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A novel stricture prevention technique in blunt urethral injury: A multi-center retrospective observational study

Yang Mi[1,*], Jingyu Wang[1,*], Jinfeng Wu[1,*], Xiaopeng Wang[2], Bin Yang[1], Ruimin Ren[1], Yangang Zhang[1], Xiaobin Yuan[3], Xuhui Zhang[3]

[1]Department of Urology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Taiyuan, Shanxi, [2]Department of Anesthesiology, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Taiyuan, Shanxi, [3]Department of Urology, First Hospital of Shanxi Medical University, Taiyuan, Shanxi, China

Purpose: Bulbar injury is the most common type of urethral injury. This study investigated the efficacy and safety of a novel technique, local urethral flushing, in preventing stricture formation after blunt bulbar urethra injuries.

Materials and Methods: This retrospective study included 205 males diagnosed with straddle injury-induced bulbar urethra injury at the Shanxi Bethune Hospital and First Hospital of Shanxi Medical University between January 2015 and January 2019. Patients were diagnosed by retrograde urethrography and classified as partial or complete urethral rupture according to the urethral integrity after injury. Complete urethral rupture patients received suprapubic cystostomy and received urethroplasty 3 months later. Patients with partial urethral rupture underwent endoscopic urethral realignment by cystoscopic guide-wire guided catheterization. Patients with both injury types were divided into 3 groups. The treatment groups received urethral flushing with 0.05% dexamethasone through a secondary ureteral catheter that locked at the urethral lesion. The blank control groups received normal saline. The negative control groups had only a single ureteral catheter placed. Patients were assessed for pain during catheterization, infection, and stenosis, and followed for at least 2 years.

Results: Stenosis rates and length were significantly reduced in the normal saline groups, and even further reduced in the dexamethasone groups. The negative control groups had significantly higher infection rates than patients in the dexamethasone or saline groups.

Conclusions: Local urethral flushing with dexamethasone could significantly decrease urethral stenosis rates and severity without increasing patients' discomfort or infection risk.

Keywords: Blunt injury; Bulbar urethra; Dexamethasone; Local urethral flushing

INTRODUCTION

Urethral injury is a common emergency in urology. In most cases, it does not endanger the patient's life, but the complications may cause long-term difficulties. Bulbar injury is the most common type of urethral injury [1]. Blunt forces

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Corresponding Author: Xuhui Zhang https://orcid.org/0000-0003-3202-1159
Department of Urology, First Hospital of Shanxi Medical University, No. 85 Jiefangnan Road, Taiyuan, Shanxi 030000, China
TEL: +86-13934226778, FAX: +86-8368397, E-mail: zhangxuhui7576@163.com
*These authors contributed equally to this study and should be considered co-first authors.

such as straddle injury and strikes to the perineum are the most common causes of closed bulbar urethral injury [2]. Complete and partial urethral injury are classified according to urethral mucosa continuity.

Strategies for treating partial and complete disruption of the bulbar urethra remain controversial. A recent report suggested that hemodynamically stable patients should undergo endoscopic realignment, and hemodynamically unstable patients should have suprapubic catheter placement and delayed management [3]. Regardless of the strategy used, the primary objective is to reduce the incidence of complications. Urethrostenosis, the most common urethral injury complication, may cause long-term distress in patients.

The increase in inflammatory secretion in the acute phase of urethral injury may be one of the most important causes of urethral stricture. In an *in vitro* experiment, dexamethasone has been confirmed to significantly reduce the local inflammatory response in the urethra [4]. This study assesses the safety and efficacy of a novel technique, local urethral dexamethasone flushing, for prevention of urethral stricture.

MATERIALS AND METHODS

This retrospective study included male patients diagnosed with straddle injury-induced bulbar urethra blunt injury, at Shanxi Bethune Hospital and First Hospital of Shanxi Medical University between January 2015 and January 2019. Most patients presented with urination disorder or bleeding at the external orifice of the urethra, and the diagnosis of urethral rupture was confirmed by retrograde urethrography (RUG). This study was approved by the Shanxi Medical University Ethical Review Board (approval number: 20150231). All patients provided written informed consent to participate in this research.

Patients were classified as having partial or complete urethral rupture, according to the urethral integrity after injury. Patients with partial urethral rupture underwent endoscopic urethral realignment by guide-wire guided catheterization using a cystoscope. These patients were divided into three groups according to the patients will as the patients were notified the additional costs because the urethral flushing was performed in the appropriate nursing facility and the potential risks associated with topical use of hormones in the urethra. These treatment group (group A), blank control group (group B), and negative control group (group C). Group A patients received urethral flushing with 0.05% dexamethasone three times per day through an additional ureteral catheter for 3 weeks. Group B patients received urethral flushing with normal saline (NS) three times per day through an additional ureteral catheter for three weeks. Group C patients had only single ureteral catheters placed for 3 weeks with no flushing. The catheter placement depth was measured by a cystoscope to ensure that the end of the second catheter was locked at the urethral lesion. A diagram of the two catheters is depicted in Fig. 1.

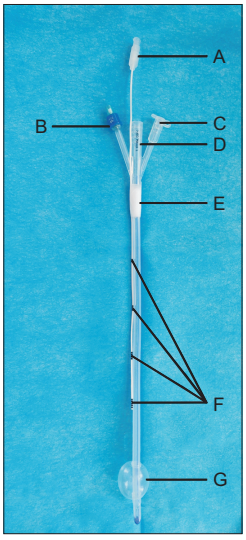

Fig. 1. The novel local urethral flushing technique. (A) A second urethral catheter (4.5 Fr) is used for urethral flushing. The placement depth is shown by the scale (F) on the catheter. Lines are marked 5 cm apart. The placement depth is measured by cystoscope to ensure the head-end of the catheter is placed at the urethral lesion. The tail-end of the catheter is closed normally *in vitro*, and only open when used. (D) A three cavity catheter (22 Fr) was placed by guide-wire guided catheterization using a cystoscope. (B) The balloon injection channel. (C) The bladder flushing channel. (G) The catheter balloon is locked in the bladder to prevent the catheter slipping from the bladder. (E) The two catheters are fixed by tape.

Complete urethral rupture patients underwent suprapubic cystostomy as the primary treatment, followed by urethroplasty 3 months later. At the time of urethroplasty, these patients were also divided into 3 groups with the same treatment as the partial rupture groups: treatment (group D), blank control (group E), and negative control (group F). The second catheter placement depth was measured during urethroplasty to ensure that the end of the second catheter was locked at the urethral lesion.

All patients were required to follow-up every 3 months in the first year, every 6 months for the second year and once a year after 2 years. The follow-up period was at least 2 years [5]. RUG and cystourethroscopy were necessary if patients had symptoms such as straining, intermittent flow, maximum urine flow rate <10 mL/min, or postvoiding residual urine volume >50 mL on ultrasound [2]. If urethral stenosis occurred, patients underwent a second operation ac-

Table 1. Patient clinical and demographic details

Variable	Group A (n=35)	Group B (n=34)	Group C (n=31)	Group D (n=37)	Group E (n=38)	Group F (n=30)
Age (y)	45.16±17.86[ab]	43.35±16.74[a]	44.31±16.86	48.31±15.56[cd]	47.67±14.71[c]	49.31±16.11
Multiple organ injury rate	8/35 (22.86)[ab]	8/34 (23.53)[a]	7/31 (22.58)	10/37 (27.02)[cd]	11/38 (28.95)[c]	8/30 (26.67)
Pelvic fracture rate	16/35 (45.71)[ab]	15/34 (44.12)[a]	14/31 (45.16)	21/37 (56.76)[cd]	21/38 (55.26)[c]	17/30 (56.67)
Follow-up duration (mo)	27.45±8.68[ab]	31.32±6.32[a]	29.21±8.21	30.41±7.11[cd]	31.89±7.32[c]	30.58±8.01

Values are presented as mean±standard deviation or number (%).
a, compared to group C, p>0.05; b, compared to group B, p>0.05; c, compared to group F, p>0.05; d, compared to group E, p>0.05.

Table 2. Urethral stenosis rate and severity by injury type and treatment group

Variable	Group A (n=35)	Group B (n=34)	Group C (n=31)	Group D (n=37)	Group E (n=38)	Group F (n=30)
Urethral stenosis rate	9/35 (25.71)[ab]	13/34 (38.24)[a]	18/31 (58.06)	13/37 (35.14)[cd]	16/38 (42.11)[c]	18/30 (60.00)
Length of urethral stenosis (cm)	0.33±0.29[ab]	0.41±0.36[a]	0.89±0.59	0.63±0.21[cd]	0.88±0.23[c]	1.01±0.59

Values are presented as number (%) or mean±standard deviation.
a, compared to group C, p<0.05; b, compared to group B, p<0.05; c, compared to group F, p<0.05; d, compared to group E, p<0.05.

cording to the length of the stricture. Internal urethrotomy of the urethral stricture was performed in patients with circular scar stenosis. Urethral stenosis resection and end-to-end anastomosis were performed in patients with stenosis <1.5 cm. Buccal mucosa urethroplasty was performed in patients with stenosis >1.5 cm in length [3].

Patient characteristics, complication rate (urinary infection, urethrodynia, acute epididymitis), and incidence of postoperative stricture formation were compared between all groups. Differences in measurement data were compared with single factor analysis of variance after normality test, qualitative data were analyzed by chi-square test, and the ranked data by the rank-sum test. Differences were considered statistically significant at $p<0.05$.

RESULTS

1. Patient's characteristics

This retrospective study included 205 males diagnosed with straddle injury-induced bulbar urethra blunt injury (100 patients with partial urethral rupture and 105 with complete urethral rupture).

Clinical characteristics were compared in groups A, B, and C in the partial urethral rupture patients. The mean age in groups A, B, and C was 45.16±17.86, 43.35±16.74, and 44.31±16.86 years, respectively. Multiple organ injury rates were 22.86%, 23.53%, and 22.58%; pelvic fracture rates were 45.71%, 44.12%, and 45.16%; and mean follow-up durations were 27.45±8.68, 31.32±6.32, and 29.21±8.21 months, respectively. None of the four clinical indices differed significantly between the groups.

In patients with complete urethral rupture, the same clinical characteristics were compared between groups D, E, and F. The mean age in groups D, E, and F was 48.31±15.56, 47.67±14.71, and 49.31±16.11 years, respectively. Multiple organ injury rates were 27.02%, 28.95%, and 26.67%; pelvic fracture rates were 56.76%, 55.26%, and 56.67%; and mean follow-up durations were 30.41±7.11, 31.89±7.32, and 30.58±8.01 months, respectively. There were no significant differences between groups for any parameter. The clinical and demographic profiles of the patients are shown in Table 1.

2. Treatment efficacy

In patients with partial and complete urethral rupture, the urethral stenosis rate and length of urethral stenosis were used to assess treatment efficacy. The urethral stenosis rates in groups A, B, and C were 25.71%, 38.24%, and 58.06%, respectively, and the length of urethral stenosis in each group was 0.33±0.29 cm, 0.41±0.36 cm, and 0.89±0.59 cm, respectively. For both parameters, the differences between all groups were significant. Similarly, the urethral stenosis rates in groups D, E, and F were 35.14%, 42.11%, and 60.00%, and the length of urethral stenosis in each group was 0.63±0.21 cm, 0.88±0.23 cm, and 1.01±0.59 cm, respectively. The differences between groups D, E, and F were significant for all parameters. The clinical and demographic profiles of the patients are shown in Table 2.

3. Complications during indwelling catheter period

Urinary infection, pain, and acute epididymitis were the most common complications during the indwelling catheter period. A visual analogue scale (VAS) was used to represent the level of pain. Urinary infection rate, acute epididymitis rate, and VAS scores were compared between groups.

In the partial urethral rupture patients, the VAS score

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Table 3. Complications during catheterization period by injury type and treatment group

Variable	Group A (n=35)	Group B (n=34)	Group C (n=31)	Group D (n=37)	Group E (n=38)	Group F (n=30)
Urinary infection patient during indwelling catheter	11/35 (31.43)[ab]	11/34 (32.35)[a]	18/31 (58.06)	18/37 (48.64)[de]	17/38 (44.74)[d]	23/30 (76.67)
Urethrodynia (Visual Analogue Scale, VAS)	3.51±1.11[bc]	3.49±1.23[c]	3.53±1.03	3.11±1.33[ef]	3.21±1.45[f]	3.23±1.39
Acute epididymitis	1/35 (2.86)[bc]	1/34 (2.94)[c]	1/31 (3.22)	3/37 (8.11)[ef]	3/38 (7.89)[ef]	2/30 (6.67)

Values are presented as number (%) or mean±standard deviation.
a, compared to group C, p<0.05; b, compared to group B, p>0.05; c, compared to group C, p>0.05; d, compared to group F, p<0.05; e, compared to group E, p>0.05; f, compared to group F, p>0.05.

(group A, 3.51±1.11; group B, 3.49±1.23; group C, 3.53±1.03) and acute epididymitis rate (group A, 2.86%; group B, 2.94%; group C, 3.22%) were not significantly different between groups. However, the urinary infection rate was significantly lower in groups A (31.43%) and B (32.35%) than in group C (58.06%). There was no significant difference between groups A and B.

In complete urethral rupture patients, the VAS score (group D, 3.11±1.33; group E, 3.21±1.45; group F, 3.23±1.39) and acute epididymitis rate (group D, 8.11%; group E, 7.89%; group F, 6.67%) were not significantly different between groups. However, the urinary infection rate was significantly lower in groups D (48.64%) and E (44.74%) than in group F (76.67%). There was no significant difference between groups D and E. The clinical and demographic profiles of the patients are shown in Table 3.

DISCUSSION

Blunt urethral injury is a common emergency in clinical practice [1]. Recovery of urethral continuity and urine drainage are important to relieve symptoms and improve prognosis. In patients with partial and complete urethral rupture, placing a successful indwelling urethral catheter is an important and efficient way to solve this problem, enabling urine drainage and providing a support surface for urethral mucosa recovery. However, it is usually difficult to catheterize patients with complete urethral rupture because of the discontinuous urethra and bleeding, which limits endoscopic vision. Therefore, in most patients with complete urethral rupture, suprapubic cystostomy is the primary treatment, followed by urethroplasty 3 months later [3] and an indwelling catheter for 3 weeks.

Urethral stricture is one of the most common and troublesome complications after catheter removal, resulting in restricted urination and even urinary retention. These patients must undergo dilatation of the urethra or secondary operations to solve this problem. There are many reasons that may induce urethral stenosis such as urinary infection, length of injury, and duration of indwelling catheter.

It has been shown that the inflammatory response plays an essential role in every phase of wound healing, and an over-reactive immune reaction could lead to keloids and hypertrophic scars [6]. Some studies have shown that local over-reactive inflammation and chronic inflammation are the main causes of urethral stricture after injury [7,8]. Dexamethasone is one of the most commonly used glucocorticoids, and the safety of its local delivery has been widely documented. The topical application of glucocorticoids in the urethra has been proven *in vitro* to significantly decrease the occurrence of urethral stricture [4,9,10].

In this study, we applied topical glucocorticoids via local urethral flushing through an indwelling catheter device. The results showed that in patients with partial and complete urethral injury, urethral flushing of 0.05% dexamethasone significantly reduced the urethral stenosis rate and the stenosis length compared to the blank control group and the negative control group. There was also a significant decrease in urethral stenosis rate and stenosis length in the negative control group, who underwent urethral flushing with NS only. We believe that the urethral flushing may decrease the local inflammatory response by reducing the inflammatory secretion concentration. However, dexamethasone urethral flushing was shown to be more effective than NS in decreasing the urethral stenosis rate and severity. This may be because dexamethasone inhibits the local over-reactive inflammatory response while the flushing action reduces the inflammatory secretions.

We also recorded rates of common complications with the indwelling catheter such as urinary infection and acute epididymitis, and the severity of pain. The results showed that the placement of the additional indwelling ureteral catheter did not increase the patients' pain, and the topical application of dexamethasone did not increase the incidence of urinary infection.

This study is limited by the retrospective design and the short follow-up time for some patients. Due to the COVID-19 outbreak in China in January 2019, many patients could

not complete more than two years of follow-up. The study results are encouraging; however, further clinical observation in a larger population of patients is needed to document safety and efficacy of the treatment. In addition, efficacy of this method in patients with patulous urethral injury needs further discussion.

CONCLUSIONS

This study presents a novel technique for local urethral flushing in patients with blunt urethral injury. The results demonstrate that local urethral flushing with dexamethasone through a dedicated indwelling catheter located at the site of injury could significantly decrease urethral stenosis rates and severity by decreasing the inflammatory secretion concentration. This simple method did not increase the patients' discomfort or infection risk and may help to achieve better outcomes for patients with such injuries.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHORS' CONTRIBUTIONS

Research conception and design: Yang Mi and Xuhui Zhang. Data acquisition: Yang Mi, Jingyu Wang, and Jinfeng Wu. Statistical analysis: Xiaopeng Wang. Data analysis and interpretation: Bin Yang. Drafting of the manuscript: Yang Mi. Critical revision of the manuscript: Ruimin Ren. Obtaining funding: Xuhui Zhang. Administrative, technical,or material support: Yangang Zhang and Xiaobin Yuan. Supervision: Xuhui Zhang. Approval of the final manuscript: Xuhui Zhang.

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