ORIGINAL ARTICLE

Effect of dexpanthenol on wound healing in penile fracture model: An experimental study

Efecto del dexpantenol en la cicatrización de heridas en un modelo de fractura de pene: un estudio experimental

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Abstract

Objectives: *In the present study, we aimed to investigate the effect of dexpanthenol on wound healing at the histopathological level on cavernous tissue.* **Materials and methods:** *Forty-four Wistar albino rats weighing 220-250 g were used. The rats were randomly divided into four groups as Group B, Group S, Group LD, and Group SD. In Group B, the incision was not repaired and left to secondary healing. In Group S, the incision line was repaired with 5/0 polyglactin suture. In Group LD, 0.25 mg/kg dexpanthenol was applied subcutaneously below the repaired wound region once a day during 14 days. In Group SD, 500 mg dexpanthenol was applied intraperitoneally once a day during 14 days.* **Results:** *No fibrosis was observed in 8 (80%) rats in group SD. Fibrosis rates were significantly lower in Group SD compared to Group B, Group S, and Group LD ($p = 0.013$, $p = 0.005$, and $p = 0.003$, respectively).* **Conclusion:** *Systemic dexpanthenol administration significantly decreased fibrosis in penile fracture model on rats.*

Keywords: *Dexpanthenol. Fibrosis. Penile fracture. Rat.*

Resumen

Objetivo: *En el estudio actual nuestro objetivo fue investigar el efecto del dexpantenol en la cicatrización de heridas a nivel histopatológico en el tejido cavernoso.* **Métodos:** *se utilizaron 44 ratas Wistar albinas con un peso de 220-250 g. Las ratas se dividieron aleatoriamente en 4 grupos como grupo B, grupo S, grupo LD y grupo SD. En el grupo B, la incisión no se reparó y se dejó para la cicatrización secundaria. En el grupo S, la línea de incisión se reparó con sutura de poliglactina 5/0. En el grupo LD, se aplicaron 0.25 mg/kg de dexpentanol por vía subcutánea debajo de la región de la herida reparada una vez al día durante 14 días. En el grupo SD se aplicaron 500 mg de dexpentanol por vía intraperitoneal una vez al día durante 14 días.* **Resultados:** *No se observó fibrosis en 8 (80%) ratas del grupo SD. Las tasas de fibrosis fueron significativamente más bajas en el grupo SD en comparación con el grupo B, el grupo S y el grupo LD (todos $p < 0.05$).* **Conclusión:** *La administración sistémica de dexpantenol disminuyó significativamente la fibrosis en el modelo de fractura de pene en ratas.*

Palabras clave: *Dexpantenol. Fibrosis. Fractura de pene. Rata.*

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Introduction

Penile fracture (PF) is defined as a traumatic rupture of the tunica albuginea of the corpora cavernosa during penile erection. Although vaginal intercourse is the most common reason for PF, penile manipulation and masturbation have also been shown to be responsible in the etiology[1]. The recommended treatment of surgery has excellent long-term results[1-3]. Although complications such as penile curvature, penile deformity, fibrosis, and sexual dysfunction are less common following surgical treatment, overall morbidity rates remain high due to inflammatory and fibrotic processes[2-4].

Dexpanthenol has been used in clinical practice for many years as it promotes wound healing[5,6]. Dexpanthenol is the molecule that is the alcohol form of pantothenic acid and accelerates anti-inflammatory effects by increasing mitotic activity. In the body, it transforms to pantothenic acid, which is a molecule that assists the coenzyme A structure, and by decreasing myeloperoxidase secretion from granulocytes, it halts the formation of free oxygen radicals, while also increasing mitotic activity which results in an anti-inflammatory effect[5,7].

The aim of this study was to investigate the effect of dexpanthenol on wound healing at the histopathological level on cavernous tissue. To the best of our knowledge, this is the first study to have examined the use of dexpanthenol in penile cavernous tissue.

Materials and methods

The study was conducted in the Experimental Animals Laboratory of Ankara Training and Research Hospital. Approval for the study was granted by the Local Ethics Committee (approval number: 0055-17.09.19). The study sample was formed of a total of 44 Wistar albino rats, each weighing 220-250 g. Both pre- and postoperatively, all the rats were housed in separate cages at 22°C and 50% humidity with free access to food and water.

On the day of the study, all the rats were administered anesthesia of 50 mg/kg ketamine under sterile conditions. At 1 h before the procedure, a single prophylactic dose of 20 mg/kg ceftriaxone was injected intramuscularly. Then, the rats were positioned supine, the genital area was shaved, and the penis area was wiped with 10% povidone iodine. A 3 Fr urethral catheter was inserted from the external meatus up to the mid-urethral level at approximately 2 cm. The experimental model of PF was created with a number 15 lancet as previously described literature[8,9] (Fig. 1). After the interventions, the rats were randomly separated into four study groups as Group B, Group S, Group LD, and Group SD, and a reference group of Group A.

Group A was the reference group with no PF applied. In Group B, the incision was made, then left for secondary healing with no repair. In Group S, the incision line was repaired with 5/0 polyglactin suture. In Group LD, the incision line was repaired with 5/0 polyglactin suture, then 0.25 mg/kg dexpanthenol was applied subcutaneously below the repaired wound region once a day for 14 days. In Group SD, the incision line was repaired with 5/0 polyglactin suture, then 500 mg dexpanthenol was applied intraperitoneally once a day for 14 days.

Six weeks later, all the rats were sacrificed using the cervical dislocation method. The penectomy was performed from proximal of the repaired region using a lancet. The penectomy material obtained from each group was placed in a 10% formaldehyde solution for pathological examination.

Histopathological evaluation using a light microscope was performed by a single independent pathologist blinded to the study groups. The penectomy material of each rat was fixed in 10% formaldehyde until macroscopic examination. Circles of tissue were cut at 4-mm intervals and then embedded in paraffin blocks, from which slices 4 micron in thickness were cut and stained with hematoxylin and eosin (HE) and with Masson trichrome for histopathological examination. Light microscopy examination was made of the preparates at ×20 and ×40 magnification. Fibrosis was evaluated as follows: 0: none, *Mild*: fibrosis in the focal area or ≤10% of the cavernous body, *Moderate*: fibrosis in >10%-≤30% of the included cavernosal tissues, and *Severe*: fibrosis in > 30% of the included cavernosal tissues. Inflammation was evaluated according to the presence of inflammatory cells such as neutrophils, lymphocytes, and monocytes. The groups were compared according to fibrosis and inflammation parameters.

Data obtained in the study were analyzed statistically using PASW 18 software (SPSS/IBM, Chicago, IL, USA). Categorical data were stated as number and percentage. Categorical variables were analyzed using the Pearson Chi-square test. A value of $p < 0.05$ was considered statistically significant.

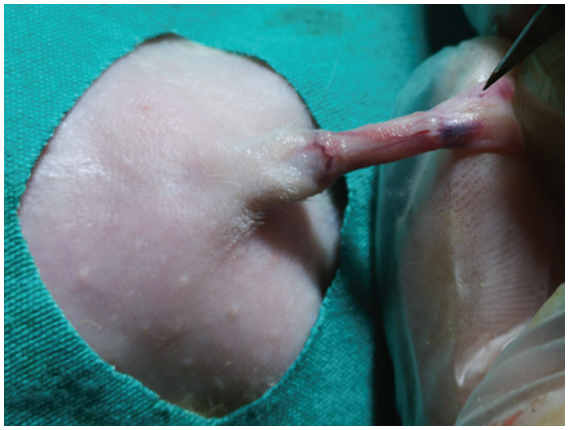

Figure 1. *Using a number 15 lancet to create a penile fracture model.*

Table 1. Fibrosis rates of the groups

Fibrosis	Group B	Group S	Group LD	Group SD	p-value
None (n %)	1 (10%)	0	0	8 (80%)	0.001*
Mild (n %)	5 (50%)	6 (66.7%)	6 (60%)	2 (20%)	
Moderate (n %)	3 (30%)	2 (22.2%)	1 (10%)	0	
Severe (n %)	1 (10%)	1 (11.1%)	3 (30%)	0	

Table 2. Inflammation rates of the groups

Inflammation	Group B	Group S	Group LD	Group SD	p-value
None (n %)	3 (30%)	6 (66.7%)	5 (50%)	8 (80%)	0.13
Observed (n %)	7 (70%)	3 (33.3%)	5 (50%)	2 (20%)	

Results

One rat in Group S died 12 h after anesthesia, possibly due to anesthesia complications. The most common complications of infection and urinary retention were not observed in any rat.

No severe fibrosis was observed in any rat in Group SD and was determined in one rat in Group B, in one rat in Group S, and in three rats in Group LD ($p = 0.001$). No fibrosis was observed in 8 (80%) rats in Group SD. The fibrosis rate was significantly lower in Group SD compared to Group B, Group S, and Group LD ($p= 0.013$, $p = 0.005$, and $p = 0.003$, respectively) (Table 1) (Fig. 2). In Group SD, total healing was observed in 8 (80%) rats.

When the groups were evaluated in terms of inflammation, the lowest inflammation rate was observed in Group SD (2 rats, 20%), with no statistically significant difference determined between the groups ($p = 0.13$) (Table 2) (Fig. 3). In the control groups (Groups B and S), fibrosis and inflammation were predominant features of the healing. More extensive fibrosis was observed in these groups than in Group SD.

Discussion

With the occurrence of PF, there can be a sudden cracking or popping sound, pain, and immediate detumescence. There is rapid local swelling of the penile shaft due to a growing hematoma, because PF includes rupture of the tunica albuginea and the enclosed corpus cavernosum[10]. When PF is diagnosed, the recommended treatment is surgical repair with closure of the tunica albuginea. Negative long-term complications such as penile curvature and deformity are kept to a minimum with this repair and the psychological well-being of the patient is not negatively affected[11]. Other complications may also be observed such as painful coitus, penile nodule formation, priapism, wound infection, and penile abscess, but the incidence rates of these can be decreased with delicate surgery.

Dexpanthenol was investigated in this study due to its well-known anti-inflammatory, wound healing, and epithelization properties. It also has the advantages of low cost and few side-effects[12,13]. The role of inflammation in wound healing is a matter of debate since excessive inflammation affects this process negatively. In the present study, fibrosis was not observed in 8 (80%) rats in Group SD. Compared to other groups, these rates were statistically significant and only two rats had mild fibrosis. Similarly, inflammation was not detected in 8 (80%) rats in Group SD, but this was not statistically significant. Interestingly, the fibrosis rate was higher in Group LD. Although mostly mild (60%), fibrosis was observed in all rats in Group LD. This could be explained by different reasons, the first being possibly the microtrauma caused by the subcutaneous application of dexpanthenol for 2 weeks, and the second reason might be that a sufficient concentration of the subcutaneously administered dexpanthenol could not reach the tunica and cavernous tissue.

A previous study by the current author group investigated the effect of intraurethral dexpanthenol in

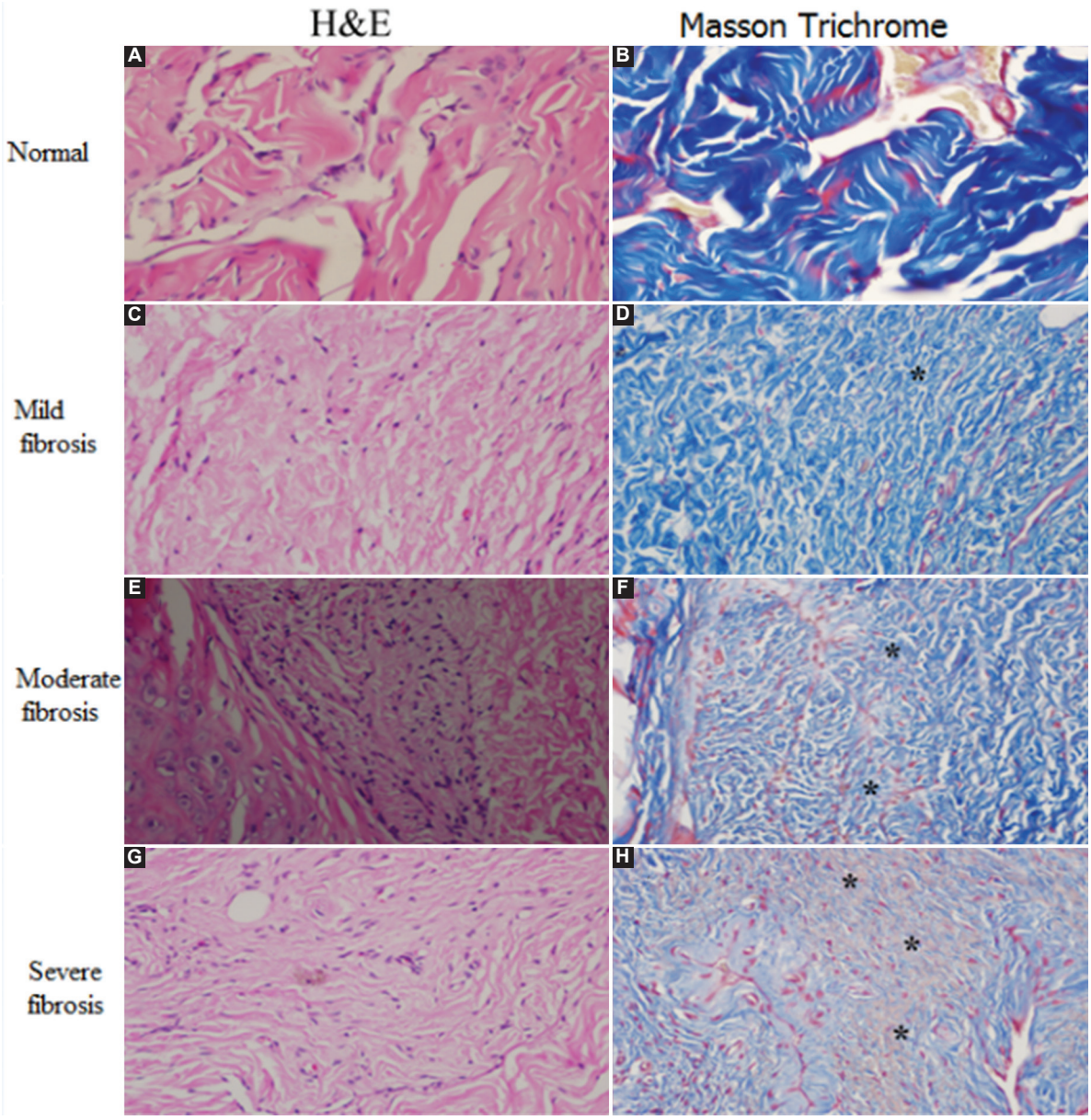

Figure 2. *Sections of rat penis (×40).* **A:** *H&E image of a normal rat penis in Group A.* **B:** *Masson trichrome image of the same rat penis in Group A.* **C:** *H&E image of mild fibrosis in Group S.* **D:** *Masson trichrome image of mild fibrosis in the same rat penis in Group SD.* **E:** *H&E image of moderate fibrosis in Group S.* **F:** *Masson trichrome image of moderate fibrosis in the same rat penis in Group S.* **G:** *H&E image of severe fibrosis in Group LD.* **H:** *Masson trichrome image of severe fibrosis in the same rat penis in Group LD. (*: areas of fibrosis).*

hypospadias repair and intraurethral dexpanthenol administration was found to significantly decrease inflammation and fibrosis. Similarly, in another study by the same group, intraurethral dexpanthenol was used in post-traumatic urethral stricture and was shown to reduce both inflammation and fibrosis[14,15]. The promising results of those two studies encouraged the current research of the effect of dexpanthenol on wound healing in a PF model. Several studies have shown that dexpanthenol accelerates wound healing after surgery and can successfully prevent scar formation[16,17]. To the best of our knowledge, this is the first study to have investigated the effect of dexpanthenol on wound healing in an experimental animal model of PF. However, the fact that it was an experimental model is a limitation of the study and there is a need for further advanced clinical studies to confirm these findings.

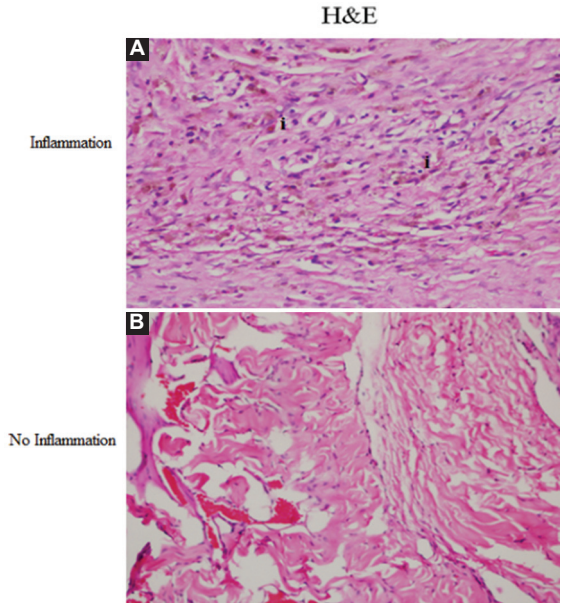

Figure 3. A: *Appearance of inflammation in Group S (×40) and* **B:** *image without inflammation in Group SD. (i: inflammatory cells).*

Conclusion

Systemic dexpanthenol administration was seen to significantly decrease fibrosis in a rat model of penile fracture. Further studies are needed to evaluate the effects of dexpanthenol therapy.

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Conflicts of interest

The authors have no conflicts of interest to declare that is relevant to the content of this article.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant Clinical Research Ethics Committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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