

The effectiveness of local steroid injection after internal urethrotomy to avoid recurrence

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Summary *Objective: Local steroid injection to the stricture region after internal urethrotomy (IU) is a promising technique to avoid the recurrence, although the effectiveness and safety of this technique is still controversial. We aimed to determine the efficacy and safety of local steroids as applied with the IU procedure.*

Material-Method: A total of 83 patients data with urethral stricture in men were examined retrospectively. Patients classified in two groups who had steroid injection with internal urethrotomy or not. Metil prednisolone 40 mg was injected with transurethral injection needle in the stricture region at the 5, 7 and 12 o'clock sites at the same session with internal urethrotomy. Procedure was considered successful if patient did not report any voiding difficulty and maximum flow rate > 15 mL/second for a voided volume of at least 150 mL after removal of the catheter. Patient's age, time to recurrence, previous recurrences were evaluated.

Results: The mean age was 56.4 (18-83) years. Of those patients 33/83 had recurrent stenosis. Nineteen out of these 33 recurrent stenosis patients were treated with local steroid injection and 14/33 had no injection. Only two patients of the steroid treated group had recurrence. Despite that 12 patients had recurrence in the steroid non-treated group. Also the primary stenosis patients showed no recurrence at the steroid+ IU group.

Conclusions: The use of local steroids with IU seems to decrease the high stricture recurrence rate following IU. When local steroids were administered with complementary intention, the disease control outcomes are encouraging. Further robust comparative effectiveness studies are now required.

KEY WORDS: Urethral stricture; Internal urethrotomy; Steroid; Recurrence.

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INTRODUCTION

Urethral stricture is a well-known disease that has been known for centuries as far as ancient Greeks, Egyptians and Hindus (1). Difficulty on managing urethral strictures is its tendency to recur. First leading cause of urethral strictures was infection but, even with development of mankind and technologies, iatrogenic instrumenta-

tions and external trauma take the lead. The actual incidence of urethral strictures developed after the transurethral resection of prostate is 2-10%, as well as radical (8.4%) and simple (1.9%) prostatectomies (2-4). There are many treatment modalities as dilatation, endoscopic urethrotomy, stent placement and urethroplasty. Internal urethrotomy (IU) and dilatation are widely used for urethral strictures less than 2 cm with a success rate of 70% but also have a high rate of stricture recurrence (5-7). Although open urethroplasty is a highly successful and durable treatment method, surgeons don't perform it so often due to its invasiveness, longer catheterization requirement and need of experienced surgery skills (8). The recurrence of stricture occurs as a result of scar that forms into the urethral epithelium and decreases the caliber of urethra (9).

There are many investigations about use of drugs such as steroids, Mitomycin C, Hyaluronidase to avoid this scar or keloid formation (10-12).

We aimed to investigate the combination of steroid injection with IU in order to avoid the recurrence of strictures and cure the patient with minimally invasive treatment.

MATERIALS AND METHODS

We present the data of patients from April 2009 to March 2014 in this retrospective study. The protocol was approved by the scientific and ethical committee of the university (2014/3255). Informed and signed consent was taken from all patients after explaining the nature of the study and the consequences of the procedure to be done in detail in their own language. Two surgeons performed internal urethrotomy with the same technique. Patients were divided into two groups by surgeons' preference to use steroid injection or not. Forty-one patients have been treated with IU adding steroid injection and 42 patients have been treated with only IU without steroid injections. Patients had option to opt out of the study at any time without compromising their right of treatment. A total of 83 male patients with diagnosed urethral strictures requiring optical internal urethrotomy were included in this study. Patients presenting for the first time for treatment

were referred to as primary, whereas those who had undergone some procedure for the treatment of stricture prior to reporting to us were referred as recurrent. In group A (IU only group); the patients underwent internal urethrotomy with cold knife. In group B (IU+ steroid group) metil prednisolone was injected to the stricture site after the internal urethrotomy with cold knife. Steroid was injected intralesional at the 5, 7 and 12 o'clock sites of urethrotomy using 22 G William's bladder injection needle (Cook Medical, Bloomington, USA). Forty mg metil prednisolone were injected for strictures less than 1 cm whereas the dosage increased to 40 mg for each cm of stricture. The patients who had recurrence after steroid injection underwent a second IU+ steroid injection session. All of the recurrences were due to the transurethral resection of prostate.

Inclusion criteria were; presence of obstructive symptoms, peak flow rate on uroflowmetry less than 15 ml/s and short segment strictures (stricture length < 2 cm) as evident on radiological studies, i.e. retrograde urethrography (RGU) and micturating cystourethrography (MCU). Exclusion criteria used were complete obliteration of urethral lumen on urethroscopy, Balanitis Xerotica Obliterans, age less than 18 years, multiple strictures, active urinary tract infection.

All patients were assessed by a history and a full physical examination, complete blood count, urine analysis, urine culture and sensitivity test, renal function tests, uroflowmetry and retrograde urethrography with micturating cystourethrography if needed. Urethroscopy was done with 20 F sheath and 0° telescope. The site and length of the stricture along with the ability of telescope to pass through the stricture was noted on urethroscopy. The procedure was performed under spinal anesthesia at lithotomy position. Antibiotic (Ciprofloxacin, 500 mg) was given just before and 12 h after procedure and continued for next 7 days twice a day. Normal saline was used for irrigation during the procedure. Post-operative catheterization has been made by a 20 F urinary catheter. Post-operative catheterization time was 7 days.

Any symptoms pertaining to recurrence were noted as reduced stream of urine (< 10 mL/second), retention of urine (> 50 ml), and burning micturition. Procedure was considered successful if patient did not report any voiding difficulty with maximum flow rate > 15 mL/second for a voided volume of at least 150 mL. Patients were followed up for at least 18 months.

Data were analyzed using SPSS software (*the Statistical*

Package for the Social Sciences, Version 14.0, SPSS Inc., Chicago, Illinois, USA). Normally distributed variables were described using means with standard deviations. Chi-square and student t test were used to compare two groups. Non-normal distributed data were analyzed using Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

RESULTS

The mean age at the presentation was 56.4 (18-83) years. Seventeen patients in the steroid group out of 41 needed 80 mg metil prednisolone due to the length of the stricture. Only 2 patients had recurrence in the 80 mg metil prednisolone treated group, whom also had a history of recurrence. So the success rate of the steroid injection was 95%. And the recurrence rate of IU only treated group was 28 % (Table 1).

Thirty-three out of 83 patients had a history of recurrent stenosis. Nineteen of these 33 patients were treated with local steroid injection and 14/ 33 had no injection. Two patients in the steroid treated group had recurrence at third and eighth month. On the contrary 12 patients had recurrence in the steroid non-treated group. Recurrence occurred at the first month in 9 patients and in the remaining patients at the second month of follow-up. Thus, for patients with history of recurrence, success rate was 89% for the first injection and 100% for the second injection.

In recurrence groups success rates of steroid injection was significantly higher than the IU only treated patients (89% versus 14.2% respectively, $p = 0.021$). Time to recurrence was significantly lower in the IU than the steroid group (1.2 ± 0.4 months, 6 ± 2.5 months, respectively, $p = 0.03$).

DISCUSSION

The main problem of urologists in relation to urethral stricture is not the disease itself but its nature of recurrence. Open urethroplasty has better results especially if performed at the early stage, but it requires a certain expertise and a long period of catheterization (13). Optical internal urethrotomy is another standard treatment of urethral strictures with varying success rates although not as good as open urethroplasty (14). In a survey conducted by the *American Urology Association*, 86% of the urologists performed IU for urethral strictures probably because of unfamiliarity and lack of expertise in open urethroplasty (15). In a study with 224 patients, the recurrence rate was reported as 68% after the first IU, 96% after the second IU and 100% after the third procedure (16). Recurrent IUs also decrease the success rates of the urethroplasty (17). So that investigators are searching for minimally invasive and curative treatment modalities for a long time.

The main pathogenesis of stricture is the fibrosis formation caused by excessive collagen synthesis and changes in the extracellular matrix of the urethral lumen due to the endoscopic instrumentations, trauma and infections (18). Spongiofibrosis occurs in varying degrees and narrows the urethral luminal caliber. So that there are some

Table 1.
Patients demographic and laboratory data.

	Only IU group (n: 42)	IU+Steroid injection group (n: 41)	p
Age (years)	61.5 ± 16.2	51.2 ± 18.5	0.397*
Follow up (month)	30.1 ± 17.3	32 ± 19	0.634*
Hemoglobine (g/dL)	14.1 ± 1.95	14.2 ± 1.5	0.838*
Neutrophile	7500 ± 2701	7617 ± 2567	0.840*
History of recurrence	14/42	19/41	0.681**
Number of recurrences			0.681**

* Student t test performed.
** Chi square test performed. $p < 0.05$ considered the statistically significance.

ideas of treating the fibrosis with antifibrotic agents such as halofugione, mitomycin C, bitoxin A, somatostatin analogues, captopril and steroids (11, 19-23). There have been a few prospective randomized clinical trials in recent literature on comparative study of steroid injection after IU over conventional cold knife for internal urethrotomy. In a study, recurrence rate after IU was reported as varying 50% to 75% in a 2 years follow up period (24). We reported a 28% rate of recurrence in the IU only treated group. Our success rates may be due to our IU technique. Common practice among urologists is one cut at 12 o' clock to incise the stricture (86.3%) (8). But a deep cut at this site may cause erectile dysfunction, extravasation and incontinence (25, 26). So we prefer to cut the 5, 7 and 12 o' clock sites to avoid above complications and to decrease the tension of the stricture. Korhonen et al injected 80 mg triamcinolone to 17 of 21 patients after IU only to the 12 o'clock position and removed the catheter the day after the surgery. Although the IU only group had a 71% recurrence rates, steroid injected group had 61% recurrence rates (27). In another study, Tabassi et al. performed internal urethrotomy and triamcinolone injection in 34/70 patients with stricture. They noted a recurrence rate of 35.2% in the steroid injected and 41.6% in IU only group. Although there were no statistically significant difference between the two groups ($p = 0.584$), time to recurrence significantly decreased in the triamcinolone treated group ($p < 0.05$) (28). In our study we observed that steroid injection prolonged the recurrence time significantly from 1, 2 to 6 months ($p < 0.03$). In addition to that, we removed the catheter at the seventh day after the surgery. Kumar et al. also reported a 95.8% success rate in patient treated with holmium laser and 80 mg of triamcinolone (29). We have found a recurrence rate of 5% in the steroid group rather than 28% in IU only treated group. Also in the patients with recurrent stenosis, the success rates were better than the IU only treated group (89% versus 14.2% respectively, $p = 0.021$). Several adjuvant therapies including injection of docetaxel, captopril, mitomycin C, hyaluronidase have been also proposed to avoid the recurrence after the IU (10, 11, 18, 23). Chung et al. studied the effectiveness of hyaluronidase injection to the stricture site and found a recurrence rate of 9.4% and 22.9% respectively in the injection and in the control group (12). A recurrence rate of 2% versus 50% was reported in patients treated with Mitomycin C injection or not, in a small study consisting of 40 patients (11). In a rabbit model, it has been shown that docetaxel significantly inhibited the urethral stricture formation (18). No complications were noted due to the steroid injections. Despite the benefits of these materials, steroids comes a step forward so as to its cost effectiveness, lower side effects and also widespread usage in general medicine.

CONCLUSION

The clinical decision of stricture-recurrence-prevention techniques should be carefully tailored to every individual patient. Steroid injection to the stricture site to avoid fibrosis is a safe and effective adjuvant therapy for short

segment strictures after internal urethrotomy. Methyl prednisolone injection during internal urethrotomy may decrease the recurrence rate significantly. As the course of urethral stricture recurrence is rather long spreading over many years, further comparative studies with longer follow-ups are required to accurately evaluate the effect of steroid injection.

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