Efficacy of holmium laser urethrotomy in combination with intralesional steroids in the treatment of bulbar urethral stricture: a randomized controlled trial

Mahmoud Amin, Ahmed A. Shorbagy, Hany M. Abdalla, Mohamed Shoeb, Waleed Mousa

Department of Urology, Faculty of Medicine, Ain Shams University Hospitals, Cairo, Egypt

Correspondence to Mahmoud Amin, MSC, Department of Urology, Faculty of Medicine, Ain Shams University Hospitals, Cairo 11772, Egypt
Tel: +20 100 567 6423;
e-mail: hodaamen90@gmail.com

Received: 02 April 2022
Revised: 18 April 2022
Accepted: 27 April 2022
Published: 04 January 2023

The Egyptian Journal of Surgery 2023, 41:708–713

Introduction
The aim was to evaluate the efficacy of holmium: YAG laser urethrotomy along with intralesional triamcinolone injection in decreasing the incidence of recurrence in the management of primary bulbar urethral stricture.
Materials and methods
A total of 124 male patients with primary short (<1.5) fresh bulbar urethral stricture disease were included in our study from 2020 to 2021. Patients were allocated randomly into two equal groups. Group A included those who underwent laser internal urethrotomy only and group B included those who underwent laser internal urethrotomy followed by injection of triamcinolone at the site of urethrotomy. A careful evaluation with uroflowmetry and ascending urethrography was *done* preoperatively. All patients were evaluated with uroflowmetry at 3 and 6 months, and retrograde urethrography was performed if needed.
Results
Each group included 60 patients. The results showed a success rate of 70 and 90% in groups A and B, respectively. In group A, eight cases (13.3%) had recurrence at the third month, whereas in group B, there was no recurrence, with a success rate of 100%. At the sixth month, 10 cases (16.7%) had recurrence in group A, whereas six cases (10%) in group B had recurrence. So, total recurrence in group A was 18 cases (30%) and in group B was six cases (10%), which was statistically different (P=0.006). In our study, we observed that the time of recurrence of urethral stricture in steroid-treated group was delayed to 6 months in comparison with nonsteroid-treated group. No major intraoperative or postoperative complications occurred. All complications were mild and managed conservatively. The difference was not statistically significant between both groups.
Conclusions
Intraurethral corticosteroid injection at the stricture site following holmium laser urethrotomy seems to be a safe and effective modality of treatment in decreasing the rate of stricture recurrence.

Keywords:
holmium laser, triamcinolone, urethral stricture, *uroflowmetry*

Egyptian J Surgery 2023, 41:708–713
© 2023 The Egyptian Journal of Surgery
1110-1121

Introduction

Urethral stricture is a common urinary tract disorder, reported since ancient times, with a significant effect on the quality of life [1,2]. Among the causes of urethral stricture are trauma and idiopathic and iatrogenic causes, for example, urethral catheterization, transurethral resection, and failed hypospadias repair [3].

The main treatment methods for urethral stricture are surgery, including endoscopic procedures to open surgical interventions. Among the methods, direct visual internal urethrotomy (IU) is widely used, using a cold-knife technique to incise short urethral strictures usually less than 2 cm, with recurrent rates ranging from 35 to 60% [4].

In recent decades, the holmium: YAG (Ho: YAG) laser has started to gain attention in the management of a urethral stricture less than 1.5 cm as an effective alternative to the gold standard cold-knife IU as it has shown a comparable outcome in both safety and efficacy [3]. However, to the best of our knowledge, long-term efficacy and recurrence conditions for holmium laser treatment have been rarely reported. Injection of steroids at the site of urethrotomy ostensibly prevents scar formation by enhancing endogenous collagenase and thus reducing the contracture rate.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

In this randomized controlled study, we aimed to evaluate the role of intraurethral steroid application simultaneously with holmium (Ho: YAG) urethrotomy in decreasing the incidence of recurrence and improving the success rate.

Materials and methods

A total of 124 male patients with urethral stricture disease, aged between 26 and 69 years, were treated in our institute from 2020 to 2021. Patients were allocated randomly into either group A or group B in a 1: 1 ratio. Group A included those who underwent laser IU only and group B included those who underwent laser IU with intralesional steroid injection. Ethical approval from the local committee at our institute was obtained. The diagnosis of urethral stricture was based on clinical history, uroflowmetry (peak flow rate is <15 ml/s), and ascending urethrography preoperatively.

Patients with single primary short bulbar urethral stricture (stricture length 0.5–1.5 cm) as evident on radiological studies were included in our study, whereas those with complete obliteration of the urethral lumen, balanitis xerotica obliterans, age less than 18 years, multiple strictures, active urinary tract infection, recurrent strictures, prior IU, prior urethroplasty, and pananterior urethral strictures were excluded from our study.

Laser device used in urethrotomy was Litho Quanta System. A 365 μm laser fiber with pulse energy from 1 to 2 J, frequency from 10 to 15 Hz, and total power 10–22.5 W was set up.

In group B, after laser urethrotomy, 80 mg of triamcinolone diluted with 5–10 ml of normal saline was injected intralesionally at the site of urethrotomy using William's endoscopic needle. At the two edges of incision site at 12-o'clock position, 1–2 ml was injected. Finally, 18-F silicone catheters were indwelled in both groups and kept for 3 days and then removed. Patients were discharged on first day postoperatively. All patients were evaluated with uroflowmetry at 3 and 6 months postoperatively, and retrograde urethrography was done only in case of symptomatic patient with uroflowmetry less than 12 m/s. We considered our procedure successful if the patient did not report any voiding difficulty, with the maximum flow rate (Qmax)=15 mL/s.

Statistical analysis

The data were coded and entered using the Statistical Package for the Social Sciences (SPSS) developed by three students at the University of Stanford (Norman H. Nie, C. Hadlai Hull and Dale H. Bent), after graduation N. Nie moved to the University of Chicago, USA, joined by Hull. The data were summarized using descriptive statistics, where mean and SD, median, and range were used for quantitative variables, and number and percentage were used for qualitative values. Statistical differences between groups were tested using χ^2–test for qualitative variables, and nonparametric Mann–Whitney test and Kruskal–Wallis test were used for quantitative variables that were not normally distributed. Correlations were done to test for linear relations between variables. *P* values less than or equal to 0.05 were considered statistically significant.

Results

A total of 124 male patients with primary bulbar urethral stricture ranged from 0.5 to 1.5 cm long were randomly allocated into one of two groups by computer random grouping, as shown in Figure 1. Mean age of the patients was 55.1 ± 9.1 years (26–69 years). The mean length of stricture in group A was 1.050 and in group B was 0.950; there was no statistically significant difference between both groups. According to the different causes of stricture, there was no statistically significant difference between both groups, as shown in Table 1.

The comparison between the mean Qmax between both groups preoperatively and 3 and 6 months after the operations is shown in Table 2. There was no statistically significant difference between both groups preoperatively, but there was a statistically significant difference in the mean Qmax between both groups after 3 and 6 months.

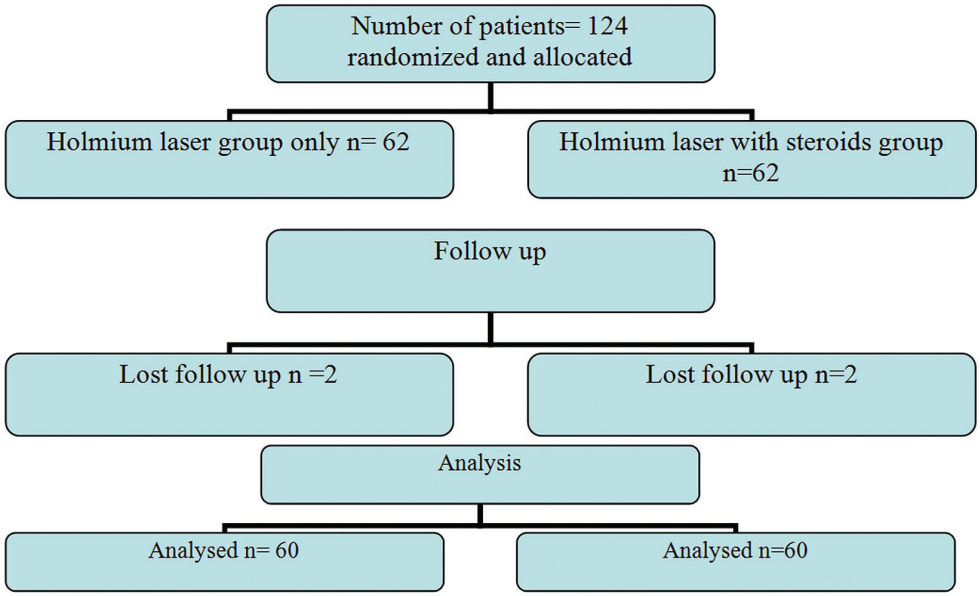
According to the recurrence of stricture, there was a statistically significant difference between both groups after 3 months. Follow-up after 6 months of operations showed that there was no statistically significant difference between both groups. The sum of total recurrence cases in both groups were statistically significant, as shown in Table 3.

Regarding the intraoperative and postoperative complications, there was no statistically significant difference between both groups (*P*=0.378 and 0.596, respectively).

Discussion

Urethral stricture is a common urological disease that impairs the patient's voiding function and quality of life. It is essential that urethral strictures are recognized early and appropriately treated [5]. Open urethroplasty has better results especially if performed at the early stage, but it requires a certain expertise and a long period of catheterization and hospital stay [6]. IU is a procedure of choice for correction of primary

Figure 1



Consort flow chart.

Table 1 Etiology of stricture

	Group		Total [*N* (%)]	*P* value
	Group A [*N* (%)]	Group B [*N* (%)]		
Cause				
Idiopathic	6 (10.0)	6 (10.0)	12 (10.0)	
Iatrogenic	24 (40.0)	30 (50.0)	54 (45.0)	
Infection	12 (20.0)	6 (10.0)	18 (15.0)	0.446
Trauma	18 (30.0)	18 (30.0)	36 (30.0)	

urethral strictures less than 1.5 cm. This intervention is minimally invasive with less morbidity and hospital stay compared with open surgery. Additionally, it is safe with low rate of perioperative complication and with a short learning curve and is easy to be repeated. However, recurrence of strictures remains its major drawback. The high rate of recurrence cannot probably be explained, but it may be related to the urethral scar tissue and excess fibrosis with lateral contracture [3].

Laser urethrotomy was first introduced in 1979, and it has been shown to be effective in a short-segment stricture less than 1.5 cm with a comparable outcome to the gold standard cold-knife optical urethrotomy. As reported by Niesel *et al.* [7], the success rate of neodymium YAG nd:yag laser was 50% and that of KTP laser was 59–61%. In addition, good results were reported by Kural *et al.* [8]. In their study of 13 patients, they reported a success rate of 69%, whereas Matsuoka *et al.* [9] in a study on 31 patients reported a success rate of 74%.

No currently available data report superiority of one laser over another. The advantage of holmium: Yag laser is its coagulation ability and shallow absorption (0.5 mm). It is presumed to reduce scar tissue formation. Spongiofibrosis occurs in varying degrees and narrows the urethral luminal caliber. So, there are some ideas of treating the fibrosis with antifibrotic agents with no or minimal complications such as halofugione, mitomycin C, bitoxin A, somatostatin analogs, captopril, and steroids [10]. Corticosteroids decrease the scar formation by reducing collagen and glycosaminoglycan synthesis and expression of inflammatory mediators [11]. There have been some prospective randomized clinical trials in recent literature on comparative study of steroid injection after IU over conventional IU methods. In our study, 124 patients were randomly allocated into two equal groups. Group A represented the holmium laser IU only, whereas group B represented the holmium laser IU with intralesional steroid injection.

In our study, there was no significant difference regarding the length and the etiology of stricture between the two groups (P=0.123 and 0.446, respectively).

Regarding the recurrence of stricture, in our study, the number of recurrent cases in group A was eight cases at the third month and 10 cases at the sixth month, with

Table 2 Qmax

	Group A							Group B						
	Mean	Median	Minimum	Maximum	SD	Percentile 25	Percentile 75	Mean	Median	Minimum	Maximum	SD	Percentile 25	Percentile 75
Pre-Qmax	9	9	7	11	1	8	10	9	9	6	11	1	8	10
Post-3m-Qmax	17	17	11	20	2	16	18	19	19	16	22	2	18	20
Post-6m-Qmax	15	16	10	19	3	15	17	18	19	10	21	3	17	19

total recurrence of 18 cases (30%). In group B, there was no recurrence at the third month, and there were six cases of recurrence at the sixth month (10%).

A study conducted by Yıldırım *et al*. [12] on 83 patients demonstrated that recurrence rate in IU by cold-knife only was 38% and in IU plus steroids was 5%. In disagreement with our study, Korhonnen *et al*. [13] injected 80 mg of triamcinolone to 17 of 21 patients after IU only at the 12-o'clock position and removed the catheter the day after the surgery. Although the IU only group had a 71% recurrence rate, the steroid injected group had 61% recurrence rate, and this may be because strictures included in the study were up to 2 cm, catheter was removed 1 day after the surgery, and longer follow-up.

Moreover, Kamyar *et al*. [14] demonstrated that the recurrence rate in IU by cold-knife was 42% and in IU plus steroids was 35%, and this may be owing to longer follow-up period.

Mazdak *et al*. [10] reported a study of 25 patients treated by IU and intraurethral submucosal triamcinolone injection. Recurrence was observed in 5 of 24 patients (21.7%), whereas 11 among 21 patients (50%) treated by IU alone reported recurrence. In another study, Tabassi and colleagues performed IU and triamcinolone injection in 34/70 patients with stricture. They noted a recurrence rate of 35.2% in the steroid injected group and 41.6% in IU only group. There was no statistically significant difference between the two groups (P=0.584) [15].

In 2012, Kumar and his colleagues treated 50 patients with a stricture length less than 3 cm by holmium laser with triamcinolone (80 mg) under spinal anesthesia. The overall recurrence rate was 24%. The success rate in patients with strictures less than 1 cm in length was 95.8%, whereas that in strictures of between 1 and 3 cm in length was 57.7% (P=0.002) [16].

Santosh Kumar reported a study on 50 patients with symptomatic urethral stricture who were treated with holmium laser urethrotomy, followed by injection of tetra-inject at the urethrotomy site. Tetra-inject was prepared by diluting a combination of 40 mg triamcinolone, 2 mg mitomycin, 3000 µg hyaluronidase, and 600 mg *N*-acetyl cysteine in 5–10 ml of saline, according to the stricture length. An indwelling 18-Fr silicone catheter was left in place for 7–10 days. All patients were followed up for 6–18 months postoperatively by history, uroflowmetry, and if required, retrograde urethrogram every 3 months. A total of 41 (82%) patients had a successful outcome,

Table 3 Rate of recurrence

	Group [*N* (%)]		Total	*P* value
	Group A	Group B		
Whole recurrence				
No	42 (70.0)	54 (90.0)	96 (80.0)	0.006
Yes	18 (30.0)	6 (10.0)	24 (20.0)	
Recurrence at 3 months				
No	52 (86.7)	60 (100)	112 (93.3)	0.006
Yes	8 (13.3)	0 (0.0)	8 (6.7)	
Recurrence at 6 months				
No	50 (83.3)	54 (90.0)	104 (86.7)	0.283
Yes	10 (16.7)	6 (10.0)	16 (13.3)	

whereas nine (18%) had recurrences during a follow-up ranging from 6 to 18 months. In less than 1-cm length strictures, the success rate was 100%, whereas in 1–3-cm and greater than 3-cm lengths, the success rates were 81.2 and 66.7%, respectively. This modality has an encouraging success rate, especially in those with short-segment urethral strictures (<3 cm) [17].

In our study, we observed that the recurrence of urethral stricture in steroid-treated group was delayed to the sixth month in comparison with the nonsteroid-treated group, where recurrence was observed earlier at the third month. In agreement with our study, Tabassi *et al*. [15] observed that the time of recurrence significantly decreased in the triamcinolone-treated group compared with the placebo group (8.08 ± 5.55 vs 3.6 ± 1.59 months) (P<0.05). Yıldırım *et al*. [12] observed that steroid injection prolonged the recurrence time significantly from 1 or 2 months to 6 months (P<0.03).

No major intraoperative or postoperative complications occurred. No patients in our study had postprocedural incontinence or impotence. All complications were mild and managed conservatively. The difference was not statistically significant between both groups (P=0.378 and 0.596, respectively). Five patients (8.3%) in group A had fluid extravasation, whereas eight patients (13.3) in group B had extravasation. In group A, seven cases (11.7%) had infection and four cases (6.7%) had scrotal swelling postoperatively, whereas in group B, 11 cases (18.3%) had infection and three cases (5%) had scrotal swelling.

However, more studies with larger population and long interval follow-up are required for better evaluation. In addition, more studies with different urethral stricture sites and larger size are required. Moreover, combination between steroids and other agents, for example, mitomycin C, hyaluronidase, and *N*-acetyl cysteine is required in an attempt to decrease the rate of recurrence after internal uretherotomy.

Conclusion

The clinical decision of stricture–recurrence–prevention techniques should be carefully tailored to every individual patient. Triamcinolone injection to the stricture site after holmium laser urethrotomy is a safe and effective adjuvant therapy for short-segment strictures, as it may decreases the recurrence rate significantly. As the course of urethral stricture recurrence is rather long, spreading over many years, further comparative studies with longer follow-ups are required to accurately evaluate the effect of steroid injection.

Financial support and sponsorship

Nil.

Conflicts of interest

There is no conflict of interest.

References

1 Wessells H, Angermeier KW, Elliott S, Gonzalez CM, Kirkby E, Kodama R, *et al*. Male urethral stricture: AUA guideline. J Urol 2016; 197:182.
2 Brandes SB, Morey AF. Advanced Male Urethral and Genital Reconstructive Surgery. New York, NY: springer; 2014. pp. 543–562.
3 Gamal MA, Higazy A, Ebskharoun SF, Radwan A. Holmium: YAG versus cold knife internal urethrotomy in the management of short urethral strictures: a randomized controlled trial. J Lasers Med Sci 2021; 12:e35.
4 Zhao LC. Management of urethral strictures. Urol Clin North Am 2017; 44:xv.
5 Anger JT, Buckley JC, Santucci RA, Elliott SP, Saigal CS. Trends in stricture management among male Medicare beneficiaries: under – use of urethroplasty? Urology 2011; 77:481–485.
6 Langston JP, Robson CH, Rice KR, Andrew Evans L, Morey AF. Synchronous urethral stricture reconstruction via 1-stage ascending approach: rationale and results. J Urol 2009; 181:2161–2165.
7 Niesel T, Moore RG, Alfert HJ, Kavoussi LR. Alternative endoscopic management in the treatment of urethral strictures. J Endourol 1995; 9:31–39.
8 Kural AR, Coskuner ER, Cevik I. Holmium laser ablation of recurrent strictures of urethra and bladder neck: prelimary results. J Endourol 2000; 14:301–304.
9 Matsuoka K, Inoue M, Iida S, Tomiyasu K, Noda S. Endoscopic antegrade laser incision in the treatment of urethral stricture. Urology 2002; 60:968–972.
10 Mazdak H, Meshki I, Ghassami F. Effect of mitomycin C on anterior urethral stricture recurrence after internal urethrotomy. Eur Urol 2007; 51:1089–1092.
11 Koc E, Arca E, Surucu B, Kurumlu Z. An open, randomized, controlled, comparative study of the combined effect of intralesional triamcinolone acetonide and onion extract gel and intralesional triamcinolone acetonide

alone in the treatment of hypertrophic scars and keloids. Dermatol Surg 2008; 34:1507–1514.

12 Yıldırım ME, Kaynar M, Ozyuvali E, Badem H, Cakmak M, Kosem B, Cimentepe E. The effectiveness of local steroid injection after internal urethrotomy to avoid recurrence. Arch Ital Urol Androl 2016; 87:295–298.

13 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; 22:263–269.

14 Kamyar T, Tabassi K, Yarmohamadi A, Mohammadi S. Triamcinolone acetonide combined with 5-fluorouracil suppresses urethral scar fibroblasts autophagy and fibrosis by increasing miR-192-5p expression. Urol J 2011; 8:13–16.

15 Tabassi KT, Yarmohamadi A, Mohammadi S. Triamcinolone injection following internal urethrotomy for treatment of urethralstricture. Urol J 2011; 8:132–136.

16 Kumar S, Kapoor A, Ganesamoni R, Nanjappa B, Sharma V, Mete UK. Efficacy of holmium laser urethrotomy in combination with intralesional triamcinolone in the treatment of anterior urethral stricture. Korean J Urol 2012; 53:614–618.

17 Kumar S, Kishore L, Sharma AP, Garg N, Singh SK. Efficacy of holmium laser urethrotomy and intralesional injection of Santosh PGI tetra-inject (triamcinolone, mitomycin C, hyaluronidase and *N*-acetyl cysteine) on the outcome of urethral strictures. Cent Eur J Urol 2015; 68: 462–465.