Original Article

To Compare The Efficacy Of Intralesional Mitomycin C Versus Traimcinolon In In Reducing The Recurrence Of Urethral Stricture After Internal Optical Urethrotomy

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Abstract

Objectives: To compare the efficacy of intralesional mitomycin C versus triamcinolone in reducing the recurrence of urethral stricture after internal optical urethrotomy.

Materials and Methods: This randomized control trial was conducted at Institute of Kidney Diseases, Hayatabad Medical Complex Peshawar from January 2016 to January 2017. We enrolled 134 patients fulfilling the inclusion criteria. Urine R/E, blood investigation followed by x-ray KUB, ultrasound of the pelvis and abdomen once done with it then will proceed to retrograde urethrogram supplemented by Uroflometry & Flexible urethroscopy. Patient were regularly followed up on 3month interval for 1 year once the Mitomycin or triamcinolone injected intralesionally with TLA needle using straight working channel Pediatric cystoscope at 12, 3 & 9 o' clock positions. On each follow up uroflowmetry, & if needed Retrograde Urethrogram (R.U.G) was performed. On last follow up R.U.G was mandatory to rule out stricture.

Results: Total 134 patients were enrolled in the study divided in to two groups Group A (Intralesinal Mitomycin) and Group B (Triamcinolone) after internal optical urethrotomy. Mean and SD of age for Group A was recorded as 47.4+14.2 and Group B was recorded as 46.58+14.27. Overall, only 29 (21.64%) patients demonstrated recurrence, whereas in the remaining 105 (78.35%) patients no recurrence of urethral stricture post procedure was documented on follow up.

In Group A the recurrence was recorded as 9 (6.71%) whereas 58 (43.28%) patients had no recurrence. In Group B 20 (14.92%) patients had recurrence whereas 47 (35.07%) patients had no recurrence. P Value= 0.021. Frequency and percentage for stricture site between the two groups were recorded as 32 (23.88%) in Bulbar, 27 (20.14%) in Penile and 8 (5.79%) both Bulbar and Penile in Group A and in Group B 35 (26.11%) were recorded in Penile, 21 (15.67%) in Bulbar and 11 (8.20%) in both sites.

Conclusion: Mitomycin C was found to be highly effective in preventing the recurrence of urethral stricture after IOU in comparison with triamcinolone.

Keywords: Mitomycin, triamcinolone, internal optical urethrotomy

INTRODUCTION:

The oldest mention of urethral stricture can be found in Greek writings [(1)]. In 1914, Hamilton Russell provided a description of the first urethroplasty surgery [(2)]. In 1974, Sachse conducted his first internal optical urethrotomy (IOU)[(2)]. Although the precise prevalence of stricture is unknown, some susceptible populations can experience a stricture incidence as high as 0.6% [(3, 4)]. Urinary tract strictures are relatively common in Pakistan, occurring between 3% and 4% of the time [(2)].

Stricture urethra is basically the shrinking of the urethra's lumen as a result of trauma or illness. It is a prevalent issue for men with high morbidity rates. With a prevalence of 0.6% in the population who are at risk, it is a reasonably common disease. A urethral stricture is brought on by injury to the urethral epithelial or the underlying corpus spongiosum. Following trauma, whether accidental or iatrogenic, infection, ischemia, inflammation, or unidentified causes, Stricture can form in the entire portion of the urethra, from the proximal to the distal [(5)].

The treatment of urethral stricture can be accomplished using a variety of techniques, from the minimally invasive IOU to more invasive methods like buccal mucosal graft urethroplasty and, in the twenty-first century, even tissue engineering. The high rate of

return in urethral strictures, however, is the biggest worry, and it has led to the development of the proverb "once a stricture, always a stricture"[5].
The most common form of care for urethral stricture is IOU. It is frequently carried out and is the treatment that urologists worldwide prefer because it is minimally invasive and has less morbidity [6].
Although optical urethrotomy is advertised to have a short-term success rate of between 80% and 100% [7, 8], the long-term efficacy of IOU is in doubt due to a high recurrence rate in various research that ranges from 20% to 60% [9]. In the present study, we want to compare the efficacy of Intralesinal Mitomycin versus Triamcinolon in the treatment of proximal in reducing the recurrence of urethral stricture after internal optical urethrotomy.

Objective: To compare the efficacy of intralesional mitomycin C versus traimcinolon in reducing the recurrence of urethral stricture after internal optical urethrotomy.

MATERIALS AND METHODS:

Study Design and setting:

This Randomized Controlled trial, was done at the Institute of Kidney Diseases, Hayatabad Medical Complex Peshawar from January 2016 to January 2017.

Sample Size:

Total sample size will be 134 (i.e. 67 in each group), using 10% recurrence rate of Mitomycin, and 30% in triamcinolone,
Level of significance = 5%,
Power of test = 95%.

Selection Criteria:

Inclusion Criteria:

- Age 20-70 years
- Male patients.
- Anterior urethral stricture of max 2 cm length irrespective of etiology based upon findings of retrograde urethrogram and supplemented by Uroflometry & Flexible urethroscopy.

Exclusion Criteria:

- Patient not giving informed consent
- Blind urethral stricture.
- Multiple urethral strictures.
- Patients with urethro-cutaneous fistula
- Previously attempted and previously failed intra optical urethrotomy.
- Patients not fit for anesthesia.
- Patients lost to follow up after 3 months in the study

Methods:

After getting approval from hospital ethical committee, Totally 134 patients were enrolled. The aim of the study were explained to the patients and informed consent were obtained from the patients/ guardian. All patients were subjected to history taking and examination for suspected urethral stricture. Urine R/E, blood investigation followed by x-ray KUB, ultrasound of the pelvis and abdomen once done with it then will proceed to retrograde urethrogram supplemented by Uroflometry & Flexible urethroscopy. All investigations were performed under strict protocol to avoid any conflict. Patient were regularly followed up on 3 month interval for 1 year once the Mitomycin or triamcinolone injected intra-lesionally with TLA needle using straight working channel Pediatric cystoscope at 12, 3 & 9 o' clock positions. On each follow up uroflometery, & if needed Reterograde Urethrogram (R.U.G) was performed. On last follow up R.U.G was mandatory to rule out stricture. All the data was recorded on structured Performa's analyzed on spss version 25.

RESULTS:

One hundred thirty four (134) patients were subjected to either Group A (Intralesinal Mitomycin) or Group B (Triamcinolon) after internal optical urethrotomy. Age wise categorization between the two groups in 20-30 years age groups is 30 (22.38%) in which both groups contained 15 patients (11.19%). Same was the situation with age group 31-40 years where 15 patients (11.19%) were recorded in both groups. In the age group of 41-50 years, overall 20 patients (14.92%) were recorded where 10 patients (10.46%) were recorded in each group. In the age group of 61-70 years, overall 34 patients (25.37%) were recorded in which 17 patients (12.68%) were recorded in each group. Mean SD for Group A was recorded as 47.4+14.2 and Group B was recorded as 46.58+14.27. Table 2. Overall, only 29 (21.64%) patients demonstrated recurrence, whereas in the remaining 105 (78.35%) patients no recurrence of urethral stricture post procedure was documented on follow up.

In Group A the recurrence was recorded as 9 (6.71%) whereas 58 (43.28%) patients had no recurrence. In Group B 20 (14.92%) patients had recurrence whereas 47 (35.07%) patients had no recurrence. P Value= 0.021. Frequency and percentage for stricture site between the two groups were recorded as 32 (23.88%) in Bulbar, 27 (20.14%) in Penile and 8 (5.79%) both Bulbar and Penile in Group A and in Group B 35 (26.11%) were recorded in Penile, 21 (15.67%) in Bulbar and 11 (8.20%) in both sites. Overall Stratification of recurrence with different effect modifiers can be seen at Table No. 2, 3 and 4. Descriptive Statistics of stricture length can be found at Table No. 5.

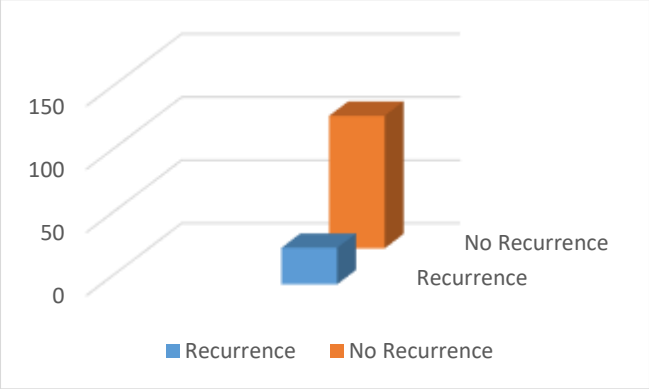

Figure 1 Distribution of patients on the basis of Recurrence and no recurrence

Table 1-0: Distribution of patients on the basis of age group (n=134)

Age Group	Groups		Total
	Group A	Group B	
20-30 years	15	15	30
	11.19%	11.19%	22.38%
31-40 years	15	15	30
	11.19%	11.19%	22.38%
41-50 years	10	10	20
	7.46%	7.46%	14.92%
51-60 years	10	10	20
	7.46%	7.46	14.92%
61-70 years	17	17	34
	12.68%	12.68	25.37%
Total	67	67	134
	50%	50%	100%

Mean ±SD	47.4±14.2	46.58±14.27	47±14.28

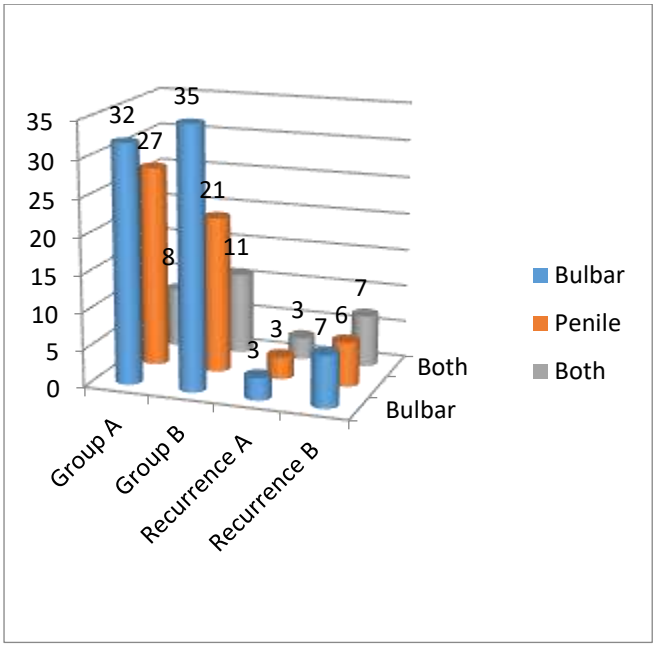

Figure 2 Location of Stricture and Recurrence in each Group

Table 2-0: Stratification of recurrence with regard to age group (n=134)

Age Group	Recurrence	Group A	Group B	Total	P Value
20-30 years	Yes	2 (1.49%)	4(2.98%)	6(4.47%)	0.361
	No	13(9.70%)	11(8.20%)	24 (17.91%)	
31-40 years	Yes	2(1.49%)	3 (2.23%)	5 (3.73%)	0.624
	No	13(9.70%)	12(8.95%)	25 (18.65%)	
41-50 years	Yes	1 (0.74%)	2(1.49%)	3(2.23%)	0.531
	No	9 (6.71%)	8(5.97%)	17 (12.68%)	
51-60 years	Yes	3(2.23%)	6(4.47%)	9 (6.71%)	0.177
	No	7(5.22%)	4 (2.98%)	11 (8.20%)	
61-70 years	Yes	1(0.74%)	5(3.73%)	6 (4.47%)	0.071
	No	16(11.9%)	12(8.95%	28 (20.89%)	
Total		67 (50%)	67 (50%)	134 (100%)	

Table 3-0: stratification of recurrence with regard to duration of disease (n=134)

Duration of Disease	Recurrence	Group A	Group B	Total	P Value
≤ 3Months	Yes	4 (2.98%)	08 (5.97%)	12 (8.95%)	0.246
	No	40 (29.85%)	38 (28.35%)	78 (58.20%)	
> 3Months	Yes	5 (3.73%)	12 (8.95%)	17 (12.68%)	0.015
	No	18 (13.43%)	09 (6.71%)	27 (20.14%)	
Total		67 (50%)	67 (50%)	134 (100%)	

Table 4-0: Stratification of recurrence with regard to stricture length (n=134)

Stricture Length	**Recurrence**	**Group A**	**Group B**	**Total**	**P Value**
≤1	Yes	4 (2.98%)	10 (7.46%)	14 (10.44%)	0.578
	No	14 (10.44%)	24 (17.91%)	38 (28.35%)	
>1	Yes	5 (3.73%)	10 (7.46%)	15 (11.19%)	0.020
	No	44 (32.83%)	23 (17.16%)	68 (50.74%)	
Total		67 (50%)	67 (50%)	134 (100%)	

Table 5-0: descriptive statistics of stricture size (length) (n=134)

INTRALESINAL MITOMYCIN					
	n	Minimum	Maximum	Mean	Means ±SD
Stricture Size	67	0.50cm	2cm	1.02cm	1.02±0.26
TRIAMCINOLON					
	n	Minimum	Maximum	Mean	Means ±SD

Stricture Size	67	0.50cm	2cm	1.22cm	1.22±0.35

DISCUSSION

Strictures of the urethra are surrounded by dense fibrosis, which is rarely accompanied with a fistulous tract connecting the prostatic and bulbar urethra. These restrictions may be the result of pelvic trauma, recurrent urethral infections, or previous surgery. Endoscopic therapy for urethral strictures is a hotly debated topic that has gained popularity over the past few decades(10). Today's standard procedure is direct vision internal urethrotomy using an optical urethrotome, which is performed with accuracy and precision and is favoured by the majority of urologists. One of the most frequent conditions seen by urologists worldwide is urethral stricture. According to a recent study, IOU is preferred by 86% of American urologists for treating anterior urethral stricture [(11)]. The primary issue is the stricture's propensity for recurrence, which is evident in patients' long-term follow-up after having any surgical procedure. Even though a number of enhancements and modifications have been made and advocated to reduce recurrence, such as repeated SCIC [(5)], recurrence once recorded has been deemed a failure of the procedure by many authors. In order to reduce this bias, SCIC was not made available to either cohort in our study group. Research avenues in various surgical specialties have been expanded thanks to the study of the antifibroblastic characteristics of first steroids and then mitomycin C. Intralesional mitomycin C has been shown to be effective in avoiding fibrosis following keloid scar excision in myringotomy [(12)] and in preventing urethral stricture in rats [(13)]. In our study, intralesional mitomycin C showed some promising outcomes in reducing urethral stricture recurrence.

To our understanding, this is the first randomized control trial comparing the effects of intralesional triamcinolon and mitomycin in our area. All individuals with urethral stricture less than 2 cm on a retrograde urethrogram were included. (RUG). The average age of the participants in our research was close to 47 years, which is consistent with the observations made by Islam et al. 180 and Khan et al. (14) that urethral stricture typically affects patients over the age of 40 years. Previously, gonococcal urethritis was the most frequent cause of urethral stricture, but today, trauma, including external and iatrogenic urethral trauma, is the leading factor in the development of urethral stricture. Stein et al. also reported an infectious aetiology in 1% of cases in their study from 2013; however, no case of urethritis was found in our study. Regarding the site, our study, which is comparable to Vanni et al's, revealed that stricture involving the bulbar urethra is the most frequent. Numerous methods, such as serial urethral dilation, low dosage oral steroids, and the use of intralesional antitumor agents, have been used to lower the risk of recurrence. A tumour-fighting drug called mitomycin C was discovered in Streptomyces caespitosus. It has been discovered to suppress the proliferation of fibroblasts and stop scarring. In 2007, Mazdak et al. [(15)] first used intralesional mitomycin C. He found that the incidence of stricture recurrence was 10% lower in the mitomycin group and 50% higher in the control group. The findings of Mazdak were contested by Mundy [(16)], who questioned his 40-patient sample size and 6-month follow-up period. Our study's sample size 70 participants in each group, with a mean follow-up of 18 months—was sufficient for tackling the aforementioned issues. In our research, stricture recurrence was significantly reduced (p0.001) from 20.4% in the control group receiving triamcinolone to 14.1% in the group receiving intralesional mitomycin. In his review paper, Vanni13 also noted that intralesional mitomycin significantly decreased the recurrence of urethral stricture. Currently, mitomycin-containing anti-fibroblast agents are used in combination with positive results. Only 20% of patients with intralesional injections experienced urethral stricture recurrence, according to Kumar et al. Only 10% of cases of recurrence with intralesional injections were good findings from a different study by Chung [(17)] as well. Intralesional triamcinolone has recently demonstrated encouraging outcomes following holmium laser optical urethrotomy, reducing recurrence by 24%; however, more research is needed to confirm the efficacy in the local population[(17)]. We have also shown that intralesional mitomycin C, as opposed to triamcinolone, can delay the onset of recurrence. After a 12-month symptom-free period, nearly 80% of patients treated with triamcinolone experienced urethral stricture recurrence; in contrast, 86.56% of patients treated with mitomycin C experienced a delayed recurrence, as noted and reported by numerous authors [(13, 18, 19)]. After successful urethral stricture treatment, Erickson et al.[(20)] also noted a substantial improvement in the MFR. As many other writers had noted, we discovered no correlation between the etiology, site, or size of the recurrence in either group. Although this is the first research in the area to compare how mitomycin and triamcinolone treat different diseases, it has some drawbacks, such as a short period of follow-up and a small sample size. It is advised that more research be done in the future to determine the likelihood of return.

CONCLUSION

The rate of recurrence of urethral stricture after IOU is high. In the present study, mitomycin C was found to be highly effective in preventing the recurrence of urethral stricture after IOU in comparison with triamcinolone.

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