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ROLE OF INTRAURETHRAL TRIAMCINOLONE INJECTION IN DIRECT VISUAL INTERNAL URETHROTOMY IN THE MANAGEMENT OF ANTERIOR URETHRAL STRICTURE AND ITS EFFECT ON RECURRENCE

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ABSTRACT

INTRODUCTION: Urethral stricture is known for a disease of recurrence since ancient egyptian times and common after internal urethrotomy[1].In modern endouroloigcal era endoscopic management takes upperhand than more invasive procedure like urethroplasty.Anterior urethra is the most common location for stricture urethra and bulbar urethra the major site of stricture accounts for 45-50%[2]. Urethral stricture can have variety of etiology like trauma or iatrogenic, infection, inflammation, ischemia or unknown etiology[3].The pathophysiology behind anterior urethral stricture manifested by a process of fibrosis which lead to a different proportions of peri-urethral corpus spongiosum tissue fibrosis known as spongiofibrosis and is associated with narrowing in urethral caliber and ultimately reduce in the urine flow. Treatment is based on the deep incision of the fibrotic area and subsequently local re-epithelialization process to the maintainance of the urethral patency.Scar forms in the epithelial lining of urethra which result in decrease in diameter of the urethral lumen[3].Iatrogenic etiology(30-80%) or trauma is the commonest cause than infection[4]. Different techniques have been described for stricture urethra but direct visual internal urethrotomy(DVIU)and instillation of triamcinolone most important additive adjuvant drug and is best suited and remains a common procedure due to its easy accessible, safety, simplicity, better learning curve and short recovery.[6-8]

MATERIALS AND METHODS: Its a retrospective observational study ontotal of 50 patients with anterior urethral stricture who underwent DVIU (Group A; n=25) and DVIU with triamcinolone injection(Group B; n=25) in the management of anterior urethral stricture disease in males.The study done during the period of march 2022 to march 2023 at Father Muller Medical College & Hospital,Mangalore. Results were compared between the two groups. The P-value < 0.05 considered statistically significant difference.

RESULTS: From the study we obseve that there were not any significant difference between age and co-morbidities in both the groups. In both the group A and B the most common age was 46-60 years. In Group A and Group B it was 48% and 56% respectively (p=0.0986).Co-morbidities (Diabetes, Hypertension ,smoking)were almost similar in both the groups. There were no significant difference in stricture location, length and causes among the two groups(p=0.627,p=0.377,p=1.000 respectively).In DVIU group alone(group A) patients came with recurrence are 2(8%) in 6 month, 4(16%) in 9th month, 3(12%)in 12th month and totally 9 patients (36%). In DVIU+triamcinolone (group B) patient came with recurrence 2 in 12th month, totally 2 patient(8%).No major complication found in both the group(p=0.837). In our study the result found to delay the recurrence but not statistically significant (p=0.231) and recurrence rate significantly less in DVIU +triamcinolone group(8%vs 36%;p =0.041,<0.05).

CONCLUSION: Intra-urethral triamcinolone injection into the urethral stricture site to avoid fibrosis and collagen growth is a safe and effective additive therapy after direct visual internal urethrotomy. No major complications were not noted due to the triamcinolone injection. Triamcinolone injection to the stricturous site seems to be cost effective,produce lower side effects and play a vital role to delay the time of recurrence and recurrence rate.

INTRODUCTION

Urethral stricture in male is known for a disease of recurrence since ancient egyptian times and common after internal urethrotomy[1]. In modern endouroloigcal era endoscopic management takes upperhand than more invasive procedure like urethroplasty Anterior urethra is the most common location for stricture urethra and bulbar urethra major site of stricture accounts for 45-50%[2]. Urethral stricture can have variety of etiology like trauma or iatrogenic, infection, inflammation, ischemia or unknown etiology[3]. Anterior urethral stricture characterized by a process of fibrosis which lead to different proportions of peri-urethral corpus spongiosum tissue fibrosis known as spongiofibrosis and is associated with narrowing of urethral caliber and consequently poor flow of urine[3]. Treatment is based on the deep incision of the fibrotic area and subsequently local re-epithelialization process to the maintainance of the urethral patency.Scar forms in the epithelial lining of urethra which result in decrease in diameter of the urethral lumen[3]. Iatrogenic etiology(30-80%) or trauma is the commonest cause than infection[4].DVIU across stricturous segment reverses fibrotic area with subsequent epithelialization. Treatment success is determined by rates of epithelialization which should occur at faster than wound contraction.As it is a simple procedure which can be performed on outpatient basis with minimal complication, DVIU has good popularity for short segment stricture less than 1cm.However, the common drawback is increase recurrence rate have been noted with this procedure and long term results are usually low with DVIU. Many additive drug have been proposed to minimize the rate of recurrence of urethral stricture and to delay time of recurrence after DVIU[5]. Local corticosteroid injection decreases the scar formation by reducing collagen,glycosaminoglycans synthesis and inflammatory mediators[6,7].Triamcinolone is most crucial drug which has antifibroblastic and anticollagenic property after instillation into the stricturous site in DVIU and easily accessible as compared to other adjuvant drugs [8,9].

Thereby we plan to evaluate the role of intraurethral triamcinolone injection in direct visual internal urethrotomy in the management of anterior urethral stricture and its effect on recurrence.

MATERIALS AND METHODS

Its a retrospective observational study on patients fulfilling the inclusion criteria and as per convenience with anterior urethral stricture who underwent DVIU (Group A;n=25) and DVIU with Triamcinolone injection(Group B;n=25) in the management of anterior urethral stricture disease in males.The study done during the period of march 2022 to march2023 in the urology department at Father Muller Medical College & Hospital. The study was approved by the institutional ethics committee by the protocol number 549/2023.

INCLUSION CRITERIA

- All male patients.
- Age between 30-75years.
- Bulbar/penile urethral stricture <1cm.
- Incomplete obliterated bulbar urethral stricture.

EXCLUSION CRITERIA

- Patients with multiple stricture.
- Prior history of urethroplasty.
- Patients having strictures with vesical calculus and enlarged prostate.

STUDY METHODOLOGY

Data was collected from patients who were included in the study.The patients in both group were analysed for age, co-morbidities (Diabetes mellitus,Hypertension,smoking),time of recurrence, recurrence rate.The stricture characteristics stricture length, stricture location, stricture causes, complications and mean follow up were assessed in both the group.

Patients included in the study was evaluated by history taking,clinical examination,ultrasound pelvis,uroflowmetry,retrograde urethrography preoperatively.Retrograde urethrography with anterior urethral stricture less than 1 cm included in the study.Patients received a single dose of third generation cephalosporin one hour before surgery.

After preliminary cystoscopy using 21Fr VIU sheath used in all cases. A 0.035inch terumo guidewire was used as a guide through the stricture during incision with sachse's knife. Incision of stricture was made at 12 o'clock position along its entire length and depth.By this way fibrous tissue was cut and intact of normal urethra. Incision was deepened in the fibrous tissue until normal urethral tissue appear and until it admitted the VIU sheath and bladder could be entered.Incision at 6 o'clock position not done because of damage of entering to rectum.Normal saline used as irrigation fluid. Thereafter 40mg/ml triamcinolone acetonide was diluted with 10ml saline injected into stricture site into four quadrants at 3/6/9/12 o'clock position . Subsequently 16 Fr per urethral catheter placed and kept for 5-7 days.

Patients were followed up for 12 months at interval of every 3 months during clinic visits by urinary symptoms, uroflowmetry and retrograde urethrogram was done when Qmax showed <10ml/sec.

Recurrence of stricture defined by those patients complaining of poor flow of urine with straining on void and uroflow shows Qmax<10ml/sec and RGU shows narrowing in the anterior urethra or require another procedure or reintervention.

Patients demographic data and variables were collected retrospectively. Data were analyzed as percentage for categorical variables and mean and standard deviation for continuous variables. Proportions were compared using chisquare test and means were compared using student T test. Non-normal data were analyzed using Mann-Whitney U test.A p value<0.05 regarded as statistically significant. All statistical variables and clinical outcome were analyzed by using SPSS version 23 software.

RESULTS

Patients demographic and clinical variables were shown in the table (1-5).The most common age in both the group is 46-60 year (Table 1). When statistically compared mean ±SD in DVIU group (53.48±2.902) and in DVIU+triamcinolone group(53.50±2.887)(Table 2) .There was not any

significant difference between age among both the group. The P value is >.05(p=0.9806;Chi square 0.322;Student T score=0.0244)which is statistically insignificant.

Regarding co-morbidities in both groups there were no statistical difference(P value >0.05). Diabetes mellitus in DVIU group was 20% and in DVIU +TRIAMCINOLONE group was 24%(p=1.000).Hypertension in DVIU group 36% and in DVIU +triamcinolone group 20%(p=0.345).Smoker in DVIU group 32% and in DVIU+triamcinolone group 16%(p=0.321) (Table 3).

There was not any significant difference in stricture location among the two groups (p=0.627;Fig1).The stricture length <0.5cm and 0.5-1cm in DVIU and DVIU +triamcinolone group 44% /28% and 56%/76% respectively(Fig2). In the study, stricture length showed no significant difference among the two group(p=0.377).The etiology for stricture urethra in the DVIU vs DVIU +triamcinolone group were iatrogenic /catheter induced (40% vs 48%),traumatic 16% in both group ,infection (8%vs 4%),unknown(36%vs 32%)(Fig3).In both group there was not any significant difference in stricture length (p=1.000).Regarding complication in the study bleeding seen in 2 patients(8% vs 8%)in both the group respectively, infection in 1 vs 2 patient (4% vs 8%) in DVIU vs DVIU+tiamcinolone group.There was no extravasation in the triamcinolone group as well as DVIU group(Fig5).No major complication found in both the group and statistically insignificant(P=0.837)(Table 4)In the study when observe for time to recurrence characteristically we noticed there was a delaying period for triamcinolone group as compared to DVIU alone. Patients came with recurrence are 2(8%) in 6 month, 4(16%) in 9th month, 3(12%)in 12th month and totally 9 patients (36%) in the DVIU group(Fig6).In DVIU+ triamcinolone patient came with recurrence 2 in 12th month, totally 2 patient(8%)(Table 5;Fig6).In our study the result found to delay the recurrence however not statistically significant (P=0.231) and recurrence rate significantly less in DVIU +triamcinolone group(8%vs 36%;P =0.041, <0.05;Table 4;Fig4).

TABLE 1: AGE DISTRIBUTION

AGE GROUP(YEAR)	DVIU GROUP	DVIU+TRIAMCINOLONE(TRIAM) GROUP	P VALUE
30-45	6(24%)	5(20%)	0.851
46-60	12()48%	14(56%)	
61-75	7(28%)	6(24%)	

TABLE 2:MEAN AGE IN YEARS

GROUP	NUMBER OF PATIENTS	MEAN AGE IN YEARS	STANDARD DEVIATION	P VALUE
DVIU GROUP	25	53.48	2.902	0.9806
DVIU+TRIAM GROUP	25	53.50	2.887	

TABLE 3:CO-MORBIDITIES

CO-MORBIDITIES	NUMBER OF PATIENTS	DVIU	DVIU+TRIAM	P VALUE
DM	11	5(20%)	6(24%)	1.000
HYPERTENSION	14	9(36%)	5((20%)	0.345
SMOKING	12	8(32%)	4(16%)	0.321

TABLE 4:STRICTURE CHARACTERISTICS

		DVIU(n=25)	DVIU+TRIAM(n=25)	P value
Stricture location	**Penile urethra**	**9(36%)**	**6(24%)**	**0.627**
	Bulbar urethra	**14(56%)**	**16(64%)**	
	Both	**2(8%)**	**3(12%)**	
Stricture length(cm)	**<0.5cm**	**11(44%)**	**14(56%)**	**0.377**
	0.5-1cm	**7(28%)**	**18(72%)**	
Stricture etiology	**Iatrogenic/catheter induced**	**10(40%)**	**12(48%)**	**1.000**
	Traumatic	**4(16%)**	**4(16%)**	
	Infection	**2(8%)**	**1(4%)**	
	unknown	**9(36%)**	**8(32%)**	
Complications	**Bleeding**	**2(8%)**	**2(8%)**	
	Infection	**1(4%)**	**2(8%)**	**0.837**
	Extravasation	**0**	**0**	
	None	**22**	**21(84%)**	
Recurrence rate		**9(36%)**	**2(8%)**	**0.041**

Fig1: STRICTURE LOCATION

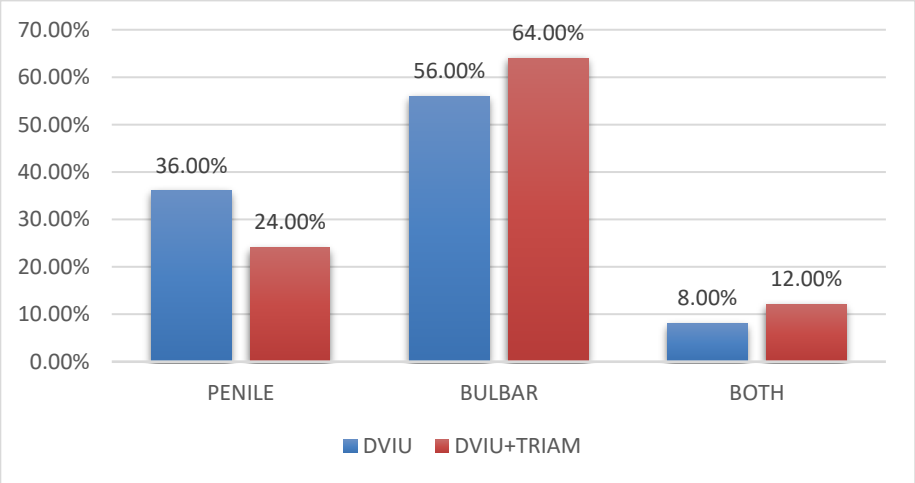

Fig2: STRICTURE LENGTH

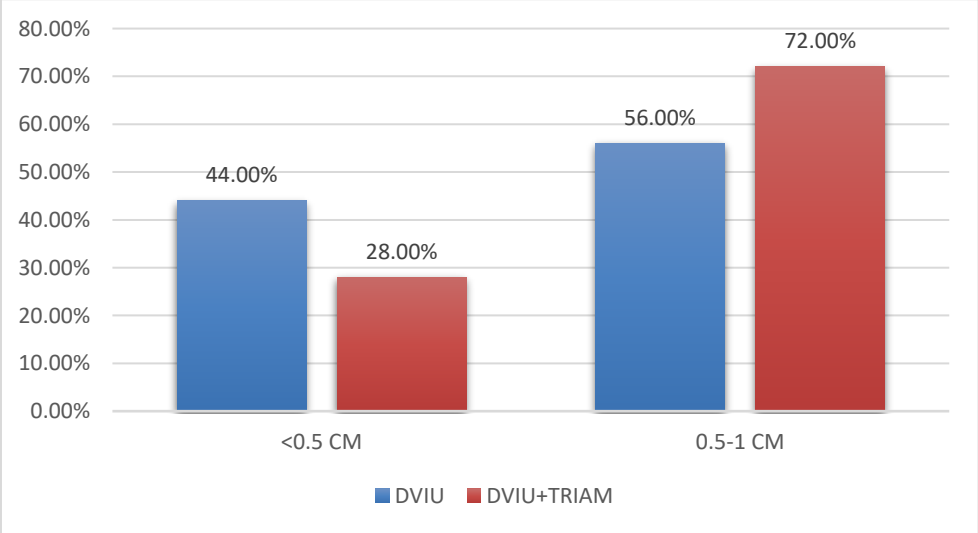

Fig3: STRICTURE CAUSES

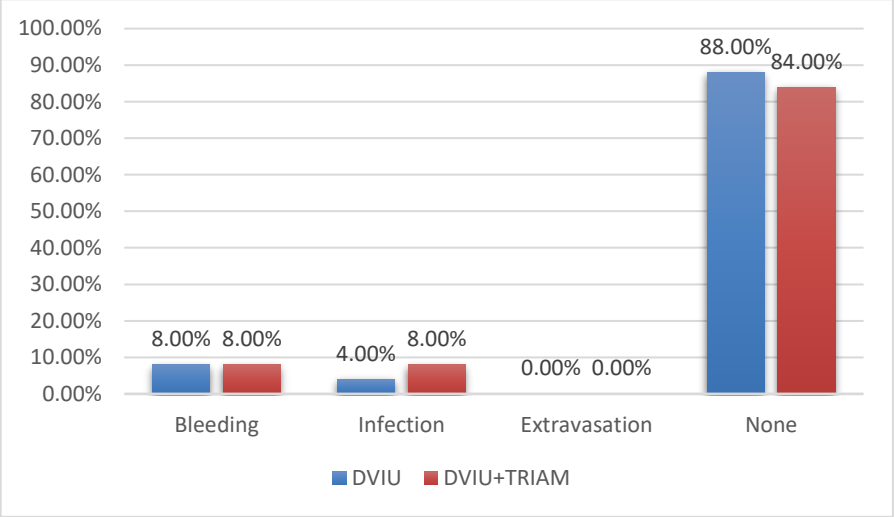

Fig4: RECURRENCE RATE

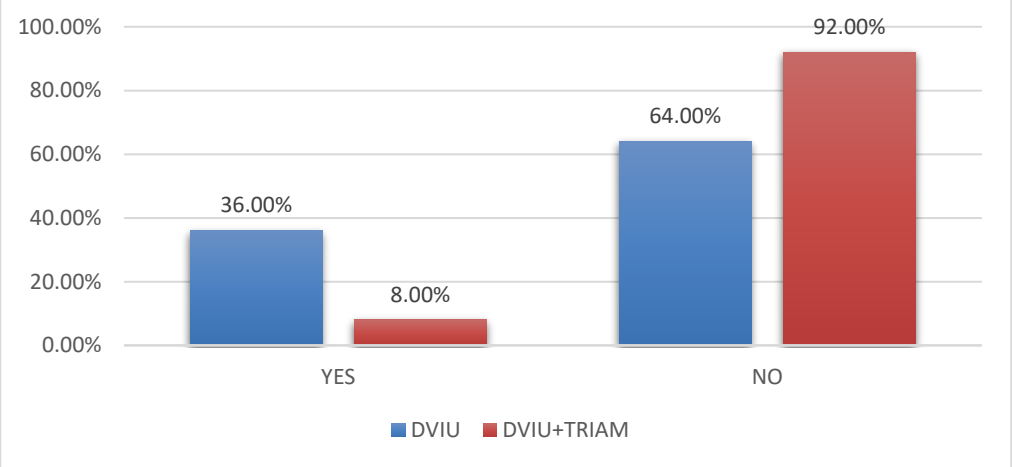

Fig5: COMPLICATIONS

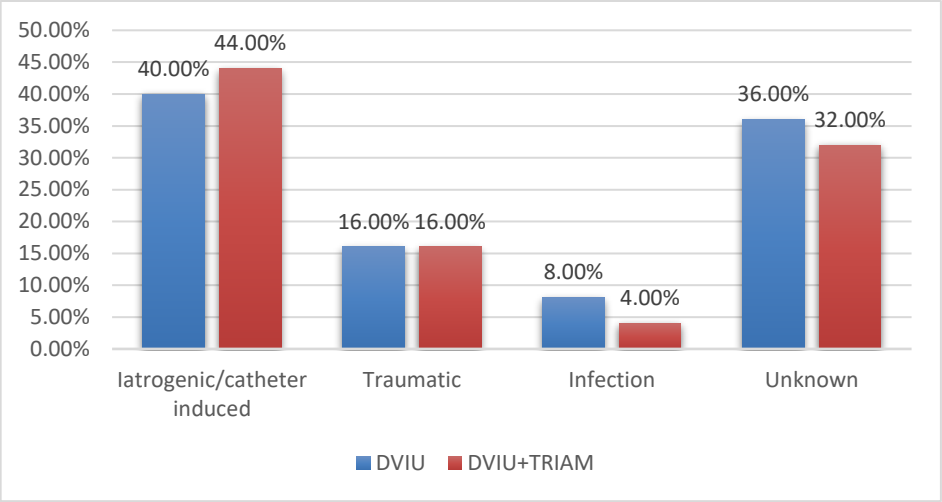

Fig6:TIME TO RECURRENCE

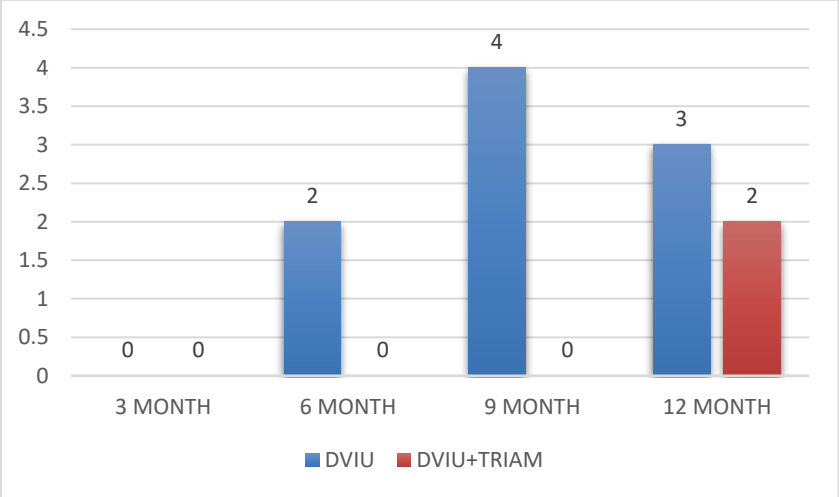

TABLE 5: TIME TO RECURRENCE

RECURRENCE	DVIU GROUP	DVIU+TRIAM GROUP	P VALUE
3 MONTH	0	0	0.231
6 MONTH	2(8%)	0	
9 MONTH	4(16%)	0	
12 MONTH	3(12)	2(8%)	
TOTAL	9(36%)	2(8%)	

DISCUSSION

Urethral stricture is known for a disease of recurrence since ancient times[1].The first DVIU was described by Ravasini in the year 1957[1]and he used electrocautery to incise the stricture while in 1971 Sachse used cold knife /sachse knife in urethrotomy[10].The most common cause of urethral stricture was infection although in the era of endourology iatrogenic cause leading the upperhand. A variety of technique including urethroplasty have been well described but DVIU as the most

common endourological intervention of choice among minimally invasive procedure for anterior urethral stricture less than 1.5cm but recurrence of stricture as one of the major disadvantage specially during a long period of observation[11-12]. As from review literature,the success rate of direct visual internal urethrotomy for urethral stricture is 30-40%[13,14] and is limited and high recurrence rate up to 65-90% with long term follow up for 2 years[13-16].Better results were observed in first intervention rather than multiple intervention which produce 0% success rate[13-16].

The probable reason behind the recurrence of stricture being the incomplete epithelial secondary healing by DVIU. The aetiopathogenesis as wound contraction narrows the urethral lumen before completion of epithelialisation[17].In multiple randomized studies mentioned about multiple radial incision as modification of previous single sachse knife incision[13-16] and leave the catheter for one week as to improve the success rate[11].

For the last decades many authors published the role of lasers in the form of Nd :YAG ,KTP, Argon ,Holmium for stricture urethra but none studies showed superior result.In a randomized study by Dutkiewicz et al compared laser vs sachse knife internal urethrotomy but safety and success rate almost similar although better and sustainable results were observed in DVIU[18].

A study by santucci et al in 2007 observed a higher recurrence rate(90%) after internal urethrotomy[19].A critical review of 365 operations in a published data reported recurrence rates 50%-75% during a long period of follow up (2 year period).In our study, the overall recurrence rate 22% and the recurrence rate higher in DVIU group was 36% almost similar to this study. The lower rate of recurrence in compare to Holm Nielsen et al study may be due to shorter follow up period[20].

A number of additive adjuvant therapies including mitomycinC[21],captopril gel[22],carboxymethylcellulose[23],hyalurornic acid, steroid have been described to minimize the recurrence rate of urethral strictures after DVIU. Gothlin and Akerlund first described local corticosteroid instillation in 1960[23] and later modified by Hebert in 1970 that intraurethral application of corticosteroid at the time of DVIU produces better result than DVIU alone[6].Submucosal injection of mitomycin C derived from streptomyces caespitosushas an important role in delaying the wound healing process by preventing growth of fibroblasts and epithelial cells and has anticollagen property and also can delay wound contraction[25].

M Shirazi et al, a phase 2 clinical trial described the application of captopril gel is a safe ,effective and nontoxic antifibrotic agent after DVIU for decreasing the recurrence with better outcome[22].In multicentre randomized control trial by Tian Y et al observed that intrurethral instillation of hyaluronic acid and carboxymethylcellulose prevent urehral stricture and cause reduction of pain after DVIU[26].Although a number of adjuvant technique proposed but their safety and recurrence rate and efficacy need to be consideredon longterm basis.

As a review literature by Mazdak et al described internal urethrotomy vs triamcinolone instillation after internal urethrotomy,studied 25 patients in which recurrence seen in 11patients out of 21(50%)and 5 patients out of 24(21.7%) in triamcinolone group[27].Korhonen et al.described intraurethral injection of triamcinolone after DVIU. In their study of total 38 patients ,21 had underwent endoscopic internal urethrotomy while 17 patients had received triamcinolone injection after internal urethrotomy. In their study, recurrence rate was 61% in patients who underwent internal urethrotomy and 71% in those who received triamcinolone[28].Hardec et al.had reported that corticosteroid injection atleast decreased the recurrence rate from 19.4% to 4.3%[29].In our

study there is a delayed time to recurrence of stricture although not significant (p=0.231) but similar to Hardec et al study.

In a study by Tabassi et al compare internal urethrotomy vs intraurethral triamcinolone injection.In their study of 70 patients ,recurrence was observed in 15 among 36 patients and 12 among 34 patients. Recurrence rate in both group found similar no statistical difference but time to recurrence significantly in triamcinolone group(8.08±5.55 vs 3.6±1.59 months)($p<0.05$)[30].Hosseini et al.intraurethral triamcinolone in 70 patients with clean intermittent catheterization after DVIU.30 patients used triamcinolone injection(experimental group) and 34 patients used water based jelly injections (control group). Recurrence rate in experimental group 30% and in control groups were 44%[31].In our study results were almost similar to Hosseini et al.study and Tabassi et al showed 8% recurrence rate in triamcinolone group ($p <0.041$;statistically significant) and time to recurrence delayed in DVIU +triamcinolone group (P value 0.231) which is not statistically significant may be due to short follow up period .In our study, we evaluated recurrence rate and the time to recurrence and data revealed that intraurethral triamcinolone injection remarkably delays the time to recurrence of urethral strictures and decrease recurrence rate after DVIU.

LIMITATION

Its a retrospective study ,the sample size is too small and follow up period is short. Further more randomized studies are required with large sample size and longterm follow up essential for precise results of steroid injection.

CONCLUSION

Intra-urethral triamcinolone injection into the urethral stricture site to avoid fibrosis is a safe and effective additive therapy after direct visual internal urethrotomy. Major complications were not noted due to the triamcinolone injection. Triamcinolone injection seems to be cost effective , produce lower side effects and plays a vital role to delay the time of recurrence .

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