

A combined retrospective-prospective cohort study for efficacy of internal urethrotomy followed by clean intermittent catheterization with and without clobetasol ointment in management of stricture urethra.

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Abstract

Direct vision internal urethrotomy (DVIU) is still a popular surgery for urethral strictures. However, its effectiveness is being questioned by many urologists owing to high recurrence rates. Development of new method to address lower efficacy of DVIU is need of the hour. We designed the current study on the basis of evidence of previous studies which used local steroid as intra-urethral injection form or ointment form and hypothesized that post DVIU clean intermittent catheterization (CIC) with clobetasol ointment (0.05%) can prevent or/and delay urethral stricture recurrence. We have compared the effect of CIC with clobetasol ointment and CIC without clobetasol in prevention and prolongation of urethral stricture recurrence after DVIU. The study included a total of 93 patients (50 patients in group A, 43 patients in group B) of primary

bulbar urethral stricture of <1.5 cm length without history of PFUI (pelvic fracture urethral injury) or straddle injury who underwent cold knife DVIU and post DVIU completed 12 months follow up. This is a prospective retrospective randomized cohort study. Group A- patients were operated at Dalela academy of urology, and post DVIU underwent CIC with 2% lignocaine jelly and 0.05% clobetasol ointment. Group B- patients operated at department of urology, King George’s medical university and post DVIU underwent CIC only with 2% lignocaine jelly without clobetasol ointment. Postoperatively patients were evaluated at 7th day, 3rd, 6th, 9th and 12th months by means of clinical evaluation, compliance to the CIC and CIC related complications (pain during CIC, bleeding during CIC, fever and orchitis) and recurrence of stricture. The authors observed parameters like

recurrence, time of recurrence after DVIU, compliance variation and complications between two groups. Group A patients were more compliant to CIC than group B, but difference was nonsignificant. CIC related complications in group A were less than group B, but difference was nonsignificant. On 12 months follow-up, recurrence was present in 4 men (10%) in group A while in 7 (16%) in group B. CIC when combined with clobetasol, decreased the number of recurrence but statistically nonsignificant contribution of clobetasol with respect to recurrence (p=0.39). CIC with clobetasol prolonged the duration of stricture recurrence (7.5 ±1.23months in group A Vs. 5.1 ±1.04 months in group B); difference was statistically significant (p value <.0001) between two groups. In this study, we followed patients till 12 months to include most crucial period of stricture recurrence, so it seems that DVIU has a good one year success rate and hope of good long term success also as most of the recurrences occur in initial 12 month of DVIU.

Keywords: Direct vision internal urethrotomy, clean intermittent catheterization, clobetasol (0.05%) ointment.

Introduction

According to a nationwide survey, direct vision internal urethrotomy (DVIU) is still the most commonly performed procedure for urethral strictures in the United States.^[1] However, high recurrence rates have been reported with the DVIU and its effectiveness also is being questioned by many urologists.^[2] The short-term success rate of DVIU varies between 39% and 73% for urethral strictures shorter than 1.5 cm, whereas, long-term recurrence rate is 56%.^[3-5] Low success rates of DVIU address the need for the development of additional new techniques and complementary strategies to prevent wound contraction

and recurrent stricture formation. In view of this philosophy clean intermittent catheterisation (CIC), intra-lesional steroids or mitomycin application have been tried to prevent recurrences with variable results.^[6,7] Local corticosteroid injection triamcinolone proposed by Hosseini^[8], Mazdak^[9] and Tabbasi^[10] in treatment of stricture urethra and concluded that this adjunctive procedure decreases stricture recurrence rate. Post DVIU, triamcinolone ointment along with CIC was used in two different randomised controlled trials (RCT) by Yesil^[11] and Gucuk^[12] in bulbar urethral stricture <1.5 cm with improved success rate. Steroidal ointment preparation of clobetasol (0.05%) can be used locally with CIC in recurrence prevention or prolongation apart from triamcinolone. On the basis of evidences of previous studies which used local steroid as intra-urethral injection form or ointment form, we hypothesized that post DVIU CIC with clobetasol ointment (0.05%) can prevent or/and delay urethral stricture recurrence. The purpose of the current study was to compare effect of CIC with clobetasol ointment (0.05%) and CIC without clobetasol in prevention and prolongation of urethral stricture recurrence after DVIU in patients with primary bulbar urethral stricture of <1.5 cm.

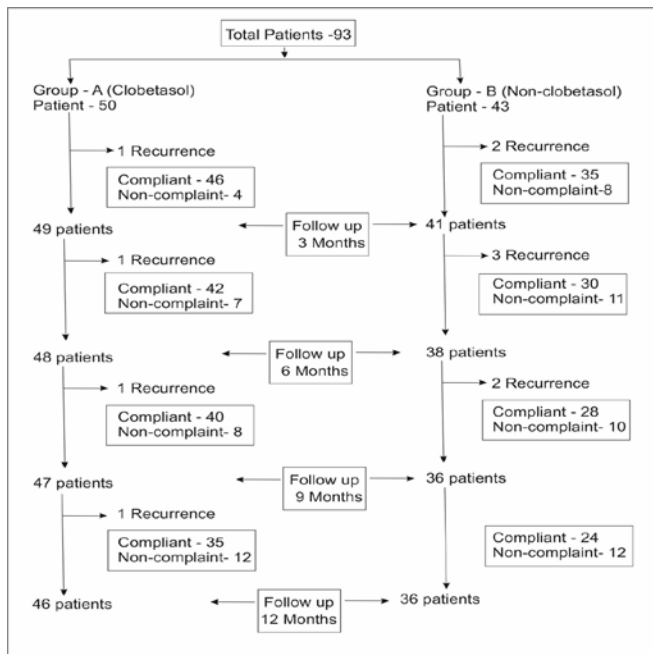
2. Aims and objectives- To compare between post DVIU CIC with and without clobetasol (0.05%) ointment in term of urethral stricture recurrence, compliance and CIC related complications.

3. Material and methods- This was a prospective and retrospective cohort study, which conducted at the Dalela Academy of Urology, Lucknow and Department of Urology, King's George Medical University (KGMU), Lucknow, From December 2018 to December 2020. Retrospective data were collected from June 2017 to December 2018. The study included

urethral surgery naïve patients who wished to undergo DVIU as a primary procedure with bulbar urethral stricture of < 1.5 cm in size. Patients with history of endoscopic or open urethral surgery, pelvic fracture urethral injury (PFUI), chronic kidney disease, consent refusal or who lost at follow-up were excluded.

A total of 93 patients who fulfilled inclusion and exclusion criteria along with 12 months follow-up were included in the study. Through simple randomization, all the patients were assigned and operated at two different urology centers thus making two groups. One arm of patients was operated at Dalela academy of urology, and post DVIU underwent CIC with 2% lignocaine jelly and 0.05% clobetasol ointment. The other group was operated at department of urology, KGMU and post DVIU underwent CIC with 2% lignocaine jelly without clobetasol ointment. Urethral stricture length was determined by using measuring scale mentioned on retrograde urethrogram (RUG) image.

Study design



All included patients were operated through DVIU by cold knife urethrotomy performed at 12'o clock

position until all the spongi-fibrotic tissue was incised. Post DVIU a 16 French per urethral catheter (PUC) was placed over guidewire. The patients were kept on PUC for 5-10 days. On the day of PUC removal, all the patients were trained individually by specialized male urology technician or by urologist himself in order to achieve the ability of self CIC at home.

Group-A was trained with CIC with 2% lignocaine jelly along with 0.05% clobetasol ointment in an amount of peanut size. Group-B was trained with CIC with 14 French K-90, lubricated with 2% lignocaine jelly. Schedule of CIC was decided as- daily for 3 months, then twice a week for 3 months, then fortnightly for 3 months and then monthly for subsequent 3 months.

Recurrence was considered if the patient was unable to pass K-90 or complain of voiding lower urinary tracts symptom for which uroflowmetry was done and if on UFR, maximum flow rate was <10 ml/min. The patients were evaluated at 7th day, and then at 3rd, 6th and 12th months by means of clinical evaluation, recurrence, compliance to the CIC and CIC related complications (pain during CIC, bleeding during CIC, fever and orchitis).

4. Results- a total of 93 men with primary, bulbar and <1.5 cm urethral stricture participated in the study. Mean age of the group A was 44.2±2.7 years and of group B was 43.7 ±2.03 years. In group A stricture consistency was soft in 32 and hard in 18 men, while in Group B stricture consistency was soft in 31 and hard in 12 men (p=0.251)

At the end of 3rd, 6th, 9th and 12th month follow-up 4, 7, 8 and 12 patients in group A, while 8, 11, 10 and 12 men in group B were non-compliant to CIC. Difference was non-significant statistically between two groups in each follow-up (p>0.005). Also, there was no significant difference present in CIC related

complications including pain during CIC, urinary tract infections, bleeding during CIC and orchitis between both groups. At tri-monthly follow-up, a total of 1, 2, 3 and 4 men (group A), while total 2, 5, 7 and 7 men (group B) developed recurrences, which was statistically non-significant. At the end of follow-up, a total of 11 men in both groups developed recurrence. In noncompliant patients of group A, on 3rd, 6th, 9th and 12th month 0, 0, 0 and 1 men while 2, 3, 1 and 0 men in group B developed recurrences, respectively. Difference was statistically non-significant. The difference was statistically non-significant in terms of

recurrence between CIC compliant and non-compliant men ($p=0.535$). Difference in recurrence rate was statistically significant in terms of length of stricture as a total of 8 men with stricture <1.0 cm, while 3 men who had stricture of 1.0- 1.5 cm developed recurrence ($p=0.02$). Mean recurrence time in group A was 7.5 months, while in group B was 6.1 months, the difference was significant in two groups ($p<0.0001$).

Table 1: Comparison of patient's data in term of recurrence.

Parameter	1st Visit- 3 month		2 nd Visit- 6 month		3 rd Visit- 9 months		4 th Visit 12 months		
	Group A (n-50)	Group B (n-43)	Group A (n-49)	Group B (n-41)	Group A (n-48)	Group B (n-38)	Group A (n-47)	Group B (n-36)	
Compliant patients	46	35	42	30	40	28	35	24	$\chi = 0.3847$ $p= 0.5351$
<i>p</i> value	$p= 0.385$		$p= 0.400$		$p= 0.802$		$p= 0.232$		
Recurrence in Compliant	1	0	1	0	1	1	0	0	
<i>p</i> value	$p= 0.385$		$p= 0.400$		$p= 0.802$		$p= 0.232$		
Non-compliant patients	4	8	7	11	8	10	12	12	
<i>p</i> value	$p= 0.128$		$p= 0.138$		$p= 0.274$		$p= 0.437$		
Recurrence in noncompliant	0	2	0	3	0	1	1	0	
<i>p</i> value	$p= 0.334$		$p= 0.158$		$p= 0.380$		$p= 0.326$		
Recurrence (compliant + noncompliant)	1	2	1	3	1	2	1	0	
Total recurrence	3 (3.22%)		7 (7.52%)		10 (10.7%)		11 (11.8%)		

Discussion

In previous studies, Santucci et al.^[13] have reported a curative success rate of DVIU of approximately 20%, whereas Pansadoro and Emiliozzi^[5] reported a curative

success rate of 30% to 35%. These low success rates of DVIU demand the need for the development of new techniques and complementary strategies to prevent wound contraction and recurrent urethral stricture.

Post DVIU CIC has been tried by Jorgensen^[14], Kjaergard^[15] and Harris^[16] which revealed that post DVIU CIC significantly improves efficacy of DVIU in urethral stricture recurrence.

The present study is a prospective-retrospective, randomized study in which CIC has been used with and without ointment clobetasol after DVIU to find out role of ointment clobetasol in post DVIU urethral stricture recurrence prevention. Participants particulars like age, stricture consistency and duration of post DVIU PUC placement in group A and group B were comparable.

Patients in group A were more compliant to CIC than group B, but difference was statistically non-significant ($p=0.370$). In both groups a total of 81 (87%), 72 (80%), 68 (79%) and 63(75.9%) men were compliant to CIC at 3rd, 6th, 9th and 12th months follow up, respectively (table 1).

In our opinion, a good number of men can be compliant to CIC if regular telephonically feedback, motivation and help is provided; and proper counselling and consequences of stricture like recurrence/ 2nd DVIU/ urethroplasty is explained, as in our experience men liked and were convinced more to do CIC rather than to go for 2nd DVIU or urethroplasty.

For the current study, each patient was contacted in every 15-20 days and was asked about CIC compliance, any difficulty during CIC and was motivated to do CIC. The year-end recurrence was present in 4 men (10%) in group A while in 7 men (16%) in group B thus CIC with clobetasol has decreased the number of recurrence though difference was statistically non-significant ($p=0.390$).

Kjaergaard et al. and Bodker et al. followed post DVIU patients with CIC for 12 months and found 19% and 22% recurrence rate, respectively.^[15] We have similar

recurrence rate in group B patients who have done post DVIU CIC without clobetasol.^[15, 17] We observed that CIC with clobetasol prolonged the duration of stricture recurrence (7.5 ±1.23months in group A Vs. 5.1 ±1.04 months in group B) and the difference was statistically significant ($p<.0001$) between both groups.

Gucuk et al. followed patients for 16 months and found out that post DVIU CIC with steroids (recurrence 20%) have better success rate than CIC without steroids (recurrence 46%).^[12]

At year-end follow-up, a total of 24 men were noncompliant to CIC in which urethral stricture recurrence was present in 7 (29%), while it occurred only in 4 (5.8%) out of 69 men who were compliant. In term of recurrence difference, it was statistically non-significant between compliant and noncompliant groups ($p=0.125$) although noncompliant group has high rate of recurrence (Table 1). Between group A and B, the complication rate was not statistically significant, although number of men who experienced complications were low in group A. In present study, CIC with clobetasol has decreased the number of recurrence without contributing towards steroid induced complications.

The result of current study are similar to a meta-analysis study by Zhang et al.^[17] which concluded that the use of local steroids along with DVIU either injectable form at the time of DVIU or as a lubricant with CIC is safe and effective in prolongation of stricture recurrence but does not have significant effect on stricture recurrence following DVIU.

Tabassi et al.^[10] showed that complication and recurrence rates in the injection triamcinolone group were lower than the control group, but the difference was not statistically significant; whereas time to recurrence decreased significantly. No complications

could be attributed to the local steroid ointment, so it appears that steroid ointment is safe to use and may delay urethral stricture recurrence. In combined, overall recurrence rate in both groups at 3rd, 6th, 9th and 12th months follow-up was 3%, 7%, 10% and 11%, respectively (Table 1.).

Hosseini et al.^[8], Kjaergaard et al.^[15], Tunc et al.^[18] and Mazdak et al.^[19] followed patients for 12 months after DVIU and found 30%, 19%, 10% and 21% recurrence rate, respectively. Most reports show that if post DVIU recurrence occurs it is most likely to do so within 3 to 12 months.^[20]

In our study, we followed men till 12 months to include most crucial period of stricture recurrence. It seems that DVIU has a good one year success rate and hope of good long term success also as most of the recurrences occur in initial 12 months post DVIU.

6. Limitations: Longer follow-up may be needed to conclude difference in stricture recurrence between two groups in a more better way statistically .

7. Conclusion: Patients with post DVIU CIC with clobetasol have more compliance to CIC, less recurrence rate, delayed recurrence and less CIC related complications than CIC without clobetasol. Post DVIU patients can have good compliance to CIC if proper follow-up and counselling is done regularly. Recurrence was high in CIC noncompliant patients in comparison to CIC compliant group, but difference was non-significant. Numbers of recurrence were distributed equally at 3rd, 6th, 9th and 12th months.

References:

1. Bullock TL, Brandes SB. Adult anterior urethral strictures: A national practice patterns survey of board certified urologists in the United States. *J Urol* 2007;177:685-90.

2. Albers P, Fichtner J, Bruhl P, Muller. Long-term results of internal urethrotomy. *J Urol* 1996;156:1611-14.
3. Brandes SB, Virgo K, Johnson FE. Adult anterior urethral stricture: A national practice pattern survey *J Urol* 2001;165:53A.
4. Stormont TJ, Suman VJ, Oesterling JE. Newly diagnosed bulbar urethral strictures: Etiology and outcome of various treatments. *J Urol* 1993;150:1725-28.
5. Pansadoro V, Emiliozzi P. Internal urethrotomy in the management of anterior urethral strictures: Long-term follow-up. *J Urol* 1996;156:73-75.
6. Mazdak H, Meshki I, Ghassami F. Effect of mitomycin C on anterior urethral stricture recurrence after internal urethrotomy. *Eur Urol* 2007;51:1089-92.
7. Korhonen P, Talja M, Ruutu M, Alfthan O. Intralesional corticosteroid injections in combination with internal urethrotomy in the treatment of urethral strictures. *Int Urol Nephrol* 1990;22:263-69.
8. Hosseini S, Kaviani A, Golshan AR. Clean intermittent catheterization with triamcinolone ointment following internal urethrotomy. *Urol J* Fall 2008;5:265-8
9. Mazdak H, Tolou_Ghamari Z, Khorrami A. Investigation of Triamcinolone Instillation in the Long-term Rate of Anterior Urethral Strictures' Recurrence. *Current Urology*. 2020;14:206-10.
10. Tabassi KT, Yarmohamadi A, Mohammadi S. Triamcinolone injection following internal urethrotomy for treatment of urethral stricture. *Urol J* 2011;8:132.

11. Yeşil S, Atan A, Polat F. A method that facilitates urethral catheterization after internal urethrotomy. *Turkish journal of urology* 2019;45:S125.
12. Gücük A, Tuygun C, Burgu B, Öztürk U, Dede O, İmamoğlu A. The short-term efficacy of dilatation therapy combined with steroid after internal urethrotomy in the management of urethral stenoses. *J Endourol* 2010;24:1017-21.
13. Santucci RA, Mc Aninch JW. Actuarial success rates of open urethral stricture repair in 369 patients. *J Urol* 2001;165:13.
14. Jorgensen JB, Mortensen T, Fischer A: Ren intermitterende kateterisation som profylakse efter operativ behandling af uretralstriktur. *Dan KirSelsk Nyhedsbrev* 1991;38:55.
15. Kjaergard B, Walter S, Bartholin J, Andersen JT, Nøhr S, Beck H. Prevention of urethral stricture recurrence using clean intermittent self catheterisation. *Jr J Urol* 1994;73:692-5.
16. Harriss DR, Beckingham IJ, Lembergher RJ, Lawrence WT. Long-term results of intermittent low-friction self-catheterisation in patients with recurrent urethral strictures. *Br J Urol* 1994;74:790-7.
17. Zhang K, Qi E, Zhang Y, Sa Y, Fu Q. Efficacy and safety of local steroids for urethra strictures: a systematic review and meta-analysis. *J Endourol* 2014;28:962-8.
18. Tunc M, Tefekli A, Kadioglu A, Esen T, Uluocak N, Aras N. A prospective, randomized protocol to examine the efficacy of postinternal urethrotomy dilations for recurrent bulbomembranous urethral strictures. *Urology* 2002;60:239-44.
19. Mazdak H, Izadpanahi MH, Ghalamkari A, Kabiri M, Khorrami MH, Nouri-Mahdavi K, Alizadeh F, Zargham M, Tadayyon F, Mohammadi A, Yazdani M. Internal urethrotomy and intraurethral submucosal injection of triamcinolone in short bulbar urethral strictures. *Int Urol Nephrol* 2010;42:565-8.
20. Naude AM, Heyns CF. What is the place of internal urethrotomy in the treatment of urethral stricture disease? *Nat Clin Pract Urol* 2005;2:538.