Fibrin Sealing in Surgical and Nonsurgical Fields
These eight volumes, which developed out of the international congress "Update and Future Trends in Fibrin Sealing in Surgical and Nonsurgical Fields" held in November 1992, present the state of the art in fibrin sealing. Initially, fibrin sealant played an important role in surgery. During the past few years, it has been increasingly applied nonsurgically and we can now say that it has become an integral component of medical treatment.

The doubts which have been raised by nonusers about the efficacy of fibrin sealant are no longer valid. The correct indication and technique continue to be basic prerequisites for effective treatment. Even today – 20 years after fibrin sealant was first used – the three most prominent effects of fibrin sealant are still hemostasis, sealing of the wound, and support of wound healing.

The problems posed by the transmission of viral infections have gained substantially in importance because of the potential transmission of AIDS via fibrin sealant. Fortunately, this is so unlikely today that it no longer represents a cause for concern, which does not mean, however, that research in this field can be discontinued.

Seven years have passed since the last series of books on fibrin sealing were published. Since then many new results have been obtained and clear indications for the use of fibrin glue in gynecology and obstetrics have emerged. The main indications are not only sutureless or suture-supporting wound closure, but also wound sealing and hemostasis; this volume presents known indications for fibrin sealing and also results of recent research to complete the spectrum.

Plastic-reconstructive and traumatological operations cannot be performed without fibrin sealant anymore, since there is no more atraumatic method of wound closure to date. In urology fibrin sealant has proved especially useful in interventions in the renal parenchyma and in pelvic organs – in particular in the prostate and genital organs. In fistula operations of the urinary bladder and in plastic-reconstructive ureter and urethra surgery the application of fibrin sealant has permitted watertight sutures and improved surgical results.

For scientists and clinicians the value of the fibrin sealing method will remain uncontested as a means of physiological tissue sealing. In this book the value of fibrin sealant in surgical and nonsurgical fields is defined and a critical view of its limitations given.

We, the editors, would like to thank all the authors for their cooperation and excellent contributions and photographs. Their work has made publication
VI  Preface

of these eight volumes on fibrin sealing possible. Special thanks are due to V. Gebhardt and his expert colleagues for efficient and constructive cooperation in the publication of these books at the Springer publishing company and to Gudrun Schrod for her untiring efforts in obtaining manuscripts, proof reading, and corresponding with the authors.

G. Schlag
D. Wallwiener
H. Melchior
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I. Gynecology and Obstetrics
Abstract

Fibrin glue has been shown to be effective in establishing hemostasis, enhancing adhesion among tissues, and stimulating tissue repair. At our institution, experience with Tissucol has been acquired mainly in three fields: conservative surgery of the uterus and/or ovaries, surgery for relief of stress incontinence, and gynecologic oncology surgery. In order to evaluate the effect of fibrin glue application on myometrial and perimetrial hematoma formation and on postoperative adhesions in 24 patients undergoing multiple myomectomy, the injection of Tissucol by Duploject on each suture line was part of the reconstruction, by layers, of the uterus. Echography was performed in all patients 10 and 30 days after surgery. Evaluation of adhesions has so far been possible in nine patients during cesarean section or laparoscopy. Comparison with historical controls collected since 1987 indicates significant reduction of febrile morbidity and formation of hematomas and adhesions. Fifty-two patients affected by first to second degree cystocele and genuine stress incontinence, proved by clinical, radiological, and urodynamic investigation, were scheduled for a Burch's colposuspension. In order to evaluate the effect of enhancing adhesiveness and fibrosis on the cure rate of stress incontinence, 18 randomly assigned patients received fibrin glue associated with the surgical procedure. Just before tying sutures suspending the vagina to Cooper's ligament, Tissucol with a low thrombin concentration (4 IU/ml) was applied, with the spray set over the paravaginal fascia. The vagina was elevated towards the corresponding ligament by the surgeon's fingers and pressure was maintained for 5 min; tamponade of the vagina was performed until the next morning. Despite more favorable clinical, radiological, and urodynamic findings in the fibrin glue treated group, no differences were found in the cure rate of genuine stress incontinence at a 2 year follow-up. In order to prevent hematomas, prolonged lymphorrhea, and lymphocele in ten patients treated by enlarged hysterectomy (Piver type II–III) and pelvic para-aortic lymphadenectomy for endometrial or cervical cancer, the retroperitoneal field was sprayed with Tissucol (thrombin 500 IU/ml), usually 5 ml for each side of the pelvis. Comparison with historical controls demonstrated significant advantages in terms of hematoma formation, quantity and duration of pelvic drains, need for postoperative blood transfusion, plasma administration and febrile morbidity. No lymphocele had become apparent by
the 1 year follow-up CT scan. Based on these data, a randomized controlled trial is currently going on.

Introduction

Fibrin glue is able to establish hemostasis, enhance adhesion among tissues, and stimulate tissue repair. These intrinsic properties have been successfully used in different gynecologic surgical procedures [1].

At our institution fibrin glue has been mainly used in radical surgery of gynecologic malignancies, specifically; (1) prevention of hematomas, prolonged lymphorrea and lymphocele formation and (2) in surgery for relief of urinary stress incontinence enhancing adhesiveness and tissue fibrosis. Here, we present results of our experience.

Materials and Methods

Between June 1990 and September 1991, 12 consecutive patients who underwent radical hysterectomy (Piver type III) and pelvic para-aortic lymphadenectomy as primary therapy for cervical cancer stage I B were enrolled in the study.

Just before reapproximation of the pelvic peritoneum by interrupted sutures, the retroperitoneal field was sprayed with high thrombin concentration (500 IU/ml) fibrin glue, usually 5 ml for each side of the pelvis. Two silicone drains were placed at the pelvic sidewall and brought out extraperitoneally through the anterior abdominal wall. Each drain was attached to a closed low suction device. The volume of fluid in the drains was measured daily and drains were removed if the total volume collected in 24 h was < 25 ml.

All patients received short-term antibiotic prophylaxis (usually cephalosporins) and low-dose subcutaneous prophylactic heparin.

Postoperative febrile morbidity was defined as two consecutive axillary temperatures > 38 °C, 6 h apart, excluding the first 24 h after surgery. Surgical site related infection was defined as the occurrence of pelvic abscess or hematoma associated with fever, pelvic cellulitis, and/or wound infection with purulent wound breakdown.

The control group consisted of 56 patients operated on at the same institution for the same indication from January 1987 to May 1990.

Routine computed tomography (CT) was introduced into the follow-up examination of our gynecologic cancer patients from 1984; this way, at least one abdominopelvic CT scan was obtained from all patients 6 – 12 months after surgery.

Results in the two groups were compared by Student’s t test for continuous measurements and by Fisher’s exact test for dichotomous measurements; the level of significance was determined as \( p \leq 0.05 \).

The urogynecologic patients group consisted of 52 patients with I–II degree cystocele, following Beecham’s classification [2], and genuine urinary
stress incontinence who were scheduled for a Burch’s colposuspension as primary therapy. Diagnosis was based on a thorough evaluation including history, complete physical examination, Q tip test, provocative water cystometry in the supine position, urethral profilometry at rest and under repeated coughing with the bladder at maximal cystometric capacity in the supine position. A diagnosis of stress incontinence had to meet the criteria of the International Continence Society [3].

By means of a randomization table [4], the 52 patients were randomly allocated to the following procedures: 28 underwent a Burch’s colposuspension performed following the operative technique indicated by Stanton [5]; in 24 the same procedure was combined with fibrin glue application. Just before tying sutures suspending the vagina to the Cooper’s ligament, low thrombin concentration (4 IU/ml) fibrin glue was sprayed over the surgically exposed paravaginal fascia; the vagina was then elevated towards the corresponding ligament by the surgeon’s fingers. Pressure was maintained for 5 min; a tamponade of the vagina was performed until the next morning.

Clinical and urodynamic evaluations were repeated at 12 and 24 months after surgery. According to the very strict criteria used by Bergman et al. [6], cure was defined as: (1) absence of history of urinary incontinence; (2) no urine loss at clinical observation and pad test; (3) negative cough urethral profiles.

Results

In the gynecologic oncology group of patients, apart from the chronological allocation of patients to the two groups, there was no identifiable selection bias.

Since 1987 no major changes have been introduced in antibiotic and antithrombotic prophylaxis, pelvic drainage systems, surgical materials or operative procedure. The surgical team has been always been led by the senior author. Data for the control group were retrospectively collected from medical records.

The two groups had no significant differences in medical history, demographic and preoperative nutritional parameters or intraoperative blood loss, as shown in Table 1. Table 2 lists some of the postoperative details regarding the two oncology groups.

In the fibrin glue treated group, duration of pelvic drains and daily drain volume were significantly lower. By the sixth day all patients were free of drains, while in the historical controls, on the same day 62.5 % had at least one drain. Probably as a consequence, the need for administration of plasma and/or albumin to support both proteinemia and nutritional status was significantly lower in the treated group.

In the historical control group the incidence of lymphoceles was similar to the figure of 20 % reported in the literature, when CT scan is incorporated into the routine follow-up [7]; no lymphocele was evident in the treated group.

Results obtained in the urogynecological group of patients with a 2 year follow-up are summarized in Table 3. No patient was lost to follow-up, as all
### Table 1. Characteristics of gynecologic oncology patients

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 12)</th>
<th>Controls (n = 12)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (range)</td>
<td>43 years (35–67)</td>
<td>46 years (32–70)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean weight (range)</td>
<td>64.5 kg (45–89)</td>
<td>67.2 kg (46–92)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean preoperative hemoglobin (range)</td>
<td>12.8 g/dl (10.4–15.3)</td>
<td>13 g/dl (10.2–15.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean preoperative serum albumin (range)</td>
<td>3.1 g/dl (2.9–4.9)</td>
<td>3.2 g/dl (2.9–4.8)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Frequency of illnesses (%)</td>
<td>4 (33)</td>
<td>22 (39)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Frequency of intraoperative blood loss &gt; 1000 ml (%)</td>
<td>4 (33)</td>
<td>20 (35)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Incidence of metastatic nodal disease at histology (%)</td>
<td>2 (16)</td>
<td>8 (14)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

n.s., not significant

a) Retroperitoneal field sprayed with fibrin glue.
b) Historical cases collected from 1987 to 1990.

### Table 2. Postoperative data of gynecologic oncology patients

<table>
<thead>
<tr>
<th></th>
<th>Patients (n = 12)</th>
<th>Controls (n = 56)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean duration of pelvic drains (range)</td>
<td>4.75 days (4–6)</td>
<td>7.1 days (5–12)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Mean volume drained in first 4 postoperative days (range)</td>
<td>110 ml (80–250)</td>
<td>185 ml (110–400)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Mean number of plasma and/or albumin units administered postoperatively (range)</td>
<td>6.5 (4–10)</td>
<td>9.5 (6–12)</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Number of postoperative transfusions (%)</td>
<td>2 (16.6)</td>
<td>8 (14.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Incidence of pelvic hematoma (%)</td>
<td>1 (8.3)</td>
<td>7 (12.5)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Incidence of surgical site related febrile morbidity (%)</td>
<td>3 (25)</td>
<td>16 (28.5)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Frequency of lymphoceles at CT scan (%)</td>
<td>0 (0)</td>
<td>14 (25)</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

n.s., not significant.
a) Retroperitoneal field sprayed with fibrin glue.
b) Historical cases collected from 1987 to 1990.
were in contact, as out-patients, with our Menopause Clinic. No major differences have become apparent among the two groups. Figure 1 shows variations in the pressure transmission ratio (PTR) and Q-tip test in the two groups.

**Discussion**

Pelvic drainage fluid contains electrolytes and proteins [8]. Since many patients are nutritionally depleted before and usually more so after radical surgery, continued fluid loss is not in these patients‘ best interest. Moreover, prolonged drainage is associated with patient discomfort, inconvenience, and expense. In our experience, spraying the retroperitoneal space with a high thrombin concentration glue is useful in reducing volume and duration of the pelvic drains, when compared with historical controls.
Table 3. Results at 12 and 24 months postoperative follow-up in urogynecologic patients

<table>
<thead>
<tr>
<th></th>
<th>12 months</th>
<th></th>
<th>24 months</th>
<th></th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Controls</td>
<td>Patients</td>
<td>Controls</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 24)</td>
<td>(n = 28)</td>
<td>(n = 24)</td>
<td>(n = 28)</td>
<td></td>
</tr>
<tr>
<td>Success rate</td>
<td>21</td>
<td>87.50 %</td>
<td>24</td>
<td>85.70 %</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>3.1 ± 1.5</td>
<td></td>
<td>3 ± 1.7</td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>Functional urethral length (cm) ± SD</td>
<td>112 ± 14</td>
<td>109 ± 15</td>
<td>110 ± 12</td>
<td>98 ± 15</td>
<td>n.s.</td>
</tr>
<tr>
<td>Pressure transmission ratio (%) ± SDc</td>
<td>14.5 ± 23.3</td>
<td>15.3 ± 21.7</td>
<td>14.9 ± 24.1</td>
<td>20.3 ± 22.5</td>
<td>n.s.</td>
</tr>
<tr>
<td>Q tip straining (degrees) ± SD</td>
<td>14.9 ± 24.1</td>
<td>20.3 ± 22.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n.s., not significant.

*Burch’s colposuspension combined with fibrin glue application on paravaginal fascia.

At our institution closure of the peritoneum is considered a fundamental step in avoiding small bowel adhesions and reconstructing the anatomy. The closure of the peritoneum associated with the use of, pelvic drains could impair its regenerative and absorptive capacities [9]. These considerations make the results of our experience all the more convincing.

Lymphocele results from continued drainage of the afferent lymphatics after removal of the regional nodes. Many factors have been indicated as risk factors including positive nodes, prophylactic heparin, and previous radiotherapy. The role of closed suction drainage is controversial [10, 11]. Our patients received low-dose subcutaneous heparin and had closed suction drains in the pelvis.

Lymphoceles are usually asymptomatic but complications such as pelvic vein thrombosis, compression of pelvic organs, edema of the legs, pain, and recurrence can occur. In our experience, spraying the retroperitoneal field with fibrin glue has been shown to provide a significant protective effect regarding lymphocele formation. This kind of effect is discussed controversially in the literature [12]. In agreement with Waclawiczek [1], we think that in order to balance the very strong fibrinolytic properties of the lymph it is important to use a high thrombin concentration fibrin glue.

In the randomized urogynecologic group there was no significant difference in age, body weight, parity, menopausal status, and chronic respiratory disease. The aim of the application of a low thrombin concentration fibrin glue was to enhance the mechanism by which colposuspension obtains elevation and stabilization of the bladder neck: fibrosis and adhesiveness among tissues [5]. No
significant differences in success rate or urodynamic parameters were appar­rent between the treated and untreated group. Both PTR and Q tip test are thought to be correlated with the ability of Burch’s colposuspension to stabilize the bladder neck, prevent its descent during stress, and enhance transmission of the intra-abdominal pressure rise to the proximal urethrae [6, 13]. Although not statistically significant, a trend towards a more long lasting elevation of the bladder neck in the fibrin glue treated group has become evident during the 2 year follow-up, although we have been unable to avoid the well known success rate decrease which occurs over time.

A randomized comparison of patients treated with Burch’s colposuspension and those withretropubic urethrocystopexy with fibrin sealant, as proposed by Jonasson et al. [14], could be of great interest.

References

Fibrin Sealing in Plastic Surgery, Gynecology, and Obstetrics

P. Kopecky and K. H. Beil

Abstract

Surgical sutures only allow interrupted tissue or wound conjugation. Moreover, suture fistulas or granulomas may occur. However, plane tissue conjugation is desirable in plastic surgery and microsurgery. By the application of fibrin sealant, skin grafts can be fixed within a few minutes. They need to be covered with a light compression bandage only for a few days. Revascularization within the fibrin layer takes place faster and with greater intensity. During the last several years, tissue adhesion by fibrin sealing has proved to be successful. For the past 10 years, we have tested tissue adhesion in many indications. We have been able to show that fibrin sealing has become a valuable tool for surgical interventions in gynecology and obstetrics. In plastic surgery it reduces the number of sutures and promotes tissue synthesis, revascularization, and hemostasis.

Introduction

Surgical sutures only allow interrupted tissue or wound conjugation. Moreover, suture fistulas or granulomas may occur. However, plane tissue conjugation is desirable in plastic surgery and microsurgery. By the application of fibrin sealant, skin grafts can be fixed within a few minutes. They need to be covered with a light compression bandage for only a few days. Revascularization within the fibrin layer goes on faster and with greater intensity. During the last several years, tissue adhesion by fibrin sealing has proved to be successful. For the past 10 years, we have tested tissue adhesion in many indications. We have been able to show that fibrin sealing has become a valuable tool for surgical interventions in gynecology and obstetrics. In plastic surgery it reduces the number of sutures and promotes tissue synthesis, revascularization, and hemostasis.

Reduction Mammaplasty and Fibrin Sealing of the Skin Flap and Areola

In patients with extensive breast hypertrophy and ptosis, we use the Ribeiro technique [1] for reduction mammaplasty, as modified by ourselves [2]. This technique avoids the unattractive vertical scar between areola and submam-
Fig. 1. The three (1–3) incisions of the Ribeiro technique [1]. The inferior line is traced in the submammary fold. Area B has to be deepithelialized. Area A has to be resected together with the upper part of the gland. Preoperatively the position of the areola was marked (M).

mary fold and prevents recurrent ptosis. In 90 operations we have never seen necrosis of the areola-nipple complex except for three patients with small peri-areolar necrosis. The surgical technique is difficult. Three circle incisions are done (Fig. 1). The inferior line is traced in the submammary fold. The inferior part of the skin is deepithelialized. After having marked an incision around the areola, the incision along the superior line is made; it is carried deeper and deeper over the mammary gland until the skin flap can be pushed upward without damaging the glandular tissue.

The incision along the middle line is then extended to the glandular tissue, leaving out the areola and the deepithelialized surrounding tissue. The excess glandular and adipose tissue is taken out with a crescent of skin. A plain deepithelialized flap remains with the areola at its extremity (Fig. 2). The medial and lateral edges of the “dermal” flap are then brought together by sutures (Fig. 3). Finally, the new breast is covered with the superior flap and sutured. In the last 20 patients we used fibrin sealant (Fig. 4). Capillary vessels grew faster under the flap and skin necrosis was diminished. Finally, the new position of the areola is marked and the areola is pulled into the new location by a few interrupted sutures at critical points. In the last 20 patients, as mentioned above, the fixation was done with fibrin sealant. Using the original method we implanted two drains. With the tissue adhesion system we needed only one drain.
Fig. 2. The Ribeiro technique [1]. Area B (see Fig. 1) has been deepithelialized. The areola has been circumcised. Area A is resected together with the upper part of the gland to the musculi pectoralis major. The upper skin flap has been prepared carefully to prevent vessel damage and to maintain good nutrition of the tissue.

**Results**

The greatest problem in thus surgical technique is the superior flap. In six patients we saw necrosis at the end of the superior flap near the submammary fold. Using fibrin sealant the adhesion of the flap is much better and hematomas are seldom. The capillary vessels grow faster under the flaps and skin necrosis is diminished. The operation time is also shortened.

**Areola Reconstruction**

In mastectomies we do breast and areola-nipple reconstruction more and more often. The new areola is formed by fibrin sealing of a free split-skin graft on the deepithelialized part of the newly built breast. The skin graft is taken from the pigmented part of the ischiocrural fold. Any subcutaneous tissue has been removed, so that a good connection between the skin graft and the deepithelialized skin area is possible. Nipple reconstruction is done by a local skate flap, or, if there is a large contralateral nipple, we transplant the upper nipple part. This is also done with fibrin sealant.
Using fibrin sealant operation time is clearly shortened: handling is easier and less suturing is required. We do not need a typical compression bandage as before. Three days after the operation, the transplanted areas are already completely nourished. No complication in wound healing has been observed with the use of fibrin sealant.

In cases of moderate breast hypertrophy, we use the reduction method developed by McKissock. Unfortunately, areola necrosis occurred in one patient. Autologous skin grafting with fibrin sealing is ideal for this type of reconstruction and for mastectomy with augmentation.
Fig. 4. The Ribeiro technique [1]. The upper skin flap has been sutured down at several points in the submammary fold. In the submamillar area it is fixed by fibrin sealant. $T$, The point for the areola is marked by a hatched line.

Rectovaginal Fistula

Recently we have seen a patient with an excessive genital prolapse. Unfortunately, she had a large rectovaginal fistula. The surgical technique was first done in the conventional way. The rectum was closed by sutures. Due to the atrophic vaginal skin and the large defect, we applied fibrin glue. The benefit of this procedure was the one layer suturing and ideal healing.

Lymphocysts and Vaginal Cysts

After puncture and draining of lymphocysts in operated gynecological carcinomas and after puncture of vaginal cysts we apply fibrin glue in order to prevent a recurrence.
Fibrin Sealing in Plastic Surgery, Gynecology, and Obstetrics

**Diffuse Hemorrhage**

In cases of oncologic surgery we sometimes see diffuse hemorrhage. Especially during cesarean section a hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome complication can be life threatening because of diffuse hemorrhage. We have found that this kind of hemorrhage can be stopped using fibrin sealant. Reoperation or excessive draining, as previously done, could be prevented.

**Fibrin Sealing in Premature Rupture of the Fetal Membranes**

Due to the intensive discussion, we would like to mention fibrin sealing in premature rupture of fetal membranes [3]. With 20 pregnancies we had good defect repair in 40%. Mostly, fibrin sealing has been done during first day after rupture. However, we have also been successful in one case of defect sealing at the 39th day [4].

**References**

“Open” Conization of the Uterine Cervix and Application of Fibrin Glue

R. Villet, V. Ezratty, P. Launey, P. Gadonneix, A. Henry, and D. Salet-Lizee

Introduction

The usefulness of conization for the treatment of cervical intraepithelial neoplasia (CIN), particularly CIN III, is widely acknowledged. Conization can be performed as therapy when diagnostic colposcopy is reliable and the transformation zone clearly visible. In such cases the height of the cone is short. When colposcopy findings are less dependable, due to the transformation zone being deep in the endocervix, conization is used as a diagnostic technique and the cone is longer (Fig. 1).

This intervention is often performed on young women, and the technique used should fulfill various criteria: (1) be reliable and allow that the cone biopsy is amenable to extensive analysis; (2) present low associated morbidity, causing no infection and no postoperative hemorrhage; (3) generate minimal sequelae, without stenosis of the cervix, so that it is easy to monitor and allows for subsequent pregnancy.

In 1975, Rubio et al. [1] described an “open technique” for conization which did not cause cervical stenosis. However, in spite of an injection of adrenaline (1:100,000) into the cervix during the operation and pre- and postoperative administration of an antifibrinolytic agent, the postoperative hemorrhage rate was 4%. In 1983 Trimbos et al. [2] compared three surgical methods for conization of the cervix: (1) Strumdorff sutures; (2) interrupted vertical sutures and (3) an open method using cauterization and no additional stitches. Simultaneously, many publications emphasized the use of carbon dioxide laser for conization [3-5]. This led us to describe a new technique of open conization using an electric knife with and without application of fibrin glue (Tissucol).

Methods and Patients

Methods

The first step of the intervention is to fit an O’Connors – O’Sullivan retractor, so that the cervix is suitably exposed. The lesions are revealed by staining with a 2% Lugol’s solution. Preoperative colposcopy results allow location of the lesions and determination of the depth of conization required, so that colpos-
copy only rarely must be conducted during the operation. Sutures are inserted in the cervix so that the needle appears just outside the zone that is negative for the iodine stain. Sutures are placed at each of the four compass points allowing the edge of the zone to be removed to be clearly defined and the cervix easily manipulated. The cervix is infiltrated with a solution of a vasoconstrictor. We use 20 ml of a 1 mg/ml etilefrin solution and intravascular injection is avoided by frequently aspirating the syringe.

Conization is done with an electric knife. The power output must be precisely regulated. We start with the current set for coagulation by carefully outlining the external edge of the section. The entire circumference of the cervix is thus outlined, and the cone can be sectioned. The current is set for sectioning and, once again, carefully regulated. The tissue is sectioned by describing a cone, after having made sure that it is precisely centered on the tip. The correct relationship between the base of the cone and its height must be maintained. It varies according to the anatomy of the cervix and the type of lesion, but generally the height of the cone is about the same as the diameter of its base. Sectioning with the electric knife continues until close to the mucosa and the conization can be completed by sectioning the mucosa with scissors. In some cases, specific cauterization may be required for hemorrhages or if blood vessels have been excessively opened. A 2/0 catgut suture is inserted at 12 o’clock to hold the cervix and to retain the silicon drain which will be fitted into the cervix.

The patients were then divided into two groups. Group A: a drain is fastened using the suture which is already in place. The vagina is plugged with a strip of iodine gauze for 48 h. Group B: fibrin glue (Tissucol) is applied on the cervix. The two components were already prepared: We used 3000 KIU/ml of aprotinin and 500 IU/ml of thrombin for a rapid setting. The Tissucol is applied with the duploject system ensuring that the two components mix. Application starts at 12 o’clock and progresses slowly across the whole surface of the cervix to the bottom. A 1 ml kit is generally enough. The drain is fastened with a catgut suture and both are then sectioned. No tent is placed into the vagina.
Patients

A total of 152 patients with CIN underwent conization. In 43 patients the transformation zone was deep in the cervix and not totally visible. In this case biopsy is not dependable and sometimes not feasible. These patients required a diagnostic conization. In the other 109 patients therapeutic conizations were performed. In spite of this difference, only the final procedure, previously described, changed: Group A (without fibrin glue) consisted of 90 patients treated between October 1988 and October 1990; their mean age was 37.3 years. In this group, patients operated on later were not included. Group B (with fibrin glue) consisted of 62 patients treated between February 1991 and July 1992, their mean age was 38.4 years. In this group all patients who underwent conization during this period were included for follow-up.

Follow-Up

All patients were seen as out-patients 1 month after the operation. In group B, seven patients were lost to follow-up and nine underwent a hysterectomy. Follow-up was available for 136 patients (group A: 90, group B: 46) for a mean duration of 7 months. All patients in group A and 26 in group B had a colposcopy. A cytologic exam was performed on the 20 remaining patients. Smears showing endocervical or metaplastic cells were considered adequate. Patient characteristics are summarized in Table 1.

Results

Immediate Complications

One patient had an infection in group A, none in group B. Seven patients in group A had hemorrhages (two patients hospitalized). In group B only two patients suffered minor hemorrhages and these did not require treatment or readmission. The mean duration of hospitalization was 60 h in group A and 36 h in group B.

Histological Diagnoses

The results of the histological examinations are reported in Table 2 and mostly confirm the preoperative diagnosis for therapeutic conization. In group A there were no cases of microinvasive or invasive carcinoma since patients operated on afterwards were excluded from the group.
Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group B&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 90)</td>
<td>(n = 62)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>37.3</td>
<td>38.4</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>36</td>
<td>25</td>
</tr>
<tr>
<td>Parous</td>
<td>54</td>
<td>37</td>
</tr>
<tr>
<td>Diagnostic conization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIN I</td>
<td>23</td>
<td>12</td>
</tr>
<tr>
<td>CIN II</td>
<td>45</td>
<td>28</td>
</tr>
<tr>
<td>CIN III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean length of follow-up (months)</td>
<td>7.1 (3-24)</td>
<td>7.0 (4-18)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>–</td>
<td>9</td>
</tr>
<tr>
<td>Loss of follow-up</td>
<td>–</td>
<td>7</td>
</tr>
<tr>
<td>Colposcopy</td>
<td>92</td>
<td>26</td>
</tr>
<tr>
<td>Smears only</td>
<td>–</td>
<td>20</td>
</tr>
</tbody>
</table>

CIN, cervical intraepithelial neoplasia.
<sup>a</sup>Treated without fibrin glue.
<sup>b</sup>Treated with fibrin glue.

Table 2. Histological results

<table>
<thead>
<tr>
<th></th>
<th>Group A&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Group B&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 90)</td>
<td>(n = 62)</td>
</tr>
<tr>
<td>Benign</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>CIN I</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>CIN II</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>CIN III</td>
<td>59</td>
<td>41</td>
</tr>
<tr>
<td>Microinvasive</td>
<td>–</td>
<td>3</td>
</tr>
<tr>
<td>Invasive</td>
<td>–</td>
<td>2</td>
</tr>
</tbody>
</table>

CIN, cervical intraepithelial neoplasia.
<sup>a</sup>Treated without fibrin glue.
<sup>b</sup>Treated with fibrin glue.

Follow-Up of the Cervix

In group A none of the patients were lost to follow-up. The 90 patients had all undergone colposcopy with a mean time of 7 months (3-24) (Table 3). The post-cone transformation zone was visible in 78 patients (86.7 %). In eight patients (8.8 %) it was not visible but Papanicolaou smears were adequate. In four patients (4.5 %) the follow-up was inadequate because there were no endocervical cells on the smears. In group B, the mean follow-up time of the 46 patients was 7 months. A colposcopy was done for 26 of them and Papanicolaou smears for the remaining 20. Only one stenosis was observed and the 20 patients followed up by smears all had adequate smears with endocervical cells.
### Table 3. Follow-up results

<table>
<thead>
<tr>
<th></th>
<th>Group A&lt;sup&gt;a&lt;/sup&gt; (n = 90)</th>
<th>Group B&lt;sup&gt;b&lt;/sup&gt; (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colposcopy</td>
<td>90</td>
<td>26</td>
</tr>
<tr>
<td>Transformation zone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visible</td>
<td>78</td>
<td>25</td>
</tr>
<tr>
<td>Hardly visible (Adequate or Invisible inadequate smears)</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Adequate smears</td>
<td>86</td>
<td>20</td>
</tr>
</tbody>
</table>

<sup>a</sup> Treated without fibrin glue.

<sup>b</sup> Treated with fibrin glue.

### Discussion

If there is general consensus on the necessity of treating CIN III, nobody knows the “ideal” technique. Destructive methods with electrocoagulation and cryosurgery must be omitted because: (1) tissue necrosis following this treatment is extensive and excessive, and persistent discharge is common. (2) healing is often accompanied by a risk of stenosis and relocation of the transformation zone into the endocervical canal. Reliable colposcopy is then impossible. It is also difficult sometimes to get a good endocervical sample for the vaginal smear so that adequate follow-up becomes difficult. This complication is avoided with carbon dioxide laser destruction, in which healing is rapid and without scanning and stenosis [4–6].

Moreover, destructive methods can not be used to treat all patients with CIN [7]. They also prevent histopathologic investigation of the lesion. For these reasons, conization seems to be the best alternative for the treatment of CIN.

The most common complication following conization is postoperative hemorrhage, which generally occurs in 10%–20% of patients [5]. Cold knife conization results in significantly more postoperative hemorrhages than laser conization, 14.3% and 2.8%, respectively, as reported by Larsson et al. [4]. Furthermore, extra sutures for hemostasis are necessary in almost half the patients in the cold knife group and, thus, stenosis is more important in this group. In our study, after “open” conization without sutures, hemorrhages occurred in seven of 90 patients (7.77%) without application of fibrin glue and in two of 62 patients (3.23%) with application of fibrin glue. Thermal injury zones in electrical and laser cervical excisional conization are the same [8, 9]. In our experience pathologic findings are not altered with electrical conization, especially as the most important pathologic zone of the mucosa is cut with scissors.

Infections after conization occurred in 6.8% of patients after cold knife conization and 2.3% after laser [5]. In our study only one patient in group A had an infection and none in group B. A very important point after cervical conization is the quality of long-term follow-up regarding absence of stenosis. The occurrence of postconization cervical stenosis depends on the technique
used, ranging from 0.8% after laser technique to 40% after cold knife conization [10].

The risk of stenosis increases with hemostatic sutures. Studying the results of cytological follow-up, Trimbos showed that reliable cytology (at least 75% of adequate smears) was 82% in cauterization against 39% in the interrupted sutures group and 52% in the Strumdorff sutures group [2]. In our study the incidence of stenosis was 4.5% in group A and 2.1% in group B, in which all the smears were adequate.

The final aspect of the cervix depends on a correct relationship between the base and the height of the cone. With this in mind, open conization with an electric knife, which owes its development to the laser technique, gives perfect anatomic results and a low incidence of stenosis. With the additional application of fibrin glue healing should be improved, morbidity is very low, and the mean duration of hospitalization can be reduced. Although patients currently leave the hospital the day after the operation, an ambulatory procedure can be done.

**Conclusion**

The use of an open technique for conization reduces the occurrence of cervical stenosis, increases the frequency with which the postcone transformation zone is visible and improves the quality of follow-up. Furthermore, the use of fibrin sealant (Tissucol) prevents complications. It may improve restitution of the anatomic integrity of the cervix and reduces the length of hospital stay after conization.

**References**

The McIndoe Operation and Cone Biopsy of the Cervix Using Fibrin Sealant

V. M. JASONNI, S. NALDI, A. AMADORI, G. GIACOMINI, A. TALLARINI, and C. FLAMIGNI

Abstract

We review 34 cases of vaginal aplasia regarding surgical treatment. Comparison between skin transplants and amnion allografts were made and the improvement obtained with the use of fibrin sealant considered. Furthermore, the use of fibrin sealant in cervix cone biopsy, performed either with laser or electrosurgery, was also investigated. The amnion allograft transplants appeared to be the treatment of choice compared to the original McIndoe surgical procedure. In both McIndoe and cone biopsy a significant improvement in terms of hemostasis and epithelialization was obtained using fibrin sealant on the scraped areas.

Introduction

Therapies for vaginal defects fall into three categories: (1) primary perineal self-dilatation [1, 2]; (2) primary operative perineal cavitation with skin grafting, as pioneered by McIndoe [3]; (3) secondary operative reconstruction either by intestinal loop interposition [4, 5] or by Williams’ labioperineal pouch construction [6]. The primary perineal self-dilatation should be recommended as the first attempt to obtain a satisfactory new space between rectum and bladder. This method may lead to very good results without the risks and discomfort involved with the surgical approaches. Self-dilatation, however, requires a certain amount of perineal elasticity and especially collaboration of the young patients. When the surgical approach is required, the McIndoe procedure is the treatment of choice. The intestinal loop interposition is not only a major operation but the results are questionable as well. In fact, despite the space offered by the cavity so obtained, intestinal secretions are present and prolapse under enhanced intra-abdominal pressure is often observed. Therefore this procedure should be avoided. The Williams’ operation offers the advantage of simplicity but the cavity is not physiological. The new space is not placed in the normal position between rectum and bladder so that it is not physiologically oriented. Nevertheless the Williams’ operation may be the method of choice for less experienced surgeons or in the rare case in which opening up a new cavity between the bladder and the rectum may be too difficult and dangerous, for
instance in patients with previous operations of the rectum or bladder. The McIndoe operation is the only surgical procedure that offers the possibility to obtain a cavity placed physiologically, but it requires a well trained surgeon because of the risks of bladder or rectum damage. The McIndoe operation has been modified in recent years. Thus, amnion or peritoneum can be used, so avoiding the necessity to obtain skin grafts. The use of fibrin sealant can be helpful in obtaining better control of hemostasis and rapid epithelialization of the new cavity. Here, we will discuss the results obtained with the original and modified McIndoe operation in 34 cases of congenital vaginal aplasia. Furthermore, the improvement offered by fibrin sealant in cone biopsy of the cervix will be considered.

**Patients and Methods**

**Subjects**

A total of 34 young women, age 16–21 years, affected by vaginal aplasia were surgically treated after failure of self-dilatation. While the first eight subjects were operated on with a skin graft, the following 26 were treated using amnion allograft transplants. In 16 patients fibrin sealant was also employed in order to improve hemostasis and epithelialization. For the same purpose, 12 patients with cone biopsy of the cervix, performed with either laser or electrocautery, were treated with fibrin sealant.

**Surgical Procedures**

Neovagina

The original technique of McIndoe vaginoplasty consists of first selecting the donor site for split-thickness skin grafts. However, this procedure presents some disadvantages related to obtaining split-thickness skin grafts and morbidity at the donor site. The fashion of ever shrinking women's bathing suits makes a donor site difficult to find, as wisely observed by Wheeless [7]. Moreover, the skin grafts implanted in the new cavity maintain histological features of the skin long after surgery (Table 1). The use of an amnion allograft that acts as a protective membrane with antimicrobial properties and weak antigenicity allows epithelialization from the vaginal margin upward into the new cavity. Amnion is then replaced by epithelium which is histologically indistinguishable from normal. The use of fibrin sealant can significantly improve this surgical procedure. It is evident that after the new space has been obtained meticulous care must be taken to ensure perfect hemostasis. This essential step may be difficult but is strictly necessary. Even minimal bleeding may compromise the final result. The fibrin sealant improves hemostasis control, especially on the scraped areas of the rectum or bladder where electrocautery might be dangerous. In addition, fibrin sealant enhances fibroblast proliferation and amnion is
Table 1. Results obtained in 34 patients with congenital vaginal aplasia

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Patients (McIndoe)</th>
<th>Mold Removed (n)</th>
<th>Vaginal space epithelialization (days)</th>
<th>Histological features at 8 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin grafts</td>
<td>8</td>
<td>10</td>
<td>6-8</td>
<td>Skin features present</td>
</tr>
<tr>
<td>Amnion allografts</td>
<td>10</td>
<td>10</td>
<td>6-8</td>
<td>Normal vaginal epithelium</td>
</tr>
<tr>
<td>Amnion allografts</td>
<td>16</td>
<td>7</td>
<td>4-6</td>
<td>Normal vaginal epithelium</td>
</tr>
<tr>
<td>+ fibrin sealant</td>
<td></td>
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</tbody>
</table>

more rapidly replaced by normal vaginal epithelium (Table 1). Once a transversal incision has been made with a scalpel, the bladder and rectum are separated by scissors that are gently and judiciously used partly as a blunt dissector and partly to snip the tissues. The new space must be opened up till the peritoneum, otherwise the neovagina will be shortened and the amnion-covered rubber mold (13 cm length; 3 cm diameter) cannot lie comfortably. Before the mold is inserted fibrin sealant is sprayed over the scraped areas and hemostasis is further controlled.

Cone Biopsy

The use of laser may permit cone biopsy of the cervix without general anesthesia and control of hemostasis without sutures, as is usually done with classical surgical procedures. However, in some cases hemostasis can be difficult and the use of electrocautery may be required. The use of fibrin sealant allows better control of hemostasis of the scraped areas. Fibrin sealant is sprayed on the cone biopsy surface (Fig. 1) and hemostatic gauze is then pressed upon the cervix. Furthermore, fibrin sealant allows more rapid epithelialization, reducing the vaginal discharges that often follow this procedure.

Fig. 1. Fibrin sealant in cone biopsy
Conclusions

The use of amniotic membranes appears to be the method of choice in the treatment of vaginal aplasia. This technique eliminates the problems related to split-thickness skin grafts. Furthermore, amnion is rapidly replaced by a normal appearing epithelium with the histological features typical of the natural vaginal epithelium. Fibrin sealant improves both hemostasis and epithelialization and should be taken into account in this surgical procedure. For the same reasons fibrin sealant should also be considered in cone biopsy of the cervix performed with laser beam. Also in this procedure, hemostasis and epithelialization are important steps that can be improved by fibrin sealant.

References

Abdominal Sacrospinal Fixation by Means of a Polydioxane Suture Ligament in Recurring Prolapse of the Vaginal Stump

D. Wallwiener, W. Stolz, S. Rimbach, E. M. Grischke, and G. Bastert

Introduction

Despite the availability of a wide range of established operative techniques, the correction of singular or multiple recidivations of prolapse of the vaginal stump with or without urinary stress incontinence still represents a challenge for the gynecologic surgeon. Vaginopexy can be performed by various approaches, e.g., by vaginal or abdominal procedures, with direct fixation or with the aid of ligament materials.

Direct fixation by suturing has the disadvantage of frequently causing complaints and relapses due to splitting of the inelastic sutures. Basic experimental surgical studies have demonstrated the polydioxane suture (PDS) ligament to be superior to the other materials used for fixation by ligaments.

Material and Methods

We treated 35 hysterectomy patients with subtotal or total prolapse of the vaginal stump, who presented with the usual problems associated with the descent, and who hoped to maintain sexual function. Sacrospinal fixation of the vaginal stump was performed by means of a PDS ligament.

Laparotomy was performed to expose the posterior pole of the vaginal stump. The entire Douglas’ pouch was resected. Subsequently, fixation of the PDS ligament to the vaginal stump and, sacrospinally, to the promontorium was performed by means of PDS sutures. Finally, the cavum douglasi was obliterated, which may be done by using fibrin sealant.

Results and Discussion

In the majority of patients, durable stabilization could be achieved by this surgical approach. In seven patients, sacrospinal fixation following laparotomy had to be combined with an additional vaginal procedure, such as colporrhaphy. The procedure has proved to be particularly effective in preventing the formation of enteroceles. Two cases of recurring descent were observed which could be attributed to a suboptimal fixation technique.
The advantages of abdominal access and the use of a PDS ligament over the vaginal procedure are elastic suspension of the vaginal stump, which helps prevent postoperative complications caused by rigid fixation, and the possibility of subtle resection of Douglas’ pouch.

Therefore, it can be concluded that in combination with thorough preoperative, clinical, and urodynamic diagnosis, the presented surgical approach has proved to be an appropriate technique, completing the spectrum of patient-specific operative therapies for stabilization of the pelvic floor.
The Marshall-Marchetti-Krantz-Hirsch-Stolz-Operation: A Retrospective Study

E. G. Coeugniet

Abstract

Transabdominal urethrocystopexy with fibrin sealant was performed in 100 women with proven urinary stress incontinence. The results were compared to another two groups of 100 women suffering from urinary stress incontinence and operated on with the Marshall-Marchetti-Krantz transabdominal technique or with the vaginal technique to Lahodny. The observation time was 4 years. Success was defined as absence of objective urine loss at coughing or straining with full bladder in an upright position.

The fibrin sealant technique is very simple, with very few postoperative complications, a very short hospitalization time, and relatively few relapses. The Lahodny technique, associated with fixation of the vagina, is indicated for patients with prolapse, large enterocele, and urethro- and cystocele. The classic Marshall-Marchetti-Krantz operation shows no advantages compared to transabdominal urethrocystopexy.

Introduction

Transabdominal urethrocystopexy is a commonly used technique for the surgical repair of urinary stress incontinence in females. All successful results seem to be related to a persistent elevation of the cervical neck and increased urethral compliance [1–3]. Approximately 120 different surgical methods have so far been reported (4). However, the ideal surgical method for treatment of urinary stress incontinence still does not exist: almost all methods used to produce anatomical corrections have been associated with substantial long-term failure rates [2, 3].

Transabdominal urethrocystopexy, in which the paraurethral and paravesical tissue at the urethrovesical junction is surgically fastened to the retropubic periostium or the rectus sheath, is the most commonly used method [3]. The procedure is easy to perform and provides an excellent view of the relevant anatomical areas. However, an unacceptably high risk for periostitis pubis has been reported when nonabsorbable sutures have been used [2].

The other procedure, fixation of the paravesical and paraurethral tissue to the fascia obturatoria and musculus obturatorius, avoids the risk of periostitis.
and osteomyelitis but increases the risk of bleedings and recurrences through suture failure.

A new vaginal method as described by Lahodny has a low recurrence rate but the operation requires much more effort by the surgical team, takes longer and needs a longer hospitalization [5].

Here, we report the results of a new procedure: a modification of the Marshall-Marchetti-Krantz-Hirsch operation by using a fibrin sealant instead of sutures [1, 2, 6–9].

We tried to compare this method with the original method of Marshall-Marchetti-Krantz [3] and with the ventral levator plastic of Lahodny [5].

**Materials and Methods**

Beginning in 1977, we started with the typical Marshall-Marchetti-Krantz operation, in 1988 with the Lahodny and with the Marshall-Marchetti-Krantz-Hirsch operation, as modified by Stolz et al. [9].

In each group we considered 100 patients, followed for a period of 4 years. All patients had urinary stress incontinence II–III, verified by complete urodynamic check-up, and a cystocele and urethrocele. Urethrocystometry was performed in all patients before surgery and 4 years after surgery.

**Operative Procedure**

One day before operation and preoperatively we used iodine-polyvinylpyrrolidone for antisepsis of the vagina. Before surgery we emptied the bladder. We did not use a Foley catheter during the operation: such an orientation marker was not necessary. A transverse incision above the symphysis was made in the skin and in the anterior rectus sheath. The rectus muscle was then separated in the midline, and each half of the muscle was retracted laterally. The anterior vesical area was mobilized and the urethra loosened. The retropubic periosteum was gently abraded: the anterior vesical area, the urethra and the urethrovaginal junction were freed of fat using pledgets.

While the assistant was holding the bladder upwards, the surgeon inserted two fingers of his left hand into the vagina. With his right hand the fibrin sealant was applied onto the vaginal fascia and the retropubic area, lifting up the vaginal wall and pressing it against the retropubic space for at least 5 min.

The fibrin sealant used was Tissucol (Immuno, Heidelberg, FRG) with two components: a fibrinogen concentration between 80 and 110 mg/ml, 500 IU thrombin/ml and 3000 KIU aprotinin/ml. Tissucol was applied by Duploject, as is available in the Tissucol kit. A tamponade was introduced in the vagina and a Foley catheter both for 24 h.

Before closing the abdomen we introduced a drain in the cavum retzii. The duration of the operation was less than 20 min, the hospitalization 6 days. Cephalosporins were given preoperatively and 24 h postoperatively as prophylaxis.
Other patients were operated on with the technique of Marshall-Marchetti-Krantz [3] or with the Lahodny ventral levator plastic [5].

Results

The use of fibrin sealing reduced the duration of the operation and of hospitalization and the frequency of complications, as compared to other techniques (Table 1).

The relapse rate after 4 years was 24% with fibrin sealing, 55% with the classic Marshall-Marchetti-Krantz operation, and 24% with the Lahodny technique.

The advantage of Tissucol is the firm and long-acting fixation of the vesicourethral junction of the retropubic periosteum without the need for sutures. Tissucol induces fibrosis during the fixation period mediated by a certain excess of fibrin [6]. The fibrosis results in consistent elevation and fixation of the paraurethral and paravesical tissue. For the induction of fibrosis it is important to apply Tissucol in a blood-oozing area, free of fatty surfaces.

The technique is free of complications, easy to perform and causes no subsequent difficulties in patients in whom reoperation had to be performed.

The frequency of relapses is near that of the technique of Lahodny. This frequency can be reduced when some precautions are taken:

1. The fibrin sealing operation cannot be used alone in females with significant vaginal prolapse. Rather, vaginal fixation is obligatory. In patients with large cystocele, urethrocele and enterocele the Lahodny technique has to be used.

2. Before operating the surgeon must personally control the quality of the fibrinogen component of Tissucol: old preparations and preparations which have not been correctly conserved may no longer contain thrombin but still be in a gel form, although no longer able to seal.

Table 1. The Marshall-Marchetti-Krantz-Hirsch-Stolz operation using fibrin sealant compared to the Marshall-Marchetti-Krantz operation and to the ventral levator plastic (Lahodny)

<table>
<thead>
<tr>
<th>Operation</th>
<th>MMKS (min)</th>
<th>MM (min)</th>
<th>VLP (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of operation</td>
<td>16.5 ± 4.5</td>
<td>46.7 ± 9.6*</td>
<td>82.8 ± 22.6*</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>6 ± 0</td>
<td>12.89 ± 3.7*</td>
<td>15.6 ± 6.6*</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>2</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Infection</td>
<td>1</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Periostitis</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Duration of bladder catheter</td>
<td>1</td>
<td>5.6 ± 2.4*</td>
<td>9.6 ± 6.7*</td>
</tr>
<tr>
<td>Duration of postoperative abnormalities</td>
<td>1</td>
<td>5.6 ± 2.3*</td>
<td>11.4 ± 7.5*</td>
</tr>
</tbody>
</table>


* p < 0.001.
3. Infections and hematomas in the cavum retzii have to be avoided through drains and antibiotic prophylaxis.
4. Postoperatively, training of the perineal muscles and weight reduction of patients with adiposis both pre- and postoperatively.

References

Urethrocystopexy with Fibrin Sealant

P. Scott and U. Gigon

Abstract

We have used fibrin sealant in a number of patients since 1987, encouraged by the good results reported in the literature. From May 1987 until April 1992, we operated on 35 patients with genuine stress incontinence (GSI) grades II–III. We replaced all sutures by fibrin sealant. Patients were checked yearly up to 5 years. Over all, 20 patients (57 %) were considered to be totally cured, with no urine leakage or urine loss during stress standing upright or in the lithotomy position. We failed to cure seven patients (20 %) and eight patients (23 %) were subjectively satisfied with the result achieved, although they experienced slight urinary loss during stress. One of the major shortcomings of the new technique is the high cost of the fibrin sealant. This point will most certainly be outweighed by the fact that a reduced number of postoperative complications will result in shorter hospital stays and as a consequence contribute to reducing costs.

Introduction

Following the widespread use of fibrin sealant in orthopedics and surgery, where it proved to fulfil expectations regarding resistance and stability, fibrin sealant was utilized to cure genuine stress incontinence (GSI) from 1982 onwards [1, 2]. Encouraged by these good results, in 1987 we started utilizing fibrin sealant as a replacement for all sutures in a number of patients.

Before 1987, we employed different Marshall-Marchetti procedures, e.g., Krantz (MMK), Burch or Cowan, for treating GSI. Our results were comparable to those published in the relevant literature [3]. We had the same percentage of complications such as rupture or tearing of sutures, long postoperative drainage of the urinary bladder and developing urgency.

Method and Material

From May 1987 until April 1992, we adopted the new method for urethrocystopexy, replacing all sutures with fibrin sealant.
We operated on 35 patients with GSI grades II–III. The average patient’s age was 50 years (range 32–70 years). The mean weight of all patients undergoing the operation was 65.9 kg (39 kg–97 kg). Parity was 2.3 (0–4 deliveries). Preoperatively all patients had a lateral cystogram with bead chain and patient history was assessed utilizing a standard questionnaire. All patients showed loss of urine following coughing or pressing and radiologically had anatomical alterations grade II, according to Green [4, 5]. Since at the time we did not have the necessary urodynamic measuring equipment, we cannot furnish any data on urinary tract pressure.

After 3 and up to 6 months, all 35 patients were reassessed by clinical examination and lateral cystogram. After this time we measured an elevation of the bladder neck (mean 1.5 cm) and an improvement of the β-angle (50°).

The patients were then checked yearly by clinical examination and standard questionnaire. Patients were informed to contact our clinic in case of subjective signs of relapse.

Operative Procedure

In 30 patients the operation was combined with an abdominal hysterectomy. After hysterectomy Retzius’ space was exposed. The anterior vesical area was mobilized and the fascia vaginalis exposed. It was important that the fascia be mostly free of fat tissue and a good hemostasis was achieved.

Subsequently, 1 ml of the fibrin sealant (Tissucol Duo S) was applied by the Duploject system to either side of the midline or the urethra. Preparatory to this, the surgeon placed two fingers of his left hand in the vagina before pressing the vaginal wall against the retropubic area for 5 min. With the sealant secured, a vaginal tamponade was placed and remained in position for 24 h. At first we inserted a suprapubic catheter, which was removed after spontaneous micturition was achieved. Of late we have tended to omit the suprapubic catheter because spontaneous micturition was always achieved on the first day. Before the patient was released from our clinic, residual urine volume was assessed by sonography.

Results

Between March 1987 and April 1992 we operated on 35 patients with proven GSI (Table 1). In 28 out of 35 patients, stress incontinence was totally cured or at least improved significantly after a follow-up period of up to 5 years. After 6 months, three out of 35 patients continued to suffer from uncontrolled urinary leakage. Two of these patients demonstrated objectively a good anatomical result, with sufficient elevation of the bladder neck. Both showed signs of sensory urge incontinence. One patient, who had undergone previous X-ray treatment for genital malignancy, continued to suffer from GSI as before and displayed a poor anatomical result. After 24 months 29 patients were examined. We noted one patient with slight uncontrolled loss of urine during stress in
Table 1. Summary of results of urethrocystopexy using fibrin sealant in 35 patients with genuine stress incontinence

<table>
<thead>
<tr>
<th>Month</th>
<th>Number of patients (%)</th>
<th>Good stress 0 (%)</th>
<th>Improved stress I (%)</th>
<th>Failure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>35</td>
<td>32</td>
<td>0</td>
<td>3 (8.5)</td>
</tr>
<tr>
<td>12</td>
<td>29</td>
<td>29</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>24</td>
<td>29</td>
<td>28</td>
<td>1 (2.9)</td>
<td>0</td>
</tr>
<tr>
<td>36</td>
<td>26</td>
<td>21</td>
<td>3 (8.5)</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>48</td>
<td>13</td>
<td>09</td>
<td>2 (5.7)</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>60</td>
<td>6</td>
<td>04</td>
<td>2 (5.7)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>35 (100)</td>
<td>20 (57.3)</td>
<td>8 (22.8)</td>
<td>7 (19.9)</td>
</tr>
</tbody>
</table>

lithotomy and standing position. She claimed to be satisfied with the result achieved. After 36 months we examined 26 patients. Two patients were found to be dissatisfied with the operation. One of them had sensory urgency. Three patients suffered from minor urinary leakage but still were satisfied with the result obtained. Some 48 months later we evaluated 13 patients and noted another two patients with slight urinary loss and a further two, suffering from total relapse of GSI. After 60 months two of six patients showed only improved results but felt the operation to be beneficial. Four patients reported complete cure from GSI.

Overall, we failed to cure seven patients (20%) from GSI. Eight patients (23%) were subjectively satisfied with the result achieved, although they experienced slight urinary losses during stress. There were 20 patients (57%) who were considered to be totally cured and suffered from no urine leakage and no urinary loss during stress upright or in the lithotomy position. We were unable to detect any difference in body weight (64.2 kg vs 66.1 kg) or parity (2.1 vs 2.3) between the complete cure and the complete failure groups. Satisfactory voiding patterns were achieved after 1–2 days. Obviously, no complications such as rupture or tearing of sutures occurred. We did not notice any signs of adverse reactions to fibrin sealant.

Conclusion

Results with overall cure rates of 80% are comparable with the results achieved with the conventional MMK procedure. The new method using fibrin sealant appears to have some advantages over the conventional procedure using sutures. Assuming that cure rates are identical, which we cannot prove because our patient numbers are too low and follow-up periods too short, the main advantage of the new method is the atraumatic technique, which prevents complications such as bladder and urethral lesions, which in turn obviously prevents strictures and fistulas. None of the patients experienced bladder voiding disturbances.

One of the major shortcomings of the new techniques is without doubt the high cost [6] of the fibrin sealant. This point will most certainly be outweighed by the fact that a reduced number of postoperative complications will result in shorter hospital stays and as a consequence contribute to reduced costs.
References

The Use of Tisseel as a Sealant and for Prevention of Postoperative Adhesions in Microsurgical Operations for Fertility

B. Larsson and A. Jonasson

Abstract

Operations for fertility include tubal anastomosis and salpingostomy, with or without salpingolysis and ovariolysis. In six women an isthmo-isthmic tubal anastomosis was performed. The edges of the serosa of the two ends of the oviducts were approximated and the anastomosis was covered with Tisseel. One patient became pregnant and patency was proved in another three patients.

Salpingostomy, combined with salpingolysis and ovariolysis, was performed in 21 women. The adhesions were excised with the aid of an isolated microelectrode. Care was taken to avoid injury to the serosa. However, in the presence of an extensive degree of periadnexal adhesions, a certain degree of injury to the serosa was impossible to avoid. These injured areas were covered with Tisseel. We found at postoperative laparoscopy that formation of adhesions was significantly prevented when denuded serosa was covered with Tisseel. The preventive effect of Tisseel might be explained by inhibition of further exudation of fibrin and by mechanical properties of the coagulated fibrin sealant.

Introduction

Intraabdominal adhesions cause major clinical problems. In women they may cause infertility and pain, besides obstruction of the intestines. Introduction of a microsurgical technique, in the 1960s, contributed to a reduction in postoperative adhesion formation [1, 2].

In women, intraabdominal adhesions are induced by either a clinically manifest or a “silent” pelvic inflammatory disease (PID), surgical trauma or endometriosis. As a rule, adhesions induced by endometriosis are more severe than those due to other causes.

There is a high risk of formation of postoperative adhesions on peritoneal areas with petechiae as a result of serosal trauma. It is thus essential to avoid trauma to the peritoneum as much as possible. The microsurgical technique is less traumatic than other procedures; however, a certain amount of trauma is sometimes inevitable, and adjuvant therapy is mandatory in such cases. A number of substances have been used in adjuvant therapy: cortisone [1], oxyphenbutazone [3], dextran [4], Surgicel [5], Interceed [6].
The aim of the present study was to evaluate the possible beneficial effect of Tisseel as a sealant in tubal anastomosis and as an adjuvant therapy in prevention of postoperative adhesion in microsurgical operations for fertility.

**Material and Methods**

The study was comprised of two series of fertility operations: (1) isthmio-isthmic anastomosis (six women) and (2) bilateral salpingostomy combined with salpingolysis and ovariolysis (21 women). The operation for fertility was performed according to the gentle, less traumatic microsurgical method previously described in detail [2].

**Tubal Anastomosis**

A tubal anastomosis was performed in two patients, in order to reverse a previous tubal resection for sterilization, and for fertility in four women infertile because of tubal occlusion.

Isthmic tubal resection combined with an end-to-end anastomosis was performed. The occluded region of the oviduct was sliced perpendicularly to the long axis by sharp dissection. Pathologic tissue was pared as thin discs from each resection and until healthy tissue – lack of fibrosis, normal muscular architecture, mucosa with normal folds – was identified, according to the salbutamol method previously described [7]. Briefly, intravenous administration of salbutamol (a β-adrenergic agonist) widens the tubal lumen in case of normal tissue without abnormal fibrosis. In order to approximate the tubal lumen, two 8–0 sutures were sewn without magnification at 6 and 12 o’clock positions in the serosa of the tubal wall. The anastomosis was then covered with a layer of Tisseel in order to strengthen the anastomosis and prevent postoperative adhesions. By use of Tisseel, a minimum number of sutures could be used for approximation of the tubal ends.

**Prevention of Postoperative Adhesions**

A gentle, atraumatic, and bloodless electromicrosurgical method was used and previously described [2]. Nonwoven sponges soaked in saline or acetate were used to keep uterus and adnexae elevated, constantly moist, and out of contact with any blood. To avoid drying of the pelvic and abdominal serosa, the peritoneal surfaces were practically continuously irrigated with saline or acetate.

Adhesions attached to the abdominal wall, pelvic wall, bowel, uterus, and/or adnexae were excised by electrosurgery with the aid of an isolated microelectrode. Care was taken not to denude any part of the serosa. Efforts were made to secure complete hemostasis. If blood escaped into the peritoneal cavity, it was aspirated in saline or acetate and never sucked up by operating
towels. Tiny bleeding capillaries were identified during irrigation, and hemostasis was secured by pinpoint electrocoagulation. If hemostasis was not achieved, a suture of the smallest possible size (10:0–6:0) was used. The use of suture material was kept to a minimum. All more or less injured or defective serosal areas were covered with Tisseel.

The sactosalpinx was reconstructed. The whitish avascular scars between the late fimbriae were identified and incised. Further incisions were made during inspection of the oviduct “from inside.” Care was taken not to cut through mucosal folds or blood vessels. The surgical procedure was performed by electrocoagulation and with the use of a very tiny-pointed and unisolated epilation needle. Hemostasis was achieved by pinpoint electrocoagulation. The intention was to create a tubal ostium, approximately 2 cm in diameter, when the mucosal edges were folded back and secured to the tubal serosa with Tisseel.

Results

Table 1 summarizes the results of tubal anastomosis. A beneficial effect of Tisseel was registered with reference to strengthening of the anastomosis after tubal resection and in prevention of postoperative tubal adhesions. In one case fibrosis was observed at the time of resection and at the follow-up laparoscopy. Although all fibrotic tissue in the isthmic part was removed (histologically verified), fibrosis developed again in the medial part of the oviduct. The prognosis is consequently poor and in vitro fertilization is recommended.

Table 2 summarizes the results of prevention of new adhesions attached to an injured serosa. The preventive effect seemed more marked on the pelvic side wall than on the oviduct.

| Table 1. The results of bilateral tubal anastomosis \( (n = 6) \) |
|---------------------|-----|
| Result              | \( n \) |
| Pregnancy           | 1   |
| Patency             | 4   |
| Occlusion (fibrosis) | 1   |

| Table 2. The distribution of adhesions before and after microsurgical treatment and Tisseel as adjuvant therapy \( (n = 21) \) |
|--------------------------|----------|----------|
| Adhesion site            | Before   | After    |
| Oviduct                  | 3.2      | 0.5      |
| Ovary                    | 2.9      | 0.3      |
| Pelvic sidewall          | 2.3      | 0.1      |

Based on an adhesion score from 0 to 4; five patients (22%) became pregnant.
Discussion

The mechanism of formation of intraabdominal adhesions is not fully understood. It is, however, well known that in peritoneal repair there is maximal deposition of fibrin during the first 2 postoperative days, which then decreases to a minimum during the following 7 days. In addition, there is increasing ingrowth of mesothelial cells from the second day until repair is completed. There is also a number of macrophages during the first 2 postoperative weeks.

Fibrin induces fibrosis as part of the repair process and during adhesion formation. When Tisseel coagulates, fibrin is formed. This fibrin is, however, broken down by fibrinolytic activators in the residues of Tisseel and in the tissues. This procedure results in normal repair with reduced potential for adhesion formation. It must be emphasized that, in prevention of adhesion, Tisseel should be applied to a completely bloodless field. In the presence of excess blood, Tisseel induces fibrosis and adhesion formation, both of which are utilized in our technique of surgical treatment of stress incontinence [8].

References

Fibrin Sealing by Tissucol in Premature Rupture of the Fetal Membranes

M. Masson

Abstract

The fetal membranes are a protective barrier against infection; however, premature rupture occurs in about 10% of cases. The premature — and especially the very early — rupture of the fetal membranes exposes the fetus to three major problems: (1) prematurity with respiratory distress (hyaline membrane disease) and deficiency of maturity for many fetal organs, e.g., kidneys; (2) problems related to anoxia and its management, e.g., ROP, enterocolitis; (3) infections due to amnionitis caused by the lack of the protective barrier. In addition, the fetus might swallow the infectious amniotic fluid and, thus, be at risk for septicemia.

For the mother, the greatest problem consists in local infection, with amnionitis, or general infection, with maternal septicemia.

Fibrin sealing with Tissucol, under very strict conditions (without any vaginal infection), offers an interesting solution, increasing not only the chances of the fetus but also the mother’s comfort and the economic costs of this condition. This procedure permits prolongation of gestation and thereby obtain better maturity of the fetus.

In addition fetal pulmonary maturity is only achieved if the fetus is able to “breathe” during its intrauterine life. This breathing permits opening of the fetal alveoli and their maturation.

The loss of amniotic fluid may induce fetal deformations by fetal compressions which are not normally absorbed by amniotic fluid. Without sealing of the amniotic membranes, the only solution is hospitalization, with strict observation to detect maternal or fetal infection and, in case of infection, artificial induction of labor resulting in a vaginal delivery or, often, in a caesarean section due to prematurity.

The use of Tissucol provides very interesting benefits for mothers both psychologically and economically.

Introduction

The problem of premature rupture of the amniotic membranes (PROM) remains a very troublesome and unsolved one for gynecologists. Naturally, this condition is even more problematic for the mother and her fetus!
The predominant concern is to minimize the risk of fetal and maternal infection. The only solution resides in prophylactic care to avoid amniotic infection and to wait for or promote fetal maturation. Many techniques are employed in attempting to continue gestation:

1. Cerclage of the cervix to prevent dilatation. This is dangerous because, in case of amniotic infection, often undetected during quick testing, the cerclage increases the risk of maternal septicemia.

2. Placing of an intra-amniotic catheter with four ducts to infuse liquid and antibiotics into the amniotic cavity. This catheter has two balloons and it is possible to infuse polyvidone iodine solution between the two balloons to disinfect the cervix. However, placement and maintenance of the catheter is dangerous and may perhaps produce infection.

The first cases of Tissucol application in 1986 [1, 2] involved cerclage of the cervix to avoid tension on the patch of Tissucol from the cervical dilatation. This method creates problems which are encountered with cerclage only. Recently, a study was published by a French team about a case of PROM for which this team applied a sealant, resulting in prolongation of gestation by 13 weeks.

**Material and Methods**

In our study, we applied Tissucol without cerclage. We think that this method is safer because, if an infection occurs, the problem is less serious and in this case, the infection is apparent in the vagina because there is no obstacle to its discharge.

**Patient Selection**

We have selected ten patients for Tissucol application and ten patients for which we have used only monitoring (controls). The ten patients that we treated with Tissucol and the ten control patients were between 16 and 30 weeks of gestation, without cervical infection, without inflammatory symptoms, had PROM of less than 24 h, no dilatation, and no fetal abnormalities, as detected by ultrasound. Treatment differences between the control and treated groups are shown in Table 1.

**Table 1. Treatment protocol for control and Tissucol-treated patients**

<table>
<thead>
<tr>
<th>Control</th>
<th>Tissucol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strict bed rest</td>
<td>Bed rest for 4 days</td>
</tr>
<tr>
<td>Inflammatory check-up</td>
<td>Inflammatory check-up during first 4 days</td>
</tr>
<tr>
<td>Vaginal disinfection</td>
<td>Vaginal disinfection during first 4 days</td>
</tr>
<tr>
<td>Vaginal bacteriological monitoring</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td></td>
</tr>
<tr>
<td>Fetal monitoring</td>
<td></td>
</tr>
</tbody>
</table>
Our methods consisted of: (1) assessing PROM visually with a speculum or positive diamine oxidase test; (2) bacteriological testing of the cervix; (3) inflammatory check-up; (4) ultrasonic check-up of the fetus and amniotic fluid.

Tissucol Application

To apply Tissucol we used a device with two syringes and a Wallace catheter, which is usually used for embryo replacement in in vitro fertilization. No anesthesia was necessary.

The breathing frequency of the fetus was recorded.

We have studied: the time between PROM and delivery; the Apgar score of the babies at birth; the outcome and well-being of the fetus; the complications which are encountered during the technique; the cost of treatment.

These data were compared with the same data for the control patients.
Results

Tissucol helps to prolong the gestation time and reduces the development of infection. It has an important role in restoring membranes:

1. Gestation can continue and a better fetal maturation is achieved, in particular pulmonary maturation.
2. If there is no cervical infection, Tissucol will reduce the development of amnionitis and fetal septicemia.
3. The amniotic fluid is secreted by amniotic membranes. By restoring the integrity of the membranes we permit the restoration of amniotic fluid which prevents fetal compression, malformation and fetal growth retardation.

Increase in Duration of Gestation

The results are apparent in the number of weeks that we gained by use of Tissucol as compared to control patients. The mean value of gestation following PROM without Tissucol application was 14 days in our control group and 59
days in the group with Tissucol application (Figs. 1–4). Thus, we succeeded in gaining an extra 45 days by the use of Tissucol.

**Apgar Scores**

The Apgar scores at 1, 3 and 5 minutes of the Tissucol and the control groups were compared. No significant difference could be observed between the two groups because the number of patients was too small.

**Consequences for the Fetus**

We did not observe any pathologic consequences for the fetus due to Tissucol application. The sealant prevented further loss of amniotic fluid, as determined by the diamine oxidase test and allowed restoration of the normal quantity of amniotic fluid, as determined by ultrasound.

In particular, no intraamniotic infection was encountered in patients treated with Tissucol.
Prolongation of gestation permitted a better weight at delivery and certainly an important reduction of the mortality and the morbidity for these babies (Fig. 5).

Once again, I must stress that the size of this study is too small to quantify the profit.

**Maternal Complications**

During delivery, one of our patients in the Tissucol group had an allergic shock reaction. It occurred during peridural anesthesia and, precisely, during the beginning of a Hemacel perfusion. We proceeded to research immunization against proteins which are included in Tissucol and all were negative. Later we found allergization against the Hemacel solution.

**Cost Savings Due to Tissucol**

The reduction in cost involves reduced duration of hospitalization. The mean duration of hospitalization was 23.8 days for the controls and 8.8 days for the
Tissucol treated patients (Fig. 6). Thus, application of Tissucol reduces hospitalization by 15 days for the mother and for her baby in intensive neonatal care.

At a cost of 7000 BEF per day, it saves society up to 200 000 BEF (4000 US $) per patient.

The decreased cost of additional treatment is also beneficial but the amount saved is difficult to specify precisely. We can, however, estimate that society is saved at least a further 26 000 BEF.

**Conclusions**

Premature rupture of the membranes remains a very important treatment problem for gynecologists. The only solution that existed until now was strict bed rest with monitoring of the inflammatory check-up.

This solution is very hard for the mother and very expensive for the community.

Therefore, Tissucol is a very interesting solution for treating PROM, as it prolongs the gestation time without major disadvantages for the mother and her baby. The cost benefit for society and the psychological and social benefit
for mother and fetus are considerable. An extensive study is necessary to confirm these results but also intensive participation is required because in a large maternity ward with 3500 deliveries per year, it took 2 years to collect these cases.

References

Fibrin Sealing Versus Combined Fibrin Sealing and Cerclage Operation in Premature Rupture of the Amniotic Membrane

W. ZIEGER and A. WISCHNIK

Abstract

In the years 1983–1987, nine patients with premature rupture of the membranes were treated by fibrin sealing without cerclage; however, only in 22% of these cases was the pregnancy carried to term. Due to this low success rate we combined fibrin adhesion with cerclage. Since 1987 we have treated 20 patients whose pregnancies were between the 28th and 33rd weeks of gestation. The combined use of cerclage and sealing improved the success rate. The pregnancies could be prolonged and were carried to term in 60% of the patients.

Introduction

Premature rupture of the amniotic membranes constitutes a risk to mother and fetus due to infection (chorioamnionitis) ascending through the cervical canal and preterm labor. The aim of all reported techniques for the management of premature rupture of the membranes (PROM) is, first, to close the leakage, to prevent both the loss of amniotic fluid and the risk of infection of child and mother, second, to encourage spontaneous epithelialization of the site of membrane leakage. In 1979, Genz [1] reported treatment of PROM with fibrin adhesion. In experimental investigations the fibrin was found to adhere to the chorionic fibers, but not to the amnion. Fibrin closes the gap in the membrane and functions like a membrane, at least to a certain extent. The seal has been shown to sustain a pressure of up to 30 mm Hg. Before the onset of labor the normal intrauterine pressure is about 12 mm Hg.

Materials and Methods

Our experience with fibrin sealing occurred during two time periods: 1982–1987 and 1987–1992. It is necessary to take a separate outlook at these two periods because in the first one we used only fibrin sealing, whereas in the second one we combined fibrin sealing with cerclage. In both time periods fibrin sealing was performed between the 28th and 33rd weeks of pregnancy, except in patients with following risk factors: (a) rupture of membranes
more than 24 h previously; (b) therapy-resistant preterm labor; (c) placental insufficiency; (d) cervical length less than 1 cm; (e) suspicion of chorioamnionitis; and (f) faulty compliance.

The patient was placed in the lithotomy position with the pelvis elevated and the head end of the gynecological chair lowered by 30°. Before performing sealing, bacteriological smears were taken, the vagina was disinfected with sterile saline, and a tocolytic agent was given intravenously.

The fibrin sealant was prepared according to the manufacturer's description. The cannula of the Duploject of Tissucol Duo S was introduced so that the tip of the cannula had advanced beyond the internal os uteri. After the fibrin...
sealant was rapidly applied, the cannula was immediately withdrawn. The patient remained immobile and in the chair for another 15–20 min. Since 1987 we have followed the method of Baumgarten and Moser [2] and carried out a cerclage using a modification technique [3] of McDonald’s. We used a cerclage with two needles, starting with the first needle at 6 o’clock, turned to the right; then, with the free second needle turned to the left, we knotted the cerclage at 12 o’clock. Fibrin sealing was then performed.

**Results**

From 1983 to 1987 nine pregnancies were treated for PROM. Rupture occurred between the 28th and 33rd weeks of gestation. Two patients were successfully treated; however, in two patients a second and third fibrin sealing were necessary and the patients developed chorioamnionitis. In four patients the pregnancy had to be stopped because of therapy-resistant labor.

The limited success rate of 22% (Fig. 1) made it necessary to change our protocol. Following the method of Baumgarten and Moser [2], we combined fibrin sealing with a cerclage (Fig. 2), using our own modification (Fig. 3).

From 1987 until now, 20 patients have been treated in this way. Twelve pregnancies could be prolonged, so that the mothers gave birth to viable full-term infants (Fig. 4). Of the eight patients in whom repair of the fetal membrane leak failed, two pregnancies developed a chorioamnionitis. Six pregnancies could not be prolonged because of therapy-resistant labor.
Discussion

The fibrin clot method was used on all 29 patients between the 28th and 33rd week of gestation. From 1982–1987, nine patients were treated with fibrin sealing only. Between 1987 and 1992, 20 patients had the combined treatment of fibrin sealing and cerclage. The success rate of the combined method of 60% vs. 22% obtained with fibrin sealing only supported our choice of a combination of fibrin sealing and cerclage. Due to the exclusion criteria, the number of reported cases is very small. It is very important that the patient be informed of the success rate and, should she choose this treatment, she must be followed up by careful clinical observation during the first few days. Based on the results of Anger [4] Baumgarten and Moser [2] and Genz [1], we believe that the combination of cerclage and fibrin sealing improves the success rate of in treatment of PROM.

References

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A New Application for Tissucol: In Vitro Fertilization and Embryo Transfer

W. FEICHTINGER, H. STROHMER, A. OBRUCA, and E. KRAMPL

Abstract

Many embryo transfers after in vitro fertilization may fail secondary to expulsion of the embryos from the uterus. Approximately 5%–8% of resulting pregnancies after embryo transfer are ectopic. It was the aim of our study to find a technique to avoid ectopic pregnancies and to improve pregnancy rate. We used a two-component fibrin sealant which also contains a fibrinolysis inhibitor (aprotinin) in various concentrations. After gaining experience in mouse embryos we used it in human embryo transfer with great success. The results of a pilot study encouraged us to perform a prospective randomized study on 546 patients (270 with fibrin sealant, 276 conventional embryo transfers). There were 47 (17.03%) orthotopic pregnancies and 6 (2.17%) ectopic pregnancies in the control group, whereas there were 51 (18.89%) intrauterine and no ectopic pregnancies in the treatment group. The difference in ectopic pregnancies was statistically significant (p < 0.05). Regarding aprotinin concentration, there was a trend towards better results with 100–150 kIU (28.5% clinical pregnancies) in comparison to 250–300 kIU (19.23%) or no aprotinin (20.41%) (not significant). Further improvements of the technique may raise the pregnancy rate when fibrin sealant is used. As was shown in our prospective randomized study, ectopic pregnancy may be completely avoided.

Introduction

For the last 10 years in vitro fertilization (IVF) and embryo transfer (ET) have been well established and widely used techniques in the treatment of infertility. The success rate fluctuates between 14% and 26% per attempt [1]. This rate appears relatively low when one considers a single attempt. However, one should not forget that the treatment is often repetitive and therefore one obtains a significantly higher cumulative pregnancy rate. The reasons for the relatively low success rate in one cycle are the following:

1. The quality of the fertilized and implanted ovum. It can be accepted that a relatively high percentage of fertilized ova discontinue their development at a relatively early stage and also soon after transfer into the uterus. Implanta-
tion therefore fails. Moreover even after a successful implantation, development may stop leading to a subsequent expulsion of the fertilized ovum.

2. Technical considerations evidenced by the immediate expulsion of the fertilized ova after implantation. This is partly due to the adherence of the ova to the catheter tip, the withdrawal of the ova by an hydraulic effect created by the retraction of the catheter out of the uterus or by physiological mechanisms; e.g., manipulation of the uterus evokes contractions which may lead to a swift expulsion of the fertilized ova [2, 3].

3. Endocrinological causes (e.g., luteal phase deficits), which in this context are not interesting.

4. An ectopic tubal pregnancy in approximately 5%–8% of resulting pregnancies after IVF and ET ensues. The reasons for this are the above mentioned uterine contractions and that the existing albeit damaged and enlarged Fallopian tubes favor entry of the ova [4–6].

From the outset it was the aim of our group to make ET safer, to prevent tubal ectopic pregnancies and to minimize migration of the transferred embryos into the cervical area or out of the cervix.

The aim of our preliminary studies was to investigate in vitro the survival of mouse embryos and their development in the presence of or directly inside fibrin glue. The description of the fibrin sealant (Tissucol, Immuno AG, Vienna, Austria) is superfluous in this context; it has been published previously [7]. However the osmolarity of the applied media for the in vitro culture is of prime significance. It was apparent to us that we should first investigate the osmolarity of the components of the ready packed commercially available fibrin glue kits. It turned out that the various charges exhibited different, slightly raised osmolarity values. Dilution of the individual glue components with sterile, repeatedly distilled water to achieve a fertilization compatible value of 280–290 mOsm/kg appeared easily feasible and was thereafter routinely adopted. The first growth studies of mouse embryos in vitro showed that when attention was paid to the correct value of osmolarity, no impediment whatsoever arose in the rate of division or of the hatched blastocysts formation [8].

Consequently the first important result of our study of mouse embryos was the possibility and necessity of determining the osmolarity of glue components for the intended use. Moreover it was demonstrated that using high glue concentrations (glue: medium = 1:40 and 1:10, respectively) a normal growth rate of mouse embryos was obtained and was statistically not significantly different from a control group of mouse embryos in a glue-free medium. Rodrigues et al. [9] found similar results and concluded that one could exclude an embryotoxic effect of fibrin glue and that it would be possible to use it in human IVF programs. (These authors, however, started out with a different hypothesis, in which they postulated that the use of a fibrin glue could improve implantation of the fertilized ovum by improved adhesion.)

Our goal was to prevent premature expulsion in both directions, with the glue remaining dissolved until implantation. Hence further in vitro trials were comprised of a study of in vitro fibrinolysis, with different aprotinin concentrations of Tissucol, in an endometrial culture.
The single result of this study was the observation that a 100 µl Tissucol clot with 100 kallikrein international units/ml (kIU/ml) aprotinin in the presence of 0.2 g endometrium (obtained from curettage of a 37 year old patient) and with 2 ml of culture medium was partially dissolved within 24 h and almost completely dissolved within 48 h. In this series of experiments all of the remaining specimens produced no results as difficulties with the endometrium cultures arose.

In a pilot study normally ongoing pregnancies were obtained in ten out of 38 patients [8]. In comparison with a nonrandomized group of 68 conventionally treated IVF patients a distinctly higher pregnancy rate was achieved (26% vs. 19% per transfer). These preliminary results were encouraging and we decided to perform further studies. In addition, we hoped that not only would we increase the success rate but also reduce or prevent tubal ectopic pregnancies after ET.

**Materials and Methods**

The fertilized ova were drawn up in the transfer catheter, both components separated by air bubbles, and this mixture was swiftly injected into the uterine fundus. The glue component consisted of the thrombin solution contained in the Tissucol 0.5 ml kit, 500 IU/ml (for faster consolidation) dissolved with already prepared calcium chloride solution and the protein concentrate Tissucol with the addition of 100 kIU aprotinin and twice distilled, sterile filtered water. The dissolution and preparation of the components was achieved with the help of the combined stir-warmer Fibrinotherm.

**Transfer Technique with Tissucol**

Fundamentally there were two alternatives from which to choose: In the “one step” injection, the components of the fibrin sealant and the embryos to be transferred are loaded as follows: (1) 10 µl of culture medium followed by an

![Fig. 1. Loading of catheter](image)
air bubble and 20 μl of bovine thrombin solution and another air bubble; (2) the embryos in 10 μl of culture medium followed by an air space and (3) 20 μl of protein-fibrinogen concentrate. Thus, the embryo containing medium separates the active components of the sealant within the catheter, the aim being to attach the ova within a fibrin glue seal onto the endometrium (Fig. 1). In the “two step” technique, first both glue components are loaded into the catheter separated by an air or medium column and thereafter a medium column containing the ova. The ova are therefore the first to be deposited in the fundus and consequently a fibrin seal is placed in the cervix distal to the ova after slight withdrawal of the catheter.

A pilot study using and comparing both techniques soon proved the superiority of the first technique by the number of resultant pregnancies (unpublished data). In addition it appeared that prophylaxis of tubal ectopic pregnancies was better with the fibrin glue seal enclosed ova than with placement of the free ova in the fundus and the fibrin sealant in the region of the internal os.

Transvaginal ultrasound examinations (Combison 320, Kretztechnik, Zpf, Austria) showed that the fibrin glue seal is easily recognizable in the uterus after transfer and can also be observed several days after ET (Fig. 2). So far, daily observations of two patients, in whom Tissucol without aprotinin additions was used, have shown that the rest of the glue can be identified ultrasonographically up to 4 days after ET in the uterine lumen. Therefore we concluded that the use of aprotinin is probably not absolutely necessary.

**Results**

**Prospective Randomized Study**

In vitro fertilization was performed in 546 patients between 23 and 39 years of age. Instead of allocating each ET the use of fibrin sealant was assigned randomly to groups, whereby each group consisted of all ETs of one week, in accordance with our programmed stimulation protocol [10]. This type of assign-
A New Application for Tissucol: In Vitro Fertilization and Embryo Transfer

Table 1. Results of prospective randomized study

<table>
<thead>
<tr>
<th></th>
<th>Glue</th>
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<tr>
<td></td>
<td>Without (%)</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>380</td>
</tr>
<tr>
<td>Pregnant</td>
<td>92</td>
</tr>
<tr>
<td>Ectopic pregnancies</td>
<td>6</td>
</tr>
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</table>

$x^2 = 8.279; p = 0.0159$.

...ment was used in order to avoid wastage of the valuable Tissucol kits. The study group consisted of 270 patients, in whom embryos to be transferred were loaded into a Wallace embryo replacement catheter (Wallace Ltd., Colchester, Essex, England) with culture medium between the two components of fibrin sealant, i.e., 20 μl of thrombin solution (500 IU/ml) and 20 μl of dissolved protein-fibrinogen concentrate. In the control group, consisting of 276 patients, conventional ET was carried out. One to three embryos per patient were transferred in both groups.

There were 47 (17.03%) orthotopic pregnancies and 6 (2.17%) ectopic pregnancies in the control group and 51 (18.89%) intrauterine and no ectopic pregnancies in the treatment group. The difference in ectopic pregnancies was statistically significant ($p < 0.05$) (Table 1).

With regard to aprotinin concentration there was a trend towards better results with 100–150 kIU (28.5% clinical pregnancies) than with 250–300 kIU (19.23%) or no aprotinin (20.41%). This is also evident if one considers that under physiological conditions implantation follows about 5–6 days after fertilization and that at this stage existing fibrin glue residues probably obstruct the nesting of the ova at higher aprotinin concentrations.

Discussion

After the prospective randomized study was completed, we continued the transfers with fibrin sealant in patients who were at high risk of ectopic pregnancy, i.e., patients with at least one patent but damaged fallopian tube (dilated fallopian tube, peripheral occlusions, etc.). In a relatively small series of such patients there was one ectopic pregnancy despite the use of the glue. We believe that this was not necessarily related to the selection of patients since in the prospective randomized study there were numerous patients with similar tubal pathology and this study showed significant reduction of ectopic pregnancies in comparison to the group without glue. The transfer technique itself also seems to be important. The catheter was pushed more or less up into the uterine fundus, where injection of the sealant occurred. Thus occasionally it may have been injected directly into the dilated tube or sactosalpinx. Waterstone et al. [11] recently found that it might be principally advantageous to put the transfer catheter no further than the internal os (“transfer to the low uterine cavity”). This may also be true for ETs using fibrin sealant.
Further improvements of the technique may raise the pregnancy rate when fibrin sealant is used. As was shown in our prospective randomized study, ectopic pregnancy may be completely avoided. Absolutely sterile handling is extremely important. The components must be freshly prepared daily. There was evidence of chorioamnionitis in some of the miscarriages at the beginning of our studies. Initially the miscarriage rate was slightly higher in the group with fibrin sealant. We then kept remaining dissolved glue for 24–48 h. It is highly likely that infections of the incubated material occurred causing a higher miscarriage rate. Preparation of fresh glue for each transfer day seems to have reduced the miscarriage rate.

From a psychological point of view it is reassuring both for patients and physicians that there is a “super glue” for human pre-embryos which could prevent early expulsion from the uterus. No bedrest after the procedure is necessary and the patients may resume their normal activities immediately.

Preliminary data from a multicenter study (J. H. Rim et al., personal communication; Z. B. Raffael et al., personal communication) seem to confirm our results (Table 2): There were a few ectopic pregnancies with the use of fibrin sealant but the number was significantly lower than in the control group. The success rates seemed to be increased.

The technique itself may still be further improved by using different component concentrations, amount of fluids, and transfer techniques.

References

Abstract

This study compares three techniques to mend rat ovaries: (1) closure with two-component fibrin sealant (Tissucol); (2) closure with two interrupted sutures of Vicryl 10/0; (3) leaving them open. Macroscopic and histological aspects of the ovaries were recorded 60 days later. The macroscopic examination was scored according to: (1) presence of adhesion; (2) size of the ovaries; (3) evidence of cysts. The histology was also assessed based on: (1) existence of macrophagic granulomas; (2) degree of fibrosis; (3) presence of germinal cysts. Using these criteria, the results with all three techniques were nearly the same; nevertheless, closure with Tissucol gave less fibrosis and less ovarian atrophy. Thus, fibrin sealing is a good alternative for ovarian repair.

Introduction

Many intraperitoneal gynecological surgical procedures, previously performed through a laparotomy incision, are currently completed by laparoscopy. This is especially true for ovarian cystectomy; however, when performed by laparoscopy, difficulty in closing the ovary still remains [1]. Suturing is difficult, but without it, in spite of hydrofloatation, ovarian bleeding may persist and cause adhesion formation [2].

Fibrin sealant (Tissucol), already used in many surgical specialities [3–5], could allow closure of the ovaries after laparoscopy and may prevent periovarian adhesion and intraovarian cystic inclusion. Before using fibrin sealant one must make sure that it does not interfere with ovarian activity and ovulation.

The purpose of this experimental study is to compare the macroscopic and histological results after partial ovariectomy in the rat. The three techniques were: leaving the ovaries open, closure with interrupted sutures of coated polyglactin (Vicryl 10/0), or closure with Tissucol.
**Material and Methods**

**Material**

We used 40 Wistar female rats, age 3–4 months and weighing 200–300 g. Among them five were used for the feasibility of the surgical procedure, while five were histological controls. The remaining 30 were separated into three lots during a first laparotomy.

**Methods**

The five first rats were used to explore thoroughly the surgical modalities. It was then decided that surgery would take place through a OPMI Zeiss microscope offering an enlargement factor ranging from five to 40. For the 30 rats, the surgical protocol was as follows:

- **First laparotomy:**
  - Anesthesia by intramuscular injection of 0.6 ml of a mixture of ketamine and chlorpromazine (10 ml of 500 mg/ml Ketalar added to 1.5 of Largactil).
  - Median xyphopubic incision
  - Intervention on the right ovary: a plastic sheet was placed such that the ovary was isolated from the rest of the open peritoneal cavity. The ovary was then sectioned in the avascular region into two halves.
  - The closure method involved either two drops of Tissucol, two interrupted sutures of coated polyglactin (Vicryl 10/0), or absence of closure, with the ovary left as it was.

The fibrin sealant was a preparation of a 300 KIU/ml aprotinin solution added to 500 IU/ml of bovine thrombin and a 40 mmol/l solution of calcium chloride. Electrocoagulation was not used and the operating field was kept moist with physiologic serum. To end the surgical process the peritoneal cavity was carefully cleared and freed from clots and blood, then filled in hydrofloatation with 5 ml of serum.

- **Second laparotomy:**
  - After 60 days, corresponding to many ovulatory cycles, the condition of the ovaries was checked by a surgeon who ignored the treatments previously undergone by the animals.

**Macroscopic Study**

Macroscopic examination was scored according to:

1. Adhesion on the surface of the ovary. Adhesion was graded from 0 to 60, according to the ovarian surface covered: 0, no adhesion; 1, one or two adhesions; 2, one fourth to one third of the surface covered; 3, half of the surface covered; 4, two thirds to three quarters covered; 5, the whole sur-
face covered. In case of very tight adhesion, not easily freed, an extra number was applied, so that the adhesion score ranged between 0 and 60.

2. The size of the ovary that was operated on was compared to the contralateral ovary. The diameter of the ovaries was measured with a caliper-square under the microscope. Three groups were used: (1) less than 8% loss in size; (2) between 8% and 15% loss; (3) more than 15% loss.

3. Absence or presence of one or several cysts.
   Following this macroscopic analysis, the ovaries were taken out and plunged in Bouin's fluid for histological examination.
   During this second laparotomy, both ovaries of the five nonoperated on control rats were also taken out.

**Histological Study**

After embedding in paraffin, the ovaries were cut at four levels and the sections stained with hematoxylin-eosin-saffron. Histology was scored according to: (1) macrophagic granulomatosis, with 0, absence of granulomas; 3, moderate granulomatous inflammation; 6, severe granulomatous inflammation. (2) importance of collagen fibrosis, with 0, no fibrosis; 3, moderate fibrosis; 6, severe fibrous degeneration. (3) absence or presence of germinal cysts.

**Results**

The macroscopic scores are summarized in Table 1. The following comments can be made: of five operated on ovaries there were one or two serous cysts with translucent wall, two among the sutured ovaries, two among the ovaries closed with sealant, and one among the ovaries left open.

Apparently, the size criterion was the only one that showed an important difference. There is evidence that the operated on ovaries closed with sealant showed less atrophy than those closed with suture or those left open. As for adhesion formation, no differences were observed.

<table>
<thead>
<tr>
<th>Table 1. Macroscopic results of each ovarian closure technique</th>
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<tbody>
<tr>
<td><strong>Technique</strong></td>
</tr>
<tr>
<td>Sutures (number of rats) 10</td>
</tr>
<tr>
<td>Tissucol (number of rats) 10</td>
</tr>
<tr>
<td>“Open” (number of rats) 10</td>
</tr>
<tr>
<td>Control (number of rats) 5</td>
</tr>
<tr>
<td>with cysts</td>
</tr>
<tr>
<td>without cysts</td>
</tr>
<tr>
<td>Size (lessening)</td>
</tr>
<tr>
<td>&lt; 8%</td>
</tr>
<tr>
<td>8%–15%</td>
</tr>
<tr>
<td>&gt; 15%</td>
</tr>
<tr>
<td>Adhesion score (0–60)</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>33</td>
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<tr>
<td>31</td>
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<td>0</td>
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<td>30</td>
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<td>33</td>
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<tr>
<td>31</td>
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<tr>
<td>0</td>
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</table>
Table 2. Histology results of each ovarian closure technique

<table>
<thead>
<tr>
<th>Technique</th>
<th>Sutures (number of rats)</th>
<th>Tissucol (number of rats)</th>
<th>“Open” (number of rats)</th>
<th>Control (number of rats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>with cysts</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>without cysts</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Macrophagic granulomatosis (0–60)</td>
<td>24</td>
<td>24</td>
<td>27</td>
<td>3</td>
</tr>
<tr>
<td>Fibrosis (0–60)</td>
<td>12</td>
<td>9</td>
<td>15</td>
<td>0</td>
</tr>
</tbody>
</table>

The histological scores corresponding to the technique used appear in Table 2. There was no difference between the three techniques for macrophagic granulomatosis and the presence of germinal cysts. The only difference was that the group treated with Tissucol presented with less fibrosis.

Discussion

Considering the results of the macroscopic observation of the ovaries, no noticeable difference seems to exist between the three techniques. Nevertheless, closure with sealant results in less ovarian atrophy and size modification.

Histologically, no trace of Tissucol was detected on any of the samples, and the results confirming macroscopic evidence do not indicate considerable differences in the three techniques. Whatever the technique, the ovarian parenchyma showed no remarkable modification: the general build-up of the ovarian parenchyma underwent little change, and inflammatory lesions or fibrosis were always slight and remained focal.

Granulomatous inflammation develops when both coated polygactin and sealant are used to close up the site, but there was no significant difference compared to ovarian nonclosure. Fibrosis tended to be somewhat more frequent in nonclosure and closure with Vicryl suture than in closure with Tissucol.

The difference in ovary size observed macroscopically could probably be linked to fibrosis: shrinking due to fibrosis was perhaps more important in ovaries closed with suture or ovaries left open.

Cysts had an equal frequency in the three techniques, one of them being revealed only through histological examination in an open ovary. Thus, the development of germinal cysts by invagination into ovarian parenchyma of the outer mesothelium was no more frequent than in the case of ovarian nonclosure.
Conclusion

This experimental study of ovarian microsurgical closure in rats indicates that fibrin sealing for ovarian reconstruction:

1. Does not cause more germinative cysts than nonclosure or interrupted sutures of coated polyglactin (Vicryl 10/0)
2. Can induce small granulomatous zones like sutures
3. Can also induce less parenchymatous fibrosis.

These data have ramifications for conservative ovarian surgery performed by laparoscopy.

In ovarian reconstruction following intraperitoneal cystectomy the sealant offers a valuable alternative to (1) the ovarian suture [1, 5, 6, 7], which is always uneasy and questionable as external material is introduced, though the technique aims at respecting peritoneal physiology. (2) ovarian nonclosure, which leaves a bleeding zone that may generate postoperative adhesion formation. Particularly, when the cyst is large, ovarian closure with Tissucol allows perfect ovarian reconstruction with no synthetic materials and no remaining bleeding zone.

Acknowledgement. We thank G. Amichot (Laboratoire de Microchirurgie des Hôpitaux) for his technical assistance.

References

II. Urology
Our Experience with Fibrin Glue in Urologic Surgery

V. Di Marino and R. Coppens

Abstract

We report on the use of a biological glue, Tissucol: (1) for standard procedures of urologic surgery, particularly in kidney surgery (major nephrotomy for removal of staghorn calculus and standard partial nephrectomy), and (2) specifically for kidney transplantations. Based on 50 observations, which account for a quarter of the authors' transplantations, the various indications of Tissucol in this type of surgery are reviewed. In particular, the method to dry up lymphoceles, frequently observed after kidney transplantations, is described. Finally, the safety of this glue, which is virus inactivated by thermal procedures, is discussed.

Introduction

Biological glues, concentrates of coagulation factors, are well known not only for their adhesive and coagulative properties, but also for their stimulating healing power. When used during surgery, biological glues reproduce the final stage of coagulation, which explains their hemostatic effect and their adhesive power (polymerization of the fibrin chains with collagen of the adjacent tissues).

In a wide range of operations in urologic surgery, we have used one such glue in particular, Tissucol, avoiding any risk of viral contamination. Tissucol is a freeze-dried plasma concentrate warmed up at 60 °C for 30 h.

Materials and Indications

From 1988–1991 we used Tissucol both in general and in urologic surgery. Here we will discuss only the specific use in urology. Our indications can be grouped as follows: renal surgery, urinary tract surgery, and transplantation surgery.

In renal surgery, 19 patients were operated on using Tissucol: two with nephrolithotomies, two with partial polar nephrectomies; ten with difficult nephrectomies (eight cases of polycystic kidneys and two kidney carcinomas); one with wedge resection for peripheral tumor, one patient with renal artery
surgery, one patient for surgical renal biopsy, and two patients with pyelotomies for extraction of lithiases.

In urinary tract surgery, there were four patients, one undergoing surgery for ureteral modeling, two with radical cystectomies; one patient with retro-pubic prostatectomy.

Transplantation surgery has been one of the most important indications. We used Tissucol five times for repairing decapsulated or injured transplants and 50 times for sealing the hilum in order to prevent post-transplantation lymph flow (including 35 patients with sealing of the vascular and urinary anastomosis). In addition, there was one sealing of urinary anastomosis, one repair of a transplant rupture, and 20 reductions of postoperative lymphorrheas and lymphoceles.

Analysis of Tissucol Use and Results

Renal Surgery

We used fibrin glue in renal surgery with the goal of sealing, hemostasis, or both.

Major Nephrotomies

It was following major nephrotomies that we found Tissucol use to be the most interesting (Fig. 1). Once the staghorn calculus was removed, hemostasis was achieved and the drains placed (pyelo-ureteral drainage and pyelic drainage), we applied a small amount of slow-adhering fibrin glue to each surface, which allowed plenty of time to adjust them. This strictly atraumatic sticking was reinforced by a few superficial interrupted sutures, with an adsorbable suture so that only the nephrostomy drain emerged from the kidney. Fast-adhering fibrin glue applied to the periphery of the kidney, at the nephrotomy zone, reinforces the superficial sutures.

Nephrectomies

We also found fibrin glue to be effective during nephrectomies.

In partial, particularly polar, nephrectomies Tissucol is indicated, especially if most of the renal capsule is preserved. Indeed, the capsule will constitute the surrounding sac which protects the parenchymal surface and caliceal sutures.

Fig. 1a–c. Use of Tissucol for the closure of a major nephrotomy which was necessary due to removal of recurring staghorn calculus. a The nephrotomy allowed extraction of the recurring lithiasis, which invaded all the pyelocaliceal cavities. At the bottom of the opening, a ureteral catheter (U) has been inserted in the proximal ureter. b The nephrotomy has been closed by interrupted superficial sutures following which Tissucol was applied on the opposing parts of the incision. From the renal convexity exit not only the ureteral catheter (U) but also a large nephrostomy drain (N). c The suture zone, which oozes slightly, has been coated with fast-adhering Tissucol. The waterproofness control, carried out by the nephrostomy drain, proved to be very satisfactory.
Fibrin glue was also used to resolve many of the problems which arose during certain difficult nephrectomies. In two cases of hemorrhagic rupture of the right suprarenal gland, during excision of enormous polycystic kidneys (which, due to their volume, made the suprarenal cleavage difficult), could have been treated simply with conservation of the remaining suprarenal part (sealing of the laceration line).

Likewise, in two cases of enlarged nephrectomies for extensive adenocarcinomas, fibrin glue proved to be very useful in treating the sites of pre- and lateral aortic curettage, which continued to bleed in spite of very careful hemostasis.

Peripheral Benign Renal Tumors

Fibrin glue also proved to be useful in the excision of peripheral benign renal tumor. We treated a patient with renal angiofibromylipoma (Fig. 2). After wedge resection of the tumor, the residual cavity was filled with a vascularized piece of the nearest fatty fascia, supported by a preliminary application of slow-adhering fibrin glue, and reapproximated to the capsule around the excised area. Fast-adhering Tissucol was then applied to the treated area.
Other Indications

Other uses of fibrin glue include:
1. Sealing of the vascular sutures in renal artery surgery, above all when oozing on a relatively inaccessible zone occurs. Tissucol allowed us to perfect the waterproofness of a posterior plane of vascular suture, which was difficult to reexpose once the anastomosis had been completed.
2. We applied fibrin glue to the suture zone in a case of pyelotomy (pyelocaliceal calculus removal) done in hemorrhagic tissue because it was very inflammatory.
3. Fibrin glue was most useful during surgical renal biopsy in a hypertensive patient. Bleeding persisted at the biopsy zone, despite closure with a U chromic catgut suture. A second suture, passed in complement, unfortunately tore at about 0.5 cm, the renal tissue, particularly fragile in this patient, perpetuating the bleeding. Fibrin glue solved the problem, immediately stopping the oozing.

Urinary Tract Surgery

Modeling Resection of Megaloureter

The waterproofness of the modeling of a megaureter was our first application of fibrin glue. Our technique is the modeling resection according to Hendren [5, 6]. Fibrin glue applied throughout the suture zone of the modeled ureter, resulted in complete waterproofness, which was not possible even with an over-and-over suture.

It is interesting to note that on postoperative urography, the ureter appeared normal not only morphologically but also functionally, flexible and without any rigidity. It excludes positively, at least in this case, any induction of scarring fibrosis by the sealing process.

Radical Cystectomies

In radical cystectomies, fibrin glue is indispensable. Indeed, at the time of bladder excision, the bottom of the pelvis, even after careful hemostasis, is still hemorrhagic, particularly when adjacent zones, invaded by the tumor, must be treated.

When a pelvic lymphadenectomy is done in conjunction with radical cystectomy, it is, above all, the diffuse oozing coming from the pelvic veins which is difficult to control, although numerous stitches are applied. Fibrin glue also succeeds here if we take care to apply it with the help of an aspirator; after the zone is treated this way, it remains dry for a short while. The only disadvantage comes from the great quantity of fibrin glue needed to obtain a good result.
Prostatic Surgery

In prostatic surgery we had to use fibrin glue only once, for a case in which the hemostatic sutures and inflation of the balloon did not provide satisfactory hemostasis. At the bottom of the prostatic fossa, around the urethral section repaired by the catheter, we applied collagenous compresses containing slow-adhering fibrin glue. The balloon of the catheter was then inflated and a slight amount of down traction was made on the distal part of the catheter. This practically suppressed any oozing; however, as a precaution, a vesical irrigation was put in place. It is interesting to note that later removal of the catheter did not cause any problem and that there was no dysuria.

Other Indications

Some other interesting indications for use of fibrin glue must be mentioned, although we have no experience regarding their use: (1) for urethroplasties and particularly at the time of the operations of Bengt Johanson [7]; (2) for urethral fistula surgery and for hypospadias surgery; (3) for treating certain vesicovaginal or vesicocutaneous fistulas.

Renal Transplantation Surgery

The numerous indications for biological glues in renal and urinary tract surgery find particularly interesting application in transplantation surgery.

As observed during the most recent of the 200 kidney transplantations we have done, sealing with fibrin glue is useful at every stage of transplantation surgery:

1. Before transplantation: for preparing or repairing certain injured transplants
2. During transplantation, not only to perfect the sutures, but also to avoid or stop oozing
3. After transplantation, in particular to treat some lymphorrhreas

Pretransplantation Use of Fibrin Glue

Transplant repair has, unfortunately, become common. The shortage of organs, itself linked to stagnation in the number of removals, the development of multiorgan removals and the practice of removal by sometimes poorly trained teams, have regrettably resulted in a lower quality of the kidneys proposed for use in transplantation.
Our Experience with Fibrin Glue in Urologic Surgery

Fig. 3A–D. Use of Tissucol for repairing renal transplant decapsulations. A Examination of the renal transplant, widely decapsulated at the time of removal (longitudinal tear of the capsule exposed by some traction forceps). B Beginning of the capsulocapsular running suture after Tissucol instillation under the capsule (note, at the end of the dissection forceps, the presence of slow-adhering Tissucol still in the fluid phase). C Final aspect of the capsular repair. As during the previous stages, the already cooled transplant is surrounded by compresses soaked with refrigerated Eurocollins liquid. D The repaired graft is plunged again into the 4°C Eurocollins liquid

Thus, some more or less decapsulated transplants, some that are contused on one pole and even some poorly removed organs are given to the transplantation teams, who, in turn, must devote several long and precious minutes to the organs.

There have been four occasions in which we had to restick or “remake” capsules whose edges were torn or pulled to pieces. They were sutured after some slow-adhering fibrin glue had been instilled subcapsularly, on the renal parenchyma surface (Fig. 3).

Sometimes the capsular damage is such that the remaining capsule is practically unusable. It is in such cases (Fig. 4) that we use a hemivicryl net, applied
Fig. 4A–D. Use of Tissucol for repairing an injured renal transplant. A Initial aspect of the transplant. Note the capsular laceration and the parenchyma injury (arrow). B Beginning of the repair by applying a vicryl net with slow-adhering Tissucol and capsular net sutures (the transplant has been very quickly plunged into 4 °C Eurocollins liquid). C Application of fast-adhering Tissucol, strengthening the repair. D The repaired transplant, in its place at the time of transplantation, after revascularization.
and stuck to one of the transplant poles and sutured to the residual capsule. This net makes a very effective neocapsule which facilitates the transplant manipulations so that they are less dangerous than the ones carried out on a decapsulated organ.

Sometimes the lesion of the transplant is not only capsular, but also affects the underlying parenchyma itself. Thus, we had to repair some sort of contused wound, fortunately superficial, of a renal pole on an organ which was otherwise unharmed.

In this case fibrin glue allowed the repair and thus the use of the transplant. Afterwards, the kidney worked perfectly.

Use of Fibrin Glue During Transplantation

We have used fibrin glue as a powder on the operating field in:
1. Sealing of the vascular anastomosis in 50 of our transplantations, among which 35 have also benefited from sealing of the urinary anastomosis
2. Sealing of the hilar fat for prevention of lymphorrheas, thereby allowing closure of certain lymphatic pedicles, without which leakage of a significant quantity of lymph would occur
3. Sealing of the transplant biopsy zones, should they ooze some blood (five cases only in our experience)

Sealing also appeared necessary (to us) in one case of early disunity of the ureterovesical anastomosis. The initial suture was associated with adherence of the ureter to the bladder, which appeared to us as worthwhile. The healing of this suture unfolded without any problem.

Posttransplantation Use of Fibrin Glue

Postoperatively, Tissucol can again periodically resolve certain problems.

Renal ruptures can be repaired with Tissucol if the parenchyma is opened and has become torn and hemorrhagic or if the dehiscence is incomplete and shallow, resembling a laceration. Such cases occur rather on edematous kidneys and in the context of rejection or tubulopathy.

The sutures may cut the renal tissue, become too wet and thereby deteriorate, even if they are tightened very carefully and with the most moderate intensity. A complementary vicryl net, itself maintained by sealing, can rescue some very difficult situations. We successfully used Tissucol only once in such a case and that despite the absence of an available vicryl net.

In our experience the most frequent use of Tissucol after transplantation concerns controlling lymph flows (lymphorrheas and lymphoceles). Lymphoceles represent one of the most frequent complications of renal transplantation surgery. The effusion of lymph, which may sometimes be considerable, can affect renal function by compressing the excretory path. Simple evacuation puncture of the lymphocele, although it is easy, remains disappointing because of almost unavoidable recurrence. This recurring character may require addi-
tional surgery for the patients. Thus we tried to develop a method of sealing with Tissucol which allowed treatment of the lymphocele during the first attempt.

It should be kept in mind that there are two ways lymphatic flow which can appear after transplantation. First, a significant quantity of lymph accumulates daily from the drains at the transplantation site. Those drains which have remained permeable can be rapidly covered with a connective cuff, which insures true partition, with preferential drainage of the lymph to the outside. The transplantation site, well drained, remains dry and progressively heals. However, the lymph collected at the end of the drains prevents their removal.

Second, the lymphatic effusion is not drained to the outside. The filled drains become clogged and are shortly removed, but subsequently a lymphocele forms which may crowd the transplant site, repulsing the peritoneum and crushing the bladder. After puncture, this effusion frequently recurs, often leading to surgical treatment (peritoneal window) which could have been avoided.

How can Tissucol be used in these two situations?

In the first case, the technique is simple and gives excellent results. The drain is first mobilized a few centimeters, so as to dissociate from its connective cuff. Then some slow-adhering Tissucol can be injected into the drain, carefully disinfected and clamped for 24 h. It will be then possible to remove it without the least effusion reappearing.

In the second case, we are faced with a real lymphatic pocket. It is evacuated at first with the help of two percutaneous drains which are put in place under local anesthesia. After some draining days, and after having checked the good position of the drains, the flow is treated as it was in the first case. However, the residual pocket and therefore of the zone of detachment due to the lymphocele make the glue spreading less perfect. As a consequence, there is possible recurrence of lymphocele after the drains are removed.

In these two cases, the vaporization of Tissucol with the help of a gaseous vector allows the best diffusion of the glue. One of the two drains is used as an injection site and the other one as a valve which allows for purging of the gas. Nonetheless, the use of compressed air, even under low pressure, in a closed cavity remains delicate and dangerous. Thus we do not use this method and have no experience with it. However, such a process must not be neglected, all the more since the use of another gaseous vector (such as CO₂), in order to pulverize the glue, could allow one to overcome the inconvenience of insufflation.

We treated 20 cases of lymphatic flow or effusion. For the simple flows (eight patients) the results have always been excellent and without any recurrence. For the lymphocele (12 patients) there were five recurrences after the first sealing, requiring a second attempt. Only two patients finally benefited from a surgical course of treatment with creation of a peritoneal window.
Discussion

Our results confirm practically all previous observations regarding satisfactory results with Tissucol. The advantages of this fibrin glue are obvious. Besides the hemostatic and adhesive effects that we have described here, we would like to stress the benefits of the two speeds of adherence that Tissucol allows. Indeed by modifying the concentration of thrombin, the speed of adherence of the clot varies: (1) slow-adhering (3 min) with a concentration of 4 IU/ml, and (2) fast-adhering (30 s) with a concentration of 500 IU/ml.

This appeared to us as extremely practical, particularly when precise adjustment of the adhering surfaces is required.

Other advantage facilitating the use of the product is the Duploject system (two syringes), which allowed us to obtain an optimal mixture and perfect polymerization, which is easy to see by the whitish aspect of the final fibrin clot. In the same way, the long Duplocaths (catheters with two separate canals) were useful to us, particularly for treating lymphoceles, as previously described.

The inconveniences of Tissucol are relatively minor, the most significant one being the amount of preparation time needed for the product. For semi-systematic use, e.g. renal transplant, preparation time is irrelevant. One only needs to allow for the preparation time up to the moment of use, and this, once matter of routine, does not pose any problems.

However, when immediate use is required during an operation, the preparation time of the solution is too long, if one adds the 10-15 min of shaking by rotation of the aprotinin-fibrinogen mixture in the Fibrinotherm (heating block at 37 °C with magnetic shaking) and the 2-3 min needed to dissolve the calcium chloride in the thrombin solution.

Indeed, it is best to wait for some 15 min or so by compressing the hemorrhagic focus and then obtaining correct hemostasis without any need for Tissucol; but each surgeon knows how endless 15 min of waiting can seem in such a context.

Another inconvenience of this biological glue is the price. Indeed the hospital administration tends to check the use of this product, all the more since interest in it increases continually.

There were practically no complications associated with Tissucol use. The only one that we can mention occurred following percutaneous biopsy of a transplant, the surface of which had been coated with Tissucol during transplantation because of a superficial injury. The histologic study of the biopsy fragment showed a thickened renal capsule with an organized fibrous structure. Was this thickness due to a reaction to Tissucol? Or was it simply due to healing of the transplant injury?

Apart from this, there was no incidence of allergic reaction or problems due to infection. Concerning HIV, all our patients are regularly monitored following transplantation. None of our transplanted patients has been seropositive.

Although we generously use betadine in our surgical fields, we avoided its use with Tissucol during polymerization of the glue, since iodine-based disin-
fectants locally disrupt this process. The same is true for rifocine, which we instill systematically in transplant surgical fields and which appears to have no harmful action on the previously formed fibrin clot.

Finally, we should note that certain lymphoceles fail to dry after intracavitary application of Tissucol. Maybe in such cases a preparation richer in aprotinin (aprotinin concentration at 10000 KIU/ml) should be used, as is recommended for urinary anastomosis (so as to offset the effects of the urokinase present in the urine). However, we have never dared to do this due to the risk of a notable inflammatory reaction (too high an aprotinin concentration would cause the persistence of some fibrin aggregates, leading to localized inflammatory and fibrotic reactions).

Conclusion

We would like to stress the great potential of Tissucol for use in urology. This fibrin glue appears to be essential for certain indications. Its properties of adherence, hemostasis, and healing are remarkable.

Without any risk or secondary effect, this glue, whose use increases continuously, will pass – and probably soon – from the stage of convenient accessory to being one of the necessary components of the urologist’s surgical equipment.

References and Suggested Reading

The Use of Fibrin Sealant in Nephron Sparing Surgery for Renal Tumors

A. LAPINI, M. CARINI, S. SERNI, S. STEFANUCCI, S. SCELZI, E. BETTI, V. CAVALLI, and M. RIZZO

Abstract

In renal surgery fibrin glue may be advantageous in all cases in which conservative procedures are required or in the presence of bleeding surfaces. In conservative surgery for renal tumors, the advantages that resulted following the use of Tissucol are represented by atraumatic sealing of the parenchyma and safe hemostasis. Here, we report our experience with fibrin glue in 67 cases of nephron sparing surgery for renal tumors.

Introduction

Fibrin glue is a sealing compound with hemostatic and healing properties which has already proven useful in many different urological situations, such as renal [1] and prostatic hemostasis [2], reconstructive procedures [3] and endoscopic maneuvers [4]. In all these conditions the compound appeared to be well tolerated and nontoxic.

Our experience with fibrin glue utilization is based on renal and prostatic surgery: orthotopic ileal bladder and endoscopic procedures. Here we report on our experience with Tissucol in nephron sparing surgery for renal tumors. In these circumstances fibrin glue utilization represents our standard method.

Material and Methods

From November 1986 to December 1992 we utilized fibrin glue in 67 patients undergoing conservative surgery for renal tumors. Surgical techniques consisted of 46 enucleations (in two patients multiple enucleations, one of which was performed ex situ) and 21 polar resections. Pathological data revealed angiomyolipoma in five patients, leiomyoma in one patient and renal cell carcinoma in 61 patients. According to the state of the contralateral kidney, conservative surgery was performed in 37 patients undergoing elective surgery: small peripheral tumors (less than 3.5 cm in diameter) were found without evidence of capsular, nodal or venous involvement and a normal contralateral kidney. Thirty patients underwent imperative conservative surgery for bilateral carci-
noma (11 cases: eight simultaneous, three subsequent) or solitary kidney (19 cases: 13 surgical, 6 functional).

In all cases we employed Tissucol (5.0 ml or 2.0 ml kit or both with thrombin 4; 1 ml of reconstituted solution contains 4 IU) using Duploject plus application needle.

**Surgical Technique**

Enucleation consisted of removal of the tumor, performing the dissection along a plane which could be developed on the renal parenchyma outside the pseudocapsule, performing what has been defined an “enucleoresection” [5]. This is a fast and simple technique which seldom requires clamping of the vascular pedicle. When the removal was completed the exposed area was sealed with Tissucol, 3–4 ml sufficing for small lesions less than 4 cm in diameter. Usually the sealed area and the renal capsule were attached with a single suture to ensure firm adhesion.

Polar resection required pedicle occlusion and surface hypothermia. Occlusion of the blood supply permitted precise, watertight closure of the collecting system and suture ligation of the large vessels.

In these conditions 5–10 ml of Tissucol are required to at least reduce large, horizontal, mattress sutures.

**Results**

Postoperative hospitalization ranged between 7 and 12 days (mean 8.6 days) for the imperative group, and between 4 and 7 days (mean 5.8 days) for the elective group.

Urinary leakage, spontaneously resolved after 5 and 8 days, was observed in two of 21 patients who underwent partial nephrectomy (9.5%). We did not observe significant postoperative hemorrhages.

Three patients died postoperatively: one of pulmonary embolism, one of massive gastric hemorrhage and one of hemothorax caused by subclavian puncture.

Mean follow-up was 23.3 months (range: 2–61 months): one patient died of unrelated causes 8 months postoperatively. Two local recurrences in patients with imperative indications were documented: one after polar resection and one after multiple enucleations. The first was treated with repeated conservative procedures, the latter with nephrectomy and subsequent hemodialysis; both patients are alive without apparent disease after 48 and 6 months, respectively, following the second operation. One patient presented with homolateral adrenal metastasis 3 years after enucleation and is alive 15 months after adenalectomy.
Discussion

During the last decade nephron sparing surgery has been proposed in situations that require preservation of renal function, such as bilateral tumor or cancer in a solitary kidney [6, 7]. Elective renal conserving surgery for small tumors, in the presence of a normal contralateral kidney, is still a matter of considerable debate.

When conservative surgery is considered for the treatment of renal tumor, different procedures are available, such as enucleation, polar resection and extracorporeal repair.

Extracorporeal repair is applied with decreasing frequency since is a complex procedure. It allows meticulous reconstruction of the vascular and pyelocaliceal system, but it considerably increase the risk of postoperative complications such as tubular necrosis and vascular thrombosis [8]. The vast majority of renal tumors can be managed in vivo: enucleation is a fast and simple technique and causes the least sacrifice of functioning renal tissue; however, its elective use is still debated and should be reserved for selected patients. Polar resection removes a wider margin of renal parenchyma around the tumor, but does not prevent local recurrence for multicentric disease [9]. It has some disadvantages over enucleation, such as more difficult hemostasis along the section line, with possibility of further ischemic lesions, urinary fistulas due to inadequate closure of the pyelocaliceal system, or vascular thrombosis secondary to pedicle occlusion, which is mandatory in this procedure.

Based on our experience with the use of fibrin glue in 67 patients undergoing conservative surgery for renal tumors, we have found that there is good hemostasis of the parenchymal surface with fibrin glue.

Since it can be applied to bleeding surfaces, renal ischemia can be avoided (enucleation) or significantly reduced (polar resection). Large sutures, which are frequently associated with necrosis of renal parenchyma, can be avoided. The collecting system, when is opened in, e.g., polar resection, can be carefully closed with a watertight line of suture, reducing the incidence of urinary fistulas. Systemic and local compatibility is good.

Using fibrin glue, there is an improved surgical technique. Consequently, hospitalization and postoperative complications are significantly reduced.

References

Fibrin Sealing in Reconstructive Operations of the Genitalia

C. SPEHR

Abstract

Fibrin sealing has been in permanent use since 1977 in reconstructive operations of infantile genitalia. This survey of 176 children, age 1–17 years, consists of 123 hypospadias, eight epispadias and 32 cases of bladder exstrophy. Thirteen patients presented with various malformations, such as adrenogenital syndrome, doubling of the penis and severe traumatic lesions. In 156 patients urethral reconstruction was performed. The following outstanding advantages of fibrin sealant were found: (1) excellent adhesive properties; (2) minimal infection rate; (3) secure hemostasis; (4) formation of tender scars and simple, uncomplicated management. These properties are illustrated by the presentation of the reconstruction of the penile shaft in bladder exstrophy.

Introduction

Scarless operation techniques are not only the dream of every plastic surgeon, but are also of decisive importance for urological surgery, especially with children. In addition to the negative impacts caused by defective scars, such as unattractive cosmetic results and grievous malfunctions, such operations with infants have to meet the necessities of puberty, for example, growth. Another “infantile complication” is the playfulness of children, which has no respect for surgeons’ admonishments for quiet behavior, fixating bandages, or staying in bed. As most of them have no pains, they don’t feel ill either. Thus the healing process has to be fast and free of complications, and a substance that shortens this process, secures hemostasis and is completely resorbed without any irritations is of greatest importance. Such a substance is fibrin sealant, which has been at our disposal since 1977.

The most important characteristics of such an adhesive are good tissue compatibility and no reaction with other substances. Both apply to fibrin sealant. It is a biological substance of the human body which is completely decomposed within 6–14 days. The time of resorption is dependent on the amount of sealant used.

Fibrin works as a guide line for the induction of capillaries into the wound. It fosters the formation of granulation tissue and reduces the danger of bacte-
rrial infection. These characteristics of fostering the healing process and reducing infections are of special importance in corrections of the urinary tract, where already minimal healing defects can lead to fistula formation or disturbances with miction. Therefore, we have been using fibrin sealant routinely for reconstructive and plastic surgery of the urinary tract and the genitals since 1977.

**Materials and Methods**

The example of a penis correction with exstrophy of the bladder will illustrate the most important aspects of using this sealant, with special attention being paid to hemostasis, sealing of sutures, fixation of large areas of skin and the possibility to substitute sutures (Fig. 1).

**Hemostasis**

Especially with operations of the genitals there is a large tendency toward formation of hematoma and edema because of many blood vessels. Accurate hemostyasis with unhindered blood circulation is therefore unavoidable for complication free healing. Punctiform as well as diffuse bleeding, as, for exam-
Fibrin Sealing in Reconstructive Operations of the Genitalia

Fig. 2. The neourethra is formed by a split-skin graft

ple, from the corpora cavernosa, can be sealed quickly by direct application of this fast sealant. If indicated, collagenic fleece can be used as a carrier. With heavy bleeding a short period of interrupting blood circulation is needed to seal the vessels, otherwise the sealant would be washed away before polymerization. Time-consuming ischemia and traumatic purse string ligations, though, are superfluous. Also unipolar electrocoagulation, with its high risk of necrosis, can be dismissed.

Sealing of Sutures

Every primarily watertight closure done with traditional techniques needs tightly set sutures. With the formation of urethrae this not only means the pos-
sibility of shortening tissue, but also the risk of insufficient blood circulation and subsequent necrosis – and thus the risk of fistula formation. In contrast, the combination of suture-sealant allows lightly sewed continuous or interrupted sutures. Thus damage caused by operation techniques can be avoided. Also splinting of the neo-urethra is no longer necessary (Fig. 2)

Sealing of Tissue and Fixation of Skin

Extensive mobilization of tissue and skin, as is necessary with such operations, causes extensive wound surfaces. In such a case, fibrin sealant can be used to seal the skin or transplant to the shaft of the penis. Its fluid consistency guarantees even the sealing of smallest splits in tissues and thus is an additional pro-
Fig. 4 a, b. Result of operation immediately and 6 months after penis reconstruction

Phylactic against fistulas. Another advantage is the property of reliably sealing the skin with the underlying tissue and thus avoiding skin sutures, as there is no more tension on the wound margins. With urethra reconstructions we therefore refer only to continuous subcutaneous or intracutaneous sutures close to the wound margins. Generally we renounce drains, as fibrin sealing completely seals different layers of tissue.

Here again we want to stress the importance of applying fibrin sealant sparingly, at most the thickness of a capillary layer. A thin net starts the induction of capillaries into the wound and the formation of granulation tissue, but a “thick carpet” hinders this vascularization process like a barrier, as Edinger et al. [2] have shown. Furthermore, prolonged fibrinolysis increases the possibility of infection. A thick carpet can also be caused unvoluntarily by summation of different sealings. To avoid this we favor one “terminal sealing” which combines the different characteristics of fibrin sealant in one single step. Prior to closure a thin tube is inserted into the wound, while a procedure with several layers also requires several tubes. After suturing, the sealant is applied via these tubes while they are pulled out slowly (Fig. 3). The still fluid sealant is evenly distributed by careful pressure and thus reaches even the smallest tissue fissures.

Another advantage of this method is the avoiding of contact between fibrin sealant and wound margins, as the sealant only develops its properties on the already outstretched skin. Thus retractions of the wound margins can be avoided. This is also of greatest importance with partial transplants and full-skin transplants, as exactly cut, well adapted skin transplants can be fixated with fibrin sealant alone if the patient avoids too much motion. With the sealing on the penis, though, it is advisable to sew the transplant loosely to the shaft and to additionally suture the wound margins. Here, too, final sealing with a thin tube has proved successful.
Results

Since 1977 we have used fibrin sealant for genital corrections in 176 children. Among these were: 123 hypospadias, 32 bladder extrophies, and eight epispadias. With 13 other patients we found various different malformations (Table 1).

In 156 patients urethral reconstruction was part of the correction. In four patients with hypospadias and two with epispadias we found fistulas without apparent cause. Because of prior operations, however, the skin conditions in all these patients were unfavorable. Two other boys showed intolerance reactions against the suture material.

In three patients with bladder extrophy, wound infection occurred probably because of too generous use of fibrin sealant. Therefore, it is necessary to apply the sealant sparingly to ensure healing without complications. It is
Table 1. Fibrin sealant

<table>
<thead>
<tr>
<th>Indication</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Hypospadias</td>
<td>123</td>
</tr>
<tr>
<td>Bladder extrophies</td>
<td>32</td>
</tr>
<tr>
<td>Epispadias</td>
<td>8</td>
</tr>
<tr>
<td>Various malformations</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 2. Complications of urethral reconstruction ($n = 156$)

<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
</tr>
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<tbody>
<tr>
<td>Fistulas</td>
<td>8</td>
</tr>
<tr>
<td>Infections</td>
<td>3</td>
</tr>
<tr>
<td>Scar contractions</td>
<td>10</td>
</tr>
</tbody>
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Absolutely not useful to fill cavities. Ten children required small scar corrections on the dorsal side of the penis after its reconstruction (Table 2). It should be noted, though, that with such long operations the wound margins can be damaged considerably by drying out. Otherwise, we found that fibrin sealant ensures tender, flexible scars even when skin tension lines could not be taken into account with the cuts (Fig. 4a, b).

**Conclusion**

There is no doubt that fibrin sealing is a great help for surgeons. It supplies a technically simple, time saving method which requires only a short phase to get acquainted with. However, it does not free the surgeon from the responsibility to use subtle, nontraumatic surgical techniques. Given these, though, fibrin sealant enhances and ensures the result of every operation.

**References**

The Use of Fibrin Adhesive Alone After Torsions of the Spermatic Cord

H.-D. NÖSKE

Abstract

Torsions of the spermatic cord must be treated in time: fast detorsion and firm fixation of the testicle in the scrotal wall. Since 1985 we have operated on more than 100 patients suffering from this dangerous condition, 70% of which were treated using fibrin glue alone to anchor the saved organ in the scrotum. In the remaining 30% torsion had resulted in loss of the testicle or semicastration. The results after fixation using fibrin adhesive alone are encouraging. We have never observed any recurrence of torsion or related complaints after using this new procedure.

Introduction

So much has been written about torsion of the spermatic cord that any detailed discussion of this condition would be repetitious [6–9, 11]. Nevertheless I shall accentuate some remarkable characteristics of this urological emergency, which requires prompt diagnosis and immediate surgical treatment for testicular survival. Torsion of the spermatic cord is predominantly a condition of the later years of childhood and the early years of adulthood. We found the average age incidence in about 250 patients to be 16 years. Moreover this phenomenon occasionally occurs also in the newborn (Fig. 1).

The disease was first described in 1840 by the Frenchman Delasiauve [1], while exploring a condition, he thought preoperatively to be a strangulated hernia. In contrast, today, torsion of the spermatic cord is a well known entity presenting a classical clinical picture with which most practitioners are quite familiar. This results in increased accuracy of diagnosis and improvement of the testicular salvage rate through quick response.

The chief predisposing cause for torsion is a developmental abnormality in the attachment of the cord to the epididymis and testis. Unknown, however, is the direct exciting cause. Sudden strain or spontaneous contraction of the cremasteric muscle is believed to bring about the twist in some mysterious way, yet in many instances torsion has occurred during sleep.

Already in 1926 Young [12], a pioneer in the field of urology, declared that surgical exploration of the involved side is the safest method for the patient.
Fig. 1. Age distribution in 255 cases of spermatic cord torsion and 47 cases of hydatid torsion

The recommended treatment for torsion is detorsion in time and firm fixation of the testis. Manual derotation may be used only as a temporizing maneuver. Diagnostic and therapeutic delay means organ loss. The salvage rate of the testicle has, for a long time, remained discouragingly poor, but in the last 15 years we have observed a significant improvement, from 40% to 75% (Fig. 2). Various often-quoted experimental preparations using dogs with torsive testes reveal that the "safe" period in which the tubules will recover is somewhere within 6 h of complete torsion (Fig. 3).

Prophylactic fixation of the contralateral healthy testicle is advisable, if any doubt concerning its viability or excess mobility is entertained, especially in patients in the dangerous age of puberty. In the case of operation for acute torsion immediate surgical fixation of the opposite side is probably the wisest course of action.

Case reports and our own experience indicate that torsion can occur after previous operations on the testis: thus, some patients had years ago undergone orchidopexy for undescended testicle, others had had therapeutic, and still others prophylactic, contralateral fixation after torsion of the other side.

**Material and Methods**

Worldwide, fixation of the testicle is performed routinely by suture technique. When, after detorsion, blood circulation returns, the testis must be firmly fixed in its proper position. Hot towels can help to restore circulation. The testicle is normally sutured to the scrotum with one or two stitches through the tunica albuginea. The following suture material is normally favored for the anchoring of the tunica albuginea to the tunica dartos layer: simple or chromic catgut, cotton, or silk. If absorbable material is being used, sufficient scarring to provide stability of the testis may not occur and a recurrence of torsion may take place after dissolution of the suture material.

According to Doerr [2], the testicle is supposedly the most irritable or vulnerable organ of the male body. Conventional sutures may cause infection, foreign body stimuli and fibrotic tissue by cicatrization; they can also cause impairment of blood supply followed by atrophy of parenchyma. Also discussed is the possibility of an impairment of the blood-testis barrier eventually followed by autoimmune orchitis.

Considering the sensitiveness of the tissue and the above-mentioned possibility of damages, we have, since 1978, tried a new method of fixation using
fibrin adhesive in orchidopexy of the retained testicle. The results were good [3, 10]; no recurrences were observed. Similar results are reported by Moradpour [5] for animal experiments performed in 1989 at the children's hospital in Zürich. In the course of fertility studies with rats fibrin sealing was used to fix artificially caused torsion of the spermatic cord using Tissucol (Immuno, Vienna). This procedure proved to be a safe, sparing and fast method of fixation. Jurincic has also reported cases of orchidopexy in children with fibrin adhesive [4].

**Results**

Since 1985 we have also preferred this tissue sparing method in torsions of the spermatic cord. Up to now we have treated more than 100 patients, 70% of whom were operated on using fibrin glue alone to anchor the saved organ in the scrotal wall. In the remaining 30% torsion had resulted in loss of the testis due to total hemorrhagic infarction. The results of this new way of fixation are encouraging and the adhesive power of fibrin glue seems to be of a very high order. In the last 7 years we have never observed any recurrence of torsion or related complaints after fibrin sealing.

The surgical technique is quite simple: After a small scrotal incision the testicle is exposed and the coats are opened. Then follows a careful detorsion and a thorough evaluation of the testis. The coats are provided with a continuous running border suture or, in adult patients, by the Winckelmann procedure. The surface of the organ and the tunica dartos layer must be bloodless and dry before glueing. Then the previously prepared fibrin adhesive is injected with the Duploject system into the scrotal space and over the tunica albuginea. Already during application of the physiological adhesive, the testis must be relocated into its proper position and kept there by external pressure of the fingers for 5 min. During fixation of the testicle in its position, the scrotal wound can be closed above a small drain with catgut.

As a rule the postoperative course without antibiotics but with elevation and cooling of the scrotum was uneventful and the patients were discharged from the hospital on the second or third day after operation. Follow-up physical examinations showed normal testicles with adequate firm fixation.

**Discussion**

The torsion of the spermatic cord treated operatively in time as well as prophylactic measures on the healthy contralateral testicle allow a firm and durable anchoring of the testis in the scrotal space. Our results show that this is possible using human fibrin adhesive alone. We therefore recommend this sutureless tissue sparing method for all situations in which the testis must be fixed in the scrotal space. These results were based on clinical experience alone without the usual randomized, prospective and comparative studies. However, he who heals is right!
References

Reconstruction of the Urethra After Radical Perineal Prostatectomy Using Fibrin Sealing

W. BOECKMANN, D. ROHRMANN, and G. JAKSE

Abstract

In urethral surgery we usually perform cystostomy or introduce an indwelling catheter for the discharge of urine. By the use of fibrin sealant urinary drainage can either be avoided or is required for a shorter period of time.

In radical prostatectomy an anastomosis between the membranous urethra and the bladder neck is necessary. Prolonged leakage at the site of anastomosis occurs in about 10% of the patients. Moreover, catheter drainage is usually needed for 2 weeks. Since we perform radical perineal prostatectomy the anastomotic site can easily be sealed with fibrin glue and collagen. The anastomosis is watertight by day 6. At present, the indwelling catheter is removed on day 10, but probably earlier removal is also possible.

Introduction

Strictures are frequent complications of injuries to the urethra. Their structure is pathologically described as spongiofibrosis, and extravasation of urine seems to be the most important pathogenic agent [1]. The incidence of anastomotic strictures after radical retropubic prostatectomy is described as being between 5% and 15% (Table 1). With a surgical technique involving the perineal approach for suturing the urethra under direct vision and additional fibrin sealing, we tried to establish a watertight vesicourethral anastomosis and thus avoid anastomotic strictures in patients undergoing radical perineal prostatectomy.
Table 1. Incidence of anastomotic stricture after radical prostatectomy

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Patients (n)</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Igel [2]</td>
<td>1987</td>
<td>692</td>
<td>5.4</td>
</tr>
</tbody>
</table>

**Material and Methods**

In a series of 18 patients undergoing laparoscopic pelvic lymph node dissection and radical perineal prostatectomy the anastomosis between bladder neck and urethra was wrapped with collagen sponge and fibrin glue (Figs. 1, 2). This group of patients was compared to 30 retrospective patients operated on in our institution with radical retropubic prostatectomy and conventional vesicourethral anastomosis without fibrin sealing. Before removing the catheter the patency of the anastomosis was proven by a cystogram between 6 and 14 days after the operation. In case of a leakage the cystogram was repeated 7 days later. To exclude an anastomotic stricture, uroflow was evaluated 3 months after the operation.

Fig. 1. Anastomosis between bladder neck and urethra after perineal prostatectomy. The anterior layer still has to be sutured
Results

After perineal prostatectomy with fibrin glue assisted vesicourethral anastomosis, only three patients had leakage in the first cystogram, leading to an average time of indwelling catheterization of 11.9 days in this group. Overall hospitalization time was 20 days; so far we have not observed anastomotic strictures in these patients or any adverse reaction due to fibrin glue.

In the group with radical retropubic prostatectomy 12 patients had a leakage of the anastomosis. Four cases of anastomotic strictures (13%) requiring further therapy (dilation, incision) occurred. Catheter lasted an average of 19.1 days, overall hospitalization time was 25.2 days (Table 2).

Table 2. Clinical results of radical perineal and radical retropubic prostatectomy

<table>
<thead>
<tr>
<th></th>
<th>Radical perineal prostatectomy and laparoscopic lymphadenectomy</th>
<th>Radical retropubic prostatectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients $,(n)$</td>
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<td>30</td>
</tr>
<tr>
<td>Age (years)</td>
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<td>48–73</td>
</tr>
<tr>
<td>Overall hospitalization (days)</td>
<td>20</td>
<td>25.2</td>
</tr>
<tr>
<td>Catheter (days)</td>
<td>11.9</td>
<td>19.1</td>
</tr>
<tr>
<td>Anastomotic stricture $,(n)$</td>
<td>0/18</td>
<td>4/30 (13%)</td>
</tr>
</tbody>
</table>

* Data from the Dept. of Urology, RWT Aachen, January 1991–August 1992
**Discussion**

Singh and Blandy [1] investigated the pathology and pathogenesis of urethral strictures in men and in an animal model. They showed that the periurethric fibrocytic reaction leads to fibrous replacement of the corpus spongiosum and they proved the important role of urine extravasation in exacerbating the inflammatory process.

Anastomotic strictures after radical retropubic prostatectomy occur in 5%–15% of cases [2–7] and may be a result of imprecise suturing behind the symphysis followed by extravasation of urine.

In analogy to the fibrin glue-mediated vasal anastomosis, which provides a reduced incidence of sperm granuloma compared to conventional two layered vasovasostomy [8], the application of fibrin in urethrovvesical anastomosis after radical perineal prostatectomy seemed effective to us.

Since laparoscopic pelvic lymphadenectomy has been introduced into urology [9], radical perineal prostatectomy has gained new interest. With this technique there is little blood loss and precise urethrovvesical anastomosis under direct vision; a nerve sparing approach was described by Weldon and Tavel [10]. Our concept was to offer a less invasive therapy of localized prostate cancer (laparoscopic pelvic lymphadenectomy and perineal prostatectomy) and to minimize its possible complications. The better results in patients undergoing perineal prostatectomy might be due to the precisely sutured anastomosis or/and the additional use of fibrin glue. The study was not designed to distinguish between the importance of these two factors.

The use of fibrin sealing at the site of anastomosis in perineal prostatectomy seemed to reduce the duration of indwelling catheterization, the incidence of anastomotic strictures, and overall hospitalization time (Table 2).

**Conclusion**

In a series of 18 patients undergoing radical perineal prostatectomy the anastomosis between bladder neck and urethra was performed by means of fibrin glue. In terms of duration of indwelling catheterization, overall hospitalization time and incidence of anastomotic strictures, the results in these patients seemed favorable compared to a group of 30 patients after radical retropubic prostatectomy with urethrovvesical anastomosis without fibrin sealing.

**References**

Comparative Study of Closing Nephrotomies in Regional Renal Hypothermia Using Techniques Saving the Parenchyma

I. Mikó, I. Furka, Z. Szabó, G. Joós, and M. Hauck

Abstract

Saving the functioning parenchyma is extremely important in renal surgery (removal of a tumor, reconstructive surgery following lithotomy and attending traumatized kidneys).

We used regional renal venous hypothermia, which we designed, in combination with two adhesives (Histoacryl and fibrin sealant) to save the parenchyma. Comparisons of results during and after surgery (dissection, angiography, histology) showed that fibrin sealant was more beneficial than other substances in hypothermia.

Introduction

Compression of the renal artery for over 20 min may become necessary when attending to traumatized kidneys, during removal of a tumor or open lithotomy of the cavernous system of the kidney, the latter also requiring simultaneous reconstruction. In these cases, in situ hypothermia serves as a means of preventing irreversible damage caused by warm ischemia and it also helps to spare the functioning renal parenchyma.

In situ hypothermia can be achieved by superficial cooling or by the perfusion method along the renal artery and/or renal vein and its collaterals (i.e. spermatic/ovarian and suprarenal veins). The latter method of cooling is especially indicated in the left kidney since, after cooling, the collaterals can be ligated and cooling is carried out without any side effects [1].

Further protection of the parenchyma in these operations is achieved by the application of bioplastics and tissue adhesives, the former having excellent hemostatic properties [2]. Urological surgery greatly relies on cyanoacrylate-based tissue adhesives, e.g., Histoacryl [3-5] and fibrinous adhesives, e.g., fibrin sealant [6–8]. These techniques also contribute to the prevention of losses of active parenchyma caused by renal sutures. Our experiments were carried out to support this approach.
Materials and Methods

The experiments were done in 35 mongrels regardless of sex or weight. Hypothermia at 20°–26°C was induced in the venous branch of the kidney, along the internal spermatic/ovarian vein, according to our own method [1]. Venous cooling was immediately following by the preparation of radial nephrotomies. After closing the cavernous system the parenchymal wound surfaces were united as follows: group 1 \((n = 7)\), Histoacryl (Braun Melsungen); group 2 \((n = 7)\), Histoacryl + Surgicel; group 3 \((n = 14)\), fibrin sealant (Immuno); group 4 \((n = 7)\), U-shaped parenchymal stitches with Dexon plus suture material.

Manageability, capability, polymerization time, and elasticity of the two kinds of adhesives together with the application of suture materials were observed during surgery contrasted with normothermal conditions. Observation of Histoacryl, fibrin sealant and suture materials lasted for 330, and 42 days, respectively. After killing the animals we searched for macroscopic changes seen along the line of nephrotomy. To judge possible changes in the vascular system and the condition of the parenchyma direct renal angiography was carried out using diluted Micropaque solution (Nicholas G.m.b.H., Vienna).

Next, tissue pieces comprising the whole width of the cortical and medullary substance of the kidney were excised. The samples were fixed in 7% neutral formalin. Sections prepared after paraffin sealing were stained with H and E.

Results

Observations During Surgery

Renal parenchyma proved to be somewhat more fragile in hypothermia than in normothermia. Despite this fact, it could be sutured easily, although the stitches pinched deeper.

Compared to normothermic conditions, polymerization times were found to be two to three times longer in hypothermia when adhesives, whether Histoacryl or fibrin sealant, were used. In hypothermia the elasticity of fibrin

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Histoacryl</th>
<th>Fibrin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymerization time</td>
<td>Twice or three times longer than in normothermia</td>
<td>Twice as long as in normothermia</td>
</tr>
<tr>
<td>Flexibility</td>
<td>Forms rigid mass</td>
<td>Unchanged</td>
</tr>
<tr>
<td></td>
<td>No change on reheating</td>
<td></td>
</tr>
<tr>
<td>Absorption time</td>
<td>Significantly slows down (detectable over 1 year)</td>
<td>Unchanged (detectable for 4 weeks)</td>
</tr>
</tbody>
</table>
Fig. 1a–d Dissection pictures. a, b Histoacryl: 330th postoperative day; c, d fibrin sealant: 42nd postoperative day
I. Mikó et al.

sealant was unchanged whereas Histoacryl formed a rigid mass which did not change even after reheating. The use of fibrin sealant did not result in changes of absorption time, although it slowed down significantly with Histoacryl. Moreover, the presence of Histoacryl could still be detected in a year's time (Table 1).

**Macroscopic Observations on Dissecting the Animals**

Well-known phenomena, i.e., uneven surface and rough scars along the line of nephrotomy, were noted in nephrotomies closed by suture material. When Histoacryl was used, these could be observed even on the 330th day. Both on the outside and incision surface of the kidney, the adhesive had not absorbed either when applied alone or in combination with Surgicel (Fig. 1a, b).

When fibrin sealant was applied, it could not be seen macroscopically, even on the 42nd day, along the line of radial nephrotomy. The site of intervention was seen only as a tiny, slightly denser scar. On incision into the kidneys no trace of the adhesive was seen on the incision surface (Fig. 1c, d).

Signs indicating slight losses in the parenchyma of the cortex, along the incision lines, were observed radiologically when Histoacryl was used (Fig. 2a). When fibrin sealant was used to close the wound, only minimal losses in the parenchyma were detected (Fig. 2b).

![Angiograms](image)

**Fig. 2a, b** Angiograms. a Histoacryl, 330th postoperative day; b fibrin sealant, 42nd postoperative day
Fig. 3a, b Histology. a Suture material, 42nd postoperative day: necrotic parenchyma in the line of nephrotomy, due to the strength of mechanical compression exerted by stitches. H and E, x20. b Histoacryl, 330th postoperative day: intact renal parenchyma with residual tissue adhesive. Double surfaces in the line of nephrotomy. H and E, x20. c Fibrin sealant, 42nd postoperative day: intact renal parenchyma without residual tissue adhesive. Very thin connective tissue strip in the line of nephrotomy. H and E, x62).

Microscopic Observations

Parts of the kidney, trapped in between the deep parenchymal stitches, became necrotic along the incision line, as a result of mechanical compression when nephrotomies were closed by suture material. A wide zone of connective tissue formed along the line of incision (Fig. 3a).

Histoacryl used to unite the surfaces in other nephrotomies was hardly digested by giant cells. The adhesive could be detected even on the 330th day in the renal tissue. A “double surface” developed along the line of incision, i.e., on both sides of the immobile adhesive, a narrow zone of connective tissue formed over the injured renal tissue. Glomeruli and tubules outside this zone were intact (Fig. 3b).

The application of Histoacryl + Surgicel bioplast resulted in a similar picture, but union between the surfaces over the double surface was also ensured by a fine connective tissue capsule.

On the 14th postoperative day, fibrin sealant, together with giant cells participating in the elimination of the adhesive, could be detected along the incision line. Next to the zone of connective tissue, already intact parenchyma could be noted. From the 42nd postoperative day on, only a fine line of connec-
tive tissue indicated the site of radial nephromyotomy. Intact renal parenchyma was found outside this zone (Fig. 3c).

**Discussion**

Based on the experiments it can be concluded that both Histoacryl and fibrin sealant are of use in regional renal hypothermia. They hold surfaces together very well, their hemostatic characteristics are good, they absorb over the time and also show histophilic properties. Their application shortens the time of surgery and lessens the effect of parenchymal losses due to suture materials since the collective tubules are not blocked. However, the polymerization time and elasticity of fibrin sealant seems more favorable than those of Histoacryl.

The above listed benefits become more significant in light of unchanged absorption times. Despite the fact that both adhesives have unambiguously proven to save the parenchyma, as compared to suture materials, fibrin sealant is preferred in hypothermia.

**References**

Watertight Sutures with Fibrin Glue: An Experimental Study

P. HOEBEKE, W. OOSTERLINCK, and R. VERBEECK

Abstract

A rat model was developed to test the watertightness of sutures and used to evaluate the value of fibrin glue in making conventional sutures watertight. Fibrin glue raised the mean hydrostatic pressure to which the skin suture resisted from 9.1 to 26.3 cm H$_2$O, thus indicating that it enhances suture watertightness. After 3 and 6 days the pressure had risen from 24.8 to 47.9 and from 56.5 to 73.3 cm H$_2$O, respectively. For bladder sutures the results are comparable.

Introduction

In urology, a watertight suture can prevent urine extravasation in the wound and eliminate the need for, or at least shorten the duration of, urinary diversion. A watertight suture can prevent the noxious effects of urine extravasation on wound healing, especially when infected, and thus reduce the incidence of complications like fistulization and fibrosis. More particularly, it can reduce the complication rate in urethral reconstructive surgery. One of the ways of achieving a watertight suture is with tissue glues. In the present study, fibrin glue is evaluated for this purpose.

Materials and Methods

Experiments were conducted with male Wistar rats, weighing between 200 and 220 g. After 12 h fasting and preoperative antibiotics (thiamphenocol 25 mg/kg body weight) the animals were anesthetized with intraperitoneal pentobarbital (25 mg/kg body weight). The abdominal wall was shaved and, after disinfection, was incised in an inverted U-shape through its full thickness. Both sides of the U incision were dissected so that a skin tube could be easily sutured without traction. The skin remained attached to its vascularization by its subcutaneous tissue. The skin flap was sutured with a running 4.0 chromic catgut to a blind tube open on one side (Fig. 1). In the experiments, which ran over several days, the remaining abdominal skin was closed over the skin tube with 3.0 silk, leaving one side of the skin tube open.
To test the watertightness of the suture line, a connector was introduced into the open end of the skin tube, and a suture was placed to prevent leakage between the connector and the tube. This was connected by a tube to a small water reservoir that could be raised progressively along a measuring scale (Fig. 2).

In the immediate postoperative experiment, a diluted methylene blue solution was used to demonstrate leakage along the suture line. By raising the fluid column, hydrostatic pressure was created in the skin tube. The fluid column was raised at the rate of 1 cm every 30 s. The pressure at which leakage was observed was registered in cm H₂O.

**Fig. 1.** Inverted U-shaped skin incision, sutured to a blind-ending skin tube

**Fig. 2.** Measuring hydrostatic pressure
For the long-term experiments, watertightness was similarly demonstrated but with contrast dye instead of methylene blue and with fluoroscopy to determine leakage. This contrast dye has a specific gravity of 1.2 so the contrast dye pressure was increased by 20% to obtain leak pressure in cm H₂O. For each observation day, a different group of rats was used.

The tissue glue that was used was a fibrin glue consisting of two components (Tissucol, Immuno France), which are brought together at the suture line by a double syringe system (Duploject). The first component is a concentrate of lyophilized human fibrinogen (total protein 120 mg/ml) and 3000 KIU/ml bovine aprotinin. The second component consists of 500 IU/ml thrombin and calcium chloride 0.04 mM/ml. When added to the fibrinogen, it induces the polymerization to loose fibrin monomers, which, in the presence of factor XIII and calcium, are converted to a stable cross-linked fibrin polymer that forms the fibrin seal responsible for the adhesive effect. The sealing can be observed as the viscous solution transforms within seconds into a white clot that binds to the suture line. The role of aprotinin is to protect the seal against naturally occurring fibrinolytic enzymes.

In the second series of experiments, the bladder was exposed by means of a suprapubic midline incision and opened longitudinally for 1 cm. The bladder was then closed with a running suture of 4.0 catgut; in one group the suture was reinforced with fibrin glue. Watertightness was measured immediately after the operation and after 3 and 6 days. This was done, as in the first experiments, by measuring the hydrostatic pressure necessary to develop leakage. The hydrostatic pressure was measured by means of a small tube inserted through the dome of the bladder and fixed with a circular suture at its entry.

**Results**

The hydrostatic leak pressures measured for skin tubes for the different groups of rats at several observation days are summarized in Table 1. The leak pressures measured in the bladder are given in Table 2.

For the first series of experiments using skin tubes, a Levene's test shows that the variances of the hydrostatic leak pressure of the different groups mentioned in Table 1 are homogeneous \((0.05 < p < 0.10)\). The results of an analysis of variance of the data in Table 1, when a two-factor factorial design was used, are summarized in Table 3. The factors considered are the post-operative time (0, 3, and 6 days after suturing) and the method (suture alone vs suture with fibrin glue) used. Table 3 shows that there is no significant interaction between the time and the method used. The time as well as the method, significantly and independently of each other, affect the hydrostatic leak pressure. On this basis it can be concluded that the application of fibrin glue does not interfere with the natural process of wound healing. However, application of the glue drastically increases the watertightness of the suture as reflected by the hydrostatic leak pressure. In fact, a Newman-Keuls' multiple range test at 95% confidence level shows that the leak pressure increases in the order: day 0, I < day 0, II < day 3, I < day 3, II < day 6, I < day 6, II,
Table 1. Hydrostatic leak pressure (cm H₂O) for skin tubes as a function of time after suturing (I) and suturing combined with fibrin glue (II)

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Method 1</th>
<th>Method 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9 12 7 8</td>
<td>21 33 22 39</td>
</tr>
<tr>
<td>3</td>
<td>19 20.5 24 21.5</td>
<td>48 37 41 57.5</td>
</tr>
<tr>
<td>6</td>
<td>55 62.5 40 50.5</td>
<td>86.5 62.5 75.5</td>
</tr>
</tbody>
</table>

where the symbols I and II refer, respectively, to suture alone and suture combined with fibrin glue.

As is seen from Table 2, for some experiments the immediately postoperative hydrostatic leak pressure for the bladder falls outside the range of our

Table 2. Hydrostatic leak pressure (cm H₂O) for bladders as a function of time after suturing (I) and suturing combined with fibrin glue (II)

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Method 1</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>24 31 32</td>
<td>52 62 80</td>
</tr>
<tr>
<td>3</td>
<td>74.5 &gt;120</td>
<td>&gt;120 74.5 &gt;120</td>
</tr>
</tbody>
</table>

where the symbols I and II refer, respectively, to suture alone and suture combined with fibrin glue.

As is seen from Table 2, for some experiments the immediately postoperative hydrostatic leak pressure for the bladder falls outside the range of our

Table 2. Hydrostatic leak pressure (cm H₂O) for bladders as a function of time after suturing (I) and suturing combined with fibrin glue (II)

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<th>Time (days)</th>
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<tr>
<td>0</td>
<td>24 31 32</td>
<td>52 62 80</td>
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<tr>
<td>3</td>
<td>74.5 &gt;120</td>
<td>&gt;120 74.5 &gt;120</td>
</tr>
</tbody>
</table>

where the symbols I and II refer, respectively, to suture alone and suture combined with fibrin glue.

As is seen from Table 2, for some experiments the immediately postoperative hydrostatic leak pressure for the bladder falls outside the range of our
Table 3. Analysis of variance of the hydrostatic leak pressure for skin tubes on the basis of a two-factor factorial design

<table>
<thead>
<tr>
<th>Source of variation</th>
<th>df</th>
<th>Sum of squares</th>
<th>Mean square</th>
<th>F</th>
<th>p</th>
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<td>11290</td>
<td>227</td>
<td>&lt;&lt;0.001</td>
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<tr>
<td>Method</td>
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<td>5434</td>
<td>5434</td>
<td>109</td>
<td>&lt;&lt;0.001</td>
</tr>
<tr>
<td>Method × time</td>
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<td>127.4</td>
<td>63.7</td>
<td>1.3</td>
<td>0.286</td>
</tr>
<tr>
<td>Residual</td>
<td>54</td>
<td>2688</td>
<td>49.8</td>
<td></td>
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</tbody>
</table>

measuring device when suturing is combined with fibrin glue. This becomes even more pronounced for the experiments after 3 days. For this reason a statistical evaluation of the data is not possible. Nevertheless, the data in Table 2 clearly show that the application of fibrin glue upon suturing of the bladder has the same beneficial effect on watertightness as in the case of the skin tubes.

Discussion

Our results demonstrate that the watertightness of conventional macroscopic suturing can be improved considerably with fibrin tissue glue. In Europe, fibrin glue (Tissucol) has been used quite extensively in animal experiments and in urological practice in the following fields: renal parenchyma lesions [1], urethral reconstruction in hypospadias [2, 3], prostatectomy [4], cystopexy, nephropexy and orchidopexy [5, 6] and in vasovasostomy [7]. However, Schultz [8] did not achieve better clinical results using fibrin glue on ureteral sutures in stone surgery, which he attributed to the peristaltic movement of the ureter causing rapid dehiscence of the clot from the ureteral surface.

The principle of fibrin sealing involves part of the naturally occurring coagulation cascade. Fibrinogen is converted to an unstable fibrin monomer in the presence of thrombin and calcium. This unstable fibrin monomer polymerizes to form a stable, cross-linked fibrin polymer that makes a physiological clot that is well accepted by the human body as it does not elicit a foreign body reaction. It even has some hemostatic activity and activates wound healing by stimulating capillary and fibroblastic growth.

This study has demonstrated that fibrin glue can enhance watertightness of skin and bladder sutures in rats. Further studies are planned to evaluate whether similar results can be obtained in suturing other urine containing structure like the pyelum, the ureters and bowel pouches.

Our results led us to use fibrin glue in the reconstruction of the urethral tube in hypospadias in order to avoid urine extravasation and infection around the newly constructed urethra. We use it under the penile skin covering the shaft and the reconstructed urethra in order to diminish bleeding between the different tissue layers. The number of patients treated, however, is still too few
to permit definitive conclusions. Many other factors influence wound healing, so that it is difficult to measure the benefits of the use of fibrin glue in clinical trials, but the experimental data are certainly favorable.

References

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