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BASIC AND TRANSLATIONAL UROLOGY

Botulinum toxin-A to improve urethral wound healing: an experimental study in a rat model

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Objectives: Tensile distracting forces caused by elements such as a muscle pull can cause widening of scars in the tissue during the wound healing process. The aim of the present study was to investigate whether induced immobilization of the urethral muscle using botulinum toxin-A (BTX-A) enhances wound healing and also reduces the amount of scar formation in an experimentally induced urethral injury in a male rat model.

Methods: Prepubertal male albino rats were divided into 2 groups: 20 rats in the BTX-A group received BTX-A injection treatment during surgery and 10 rats in the control group received 0.9% saline solution injection. The penile skin was incised circumferentially and degloved. To make the urethral injury at a location approximately 15 mm proximal to the external meatus, the urethra was cut transversally with scissors, from the 2-o'clock to the 10-o'clock position and then sutured by a single suture at the 6-o'clock position. To evaluate chronic inflammation and fibrosis, the rats were killed, and the injured portions of the urethras were harvested for histopathologic examination after a follow-up period of 21 days.

Results: On histopathologic evaluation, the control group rats had a more severe fibrotic change in the urethral tissue compared with the BTX-A injected rats, which showed a mild fibrotic change. The mean +/- SD and median fibrosis score was 2.4 +/- 0.5 and 2 in the control group and 1.5 +/- 0.5 and 1 in the BTX-A group, respectively ($P < .01$ and $P < .01$, respectively).

Conclusions: The results of our study have shown that BTX-A prevented increases in collagen content during urethral wound healing.

Editorial Comment

This is a very interesting and inventive study that certainly will open new avenue for treatment of urethral stricture disease. In fact, using biochemical and stereological methods, we have recently found that, when compared to age-matched controls, there is no fibrosis and no collagen increase in the urethral edges of

male patients submitted to end-to-end anastomosis for treating bulbar urethra stenosis (1). Therefore, in well conducted cases, with anastomosis of fibrosis-free urethral edges, the fibrosis that could compromise the results may be a consequence of tensile forces in the anastomotic area and probably BTX-A would help in avoiding it.

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Comparisons of the responses of anterior and posterior human adult male bladder neck smooth muscle to in vitro stimulation

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Objective: To evaluate differing methods of stimulation on strips of human bladder neck smooth muscle and compare muscle taken from the anterior and posterior aspects.

Materials and Methods: Samples of adult human male bladder neck muscle were obtained from patients undergoing open radical prostatectomy. Muscle was taken from either the anterior or posterior (nine and six patients, respectively) aspects of the bladder neck. Muscle strips dissected from these samples were suspended in the Brading-Sibley organ bath. The strips were superfused with 100 mm KCl-enriched Krebs' solution for 4 min to determine viability. This allowed experimentation on 17 strips from the anterior aspect of the bladder neck and 13 from the posterior bladder neck. These remaining strips were then superfused either with various concentrations ($\times 10^{-7}$) to $\times 10^{-3}$ m) of carbachol or noradrenaline in Krebs' solution, for 15 s. A further set of strips (eight from anterior, six from posterior) was suspended and responses to electrical field stimulation (EFS) with varying parameters were measured. Each EFS experiment was repeated after a 15 min exposure to 10^{-3} m atropine, and again after a 15 min exposure 10^{-7} m tetrodotoxin (TTX). Tension responses produced in these series of experiments were measured using strain gauges and analysed using data acquisition software. Student's t-test was used for the statistical analysis.

Results: All muscle strips included in the study responded to EFS. The magnitude of this contraction is frequency dependent. The contractions were abolished by superfusion of the muscle strips with atropine. There was no further suppression of the contractile response on addition of TTX. Posterior bladder neck samples had a greater mean contractile response per unit mass than anterior strips at all frequencies of >1 Hz, and significantly more at 20 and 30 Hz. There was a concentration-dependent response in bladder neck contraction to carbachol but only in the strips from the anterior bladder neck at concentrations of $<10^{-3}$ m. Posterior bladder neck strips did not significantly contract upon application of carbachol. Similarly, there was a concentration-dependent response to noradrenaline. Responses to noradrenaline were not uniform around the bladder neck, but not significantly different. Carbachol was the more 'potent' stimulator in anterior smooth muscle strips, but again the differences between agonists were not statistically significant.

Conclusion: These experiments show physiological variability around the circumference of the human male bladder neck. The posterior bladder neck shows significantly stronger contraction to alpha-adrenergic agonists compared with cholinergic agonists; the anterior bladder neck does not have a similarly significant differential response. The uniform response to noradrenaline may underlie the bladder neck's role in the prevention of retrograde ejaculation. The differential responses to carbachol may reflect differences in the embryological derivation of the anterior and posterior bladder neck fibres or in their innervation. Some of these differences may have clinical importance through the action of therapeutic agents.

Editorial Comment

The authors of this elegant in vitro study show by the first time, in the best of my knowledge, that exist important physiological variability in the human male bladder neck. They found that the posterior bladder neck presented significantly stronger contraction to alpha-adrenergic agonists when compared with cholinergic agonists. On the other hand, the anterior bladder neck did not have a similarly significant differential response. The authors also found a uniform response to noradrenaline and this might underlie the role of bladder neck in avoiding retrograde ejaculation. Also, the authors speculated that differential responses to carbachol may reflect differences in the embryological origin of anterior and posterior bladder neck fibers or in their innervation.

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RECONSTRUCTIVE UROLOGY

A new suture material for hypospadias surgery: a comparative study

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Purpose: We compared the results of hypospadias repair using polyglytone versus polydioxanone to evaluate the potential benefit of using a suture with a rapid absorption time.

Materials and Methods: A total of 100 patients 8 to 24 months old affected by distal isolated penile hypospadias were considered for this study. Patients were randomized and assigned to 2 different groups according to the suture material used during the surgical procedure (tubularized incised plate repair with or without preputial reconstruction). Polyglytone was used in group A and polydioxanone was used in group B. All patients were evaluated at 4 intervals (1 week, 1 month, 6 months and 2 years postoperatively). Persistence of sutures on penile skin, urethral fistulas, skin dehiscence, infection and skin tracks were recorded. Statistical analysis was performed using chi-square test.

Results: Follow-up data documented the absence of significant differences in terms of urethral fistula rate, skin dehiscence and acute skin infection. Persistence of sutures and multiple skin tracks at long-term follow-up were significantly greater in patients in group B.

Conclusions: Both sutures are adequate for hypospadias surgery in small children. The use of a rapid absorption monofilament may allow much more rapid disappearance of the skin sutures. In the long term this outcome means almost complete absence of suture tracks. No statistically significant difference in terms of urethrocutaneous fistula was observed, suggesting that the tensile strength of polyglytone is adequate.