THE EFFICACY AND SAFETY OF TOPICAL TRIAMCINOLONE IN REDUCING URETHRAL STRICTURE RECURRENCE FOLLOWING INTERNAL URETHROTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objective: *This systematic review aims to determine the efficacy and safety of topical triamcinolone in reducing urethral stricture recurrence following internal urethrotomy procedures.* ***Material & Methods:*** *A systematic literature search was performed in Cochrane Library, Pub Med and Google Scholar with the related keywords. The statistical analysis was conducted using a Review Manager v.5.4.1.* ***Results:*** *We identified 6 RCTs with a total of 316 patients diagnosed with urethral stricture undergoing internal urethrotomy. The statistical analysis appeared tol ower the recurrence rate significantly inpatients undergoing internal urethrotomy with the adjuvant therapy of topical triamcinolone (RR 0.55, 95% CI 0.38 – 0.78, p = 0.0008).* ***Conclusion:*** *Additional treatment with topical triamcinolone has the benefit of declining the recurrence rate ofurethral stricture following internal urethrotomy.*

Keywords: *Triamcinolone, urethral stricture, internal urethrotomy.*

ABSTRAK

Tujuan: *Tinjauan sistematis ini bertujuan untuk mengetahui efikasi dan keamanan triamcinolone topikal dalam mengurangi striktur uretra berulang setelah prosedur uretrotomi interna.* ***Bahan & Cara:*** *Penelusuran literatur sistematis dilakukan pada Cochrane Library, Pub Med dan Google Scholar dengan kata kunci terkait. Analisis statistik dikerjakan menggunakan Review Manager v.5.4.1.* ***Hasil:*** *Kami mengidentifikasi sebanyak 6 uji acak terkontrol dengan total 316 pasien yang didiagnosis dengan striktur uretra yang menjalani uretrotomi interna. Hasil analisis statistik menunjukkan penurunan tingkat kekambuhan striktur secara signifikan pada pasien dengan pengobatan tambahan triamcinolone topikal (RR 0.55, 95% CI 0.38 – 0.78, p = 0.0008).* ***Simpulan:*** *Terapi tambahan dengan triamcinolone topikal terbukti bermanfaat dalam menurunkan tingkat kekambuhan striktur uretra setelah prosedur uretrotomi interna.*

Kata kunci: *Triamcinolone, striktur uretra, uretrotomi interna.*

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INTRODUCTION

Urethral stricture is a narrowed segment of the anterior urethra resulting from spongiofibrosis. The incidence of urethral stricture is estimated at approximately 229-627 per 100.000 males, with the anterior part of the urethra (92.2%) representing the most frequently affected, subsequently followed by the bulbar urethra (46.9%).[1] Idiopathic, iatrogenic (catheterization and transurethral surgery), inflammatory, and trauma (pelvic fracture) are the most common causes of urethral stricture.[2] Urethral stricture not only results in significant morbidity and affects the patient's quality of life (QoL)[3] but also incurs considerable costs for treatment and burdens the healthcare system due to the possibility of recurrence.[4]

Urethroplasty is regarded as the gold standard therapy for urethral stricture due to its great long-term efficacy and minimal recurrence rate.[5] However,urethroplasty is not always feasible and necessary to seek a specialized tertiary center. Direct vision internal urethrotomy (DVIU) is widely considered the most common minimally invasive procedure for managing urethral stricture.[6] None the less, because of its substantial rate of recurrence

which ranges from 9 to 60%, this kind of treatment is only suggested in certain circumstances, like primary stricture shorter than 2 cm and non-obliterative in the bulbomembraneous urethra.[7-9]

Many complementary procedures such as in dwelling catheterization, intermittent self-catheterization (ISC), and urethral stenting have been proposed to deal with this problem. The addition of corticosteroids to these treatments may further improve outcomes by stimulating the action of endogenous collagenases and down regulating collagen deposition. This allows for a healthier healing process of the mucous membranes, reduces the excessive formation of scar tissue, and declines the risk of restenosis in the urethral lumen.[10-11] Corticosteroids like triamcinolone, can be administered through intra lesional injection or topical application, such as instillation within the urethral lumen or as a catheter lubricant.[10,12] The topical administration of corticosteroids is very simple and inexpensive in practice. However, there is still lacking evidence to support the use of corticosteroids in the literature.

OBJECTIVE

This systematic review and meta-analysis aims to analyze the efficacy and safety of topical triamcinolone in preventing recurrent urethral stricture after internal urethrotomy procedures.

MATERIAL & METHODS

This study was conducted in compliance with the Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 (PRISMA) Protocol.[13] The articles were searched using Pub Med, Cochrane Library, and Google Scholar data bases up to June 2023. Keywords related to urethral stricture, urethrotomy, corticosteroids, or triamcinolone were searched.We applied the following inclusion criteria:(1) Randomized controlled trials (RCTs) comparing topical corticosteroids use (administered as a catheter lubricant or intra luminal instillation) versus no corticosteroids after DVIU,(2) adult (≥ 18 years) male patients diagnosed with urethral stricture

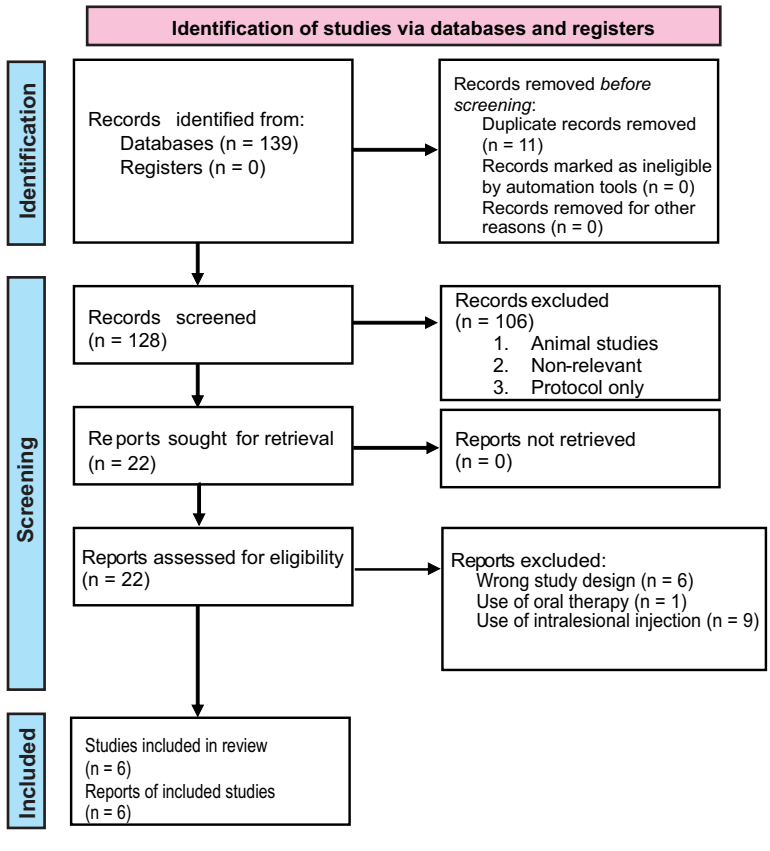

Figure 1. PRISMA flowchart diagram of the search strategy.

Table 1. Baseline characteristics of the included studies.

Author	Design	Group	n	Mean age ± SD (years)	Stricture etiology, n (%)	Stricture location	Mean stricture length ± SD (cm)	Intervention	Follow-up (months)	Recurrence rate (%)
Mazdak et al. 2020	RCT	Intervention Control	33 33	43.6 ± 16.3 50.2 ± 18.0	Traumatic 34 (51.5), inflammation 13 (19.7), idiopathic 19 (28.8)	NS	1.9 ± 1.3 1.7 ± 0.3	Intraurethral lumen instillation with triamcinolone	36	4/33 16/33
Regmi et al. 2018	RCT	Intervention Control	27 28	37.2 ± 1.6 36 ± 1.7	Traumatic 26 (47.2), inflammatory 12 (21.9), other 17 (30.9)	NS	0.93 ± 0.33 1.07 ± 0.32	Catheter lubricated with triamcinolone	12	6/27 13/28
Ergun et al. 2015	RCT	Intervention Control	30 30	61.2 60.7	Iatrogenic 48 (80), idiopathic 12 (20)	NS	NS	Catheter lubricated with triamcinolone	24	9/30 10/30
Yesil et al. 2013	RCT	Intervention Control	22 19	45.1 ± 8.0 47 ± 8.8	Instrumentation 12 (29.0), trauma 3 (7.0), infection 7 (17.0), idiopathic 19 (46.0)	Bulbar	NS	Catheter lubricated with triamcinolone	36	3/22 3/19
Gucuk et al. 2010	RCT	Intervention Control	15 15	31.2 ± 8.3 35.2 ± 7.9	Trauma 9 (30), infection 4 (13.3), instrumentation 7 (23.3), idiopathic 10 (33.3)	Bulbar	0.83 ± 0.27 0.83 ± 0.19	Catheter lubricated with triamcinolone	16.4 ± 2.97	3/15 7/15
Hosseini et al. 2008	RCT	Intervention Control	30 34	37.7 ± 17.1 34.5 ± 13.3	Urethral distraction 29 (45.6), straddle injury 12 (18.4), catheter 10 (15.7), other 13 (20.3)	NS	0.85 ± 0.40 0.90 ± 0.30	Catheter lubricated with triamcinolone	12	9/30 15/34

RCT: randomized controlled trial; NS: not specified

undergoing DVIU, irrespective of the etiology, length, location, or history of prior treatments. We excluded studies that involved intra lesional injection of corticosteroids,case reports, animal studies, and systematic or narrative reviews.

All authors independently carried out the data extraction. The extracted data included the source, methods, sample characteristics, and intervention. Additionally, the results of each study were cross-checked using a standard form by each reviewer. The authors had a discussion to settle any differences. Other authors are consulted to resolve the disagreement if this author is unable to reach a consensus, and the majority vote is used to make the final decision. We extracted and presented all of the data in the tabulation table.

Study heterogeneity was analyzed using the I2 statistics and P-values.[14] We selected a random-effects model if there was considerable heterogeneity (I2>50%, P<0.05). Conversely, we applied a fixed-effect model (I2<50%, P > 0.05). We represented the primary outcome of this study as a risk ratio (RR) with a 95% confidence interval (95% CI). We performed statistical analysis with software namely Review Manager v.5.4.1 to generate the forest plots containing a pooled analysis.

RESULTS

We evaluated a total of 139 records by searching multiple databases. After eliminating the duplicates, we scrutinized 128 studies and investigated 22 articles. Ultimately, we identified six RCTs 14-19 qualified to be included in the pooled analysis with 316 patients diagnosed with urethral stricture who underwent DVIU intervention. The study selection process followed the PRISMA guidelines described in Figure 1.

An overview of the baseline characteristics of the study is displayed in Table 1. All of the included studies were prospective RCTs that evaluated the efficacy of the administration of topical triamcinolone, either through intraluminal instillation or lubricated catheterization, as an

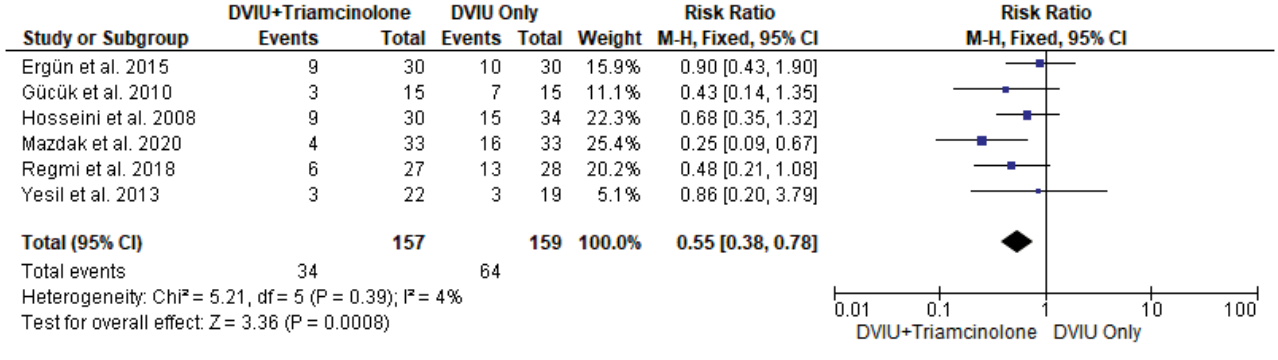

Figure 2. Forest plot analysis of the recurrence rates between the triamcinolone group compared to the control group.

adjunct treatment after internal urethrotomy. No significant difference from each trial was found in the length of urethral stricture. The majority of the strictures were primary ones, and the etiology of the strictures varied, as shown in Table 1.

We incorporated six RCTs 14-19 to determine the rate of urethral stricture recurrence the DVIU procedure. The study comprised 157 patients who received additional treatment with topical triamcinolone, while the control group consisted of 159 patients. Based on the forest plot analysis shown in Figure 2, patients undergoing DVIU with additional topical triamcinolone therapy showed a significant reduction in the recurrence rate of urethral stricture compared to the control group (RR 0.55, 95% CI 0.38 – 0.78, p = 0.0008). A fixed-effect model for statistical analysis was set up because of low evidence of heterogeneity among the studies (P = 0.39, I2 = 4%).

Of all six RCTs, three studies noted that there were no adverse events in their trial. Regmi et al., Ergun et al., and Hosseini et al. reported no local or systemic complications related to the administration of topical triamcinolone in their trials.15,17,18 However, none of the studies provided detailed information on complications related to the treatment. Gucuk et al., Yesil et al., and Mazdak et al. did not report adverse event outcomes in their trials.[16,19,20] Thus, a meta-analysis was insufficient due to the lack of data.

DISCUSSION

This systematic review investigated whether topical triamcinolone is effective and safe to decline recurrent urethral stricture following internal urethrotomy. There was a total of six including RCTs 14-19, in which 157 patients underwent DVIU followed by the topical administration of triamcinolone as a catheter lubricant or intraluminal instillation on the urethra, and 159 patients underwent DVIU procedures followed by catheter lubrication without triamcinolone.We discovered that the recurrence rate of urethral stricture was significantly lower in patients who received topical triamcinolone following DVIU (RR 0.55, 95% CI 0.38 – 0.78, p = 0.0008). This finding supports the use of topical corticosteroids as adjuvant treatment after the DVIU procedure.

Internal urethrotomy or DVIU is frequently employed as the initial treatment for primary short urethral stricturesless than 1.5 cm.[1] Although DVIU can efficiently remove the scar epithelium to facilitate secondary wound healing, this procedure no longer ensures an approximation of the epithelium. Therefore, if epithelialization progresses before wound contraction, DVIU will only be effective, or stricture recurrence is undesirable.[21] The addition of topical agents like corticosteroids to this mode is intended to minimize stricture recurrence rates. This might be explained by the use of corticosteroids on the torn mucosal strip, which occurs after dilating the stenosis, resulting in reduced collagen deposition and stimulation of endogenous collagenase enzymes. Rapid tissue re-epithelialization is promoted to prevent the development of excessive scar tissue and restenosis.[10,11]

Our findings in this systematic review are parallel with the systematic review by Verla et al., regarding the combination of intermittent self-catheterization (ISC) with topical corticosteroids after DVIU procedures. They found that the recurrence rates in groups of patients who performed ISC using a lubricated catheter with corticosteroids were significantly lower than without corticosteroid lubricant in a short-term period.[12] However, all of the studies in this review used only one mode of topical corticosteroid application as a catheter lubricant. In our systematic review, we included the study by Mazdak et al. that used an intraurethral instillation of triamcinolone providing statistically significant results in reducing the rate of stricture recurrence.[20]

It is important to note that all studies included in this meta-analysis focused on the primary, isolated, and short strictures located in the bulbomembranous segment, which was predominantly managed with DVIU alone. Therefore, the findings of this study cannot be utilized to provide recommendations for other patient subgroups.

Undeniably, this systematic review is not without limitations. We solely investigated the analysis of the effectiveness of topical triamcinolone to minimize urethral stricture recurrence after internal urethrotomy. However, due to the lack of data, we are unable to further analyze the safety of topical triamcinolone. The safety profile of topical triamcinolone or other corticosteroids in patients undergoing internal urethrotomy should be the main focus of future studies. Ultimately, only six RCT studies were incorporated into this study. Thus, a meta-analysis comprising a greater number of randomized controlled trials is mandatory to validate the results.

CONCLUSION

In conclusion, topical corticosteroids (triamcinolone) application to the urethra as a catheter lubricant or instillation into the urethral lumen may decline urethral stricture recurrence following internal urethrotomy procedure.

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