ORIGINAL RESEARCH

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Histopathological effects of fibrin glue on penile fracture in a rat model

Abstract

Purpose: To evaluate both histopathological effects and potential clinical application of fibrin glue on the penile cavernosal tissue.

Methods: Experimental penile fracture was formed by incising from the proximal dorsal side of the penis in 32 Wistar Albino rats. The rats were randomly assigned to four main groups of eight animals each. In the control group, the incision was not repaired and it was left to secondary healing. In the primary repair group, the incision was primarily repaired. In the fibrin glue group, glue was applied only to the incision. In the final group, fibrin glue was applied to the incision following primary repair. Three weeks later, penectomy tissue was examined histopathologically.

Results: When the control group was compared with primary repair+fibrin glue group, the differences in cavernous tissue healing with fibrosis and inflammation were statistically significant ($p = 0.04$ and 0.01 , respectively). The primary repair+fibrin glue group, showed the best cavernous healing with fibrosis observed in only one rat. There was no significant difference between the control group and the other groups according to cavernous tissue healing with fibrosis and inflammation ($p = 0.11$ and 0.12). Hyperemia was observed in the all groups of rats.

Conclusions: Fibrin glue can be used in cavernoseal surgeries due to its adhesive and potentially anti-inflammatory features.

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Penile fracture is defined as a traumatic rupture of the outer longitudinal layer the tunica albuginea of the corpora cavernosa. The pathologic lesion causes haematoma, swelling and skin discoloration. There is some controversy about the treatment approach for penile fracture. In older studies, a conservative treatment, consisting mainly of cold compresses with antibiotics and anti-inflammatory drugs, was recommended [1]; however, 10% to 30% of patients who were treated conservatively experienced penile deformity, suboptimal erections and difficulty during coitus [2]. Today, immediate surgical treatment is widely accepted as the treatment of choice due to the excellent long-term results that have been reported [3,4].

Fibrin glue is a material that has haemostatic, sealant and adhesive properties. It promotes many healing functions, including angiogenesis, collagen synthesis, wound contraction and epithelialization in wound repair [5-9]. The use of fibrin glue has been an important advance for haemostasis and tissue adhesion in a variety of surgical applications [6,10]. Fibrin glue causes both haemostasis and enhances healing [11-14]. The presence of stabilized fibrin structure stimulates the growth of fibroblasts and this combined effect on wound healing is essential for fibroblastic action.

In this experimental study, the histopathological effect of using commercially available fibrin glue ('Tisseel', Baxter Healthcare Corp., Irvine, California) on cavernosal tissue of rats, and its possible use in penile fracture repair and other penile cavernosal procedures was investigated.

Methods

Experimental Conditions

In this study 32 male Wistar Albino rats (weighing 250–350 g) were obtained from the Experimental Animal Research Center, Medical Faculty, Inonu University, Malatya, Turkey. The animals were kept in a temperature ($21 \pm 2^\circ\text{C}$) and humidity ($60 \pm 5\%$) controlled room in which a 12/12 hour light–dark cycle was maintained. The rats had free access to food and water. The experiment was performed in accordance with the Guidelines for Animal Research from the National Institute of Health and was approved by the Committee on Animal Research at Inonu University, Malatya, Turkey.

Penile Fracture

The rats were placed in supine position after general anesthesia (ketamine 70 mg/kg, xilazine 10 mg/kg i.p. before operation). The genital area of the animals was shaved using an electrical clipper, and the penile skin of each animal was cleaned with 10% povidon iodine before creating the incisions. A 3F ure-

thral catheter was pushed approximately 2 cm up to the mid-penile level from external meatus. Experimental penile fracture model was formed with a number 15 lancet as described in previous literature [15].

Experimental Groups

Thirty-two rats were randomly divided into four groups, each containing six rats as follows:

Control (group C): Penile fracture was performed, but the incision was not repaired; it was left to secondary healing.

Primary repair group (group P): Penile fracture was performed and the incision was repaired with 6-0 polydioxanone suture.

Fibrin glue group (group F): Penile fracture was performed and the incision was repaired with Tisseel fibrin glue.

Primary repair +Fibrin glue group (group PF): After penile fracture was performed the incision was repaired with both 6-0 polydioxanone suture and Tisseel fibrin glue.

After penile fracture, all animals were observed for three weeks. At the end of the observation period, all rats were sacrificed using ketamine (70 mg/kg) and xylazine (10 mg/kg), injected intraperitoneally. Researchers then performed penectomies and the penectomy material of each group was placed separately into 10% formaldehyde solution for pathological examination.

Pathological Evaluation

Approximately 0.5 mm sections were prepared from the penectomy material, including the repaired region. The material was sectioned and then stained with haematoxylin eosin dye and alcohol fixative over a period of 24 hours. The sections were examined by a pathologist in blinded tests. The groups were compared according to fibrosis, hyperemia and inflammation parameters.

Statistical Analysis

The data were analyzed using SPSS version 13.0 for Windows. All values were expressed as mean $\pm$ SD. Comparisons of all the groups according to histopathological features were made based on Fisher's exact test. $P \leq 0.05$ was considered significant.

Results

Microscopic observations were used as the criteria for evaluating success in our study. The results of histopathological examination are summarized in Table 1.

TABLE 1. Histopathological features of all experimental groups

Histopatological Features	Group C n = 8	Group P n = 8	Group F n = 8	Group PF n = 8
Cavernosal tissue healing with fibrosis, n (%) *	6 (62.5)	4 (50)	3 (37.5)	1 (12.5)
Presence of inflammation, n (%) **	7 (87.5)	3 (37.5)	3 (37.5)	1 (12.5)
Presence of hyperemia, n (%)	8 (100)	8 (100)	8 (100)	8 (100)

P : Primary repair, F: Fibrin Glue,

According to Fisher's exact test

* p= 0.60 for group C vs. group P and p= 0.31 for group C vs. group F and p=0.041 for group C vs. group PF

** p= 0.11 for group C vs. group P and p= 0.12 for group C vs. group F and p=0.01 for group C vs. group PF

In the control group (group C), healing with fibrosis, hyperemia and chronic inflammation were predominant features. Chronic inflammation was seen more extensively in this group than in the others (Fig. 1). This group was the worst with regard to cavernous healing (Fig. 2). The primary repair+fibrin glue group (group PF) showed the least inflammation (Fig. 3). Hyperemia was observed in all rats (100%) and fibrosis was observed in six rats (62.5%)

In the primary repair group (group P), hyperemia was observed in all rats (100%). Fibrosis was a feature observed in four rats (50%). In the fibrin glue group (group F), fibrosis and inflammation were observed in three rats (37.5%).

In the primary +fibrin glue group (group PF), fibrosis were observed in only one rat; therefore, this group was the best in regard to cavernous healing (Fig. 4). When the control group was compared with group PF, the hyperemia were not statistically significant ($P > 0.05$), but there was a significant difference between group C and group PF with regards to fibrosis and inflammation ($P < 0.05$). When group P was compared with group F, the differences in cavernous tissue healing, fibrosis and inflammation were not statistically significant ($P > 0.05$).

Discussion

Penile fracture is a traumatic rupture of corpus cavernosum. The tunica albuginea has a high tensile strength requiring a pressure in excess of 1500 mmHg to achieve rupture [16]. Injury to the tunica albuginea should be repaired immediately after diagnosis [17] and immediate surgical repair is the optimal method of management. The aim of immediate repairs to preserve the tunical integrity that is essential for erection and to avoid the complications of conservative management, i.e., penile curvature and deformity, fibrosis and sexual dysfunction [18].

In this study, penile fracture was repaired with conventional suture in the rats with experimental penile fracture. Although

considered a standard method in repairing penile fracture, suturing may cause an inflammatory reaction affecting the regeneration process [19]. Repair with fibrin glue, a method extensively applied in Europe, is an alternative to conventional suture repair.

Fibrin glue is a agent that has been approved for haemostasis in the Europe. It is used for wound repair to promote healing and has been tested in a variety of animal models. Fibrin sealant has been used during many surgical procedures. Fibrin glue has been shown to have a beneficial effect in various applications of urological surgery, including priapism, aortocaval fistulas after nephrectomy and erectile dysfunction due to veno-occlusive dysfunction [20,21].

Although fibrin glue appears to be uniformly detrimental for interosseous and osteochondral healing, ligament repair or bowel anastomosis [22], it is reported as being uniformly beneficial for meniscus repair, corneal and scleral healing and periodontal healing [22]. Fibrin glue has been found to be effective for the prevention of intra-abdominal adhesions [23-25].

Studies on cutaneous wound healing and nerve anastomosis have shown favourable outcomes. Suria, *et al.* showed that sutures lead to an inflammatory reaction that may affect the regeneration process in repairing nerve lesions in an experimental study [26]. Roberto, *et al.* showed that a combination of both suture and fibrin glue techniques provided better conditions for nerve regeneration than sutures alone after sciatic nerve transection in a rat model [27]. In previous studies of experimentally induced penile fracture, agents such as Ankaferd Blood Stopper (ABS) and electrocoagulation have been used, but these agents did not prevent the development of fibrosis in erectile tissues [28,29].

In this study, the histopathological effects of the clinical use of fibrin glue was evaluated on penile cavernosal tissue. Complications were found to be lower in group PF when compared with group C. The most significant improvement was found in group PF. These results may be due to the adhesive, and possibly anti-inflammatory properties of fibrin glue; how-

FIGURE 1. Control group: severe inflammation was seen (H&E X400)

FIGURE 2. Control group: severe fibrosis was seen (H&E X400)

FIGURE 3. Primaryrepair+fibrin glue group: mild inflammation was seen (H&E X400)

FIGURE 4. Primaryrepair+fibrin glue group: mild fibrosis was seen (H&E X400)

ever, further studies are required to clarify the exact mechanisms of the activity of fibrin glue following primary repair in penile fractures.

Conclusions

Our results indicate that use of the combined technique of primary repair with both sutures and fibrin glue provides better regeneration as compared with the use of fibrin glue alone. Therefore, the use of fibrin glue should be considered in cavernoseal surgery due to its adhesive and potentially, anti-inflammatory properties.

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