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A PROSPECTIVE, COMPARATIVE STUDY ON THE EFFECT OF MITOMYCIN C ON ANTERIOR URETHRAL STRICTURE RECURRENCE AFTER INTERNAL URETHROTOMY

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ABSTRACT: INTRODUCTION: Direct visual internal urethrotomy (DVIU) is the most commonly performed procedure for bulbar urethral stricture disease of length 10mm or less. DVIU alone, classically, has a poor long-term success rate. The objective of this prospective study conducted at VIMS Bellary from Sep 2012 to Aug 2013 is to compare the effect of submucosal injection of mitomycin-C after DVIU on recurrence rate of bulbar urethral stricture with DVIU alone. **MATERIALS AND METHODS:** Forty five male patients with bulbar urethral strictures of 10mm or less were included in the study with every alternate patient undergoing DVIU was injected urethral submucosal Mitomycin-C(0.1mg) at the urethrotomy site. Mitomycin C injected in 23 patients. Mean stricture length, as measured by retrograde urethrography (RUG) was 0.75 cm. Mean preoperative uroflow was 10.5ml/sec. The patients were re-evaluated after 6 months and 1 year by uroflow, USG abdomen and RGU, and the stricture recurrence rate was compared between the two groups. **RESULTS:** Analysis of the results revealed a stricture recurrence rate of 47% in the DVIU only group while the recurrence rate in the Mitomycin C group was only 13%. This difference was statistically significant. The mean uroflow of the recurrences in the Mitomycin C group was 13 ml/sec, and DVIU group 11.75 ml/sec. **CONCLUSIONS:** Submucosal injection of Mitomycin C after DVIU is effective in reducing the rate of early recurrence in our short term follow up study. However further studies are required to know the long term results. In our study aetiology of stricture has no relation to the recurrence rate after DVIU.

KEYWORDS: Anterior urethra, internal urethrotomy, Mitomycin.

INTRODUCTION: Urethral strictures can occur due to trauma, infection, ischemia, inflammation, or unknown causes. As a result, scar tissue forms in the epithelium, which leads to decrease in caliber of the urethral lumen. Stricture can develop in any part of the urethra from the prostatic urethra to the meatus. Different techniques have been described for treatment of urethral strictures, depending on the stricture length, location, and depth of scar. Direct Visual Internal Urethrotomy (DVIU) is a worthwhile method for treating bulbar urethral strictures which are less than 1.0 cm in length. This approach is appealing both for urologists and patients as it is minimally invasive. However high recurrence rates have been reported with this technique.^{1,2}

Several adjuvant therapies, including brachytherapy, injection of captopril, steroids and mitomycin C have been proposed to minimize the recurrence rate of urethral strictures after Direct visual Internal urethrotomy (DVIU)^{3,4,5} Mitomycin C is an alkylating antineoplastic antibiotic derived from *Streptomyces Caespitosus*. It acts by inhibiting DNA synthesis by cross-linking DNA between adenine and guanine. It is useful in delaying the healing process by preventing replication of fibroblasts and epithelial cells and inhibiting collagen synthesis. It is also proposed that it can delay

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wound contraction. The drug has been used to prevent the development of fibrosis after myringotomy and trabeculectomy and has improved the success rate of these procedures.⁵

In this comparative study, we investigated the results of urethral sub mucosal injection of mitomycin C (0.1mg) at the urethrotomy site, on the recurrence rate of the stricture following direct visual internal urethrotomy (DVIU). The patients were re-evaluated after 6 months and 1 year by uroflow, USG abdomen and RGU, and the stricture recurrence rate compared with control group.

MATERIALS AND METHODS: We performed a prospective, comparative study on patients with urethral stricture who presented to urology department of VIMS, Bellary, Karnataka, India, from September 2012 to August 2013. Forty five male patients with bulbar urethral strictures of 10mm or less were included in the study with every alternate patient undergoing DVIU was injected urethral submucosal mitomycin C (0.1mg) at the urethrotomy site. The stricture length was measured by pre-operative retrograde urethrogram (RGU). Patients with previous urethroplasty, urethral manipulation (urethrotomy or urethral dilatation), urethral strictures longer than 1.0 cm, neurogenic bladder, lichen sclerosis, urinary tract infection, history of immunodeficiency disease, and use of corticosteroids were excluded from the study.

Mitomycin C was injected in 23 patients. Mean stricture length, as measured by retrograde urethrography (RUG) was 0.75 cm. Mean preoperative uroflow was 10.5ml/sec. The patients were re-evaluated after 6 months and 1 year by uroflow and the stricture recurrence rate was compared between the two groups. Retrograde urethrography (RUG) was done in all patients under fluoroscopy.

Failure was defined as a need for repeat of surgical intervention during the follow up period. Recorded complications were dysuria and bleeding.

SURGICAL TECHNIQUE: Pre-operative evaluation consisted of history taking physical examination, retrograde urethrography, USG abdomen and cystoscopy. Furthermore, patients received a single dose of a first-generation cephalosporin half an hour before the surgery. First, by using a cold knife, DVIU was done through stricture site at 12 o'clock position endoscopically, only fibrous tissue was cut and normal healthy urethra was remained intact. The incision was continued until the 21 F sheath could pass through the stricture site into the bladder. Subsequently, mitomycin C (0.1mg in one ml) was injected into both sides (0.5ml each) of cut fibrotic tissue at around 11 and 1 o'clock positions by using William cystoscopic injection needle. Thereafter, an 18 F Foley catheter was inserted and left in place for 3 to 5 days. After removal of the catheter, patients were followed up for 6 to 12 months for development of any complications. Follow up visits included history taking, questions about urinary symptoms, uroflow as well as retrograde urethrography, USG abdomen and cystoscopy if indicated. Follow-ups were scheduled every 3 months and whenever patients had any complaints.

Patients were not taught self-dilatation of urethra because it may confound the results.

RESULTS: Analysis of the results revealed a stricture recurrence rate of 47% in the DVIU only group while the recurrence rate in the Mitomycin C group was only 13%. Statistical analysis done by applying fisher exact test, and got the significant difference with p value of 0.023. The mean uroflow of the recurrences in the mitomycin C group was 13 ml/sec, and DVIU group 11.75 l/sec. In our study both groups had similar number of patients with respect to aetiology, hence no relation of aetiology was referred to recurrence rate of stricture.

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DISCUSSION: Direct visual Internal urethrotomy (DVIU) has been suggested as a procedure of choice for correction of the urethral strictures shorter than 1.0 cm; however, recurrence has been remained as its major drawback.^{3,4} Holm-Nielsen and colleagues reported recurrence rates ranging from 50% to 75% during a 2-year follow-up period⁶ In our study, the overall recurrence rate was 28% and the recurrence rate in the control group was 47%, which is consistent with the findings of Holm-Nielsen and colleagues. The reason for lower recurrence rates may be due to shorter duration of follow-up in our study.

A study conducted by H. Mazdak and colleagues from Isfahan, Iran where mytomycin C was injected submucosally after DVIU and recurrence rate compared. Analysis of the results revealed a stricture recurrence rate of 50% in the DVIU only group while the recurrence rate in the Mitomycin C group was only 10%. This difference was statistically different. The mean caliber and length of the recurrences in the Mitomycin group were 1.3 mm and 0.71 cm respectively while the values for the DVIU only group were 1.2 mm and 0.84 cm.⁵

In our study as shown in table 1 and 2, DVIU group had 22 patients with mean age of 30.1 yrs, mean uroflow of 9.9ml/sec, mean stricture length 0.78cms, one complication in the form of bleeding and recurrence rate of 47%. Mytomycin C group had 23 patients with mean age of 33.2 years, mean uroflow of 10.5 ml/sec, mean stricture length of 0.75cms, two complications in the form of dysuria and bleeding, and recurrence rate of only 10%. Bleeding was managed with perineal compression. Recurrence rate between two groups is statistically significant with p value of 0.023 and almost consistent with study conducted by Mazdac and colleagues

CONCLUSION: Submucosal injection of Mitomycin C after DVIU is effective in reducing the rate of early recurrence in our short term follow up study. However further studies are required to know the long term results and require multicentric randomized control trials for definitive evidence.

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GROUP	DVIU	DVIU With MYTOMYCIN C
No. of patients	22	23
Mean age	30.1 yrs	33.2 yrs
Mean uroflow	9.9 /ml/sec	10.5 ml/sec
Mean stricture length	0.78 cms	0.75 cms
No. of complications	1	2

TABLE 1

GROUP	DVIU	DVIU WITH MYTOMYCIN C
No of recurrences	10	3
% of recurrences	47 %	13 %
Mean uroflow of recurrent patients	11.75ml/sec	13 ml/sec

TABLE 2

SL. No.	Etiology	Number
1	Inflammatory	22
2	Iatrogenic	6
3	Traumatic	12
4	Idiopathic	5

TABLE 3

Fig. 1: William cystoscopic injection needle

Fig. 2: ASU Depicting Short bulbar urethral stricture

Fig. 3: Stricture incised at 12° C (White arrow)

Fig. 4: Injection of mitomycin-C at 11° Clock Position

Fig. 5: Injection of mitomycin-C at 1° Clock Position

Fig. 6: Post DVIU RGU (6 months)

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