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Is Mitomycin-C Really Effective in Reducing The Recurrence Rate of Stricture Urethra After Internal Urethrotomy?- Our Institutional Study

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ABSTRACT:
INTRODUCTION:
The recurrence rate of optical internal urethrotomy (OIU) alone in the treatment of urethral stricture is approximately 50%.Pharmacological adjuncts to OIU,which can be injected at the site of OIU to significantly reduce the recurrence rate have been studied. One among such drugs is mitomycinC.If addition of this drug significantly lowers the recurrence rate of stricture formation,it will be very useful in the long term outlook of these patients.
AIM:
To study the efficacy of mitomycin C in reducing the recurrence rate of urethral stricture in patients undergoing Optical Internal Urethrotomy(OIU).
METHOD:
40 patients with symptomatic urethral stricture after proper evaluation were divided in to 2 groups,group A(OIU alone) and group B (OIU with 0.1 mg submucosal mitomycin C injection after OIU with 3.7 Fr 37 cm injection needle).All patients were followed up for 6 to 9 months based on history,uroflowmetry monthly and Ascending Urethrogram (AUG) every 3months.
RESULTS:
Recurrence rate in group B(mitomycin C) was 10%(2 out of 20 patients),in group A(OIU alone) was 45%(9 out of 20 patients).Success rate was 90% in group B,55% in group A.
CONCLUSION:
Mitomycin C significantly reduces the recurrence rate of urethral stricture following OIU.Proper use of this drug can be useful in long term management of such patients,as seen in our study.
KEYWORDS*: Stricture urethra,Mitomycin C,Optical Internal Urethrotomy*

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I. Introduction:

Urethral stricture disease has always been a challenge for urologists. Different treatment modalities that are used for treatment of urethral stricture disease are dilatation, urethrotomy, stent placement and urethroplasty.

Urethrotomy is one of the minimally invasive treatment options for short (<1 cm) strictures within the bulbar urethra.

Pansadoro and Emiliozzi have shown that the **recurrence rate of optical internal urethrotomy (OIU) alone is approximately 50%[6].**This is because,OIU does not provide an epithelial approximation but rather aims to separate the scarred epithelium so that healing occurs secondarily. If epithelialization progresses completely before wound contraction significantly narrows the lumen, the internal urethrotomy may be successful. If wound contraction significantly narrows the lumen before the completion of epithelialization,the stricture recurs[8].

Stricture often recurs within 1 year, although recurrences have been noted after more than 10 years. The low success rate and the recurrence of stricture despite such treatment options have prompted the search for new treatment methods[9].

Several adjuvant therapies like brachytherapy, injection of captopril, steroids and mitomycin C have been proposed to minimize the recurrence rate of urethral strictures after Internal urethrotomy[2,3]. Mitomycin C prevents replication of fibroblasts and epithelial cells,inhibits collagen synthesis & delays wound contraction[4].

This study evaluated the efficacy of mitomycin C in reducing the recurrence rate of urethral stricture in patients undergoing Optical Internal Urethrotomy(OIU).

AIM OF THE STUDY:
To study the efficacy of mitomycin C in reducing the recurrence rate of urethral stricture in patients undergoing Optical Internal Urethrotomy (OIU).

II. Materials And Methods :

We conducted this prospective double blinded randomized study from April 2018 to July 2019 at the Department of Urology in Government Medical College and Hospital,Dharmapuri.Sample size was 40 patients & was attained based on the following method.

Two-sided significance level(1-alpha):	95
Power(1-beta, % chance of detecting):	80
Ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed with Outcome:	50
Percent of Exposed with Outcome:	9.9
Odds Ratio:	0.11
Risk/Prevalence Ratio:	0.2
Risk/Prevalence difference:	-40

	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size - Exposed	21	**20**	24
Sample Size-Nonexposed	21	**20**	24
Total sample size:	42	**40**	48

References

Kelsey et al., Methods in Observational Epidemiology 2nd Edition, Table 12-15
Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 &3.19
CC = continuity correction

INCLUSION CRITERIA:

1) Patients in 18-70 years age group,
2) Patients with symptomatic bulbar urethral stricture <1 cm in length,
3) Partially obliterated bulbar urethral stricture
4) Patients not willing for end to end anastomotic urethroplasty
5) Patients with no clinical or psychological contraindications to anesthesia or surgery
6) Patients who are willing & compliant for the study.

EXCLUSION CRITERIA:

1) Stricture length more than 1 cm,
2) Completely obliterated urethral stricture,
3) Posterior urethral stenosis,
4) Patients with co existent neurogenic bladder &
5) Previous urethral surgeries.

III. Methodology:

Proper history taking & clinical examination were done to look for evidence of urethral stricture like BXO changes over prepuce/glans & urethral thickening. Patients fulfilling the inclusion & exclusion criteria were included in the study. Informed consent was properly obtained from all patients.

All patients were initially counseled regarding the

1) Natural course of the disease,
2) About the surgery and mitomycin C instillation,
3) Risks of surgery &
4) Need for regular follow up.

They were randomised in to 2 groups (group A & B) based on simple random sampling method.
Group A- 20 patients,who underwent OIU alone
Group B- 20 patients,who underwent OIU with adjuvant mitomycin C instillation near the site of OIU,

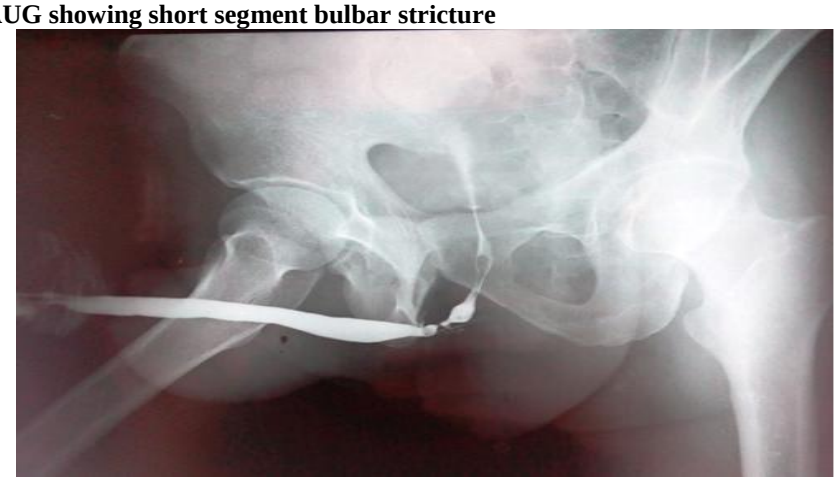
All relevant preoperative investigations were done namely,

1) Urine sugar,albumin & deposits,
2) Urine culture & sensitivity,
3) Blood sugar,serum urea & creatinine,
4) Ultrasound Kidney,Ureter & Bladder

- Kidney size & cortical thickness
- Corticomedullary differentiation status
- Pelvicalyceal system dilatation if any,calculi if any
- Bladder wall thickness,calculi/growth if any
- Prostate size & PVR

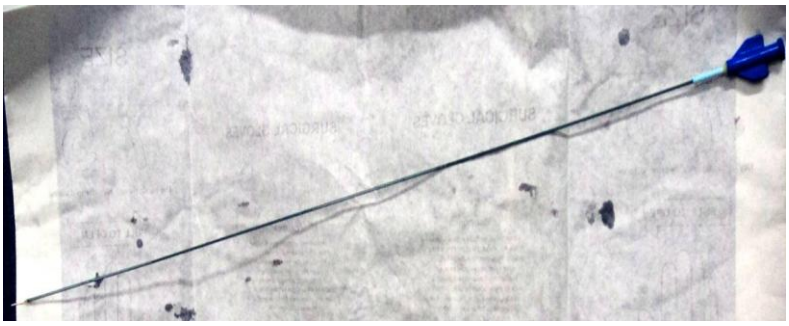
5) Uroflowmetry-curve pattern,voided volume,Q max,Qave,voiding time,PVR
6) Retrograde urethrogram

Pre operative AUG showing short segment bulbar stricture



Under spinal anesthesia,OIU was done at 12 O clock position with 21 Fr
OIU sheath,active working element & sachse cold knife.After doing OIU,0.1mg mitomycin C was injected submucosally at 11 & 1 O' clock position with 3.7 Fr 37cm injection needle.Bladder was decompressed with 14 or 16 Fr silicone foley catheter.

Mitomycin C injection needle



Submucosal injection of mitomycin C at 11 O clock position

Urethral foley catheter was removed after 14 days.Patients were advised to review to our OPD every month.AUA symptom score assessment,genitalia examination & Uroflowmetry were done on every visit.Retrograde urethrogram was done on every 3rd month.

Recurrence was defined as,if in uroflowmetry study if the curve pattern is of plateau type/if Qmax is less than 10 ml/s or if there is evidence of stricture in AUG.

IV. Results:

Median follow up period was 7.5 months.No complications were reported after mitomycin C instillation.Recurrence rate in group A(OIU alone) was 45%(9 out of 20 patients) and in group B(adjuvant mitomycin C) was 10%(2 out of 20 patients) and it was statistically significant (p value 0.03 based on fisher' s exact test).Median time for recurrence was 5 months in group A(OIU alone) & 7 months in group B(mitomycin C). 11 out of 13 recurrences were treated with end to end anastomotic urethroplasty.Remaining 2 patients were not willing for urethroplasty & hence treated with OIU.

Success rate is 90% in group B(mitomycin C),55% in group A(OIU alone).

OUTCOME	TREATMENT			
	WITH MITOMYCIN C (GROUP B)		WITH OUT MITOMYCIN C (GROUP A)	
	NUMBER	PERCENTAGE (%)	NUMBER	PERCENTAGE (%)
RECURRENCE	2	10	9	45
WITHOUT RECURRENCE	18	90	11	55
SUM	20	100	20	100

Post operative AUG

V. Discussion:

Mitomycin C is an alkylating antineoplastic antibiotic derived from Streptomyces caespitosus. It acts by cross-linking DNA between adenine and guanine, thereby inhibiting DNA synthesis. It also suppresses cellular RNA and protein synthesis and is not cell cycle specific. Therefore, it is useful in delaying the healing process by preventing replication of fibroblasts and epithelial cells and inhibiting collagen synthesis. It is proposed that it can delay wound contraction. Other studies on mitomycin C have shown its efficacy in preventing fibroblast proliferation and development of fibrosis after myringotomy and trabeculectomy, thus improving the success rate of these procedures[10].

OIU has been suggested as a procedure of choice for correction of the urethral strictures shorter than 1.0 cm; however, recurrence is its major drawback[1]. Holm-Nielsen and colleagues reported recurrence rates ranging from 50% to 75% during a 2-year follow-up period[5].A study conducted by H. Mazdak and colleagues from Isfahan, Iran where mitomycin C was injected submucosally after OIU and recurrence rate compared[4]. Analysis of the results revealed a stricture recurrence rate of 50% in the OIU only group while the recurrence rate in the Mitomycin C group was only 10%. This difference was statistically significant.

In our study,recurrence rate was 45% in OIU alone group & 10% in mitomycin C group,which was statistically significant(p value 0.03).One of our study limitation is the short follow up period.

VI. Conclusion:

Mitomycin C significantly lowers the recurrence rate of urethral stricture if given after doing OIU,as evident in our study.It is safe,easily available & cheaper drug. However further studies are required to know the long term results and require multicentric randomized control trials for definitive evidence.

References:

[1]. Santucci RA, Eisenberg L. Urethrotomy has a much lower success rate than previously reported. J Urol. 2010; 183: 1859– 62.
[2]. Mazdak H, Izadpanahi MH, Ghalamkari A, Kabiri M, Khorrami MH, Nouri-Mahdavi K, et al.Internal urethrotomy and intraurethral submucosal injection of triamcinolone in short bulbar strictures. Int Urol Nephrol. 2009.
[3]. Shirazi M, Khezri A, Samani SM, Monabatti A, Kojoori J, Hassanpour A. Effect of Intraurethral captopril gel on the recurrence of urethral stricture after direct vision internal urethrotomy:Phase II clinical trial. Int J Urol. 2008; 15: 562– 4.
[4]. Mazdak H, Meshki I, Ghassami F. Effect of mitomycin C on anterior urethral stricture recurrence after internal urethrotomy. Eur Urol. 2007; 51: 1089– 92.
[5]. Holm-Nielsen A, Schultz A, Moller-Pedersen V. Direct vision internal urethrotomy: A Critical review of 365 operations. Br J Urol. 1984; 56: 308– 12. [PubMed]
[6]. V. Pansadoro and P. Emiliozzi, " Internal urethrotomy in the management of anterior urethral strictures: long term follow up," *Journal of Urology*, vol. 156, no. 1, pp. 73– 75, 1996.
[7]. Santucci RA, Joyce GF and Wise M: Male urethral stricture disease.J Urol 2007, Jordan GH, Schlossberg SM. Surgery of the penis and urethra. In: Retik AB, Vaughan ED, Wein AJ, editors.Campbell' s urology. ed. 11. Philadelphia
[8]. Bradner WT. Mitomycin C: a clinical update. Cancer Treat Rev 2001;27:35– 50
[9]. Fontana H, Nouri-Mahdavi K, Caprioli J. Trabeculectomy with mitomycin C in pseudophakic patients with openangle glaucoma: outcomes and risk factors for failure.Am J Ophthalmol 2006;141:652– 9

Dr.R.Gopi Saravanan. "Is Mitomycin-C Really Effective in Reducing The Recurrence Rate of Stricture Urethra After Internal Urethrotomy?- Our Institutional Study"." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(07), 2022, pp. 10-15.