

Efficacy and Safety of Optilume; A Drug-Coated Balloon Treatment for Anterior Urethral Stricture

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ABSTRACT

Objective: To determine the efficacy and safety of Optilume; a drug-coated balloon (DCB) treatment for anterior urethral strictures.

Methodology: This multi-centered descriptive case series study was carried out in the Department of Urology and Renal Transplant, Sharif Medical City Hospital, Lahore and the Department of Urology, National Hospital & Medical Center, Lahore on thirty cases presenting with ≤ 3 cm strictures in the anterior urethra. This study was conducted from November 2021 to October 2022. Follow-up was done at two weeks, 3 months, 6 months, and one year. The primary efficacy endpoint was an improvement in International Prostate Symptom Score (IPSS), secondary outcomes included post micturition residual urine (PMRU), maximum urinary flow rate (Qmax), the International Index of Erectile Function (IIEF), and quality of life. The variables were analyzed by computer-based software and descriptive statistics were used to present the outcomes.

Results: A total of 30 patients were treated with Optilume DCB, 13(43%) patients completed one year follow-up and 17(56%) completed 6 months follow-up. Eighteen (60%) patients had a history of endoscopic treatment. There were no treatment-related side effects after one year of treatment. Success was achieved in 100% at a mean follow-up of 8.4 months and the baseline mean change in IPSS score was 18 at one year. Quality of life, Qmax flow rate, and PMRU improved significantly from the baseline.

Conclusion: One year treatment data shows that Optilume DCB is safe and effective for the treatment of recurrent strictures of the anterior urethra as it showed a significant improvement in the present study.

Keywords: Anterior urethral strictures. Quality of life International Prostate Symptom Score.

INTRODUCTION

Urethral stricture is a morbidity that could result due to inflammation, ischemia or any traumatic process. All these issues lead to the formation of scar tissue and consequently become the reason for low urine flow rate.¹ The annual cases that have been presented with this condition range from 200 to 1200 cases per 100 thousand which multiplies as the age of the population increases. In industrialized countries, its prevalence is less than 10%.² In addition to difficulty in treating urethral strictures, stricture recurrences are common.³

The treatment of urethral stricture disease has evolved over time from minimal invasive endoscopic procedures to urethroplasty. But recurrence rate of stricture is high for endoscopic treatments. Endoscopic management of anterior urethral strictures is made easier with Optilume DCB.⁴ Optilume DCB is an alternative to repeated urethroplasty and dilatations. Optilume DCB is an ideal option for patients undergoing repeated endoscopic urethral procedures and for patients who are not willing for urethroplasty or

are unfit for surgery.⁵

Optilume DCB coating has paclitaxel that has hydrophobic and lipophilic properties making it an ideal anti-proliferative agent for uptake and residency in urothelial tissue.⁶ It inhibits the post-procedure inflammatory response and provides sustained symptom improvement. Paclitaxel is anti-mitotic, anti-microtubule, anti-fibrotic, and anti-proliferative drug, thus stopping new tissue growth and prevents fibrotic scarring that leads to stricture recurrence.^{6,7}

Optilume DCB is a dynamic compliant balloon that expands at high pressure, expanding the lumen and creating microfissures in the urethral tissue. Upon inflation, the coating releases paclitaxel directly into the fissured tissue. Paclitaxel is absorbed by the urothelium where it resides for more than 30 days, preventing cell proliferation and fibrotic scar tissue generation.⁸

The present study was conducted to determine the efficacy and safety of Optilume, a drug-coated balloon treatment for anterior urethral strictures. Very less literature is available on the efficacy of Optilume DCB. So, the study will help in the evaluation of Optilume DCB in improving the overall quality of life in men with urethral strictures.

METHODOLOGY

This was a multi-centered descriptive case series study. This study included 30 male patients after the hospital's ethical committee approved the protocol. The sample

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elements were collected by non-probability consecutive sampling method. The study was carried out for a duration of one year starting from November 2021 to October 2022 in the Department of Urology and Renal Transplant, Sharif Medical City Hospital, Lahore and the Department of Urology, National Hospital & Medical Center, Lahore. Patients with single anterior urethral stricture measuring ≤ 3 cm in length on urethrogram, IPSS >14 , a maximum flow rate of 10 mL/sec, and at least 0-5 prior endoscopic stricture treatments were included in this study. Patients with prior urethroplasty, radical prostatectomy, penile prosthesis, artificial urethral sphincters, a neurogenic bladder, or pelvic radiation were excluded from this study.

Optilume DCB was performed on all patients. Optilume DCB 30 French (Fr) and 5 cm in length was used and balloon was inflated at a pressure of 10-12 atm for 7-10 minutes. Stricture dilatation was confirmed visually on urethroscopy. Patients were followed-up at 14 days, three months, six months, and 12 months. Each follow-up included IPSS, maximum flow rate, PMRU, and IIEF.

A key safety endpoint was urethral fistulas, urinary retention >14 days' posttreatment, stress incontinence, or urethral rupture associated with treatment. International Prostate Symptom Score improvement of 50% relative to a baseline without retreatment was our primary efficacy endpoint. If the IPSS improvement at the last follow-up did not reach 50% or retreatment was required, the patient was considered to have failed treatment. In addition to sexual function and overall

satisfaction, Qmax, and PMRU were secondary endpoints.

STATISTICAL ANALYSIS

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23. Quantitative data was presented with the use of mean & standard deviation. Qualitative data was presented with frequency & percentage. Paired t-test & repeated measures ANOVA was used to determine the mean difference in the significant difference of the mean value changes for baseline to the follow-up visit. A p-value of ≤ 0.05 was taken as significant.

RESULTS

The mean age of the study patients was 50 ± 14.34 years and its range was 20-80 years. The suprapubic catheter was noted in 5 (16.67%) cases. On clinical investigation of the stricture aetiology, it was observed that 13 (43%) cases were iatrogenic, 11 (36%) cases were idiopathic, and 6 (20%) cases were traumatic. The majority of the cases [10 (33%)] had only one previous endoscopic treatment (Table 1).

There were no treatment-related side effects like urethral rupture, stress incontinence, and urinary retention. Among 10 encountered adverse events in our study participants, 16% had urinary tract infections, 6% had fevers and 6% had dysurias. At a mean follow-up of 8.4 months, 30/30 (100%) of men achieved functional treatment success.

The mean change in the IPSS score from baseline to 12th month follow-up was 18 ± 0.04 , IPSS quality of life score was 4 ± 0.19 , overall satisfaction score 1.9 ± 0.26 ,

Table 1: Patient Demographics and Urological Variables

Variables		Values
Age (Years)	Mean \pm SD	50 \pm 14.34
	Range	20-80
Gender Frequency & Percentage	Male	30(100%)
Suprapubic Catheter at Baseline Frequency & Percentage		5(16.67%)
Stricture Aetiology Frequency & Percentage	Iatrogenic	13(43.3%)
	Idiopathic	11(36.67%)
	Traumatic	6(20%)
Stricture Length in mm Mean \pm SD (n)		15 \pm 4.2(30)
Pretreatment Direct Vision Internal Urethrotomy		1/30(3.3%)
Number of Previous Endoscopic Treatments Frequency & Percentage	0	3(10%)
	1	10(33.3%)
	2	8(26.7%)
	3	6(20%)
	4	2(6.7%)
	5	1(3.3%)

Table 2: Mean Changes in the Study Variables from Baseline to the Follow-up Visits

Category	Baseline Mean±SD (n)	3 Months Mean±SD (n)	6 Months Mean±SD (n)	12 Months Mean±SD (n)	p-value
IPSS	25±3.56(30)	9.1±6.3(30)	8.6±5.18(30)	7±3.6(13)	0.00*
IPSS Quality of Life	4.6±0.76(30)	0.9±1.52(30)	0.8±0.89(30)	0.6±0.95(13)	0.00*
IEF: Overall Satisfaction	6.3±2.67(30)	7.8±2.53(30)	7.4±2.87(30)	8.2±2.41(13)	0.00*
Qmax (mL/sec)	5.3±2.56(30)	22±12.54(30)	21.6±10.78(30)	18±10(13)	0.00*
PMRU (mL)	150.4±104.6(30)	41.5±36.56(30)	35.2±42.84(30)	26.4±31.08(13)	0.00*

*Significant p -value ≤ 0.05

Qmax score was 12.7 ± 7.44 & PMRU score was 124 ± 73.52 . All the mean changes were significantly different when compared with the baseline (Table 2).

DISCUSSION

Urethral strictures are nowadays a common problem among the men above 40 years and cause a substantial economic burden. The epidemiology of urethral strictures varies as it depends on multiple factors that enhance its chances to occur in a population. Moreover, the incidence of this disease is widely due to the underlying risk factors that need to be addressed.⁶

Our results showed that at a mean follow-up of 8.4 months, 30/30 (100%) of men achieved functional treatment success. The mean change in the IPSS score from baseline to 12th month follow-up was 18 ± 0.04 , IPSS quality of life score was 4 ± 0.19 , overall satisfaction score 1.9 ± 0.26 , Qmax score was 12.7 ± 7.44 & PMRU score was 124 ± 73.52 . All the mean changes were significantly different when compared to the baseline. Another multi-centered study included 53 patients with recurrent strictures with 1 to 4 prior endoscopic treatments. These patients were treated with Optilume and forty six patients completed their follow-up after 24 months. Thirty two patients had at least 50% improvement in IPSS without retreatment. The mean baseline IPSS was improved from 25.2 to 6.9 after 24 months ($p < 0.0001$). Flow rate, post void residual urinary volume, and quality of life significantly improved from baseline. They concluded that Optilume is safe for the treatment of urethral strictures and it has good efficacy.⁹

A single-blind randomized controlled trial was conducted on 127 patients. The trial reported that Optilume is a safe treatment option and it is superior to direct vision internal urethrotomy.¹⁰ In our study, there were no treatment-related side effects like urethral rupture, stress incontinence, and urinary retention. Among 10 encountered adverse events in our study participants, 16% had urinary tract infections, 6% had fevers, and 6% had dysurias.

A study conducted by Virasoro et al. showed that there were no serious adverse events reported within 90 days of the treatment. There were seven cases of cystoscopic recurrence, five retreatments, and two patients left the

study early due to symptom recurrences.⁸ Another study reported no significant device-related side effects. They found fever in 8%, headache in 6%, urinary tract infection in 17%, dysuria in 7%, and acute urinary retention in 6%.⁹

The results of this study are in line with the findings of the ROBUST I study with 1 year, 2 years, and 3 years follow-up. However, further ROBUST I study findings after 2nd and 3rd year follow-ups showed that Optilume paclitaxel-coated balloons were effective in treating recurrent strictures.^{11,12} According to literature reports, 50% to 0% of those with 2 and 3 prior interventions experienced success following endoscopic treatment of recurrent urethral strictures.^{12,13} After three years of treatment with Optilume DCBs, 77% of patients remain free from repeated interventions. With the Optilume drug-coated balloon, paclitaxel is circumferentially delivered while dilation is taking place. In minimally invasive vascular applications, paclitaxel serves as an anti-fibrotic & anti-proliferative coating to prevent restenosis.¹⁴

In the management of urethral strictures, the Optilume drug-coated balloon represents as a significant advancement. Before urethral dilatations and visual internal urethrotomies were available treatment modalities.^{2,15} When these techniques failed, men had no choice but to undergo urethroplasty. With the Optilume drug-coated balloon, one can avoid repeated dilatations and urethroplasty for the rest of the life. Patients who are poor surgical candidates or decline urethroplasty may benefit from this treatment as an alternative to current endoscopic management. Paclitaxel's anti-proliferative properties reduce collagen reformation when applied locally to scar tissue.^{16,17}

Radiation therapy, penile urethral strictures, bladder neck contractures, or lichen sclerosis may have adversely affected the DCB.¹⁸ The results of this study are consistent with the ROBUST study except a minor deflection in the adverse reactions. Resultantly, it is not wrong to conclude that the introduction of Optilume DCB is a good addition to available treatment options for urethral strictures.

CONCLUSION

Optilume DCB is a safe procedure with low symptomatic recurrence rates one year after the procedure. It has not only successfully addressed the issue, but also caused an improvement in the quality of the life. We recommend that Optilume DCB should be opted by the urologists for the management of urethral strictures.

LIMITATIONS & RECOMMENDATIONS

Like every clinical research, this study also has limitations. Due to financial constraints, the study could only be conducted up to a follow-up of one year with the selection of cases who already had urethral stricture disease. Due to the absence of real aetiology & cause of this condition, the results are a little less precise. Moreover, the smaller sample size and the corresponding results may be less important for a wider population. Hence, considering this weakness of the study, we recommend that more such studies are needed to be carried out on the same analogy on a larger sample size with ample financial assistance. Future studies should also address the wider geographical population for a better understanding of the results, treatment options, and effectiveness of Optilume DCB.

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