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Role of Steroids in Reducing Recurrence of Urethral Stricture after Direct Vision Internal Urethrotomy

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ABSTRACT

Background: Recurrence of urethral strictures is the most frequent and bothersome complication, with majority of stricturesrecurring after optical internal urethrotomy. The objective of this study was to establish the role of oral steroid therapy after direct vision internal urethrotomy (DVIU) in minimizing recurrence of urethral stricture.

Methodology: It was a randomized controlled trial carried out at Armed Forces Institute of Urology, Rawalpindi from January 2018 to March 2021. A total of 180 male patients with urethral stricture of ≤2 cm were included. Patients with traumatic stricture, post-anastomotic urethroplasty strictures, neurogenic bladder and history of steroid intake were excluded. Patients were randomly categorized into two groups i.e. Group A patients were given oral prednisolone (6 mg tablet twice daily for 4 weeks) while group B was control group. Patients were followed up to 12 months for recurrence of stricture.

Results: The mean age of patients in group A was 44.38 ± 8.03 years while in group B was 46.64 ± 6.66 years. The mean length of stricture in group A was 0.93 ± 0.26 cm and in group B was 0.95 ± 0.27 cm. Recurrence of stricture was seen in 18 (20.0%) patients in group A (oral steroids group) and 42 (46.67%) patients in group B (no oral steroids) with p-value of 0.0001.

Conclusion: Oral prednisolone therapy after internal urethrotomy waseffective in decreasing the rate of recurrence of urethral stricture.

Keywords: Oral, Recurrence, Steroid, Urethral Stricture.

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [3, 4] Critical analysis and manuscript review; [5,6]Data analysis; Manuscript Editing.

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Introduction

Urethral stricture is narrowing of the anterior urethral caliber. Any insult to the urethra disrupts the pseudostratified columnar epithelium, causing the extracellular tissue in the corpus spongiosum to scar during healing and ultimately fibrosis.[1, 2]Urethral stricture is the most frequent cause of admissions in urological department. Not only it adversely effects the quality of life of the patients but in addition increases the cost of treatment and financial burden to the patient due to sequelae of urinary stasissuch as urinary tract infections, bladder stones, fistulas and extreme cases renal failure.[3, 4]

Male population is highly susceptible to urethral stricture due to long length of urethra. Majority of strictures (80%) are iatrogenic and usually occurs at the level of membranous urethra. Urinary procedures such as catheterization, cystoscopy, transurethral prostate surgeries result in injury to urethra, which heals with fibrosis resulting in stricture.[5, 6, 7] Other causes of urethral strictures include infection of urethra (commonly due to gonococcus or chlamydia) and malignancy of urethra.[8] Urethral stricture disease may be asymptomatic or may present with certain symptoms like weak urinary stream, urinary hesitancy, dribbling, urinary retention or recurrent urinary tract infections.[9, 10]

Current management options for urethral stricture include urethral dilatation, direct vision internal urethrotomy (DVIU), urethroplasty, and regenerative therapies. Direct vision internal urethrotomy is the most widely used procedure for urethral stricture.[10] Despite of expert surgical hand, recurrence is the most common and unwanted complication of DVIU. Recurrence risk is also associated to the length of the stricture, the location of the stricture and follow-up length since the procedure. In addition, the risk of recurrence increases exponentially after subsequent urethrotomy.[11, 12] Different methods have been used to decrease the risk of recurrence following DVIU. Some studies have shown promising results when local steroid or mitomycin injections are used following DVIU to reduce the risk of recurrence. Some centers have also proposed self-catheterization to reduce recurrence.[6, 11]While many trials have shown reduced recurrence with intralesional steroids use, there is limited data on oral steroids for this purpose.[13]Therefore, this study was conducted to establish the role of oral steroids after DVIU to prevent the recurrence of strictures in the local population.

Methodology

This randomized controlled trial was conducted at Armed Forces Institute of Urology (AFIU), Rawalpindi from January 2018 to March 2021.The study was registered at ClinicalTrials.gov Identifier: NCT05069883.A sample size of 180 patients was computed (n=90 in the oral steroid group, n=90 in the control group) at 80% power and 95% confidence interval, considering estimated percentage of 19.44% and 36.11% of recurrence in the steroid group and control group, respectively.[5]This study was approved by ethical review committee of AFIU**.** All male patients between the age group of 20-60 years presenting with urethral stricture of length ≤2 cmresulting from iatrogenic or inflammatory causes with urine flow of less than 15 ml/min on uroflowmetry and dilation of proximal urethra and prostatic ducts on retrograde urethrogram were enrolled in the study after taking informed consent. Patients with urethral stricture after anastomotic urethroplasty, patients with stricture after transurethral resection of prostate, patients with neurogenic bladder, patients with history of steroid intake and patients with extravasation during optical internal urethrotomy (OIU) were excluded from the study.

Patients were randomly distributed into two equal groups A and B. Randomization was carried out through lottery method. In both groups direct internal visual urethrotomy (DVIU) was performed

under spinal anesthesia by consultant urologist (at least three years of post-fellowship experience). In DVIU, a urethrotome (21 Fr) was inserted into the urethral orifice and advanced up to stricture. The stricture was then incised at 5, 7 and 12 o' clock position with a cold knife under the guidance of guide wire. The urethrotome was then advanced till it reaches the urinary bladder. Once the uretherotome reached the urinary bladder,it was removed and a 16 French Foley's catheter was inserted over the guide wire which was kept for 7 days. Group A patients were given predisolone 5 mg tablet twice daily for 4 weekswhile group B patients were given placebo(specially designed pill) and double blinding ensured. Patients were then followed weekly for first month then monthly for next 6 months. Recurrence was measured in terms of restricted urine flow (<15 ml/min) on uroflowmetry and/or dilation of the proximal urethra and prostatic ducts (on retrograde urethrogram) after six months of treatment. All the data (age, length of stricture, site of stricture and efficacy) was recorded on a specially designed Performa.

Statistical analysis was performed using SPSS version 25. Quantitative variables such as age, duration of stricture and length of stricture were expressed as mean and standard deviation (SD). Qualitative variables like site of stricture (penile/bulbar/membranous/prostatic) and recurrence of stricture were presented as frequency and percentage. The recurrence of stricture was compared using a chi-square test. Stratification was done for age, duration of stricture, site of stricture and length of stricture. Post- stratification chi-square test was applied to see their effect on recurrence of stricture. A p-value ≤ 0.05 was considered as statistically significant.

Result

Mean age of patients in the study population was 44.95 ± 7.98 years with an age range of 20-60 years. Majority of the patients 55 (70.51%) were lying between the age group of 41 to 60 years. Baseline characteristics of the patients in both groups are elaborated in table 1.

Table I: Baseline characteristics of the patients (n=180)

Baseline Characteristics	Group A (n=90) (Mean ± SD)	Group B (n=90) (Mean ± SD)
Age (years)	44.38 ± 8.03	46.64 ± 6.66
Duration of strictures (months)	4.33 ± 1.57	4.38 ± 1.53
Length of stricture (cm)	0.93 ± 0.26	0.95 ± 0.27

Patients were further divided in both groups according to site of stricture. In group A, 11(12.2%) patients presented with a stricture in penile urethra, 44 (48.9%) patients bulbar urethra, 15 (16.7%) patients membranous urethra and 20 (22.2%) patientswith prostatic urethra. In group B, 13 (14.4%) patients developed stricture in penile urethra, 45 (50%) patients in bulbar urethra, 14 (15.6%) patients in membranous urethra and 18 (20%) patients in prostatic urethra. Both groups showed maximum number of patients presenting with a stricture in bulbar area.

Recurrence of stricture was observed in 18 (20.0%) patients in group A (oral steroids group) while 42 (46.67%) patients in group B (no oral steroids) with p-value of 0.0001. Stratification for recurrence among the groups with respect to age, site of stricture, length of stricture and duration of stricture is shown in Table 2. Majority of the stratified groups showed significant difference in recurrence between

group A and B. However, no statistically significant difference was noted between the groups in or prostatic area and with a stricture of less than four months duration.

Table II:Stratification of efficacy in both groups according to age, length of stricture, site of stricture and duration of stricture in both groups(n=180)

Variables		Group A (n=90)		Group B (n=90)		p-value
		Recurrence		Recurrence		
		Yes	No	Yes	No	
Age(years)	20-40 years	10	28	10	08	0.033
	41-60 years	08	54	22	40	0.0001
Length(cm)	≤1 cm	16	46	30	29	0.005
	1-2 cm	02	26	12	19	0.004
Site of stricture	Penile	06	05	02	11	0.043
	Bulbar	04	40	26	19	0.0001
	Membranous	01	14	05	09	0.054
	Prostatic	07	13	09	09	0.350
Duration (months)	≤4 months	12	24	06	30	0.102
	>4 months	06	48	36	18	0.0001

patients presenting with a stricture in membranous

Discussion

There are multitude of surgical options for the management of urethral strictures depending upon the site, etiology and length of stricture. Different surgical procedures include urethral dilation, internal urethrotomy and reconstructive procedures such as urethroplasty. Urinary diversion is usually required for long stricture in those patients which are not fit for complex surgical procedures. These surgical procedures can be done easily in any ambulatory settings; however, the main concern is risk of high recurrence of stricture. There is still lack of consensus on the best available solution to lessenthe recurrence of strictures. Our study aimed to demonstrate the role of oral steroid therapy after DVIU in reducing the rate of stricture recurrence.[14]

In this study, there is a low recurrence rate of stricture after internal urethrotomy with patients taking oral steroid therapy as compared to the patients without taking oral steroid therapy. Similarly in a study conducted by Gupta et al[15], the recurrence rate of urethral stricture after internal urethrotomy with oral steroid therapy was reported as 19.4% while it was 36.1% in control group, a finding concurrent with our study. Mazdak et al[16] carried out a clinical trial in 50 patients with urethral stricture. According to this study, patients taking oral steroids after internal urethrotomy had recurrence rate of 21.7% while patients with only internal urethrotomy had recurrence rate of 50% after a mean follow-up time of 13.7 ± 5.5 months. These results are also in concordance with our study. This study demonstrated that there was an increased efficacy of oral steroids in patients with stricture less than 1 cm as compared to those with stricture more than 1 cm. Kumar et al[17] conducted a study with total of fifty patients with less than 3 cm urethral stricture managed with Holmium laser with intralesional steroid (triamcinolone). The recurrence in patients presenting with strictures less than 1 cm in length was 4.2%, while patients who developed urethral strictures of 1 to 3 cm in length, the recurrence was 42.3%. These results are similar to our study.

Furthermore, there is also role of intralesional steroid therapy in reduction of stricture recurrence. A study conducted by Modh et al[18] evaluated the role of intralesional steroid after optical internal urethrotomy. The study concluded that high doses of steroid injections played a definite role in

reduction of recurrence rate of strictures. In another placebo-controlled trial conducted by Tabassi et al[19], 70 patients treated with internal urethrotomy were enrolled, 34 were given intraurethral submucosal triamcinolone injection and rest 36 were taken as the control group. The study demonstrated that the steroid group had significantly decreased time to recurrence (8.08 ± 5.55 months) as compared to the control group (3.6 ± 1.59 months). There was no associated complication from steroid injection in the study.

Finally, there is also role of local steroid in lessening stricture recurrence after internal urethrotomy. A systematic review of eight studies with patient population 0f 203 patients done by Zhang et al[20] in 2014 reported that DVIU with steroid therapy were shown to have significant reduction in recurrence time as compared to DVIU alone (10.14 months in steroid group versus 5.07 months in control group, $p < 0.00001$).

Our study has certain limitations. Firstly, it was a single center study. Secondly,we assessed the efficacy of steroids at a fixed dose. Lastly, we had a follow up of 6 months. There is a need for more vast research studies assessing the efficacy of steroids at different doses with longer follow ups.

Conclusion

Oral prednisolone therapy after internal urethrotomy was effective in decreasing the rate of recurrence of urethral stricture.

Recommendation

Oral prednisolone therapy for 4 weeks after optical internal urethrotomy should be considered in selective patients of urethral stricture to reduce the risk of recurrence.

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