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ORIGINAL ARTICLE

Role of Mitomycin C in Management of Anterior Urethral Stricture

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ABSTRACT

Background: Urethral stricture disease can result from any of the following causes inflammatory, ischemic or traumatic processes. Many risk factors of urethral stricture disorder have been documented. Urethral stricture disorder is a disease of antiquity. Recurrence of the stricture is the most common adverse outcome of surgery.

Objective: To compare the clinical recurrence rate in urethral stricture after direct vision internal optical urethrotomy followed by intralesional injection of mitomycin C inoculation and internal optical urethrotomy alone.

Study Design: Randomized control trial

Place and Duration of Study: Department of Urology, Jinnah Hospital, Lahore from 1st July 2019 to 31st January 2021.

Methodology: Eighty patients were enrolled and they were divided into two groups; group A and group B. Group A was treated with intralesional mitomycin C and group B with internal optical urethrotomy alone. The patients were followed up for 6 months and clinical outcome and recurrence were noted.

Results: The patients' average age was 47.91+16.19 years. About 65 (81.25%) strictures reported were caused by iatrogenic and 15(18.75%) strictures caused by infection. The recurrence of weak urinary stream occurred in 28 patients and it was found significantly higher in control group 21(52.5%) as compared to group given mitomycin C 7 (17.5%)

Conclusion: Both intralesional mitomycin C inoculation and internal optical urethrotomy has better outcome than internal optical urethrotomy alone.

Keywords: Intralesional mitomycin C, Urethral stricture, Urethrotomy.

INTRODUCTION

Stricture of urethra is partial or complete tapering of the normal caliber of the urethra which may or may not affect urine outflow.[1] Injuries to the urinary tract, including the epithelium or the underlying spongy corpus spongiosum, can lead to scarring, which can lead to hardening of the urinary tract, which can adversely affect the quality of urinary outflow stream.[2]

Approximately 229-627 per 100,000 population is affected by urethral stricture mainly the anterior urethra is affected. Various etiological determinants are said to linked with disease of urethral stricture, including infections and diseases of sexually transmitted origin, inflammatory causes, external trauma affecting the perineum, iatrogenic trauma, catheterization, instrumentation or urethral surgery.[3] Its prevalence is high in both the developed and as well as under-developed countries and it has been speculated from the literature that nearly 4% of the indoor patients suffer from urethral stricture.[4] The incidence of stricture with increasing age as compared to younger patients suffering from stricture urethra were seen.[5]

Even though urethra can be affected at any point throughout its entire continuity, roughly 50% of the patients that present with urethral stricture are having bulbar urethral involvement. of many etiological factors most familiar are idiopathic causes, iatrogenic causes (including urethral catheterization and urological surgeries), infective (inflammatory) causes and pelvic and perineal traumatic injuries (pelvic bone fracture resulting break in continuity of urethra).[2] Regional differences have been reported in stricture etiology in multi-center cohorts.[6] The infective or inflammatory type was considered to be more common but with increase in education level, public awareness programs and introduction of modern antibiotics, incidence of post-infective and inflammatory causes has been markedly reduced in developed countries where these strategies are used effectively.[7] On contrary, urethritis still remains a major etiological factor to the stricture urethra in developing countries.[8]

The most common site involved in stricture urethra is anterior urethra followed by posterior or proximal urethra.[5] Clinical presentation and symptoms depend upon the cause of stricture, site and length of the involved part in the stricture urethra. Common clinical picture of the stricture patients include increased straining while attempting to urinate, poor urinary stream, post-void dribbling, incomplete bladder emptying or urine retention resulting in recurrent urinary tract infections.[9] Some patients may present with failure to ejaculate, impotence that is the cause of infertility.[4]

Treatment modalities in management of stricture urethra depends primarily on attributes of urethral stricture i.e., length, site and character of the urethral stricture and as well as available options and expertise of the treating clinician.[10] Enlisting few, these procedures include urethral dilation using metal sounds or bougies, direct vision internal optical urethrotomy and high pressure balloon dilation.[11] Although urethral stricture disease is of high prevalence still there is no consensus in the management strategy of the disease.[12]

Current urethral stricture disease management options include either endoscopic or surgical procedures involving open techniques or both of them but all procedures are having a variable profile of success rate.[13] The direct vision internal optical urethrotomy (DVIOU) involves incising the strictured segment of urethra to dilate the urethral caliber mainly for stricture lengths 10-15 mm and involving the bulbar part of urethra.[14] Endoscopic treatments mainly incise the urethra at stricture site at 12'O clock but results are often not adequate with more stricture recurrence rates of 60-80 percent at longer duration of follow-up.[15] Longer stricture lengths more than 20mm, involving other sites than bulbar part, recurrent, penile or anterior urethral strictures of shorter length that were previously treated with DVIOU but come up with recurrence are often managed with open surgical techniques involving reconstruction with somewhat better outcome but this technique is more invasive and requiring more resources in the population with urethral stricture disease.[16] Moreover, open surgical techniques demand require a higher level of surgical expertise compared to endoscopic procedures and can be less suitable for a surgically unfit group of patients with high age of comorbidities ease due to increased anesthesia and surgical time. Therefore, optimalisation of current endoscopic procedures is necessary.[14] Post-surgical complications include bleeding or hematuria, pelvic pain, prostatitis, urinary retention, peri-urethral abscess, epididymo-orchitis and recurrence of the stricture.[17]

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Mitomycin C has been used in various surgical procedures i.e. myringotomy, trabeculectomy and after keloid scar excision to reduce recurrence rate in humans and animals.[18] The promising results with the use of intralesional injection of mitomycin C during treatment of bladder neck contracture with radial urethrotomy.[19]

Mitomycin C, hyaluronic acid and carboxymethyl cellulose result in better improvements in the rate of recurrence of stricture in low-risk group. But, these improvements in the outcomes in the patients under trials of mitomycin C and steroids decrease with a long follow-up. Although local instillation of mitomycin C or hyaluronic acid and carboxymethyl cellulose can result in better outcome in terms of recurrence of stricture following endoscopic interventions, but still a larger randomized controlled trial with longer duration of study is mandatory to assess the clinical outcomes.[13]

MATERIAL AND METHODS

This randomized controlled trial was conducted in the Department of Urology Jinnah Hospital, Lahore from 1st July 2019 to 31st January 2021. The sample size was calculated with 1% level of significance, 95% power of test with expected percentage with mitomycin C as 10% and without mitomycin C 50% were 80 patients.[20] The patients were divided into two groups; group A and group B. Group A was treated with intralesional mitomycin C inoculation and group B with internal optical urethrotomy alone. All patients age above 18 years, newly diagnosed urethral strictures, stricture length less than 20 mm, infective and iatrogenic strictures, anterior urethral strictures only and spongial tissue grade 1-3 were included. Patients who have blind urethral strictures, multiple urethral strictures, recurrent stricture after failed internal optical urethrotomy, traumatic urethral strictures, history of urethroplasty, posterior urethral strictures and spongial tissue grade 4-5 were excluded. Demographic data of patients was obtained. The severity was assessed by urethral ultrasonography. Anesthesia was either spinal or general. All the patients undergoing procedure were injected with injection ceftriaxone 1gm intravenously. Urethrotomy using cold knife was done using urethrotome 20F (wolf) and incision at 12O' clock in urethra. Mitomycin C 0.1 mg was diluted in 2 mL of saline and was injected intralesionally at 1.5, 7 and 11O' clock position (0.5 ml at each site) using cystoscopic needle. Securing hemostasis and viewing bladder and urethra after injection, 16 Fr catheter placed and balloon inflated with distilled water and kept for 7 days. Injection ceftriaxone 1 gm intravenous BID and injection diclofenac sodium 75 mg intramuscular BID was given on first post-operative day. After that Tab ciprofloxacin 500 mg BID (7 days) and tab diclofenac sodium 50 mg BID (3 days) will be given to all the patients postoperatively. Patient was discharged after 24 hours. Upon post-operative follow-up urinary symptoms of patients were recorded. Retrograde urethrography and urethral ultrasonography done if patient complaints of lower urinary tract symptoms (reduced stream of urine). Patients were kept on a regular follow-up schedule of monthly visiting Jinnah hospital for 6 months. Procedure will be considered successful if patient remained symptom free for at least three months. The data was entered and analyzed through SPSS-26. 't' test and Chi square test were applied. P value <0.05 was taken as significant.

RESULTS

The mean age A group patients was 45.97±15.40 years whereas the mean value of age in group B patients was 49.80±16.90 years. The mean grading of stricture among A group was 2.079±0.67 whereas in B group was 2.08±0.79. There were insignificant (P>0.05) difference between the groups were found (Table 1). In group A, 33 (82.5 %) patients had iatrogenic stricture whereas 7 (17.5%) patients had stricture caused by infection. Similarly in group B, 32 (80%) patients had iatrogenic stricture whereas 8 (20%) patients had stricture caused by infection. Statistically insignificant (P>0.05) difference was found in causes of strictures (Table 2). The mean stricture of length in group A was 1.167+0.46 whereas in group B was 1.164+0.46. There was statistically insignificant (P=0.974) difference and the mean length on retrograde urethrogram in group A was 1.185±0.44 whereas in group B was 1.160±0.45. The insignificant (P=0.803) difference statistically was found (Table 3). The recurrence of wean urinary stream was occurred in 28 (35%) patients while in remaining patients, it was not observed and weak urinary stream in group A found in 7 (17.5%) patients whereas the recurrence of weak urinary stream in group B found in 21 (52.5%). Statistically significant (P=0.001) difference was observed (Table 4).

Table 1: Comparison of age and ultrasound grading of stricture in both groups

Variable	Group A	Group B	P value
Age (years)	45.97±15.40	49.80±16.90	0.825
Ultrasonographic grading of stricture	2.07±0.67	2.08±0.79	0.957

Table 2: Comparison of causes of stricture with respect to study groups

Causes of stricture	Group A	Group B	Total	P value
Iatrogenic	33(82.5%)	32(80%)	65 (81.25%)	0.7745
Infection	7(17.5%)	8(20%)	15(18.75%)	

Table 3: Comparison of length of stricture and length on retrograde urethrogram in both groups

Variable	Group A	Group B	P value
Length of stricture	1.16±0.46	1.164±0.46	0.974
Length on retrograde urethrogram	1.185±0.44	1.16±0.45	0.803

Table 4: Comparison of recurrence of weak urinary stream with respect to study groups

Recurrence	Group A	Group B	Total	P value
Yes	7(17.5%)	21(52.5%)	28 (35%)	0.001
No	33(82.5%)	19(47.5%)	52 (65%)	

DISCUSSION

The urethral stricture is a disorder that is always a challenge to the urologists. It is one of the classical urologic diseases, which is known and rests a conjoint problem yielding huge morbidity. Various modalities in management are used to treat the urethral stricture disease and these are the dilatation, stent placement, urethrotomy and the urethroplasty. The mitomycin C is an antitumor antibiotic secluded from streptomyces caespitosus (SC). It frequently inhibits the fibroblast proliferation and thwart scar creation. Many techniques implemented in shrinkage the stricture recurrence once after internal optical urethrotomy (IOU), like the lengthy catheterization and a self-clean intermittent catheterization with capric IOUs success. The mitomycin C has properties like anti-collagen and anti-fibroblast and used in trabeculectomy, in myringotomy, and after keloid scar editing in contemporary surgical practice.[21,22] It has reported about 86% of the urologists in US prefer the IOU in anterior urethral stricture management.[23]

In this study there is statistically insignificant difference found between the study groups with recurrence rate of stricture urethra after internal optical urethrotomy. In our study the recurrence of weak urinary stream occurred in 4 (5%) patients. In mitomycin C group the recurrence occurred in 39(97.5%) patients whereas in other the recurrence occurred in 37(92.5%) patients (p=0.615). Mundy and Andrich[17] showed results in favor of present study. Mazdak et al[20] showed promising results with mitomycin C after internal optic urethrotomy in urethral stricture and only 10% of the patients in mitomycin C group developed recurrence as opposed to 50% in the control group. Kumar et al[24] reported that recurrence rate (overall) once after the second technique was 5.8%, which is with a success rate of 94.2%.

On the other hand, Pervez et al[25] documented that 11 patients (14.1%) in group A and in 27 patients (36.9%) in group B were reported with urethral stricture recurrence (p=0.002). The mitomycin group also exhibited recurrence delay when comparing with the control group. The mitomycin C was observed as

extremely effective in precluding the urethral stricture recurrence once after the IOU.

The study conducted by Chung et al[26] reported with the positive recurrence outcomes in almost 10% of the cases with intralesional injections. Thus, in future, we will recommend adding mitomycin C with internal optical urethrotomy in order to improve outcome and decrease chances of recurrence.

CONCLUSION

Both intralesional mitomycin C inoculation and direct vision internaloptical urethrotomy alone are equally efficacious in terms of recurrence rate of urethral stricture after endoscopic treatment of urethral stricture.

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