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Conservative Management of Penile and Urethral Lichen Sclerosus: A Systematic Review

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Purpose: We evaluate the efficacy and safety profiles of currently available conservative management options for penile and urethral lichen sclerosus.

Materials and Methods: A systematic review of existing literature on lichen sclerosus was conducted utilizing the PubMed, Embase, and Web of Science databases. References were assessed for relevance to nonsurgical management of male genital lichen sclerosus by title and abstract by 3 independent reviewers, then reviewed in full and in duplicate by 5 independent reviewers.

Results: Seventeen studies describing conservative management of histologically confirmed penile and urethral lichen sclerosus in male patients were included in the final review. We present available evidence supporting the use of 4 major treatment modalities represented in the existing literature: topical corticosteroids, tacrolimus, platelet-rich plasma, and CO_2 laser. We also briefly discuss the limited studies on the use of oral acitretin and polydeoxyribonucleotide injections. Outcomes assessed include symptoms, clinical appearance, quality of life, sexual satisfaction, adverse effects, and long-term efficacy of treatment.

Conclusions: Topical corticosteroids remain the mainstay of conservative management of penile and urethral lichen sclerosus, with current literature supporting the use of other therapies such as tacrolimus and platelet-rich plasma as alternatives or adjuvant treatments when escalation of treatment is necessary. Future research should further explore the efficacy and safety of newer therapies through additional controlled clinical trials in the targeted population.

Key Words: lichen sclerosus et atrophicus, male genital lichen sclerosus, urethral stricture, conservative management

Penile lichen sclerosus (LS), also known as balanitis xerotica obliterans, is a chronic inflammatory disease of the glans penis and foreskin. LS is more common in the uncircumcised and can affect all age groups.[1,2] Cross-sectional studies have suggested a prevalence in males of 0.0014% to 0.07%, compared with at least 1% for females.[3-8] Penile LS causes symptoms including pruritis, burning sensation, and pain, and can lead to significant complications including phimosis, buried penis, urethral stricture, and malignant transformation to squamous cell carcinoma.[5,9,10] Surgery has classically been the centerpiece of treatment; however, high recurrence and complications rates from surgery have created a growing need for robust conservative therapeutic options.[11]

While many options for conservative management have been described in women, most studies in men have focused on topical corticosteroids and surgery. Topical corticosteroids in adult

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males can effectively control symptoms in 59% to 88% of cases; however, corticosteroids are not curative and may have the potential to trigger latent infections such as human papillomavirus.[12-16] Less commonly utilized second line treatments include tacrolimus, topical androgens, ultraviolet radiation, and oral acitretin but existing literature has largely focused on the treatment of vulvar LS with these modalities. CO_2 laser therapy is also available as a less-invasive procedural approach that can be done under local anesthesia.

Given this context, our systematic review aims to describe the current evidence regarding conservative management options for penile and urethral LS. Herein, we summarize the evidence for use of the main conservative treatment options explored in the current literature and we assess the efficacy and safety of each treatment.

MATERIALS AND METHODS

Search Strategy

Following a registered protocol (PROSPERO CRD42022324674), we systematically searched PubMed, Embase, and Web of Science up to June 19, 2023. We focused our search on LS and male genital disease (Figure 1 and Supplementary Appendix 1, https://www.jurology.com). We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement guidelines.[15] Ethical approval was not indicated because this review does not constitute human subjects research.

Eligibility Criteria

Studies published as clinical trials, cohort studies, case control studies, and case series with greater than 3 patients were included. Reviews, letters to the editor, communications, and case reports were excluded. We only considered articles published in the English language. For inclusion, studies had to assess the efficacy of a

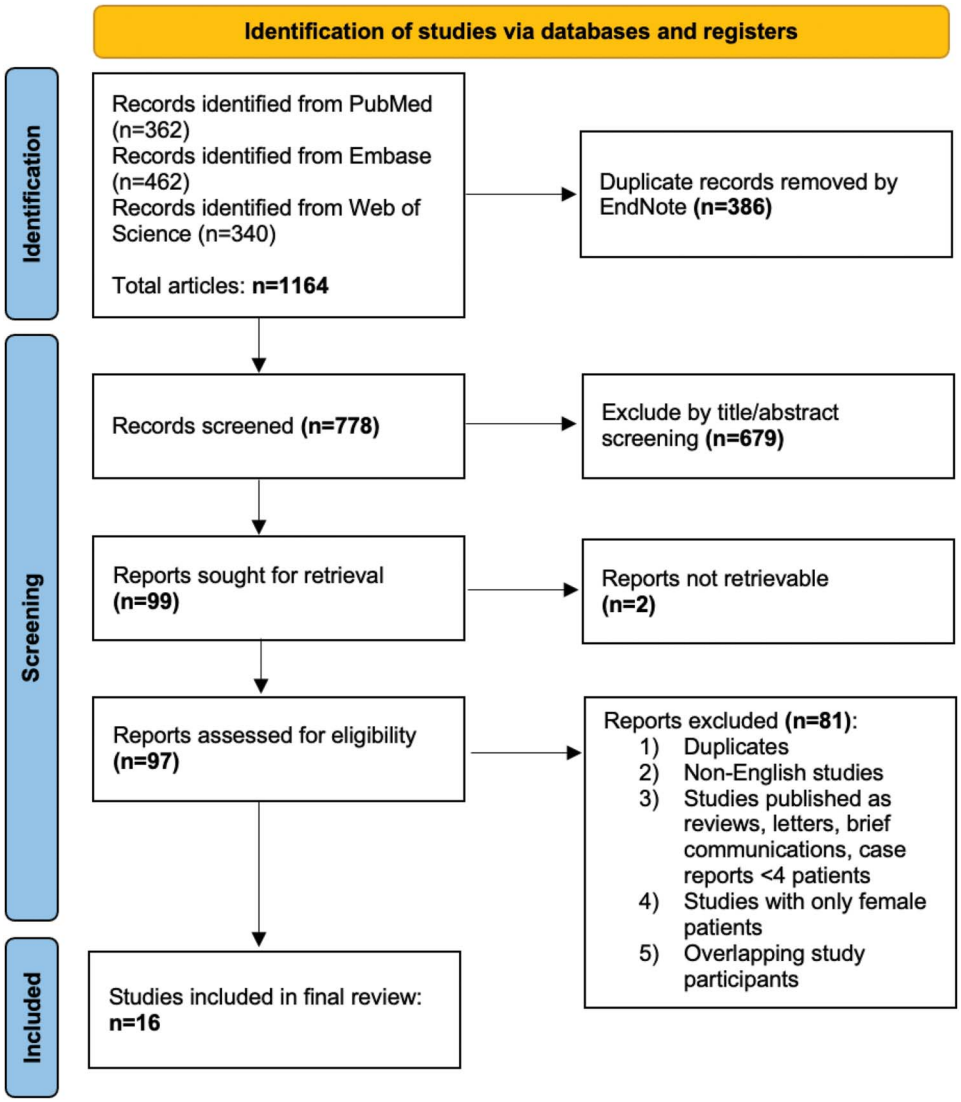

Figure 1. Methodology for systematic review of articles. Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 flow diagram for new systematic reviews including searches of databases and registers only.

nonsurgical treatment for LS in male patients. We included CO_2 laser vaporization as a conservative procedural treatment option. Studies solely examining incidence or classification of LS or efficacy of surgical treatments were excluded. Studies including female patients were only included if data was stratified by sex. No medical librarian was consulted for this review. Our search included gray and white literature, but we did not find any that satisfied inclusion criteria.

Data Collection and Abstraction

Articles were screened for relevance by title and abstract by the reviewers (C.S., N.H., M.N.). In addition, all references of included studies, existing review articles, and treatment guidelines were screened. After applying initial exclusion and inclusion criteria, 5 independent reviewers (C.S., N.H., M.N., U.G., J.G.) conducted a full text review to ascertain final inclusion. Every record was screened by 2 reviewers independently and in duplicate. Disagreements were resolved by a senior investigator (C.J., B.N.B.). Methodology for systematic review of articles as outlined in the PRISMA Flow Diagram can be found in Figure 1. Data collected from articles include patient demographics, disease history, treatment details, reported adverse effects, and treatment efficacy defined as resolution of symptoms or reduced need for further intervention. A meta-analysis was not performed due to the heterogeneous outcomes assessed by the studies. Risk of bias was assessed using the Newcastle-Ottawa Scale and the Cochrane Risk of Bias assessment version 2.[16]

RESULTS

Description of Studies

Of 778 articles initially identified from our search strategy, 16 articles met inclusion criteria. These studies include 507 male patients and 6 treatments: clobetasol propionate, tacrolimus, platelet-rich plasma (PRP), CO_2 laser vaporization, acitretin, and polydeoxyribonucleotide (PDRN) injection (Figure 2).[17-20] All studies recruited adult men aside from 1 study examining the use of topical tacrolimus in boys. The median Newcastle-Ottawa Scale quality rating was 6 stars (Supplementary Appendix 2, https://www.jurology.com).

Topical Corticosteroids

We identified 3 clinical studies assessing the efficacy of topical clobetasol propionate 0.05% applied twice

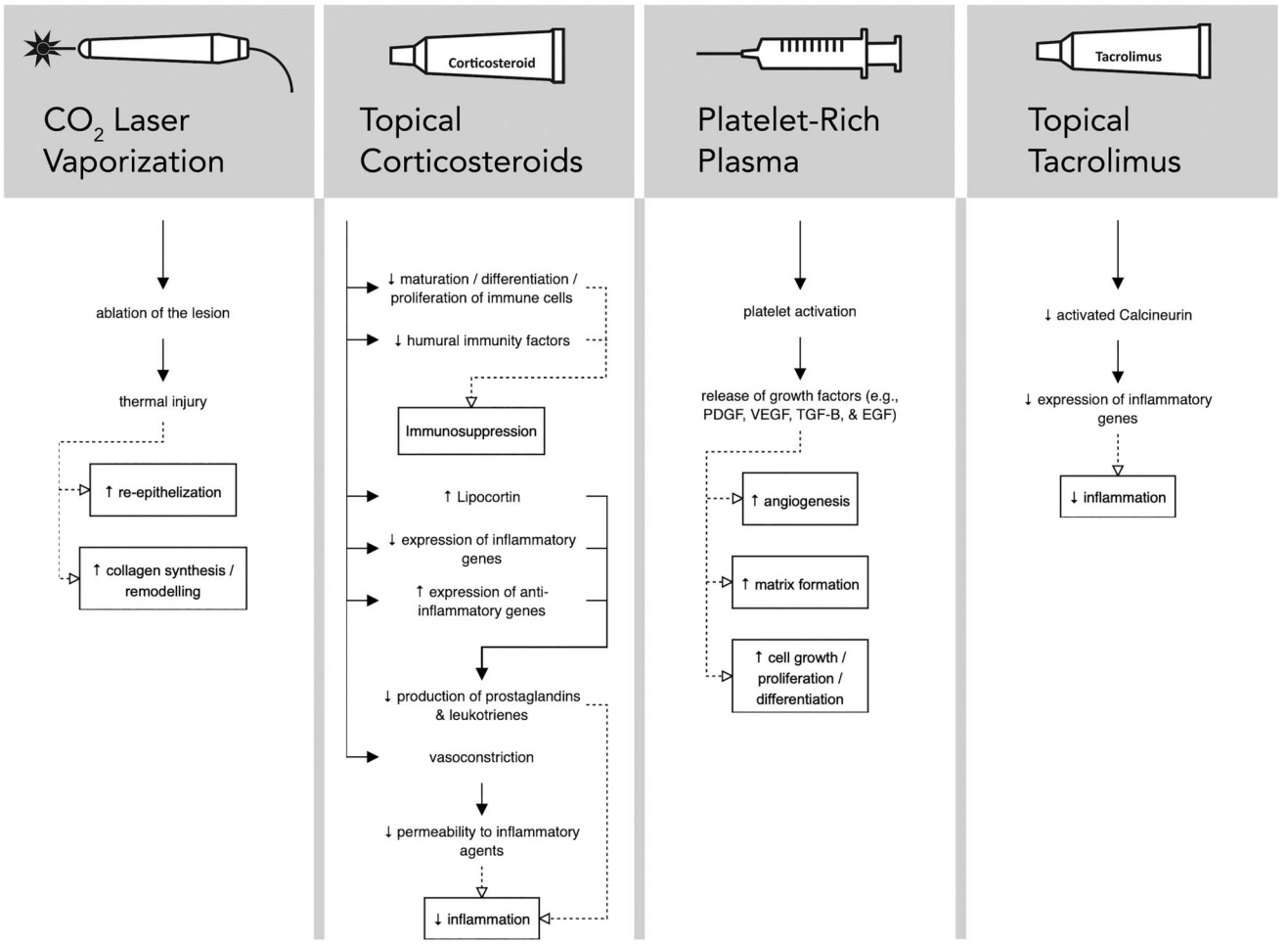

Figure 2. Lichen sclerosus conservative treatment mechanisms of action. EGF indicates endothelial growth factor; PDGF, platelet-derived growth factor; TGF-B, transforming growth factor beta; VEGF, vascular endothelial growth factor.

daily in patients with histologically confirmed penile or urethral LS (Supplementary Appendix 3, https://www.jurology.com).[14,21-23] Treatment duration of these studies varied from 2 to 12 weeks. No control treatments were given.

External Application

In a retrospective cohort study conducted by Dahlman-Ghozlan et al, 22 men with histologically diagnosed penile LS were treated with once or twice daily application of clobetasol propionate 0.05% for 2 to 16 weeks, with most patients (59%) applying twice daily for a mean of 7.1 weeks.[14] Nine patients (41%) had received some form of prior treatment for LS, including circumcision, meatal dilatation, frenuloplasty, and previous topical corticosteroid or androgen use. Based on self-completed nonvalidated questionnaires, the degree of perceived itching, burning/soreness, pain/discomfort during erection, dyspareunia, tightness of the foreskin, and reduced urinary flow by patients were significantly reduced both immediately after treatment and at long-term follow-up (mean: 14.6 months) when compared to before treatment ($P < .001$ to $P < .1$). At an average of 14.6 months of follow-up, 9 patients (43%) were determined to be clinically free of LS on exam and 5 patients (23%) reported being asymptomatic. Six of the remaining 12 patients were eventually referred for surgical management despite a second course of topical clobetasol. Three patients showed microscopic signs of human papillomavirus infection by biopsy after treatment, and 1 patient had a recurrence of genital herpes 4 weeks after treatment.

In another retrospective cohort study by Kyriakou et al, 41 patients with biopsy-proven LS were treated with topical clobetasol propionate 0.05% twice daily for 8 weeks.[21] Clinician assessment was recorded via the Investigator's Global Assessment (IGA), a 4-point scale to quantify disease severity through degree of inflammation and lichenification. Patient-reported outcomes were recorded via a 10-cm visual analogue scale which measured degree of pruritis and the Dermatology Life Quality Index (DLQI) surveys which measured disease impact on factors related to quality of life (QoL).[24] Between baseline and 8 weeks of treatment, 37 patients (90.2%) showed significant improvement in scores in all 3 domains ($P < .001$) and the mean scores for each domain improved by 70% to 75% of the scale values. For the remaining 37 patients, maintenance therapy was continued with either methylprednisolone aceponate 0.1% cream twice daily (n = 17) or tacrolimus 0.1% ointment once daily (n = 20) until week 20, at which point continued improvement of 24% to 87% was again noted in all 3 domains compared with week 8. No significant differences were reported between patients treated with methylprednisolone and tacrolimus.

Intraurethral Application

Hayden et al conducted a retrospective cohort study of 42 patients with biopsy proven LS related urethral stricture disease who were referred for treatment with intraurethral topical 0.05% clobetasol proprionate.[23] Thirty-five patients (83.3%) had previously undergone surgical treatment such as circumcision or urethroplasty, and 8 patients (19%) had previously tried topical medical therapy with either clobetasol, testosterone, or triamcinolone. Twelve percent had disease limited to the meatus, 36% had disease extending to the penile urethra, and 52% had disease involving the bulbar urethra. The 2 primary outcomes assessed were voiding function per the AUA Symptom Score (SS) and voiding-related QoL per the AUA SS QoL bother index. Clobetasol was applied in a tapered fashion: once daily for 1 week, every other day for 2 weeks, every third day for 3 weeks, every fourth day for 4 weeks, then on an as-needed basis. Thirty-six (85.7%) patients experienced significant improvement after clobetasol treatment, with the median AUA SS score decreasing from 12 to 8 ($P = .017$), and median AUA SS QoL bother index score decreasing from 4 ("mostly dissatisfied") to 2 ("mostly satisfied"; $P < .001$).

Tacrolimus

The use of tacrolimus in the treatment of histologically proven male genital LS in conjunction with surgical management or as postoperative adjuvant treatment was assessed in 1 prospective randomized study and 2 prospective nonrandomized studies (Supplementary Appendix 4, https://www.jurology.com).[25-27] The randomized study used topical and intraurethral clobetasol as a control. Control treatments were not used in the other 2 studies.

In the prospective randomized cohort study conducted by Choudhury et al, 67 patients with meatal stenosis and penile urethral stricture with histopathologically proven LS were divided into 2 groups.[27] Group 1 (n = 35) was treated with ointment clobetasol 0.05% applied on the penis and in the urethra for 3 months. Group 2 (n = 32) was treated with ointment tacrolimus 0.03% applied in the same fashion for 3 months. At 3 months, both groups saw 12-point improvement in International Prostate Symptom Score ($P = .94$). Group 1 saw a 5-mL/s increase in maximum flow rate vs a 4-mL/s increase in group 2 ($P < .01$). Group 1 patients were also less likely to have an additional procedure during the study period (3% vs 25%, $P = .05$).

Dey et al conducted a nonrandomized prospective cohort study in which 20 patients with LS involving the anterior urethra were treated with intraurethral instillation of 1 g 0.03% tacrolimus twice daily for 6 weeks.[25] All patients underwent cystostomy with a suprapubic tube (SPT) prior to treatment to allow for

increased tacrolimus intraurethral dwell time and patients with meatal stenosis also underwent meatotomy. After 6 weeks of treatment, 75% of patients showed a significant decrease in postvoid residual (mean decrease 126.3 cc) and significant increase in maximum flow rate (mean increase 6.4 mL/s) compared to baseline. SPTs were clamped at 6 weeks to allow for voiding per urethra with continued once-daily instillation of tacrolimus. Improvements were sustained at 3 months of follow-up, and SPTs were removed at that time. The most commonly reported side effects were perineal heaviness and urethral discomfort during initial instillations and all patients remained sexually active during treatment.

Another nonrandomized prospective cohort study by Ebert et al examined the use of 0.1% tacrolimus topical ointment as adjuvant and therapeutic treatment for disease control in 20 boys (mean age 9.7 years old, range 5.2-16.1) diagnosed with penile LS who underwent circumcision.[26] After surgical treatment, 9 patients (45%) had minimal residual lesions and 11 (55%) were lesion-free. Topical tacrolimus was applied twice daily to the glans and meatus for 3 weeks in all patients postoperatively. For the 9 patients with residual disease, for whom tacrolimus treatment had both adjuvant and therapeutic effects, full clearing of clinical disease on exam was noted in all patients. One of these patients had recurrent disease at 6 months, which was cleared by another 3-week course of topical tacrolimus. For the 11 patients with true adjuvant treatment, all patients had full clearance of disease except 1 who had recurrence at 8 months. His disease was also cleared by another 3-week treatment course.

PRP

Autologous PRP injection for treatment of penile LS was assessed in 2 cohort studies[28,29] and 1 prospective open-arm study (Supplementary Appendix 5, https://www.jurology.com).[30] All patients were males with histologically proven LS and proven failure of previous treatment, most commonly ultrapotent steroids. Outcomes were assessed using the DLQI and the IGA scale. No controls were used.

In a prospective cohort study conducted by Casabona et al, 45 patients with penile LS who failed to improve after at least 6 months of ultrapotent topical corticosteroid therapy received 2 to 10 autologous PRP injection treatments to affected sites.[28] The PRP was made through 2 centrifuges of the patient's own 50-mL blood sample and was injected in 2-cc treatments into the scar tissue or area of splitting. Corticosteroid therapy was stopped at the time of treatment. There was a significant reduction in DLQI scores (9.42±4.75 to 1.69±1.20, $P < .001$) between pretreatment and posttreatment follow-up (median: 18 months), thus indicating a significant increase in reported QoL. Six-point IGA scores also showed a significant reduction (3.24±0.77 to 1.20±0.69, $P < .001$), indicating significantly decreased severity of clinical disease. Topical steroid therapy was not restarted by any patient, and only 1 patient later underwent circumcision for continued voiding symptoms.

Navarrete et al conducted a similar prospective single-arm cohort study assessing PRP treatments in 4 patients with penile LS who failed to achieve complete response with at least 6 months of ultrapotent corticosteroids or circumcision.[30] Patients received autologous PRP treatment with follow-up every 6 months until a mean of 18 months. DLQI scores were found to be decreased between baseline and at time of final follow-up (6.25±4.48 to 1.25±2.45), although statistical significance was not reported. Despite minimal change in visual clinical severity by IGA evaluation (3.63±0.73 to 3.25±0.49), all patients reported being completely asymptomatic (dyspareunia, pain on erection, pruritus, stinging sensation) by 10 months. The only adverse effect reported during treatment was balanitis in 1 patient which was resolved with oral treatment.

Another prospective cohort study by Tedesco et al investigated the effect of autologous PRP injection on QoL in 43 male patients with proven failure of previous treatment for LS.[29] Three PRP treatments were given with 15 days in between each treatment, with final follow-up occurring 6 months posttreatment. Median DLQI score was 6 at baseline and 3 at final follow-up, with patients reporting most significant symptomatic improvement in terms of pruritus (37.2%-9.3%, $P < .004$) and dyspareunia (34.9%-11.6%, $P < .004$). Treatment was well tolerated by all patients without adverse effects.

CO_2 Laser Vaporization

The use of defocused and fractionated CO_2 laser vaporization was assessed in 3 cohort studies,[31-33] with an additional 14-year follow-up conducted for 1 study (Supplementary Appendix 6, https://www.jurology.com).[34] In all studies, male patients with histologically diagnosed LS of the penis or urethra were treated with 1 to 3 sessions of CO_2 laser vaporization. No controls were used.

In a prospective cohort study conducted by Ferrara et al, 10 patients with penile LS underwent 3 ablations each with a fractionated CO_2 laser at 10 W to 15 W.[31] All patients were previously on corticosteroid therapy which was stopped at least 4 weeks prior to starting CO_2 laser vaporization treatment. Patients reported an increased QoL as measured by a significant decrease in DLQI scores between the first and last treatments (11.2±5.5 to 4.9±3.6, $P < .001$). Researchers also collected MenLas Patient Scale and MenLas Observer Scale data, which described patient evaluation of symptoms and clinician evaluation of clinical signs such as loss of

elasticity and hyperkeratosis. Significant decreases in scores on both the MenLas Observer Scale (13.6±4.5 to 6±2.7, $P = .001$) and MenLas Patient Scale (29.5±6.4 to 15±4.9, $P < .019$) indicated a decrease in both clinician and patient perception of LS symptoms. Sexual function as assessed by the Male Sexual Health Questionnaire increased significantly between the first and last treatments (94.3±20 to 107.3±15.9, $P = .047$). At 6 months of follow-up, no patient showed any sign of relapse or need for further topical steroid therapy.

In a retrospective cohort study, Windahl and Hellsten studied 62 patients with penile LS of the glans and foreskin treated with either 1 or 2 sessions using a defocused beam at 15 W to 20 W.[32] Successful treatment was defined as no local symptoms or visible lesions at time of follow-up, with 47 patients (76%) determined to be successfully treated. Notably, 10 patients with residual symptoms had glanular disease involving the frenulum. Reported side effects of treatment included moderate discomfort for 4 to 6 weeks and charring of treatment site, which reepithelialized from normal margins over 6 to 8 weeks. A long-term follow-up was conducted with 50 of the original patients, with an average time to follow-up of 14 years.[34] At this time 40 patients (80%) reported no local symptoms or visible lesions.

CO_2 laser vaporization for concurrent penile and urethral LS has also been explored. In a prospective cohort study, Kartamaa and Reitamo treated 4 patients with penile LS with 1 session utilizing a defocused beam at 5 to 6 W. They also treated 1 patient with concurrent penile and urethral LS with 3 sessions using a defocused beam at 16 W.[33] All penile lesions were successfully treated per clinical appearance. The patient with urethral lesions recurred 3 times despite multiple sessions due to technical difficulties in reaching lesions in the proximal fossa navicularis. Although he had improved symptoms between each treatment, the patient was eventually referred from dermatology to a urologist for surgical management. For all patients, skin charring during treatment of penile lesions was reported, as well as superficial fibrosis of treated areas. There were no instances of postprocedural infection, loss of sexual function, or distinct pigmentary changes.

Oral Acitretin

We retrieved 1 double-blind, randomized, controlled trial (RCT) by Ioannides et al, assessing the use of oral acitretin for severe LS in 49 patients.[35] Acitretin exhibits anti-inflammatory and antiproliferative effects by reducing the expression of proinflammatory cytokines such as interleukin 6 and normalizing epithelial keratinocyte differentiation.[36] All patients had LS refractory to at least 1 cycle of treatment with topical ultrapotent steroids, with all LS medications discontinued 30 days prior to the study. The treatment group received acitretin 35 mg daily by mouth for 20 weeks. Prior to treatment, authors estimated the severity of disease through DLQI and a nonvalidated scale called the total clinical score, which includes domains for clinician evaluated features and patient-reported symptoms. Complete response was defined as total clinical score = 0 at week 20, and partial response was defined as a decrease of at least 4 points between baseline and week 20. In the acitretin group, 12 of 33 (36.4%) achieved a complete response, and 12 of 33 (36.4%) achieved a partial response at week 20. In comparison, only 3 of 16 (18.8%) of patients in the placebo group achieved either a complete or partial response. Additionally, the mean DLQI score of the acitretin group decreased from 12.27 to 6.67 ($P < .005$), indicating a significant increase in QoL. Despite these results, several side effects were experienced by the acitretin group, including cheilitis (75.8%), skin peeling (48.5%), moderate hyperlipidemia (42.4%), pruritis (30.3%), and slight increase in liver enzymes (27.3%).

PDRN Dermal Infiltration

Laino et al conducted a nonrandomized prospective cohort study with 28 men to assess the efficacy of PDRN in conjunction with topical 0.05% clobetasol propionate for treatment of penile LS.[37] PDRN is thought to improve tissue regeneration and wound healing through activation of A2 receptors and offering purine and pyrimidine rings for the salvage pathway.[38] Clobetasol was applied nightly for 4 months in both control and treatment groups, and the treatment group additionally received 8 PDRN treatments over the 4 months. Patients were assessed at the end of treatment and 6 months after treatment cessation. Primary outcomes include clinical severity per IGA scoring and QoL per DLQI scoring. Both treatment and control groups showed a significant decrease in IGA and DLQI scoring at 4 months of follow-up ($P < .001$ and $P < .003$). An IGA score reduction of $> 50\%$ was achieved in 64.3% of the treatment group ($P = .007$) as compared with 14.3% in the control group.

A prospective cohort study by Zucchi et al assessed the effectiveness of PDRN infiltration in a cohort of 21 men with clinically diagnosed penile LS.[39] All patients were treatment naïve and received two 10-week sessions of weekly local PDRN injections. Primary outcomes were QoL per DLQI and sexual function per IIEF-5 (5-item version of the International Index of Erectile Function). There was a significant decrease in DLQI from pre- to posttreatment (15 to 4, $P < .001$) indicating improved QoL. No significant changes in International IIEF-5 were observed. In a subjective evaluation of the treatment process, 17 patients (80%) indicated their posttreatment status as "improved" with increased foreskin suppleness and decreased

Table 1. *Assessment of Adjuvant Therapies to Surgery and Treatments After Failing Surgical Therapy for Lichen Sclerosus*

Authors	Treatment Hx	Site	Technique	Frequency of application	Results
Dahlman-Ghozlan et al (1999)[14]	Prior surgical treatment[a]	Penis	Topical 0.05% clobetasol cream	Average 2 times/d for 7.1 wk	9/21 (43%) clinically free of LS on exam, 100% reported reduced symptoms at follow-up (average 14.6 mo)
Hayden et al (2020)[23]	Prior surgical treatment[a]	Urethra	Intraurethral topical 0.05% clobetasol cream	2 times/d for 4-8 wk	36/42 (85.7%) did not require any subsequent surgical management at follow-up (average 8.4 mo)
Ebert et al (2008)[26]	Adjuvant treatment postcircumcision	Penis	Topical 0.1% tacrolimus	2 times/d for 3 wk	18/20 (80%) complete response without relapse at follow-up (average 13 mo)
Dey et al (2017)[25]	Cystostomy ± meatotomy prior to intraurethral instillation	Urethra	1 g 0.03% tacrolimus instillation	2 times/d for 6 wk, then 1 time/night for 3 mo	15/20 (75%) showed significantly improved postvoid residual and flow rate at 3 mo

Abbreviations: Hx, history; LS, lichen sclerosis.
[a] Not specified how many patients in study received prior surgical vs medical treatment.

irritative symptoms. Three patients reported worsening symptoms and 1 reported no change. No adverse effects were reported.

DISCUSSION

In this study, we systematically reviewed the existing literature on conservative management of penile and urethral LS. We catalogue the different treatment options including both medical and conservative procedural treatment options thereby expanding upon prior reviews which have largely focused on vulvar LS or male surgical management.[40-42] We also include details on treatment mechanism and outcomes, finding that topical corticosteroids, tacrolimus, PRP, CO_2 laser, oral acitretin, and PDRN injections all have evidence of therapeutic efficacy for penile and urethral LS.

Although there may not be a one-size-fits-all gold standard for LS, based on the available literature, the external and internal (intraurethral) use of the topical ultrapotent corticosteroid clobetasol propionate remains the treatment of choice at our institution and a mainstay of conservative management of penile and urethral LS. It has the most robust evidence in support and an excellent safety profile among the conservative treatment options.[40-42] The current evidence supports the use of topical 0.05% clobetasol propionate as not only an effective initial therapy, but as a useful adjuvant treatment to surgery as well as alternative to prior failed therapy (Table 1).[14,23] In the selected studies detailed in this review, patients experienced significant improvement in symptoms as assessed by measures such as the visual analogue scale, DLQI, AUA SS, and AUA SS QoL bother index, which measure QoL and symptoms such as degree of pain and pruritis. This improvement in clinical severity has also been verified by clinician observations per the IGA scale. In our opinion, topical corticosteroids should be the first-line conservative management in most situations, and our practice patterns mirror those described by Belsante et al in a review article from 2015.[42]

Previous studies have shown success with the calcineurin inhibitor tacrolimus for both primary and maintenance treatments for LS in both women and men.[43,44] However, the recent study by Choudhury et al showed tacrolimus to require more procedures and cause more side effects during treatment when compared with steroids.[27] We therefore recommend tacrolimus only for patients who either cannot tolerate or fail corticosteroid therapy (Table 1). In addition to tacrolimus, systemic treatment with the retinoid acitretin for LS in men has been studied in a double-blind, placebo-controlled study with promising results.[35] Despite the positive clinical response, most patients experienced 1 or more adverse effects from systemic acitretin use. This is important to consider when discussing treatment options with patients since alternatives such as corticosteroids and tacrolimus have superior and more well-studied safety profiles.

For patients who fail corticosteroid treatment and do not wish to proceed directly to surgery, there is evidence for the use of other therapies such as PRP injection or CO_2 laser vaporization (Table 2).[42,45] These options may be offered by the clinician after taking into consideration factors including site of disease, clinical severity, and patient preferences. In the 3 studies investigating PRP detailed in this review, all patients involved had previously failed topical corticosteroid therapy but showed significant improvements in DLQI and IGA scores after PRP treatments. PRP is thought to lead to reduced symptoms through anti-inflammatory mechanism, as has been seen suggested in treatment of knee osteoarthritis.[46,47] Similarly, patients who previously failed corticosteroid treatment and subsequently underwent CO_2 laser vaporization experienced significant improvements in MenLas Patient Scale, MenLas Observer Scale, and DLQI scores.

Despite the variety of nonsurgical treatment options available, some cases of penile and urethral LS are refractory to conservative treatment and may require surgical intervention.[48,49] The specific surgical technique chosen depends on factors such as disease

Table 2. *Assessment of Treatments After Failing Prior Corticosteroid Therapy*

Authors	Treatment Hx	Site	Technique	Results
Casabona et al (2017)[28]	At least 6 mo corticosteroid therapy	Penis	Autologous PRP 2-10 treatments (median = 4)	45/45 (100%) significant reduction or disappearance of symptoms at 18 mo
Navarrete et al (2020)[30]	At least 6 mo corticosteroid therapy, or circumcision[a]	Penis	Autologous PRP 1-2 treatments	4/4 (100%) asymptomatic by 10-mo follow-up
Ferrara et al (2020)[31]	Previous treatment with corticosteroids	Penis	Fractional CO_2 laser at 10-15 W 3 sessions	10/10 (100%) no relapse of disease or need for additional topical corticosteroid therapy at 6 mo
Ioannides et al (2010)[35]	At least 1 cycle of corticosteroid therapy	Not specified	Acitretin 35 mg po daily 20 wk	12/33 (36.4%) achieved partial response, 12/33 (36.4%) achieved complete response at 20 wk

Abbreviations: Hx, history; po, orally; PRP, platelet-rich plasma.
[a] Not specified how many patients in study received prior surgical vs medical treatment.

site, extent of disease, and symptomatology, but common procedures include circumcision, meatoplasty, and urethroplasty.[40,42] The available literature on nonsurgical management as outlined in this study supports reserving surgical intervention until conservative management has been exhausted, except when foreskin is involved in which circumcision may be considered first line. In such situations conservative treatment can still be used as an adjuvant or as postsurgical maintenance therapy to improve or maintain results. For example, there is evidence that topical corticosteroids are effective in treating refractory disease after surgical management[14,23] as well as evidence supporting the use of topical tacrolimus in the postoperative setting as an adjuvant therapy (Table 1).[26]

Although this review highlighted the evidence behind current treatment options for LS, there are several limitations. First, there is an evident lack of RCTs examining the conservative management options for LS in the male population, likely due to the low prevalence of disease compared with the female population. Of 16 studies meeting our inclusion criteria, only 1 RCT was retrieved. Secondly, due to the small sample sizes of several studies, the ability to extrapolate findings to a larger population may be limited. Future studies with larger cohorts in controlled trials are necessary to fully understand and compare the efficacy and safety profiles of existing treatment options. We are also limited in our ability to draw conclusions regarding long-term efficacy and side effects because, with a few exceptions, most studies had a maximum follow-up time of 3 to 18 months. Very few of the studies had a definition of "success," making it difficult to compare the efficacy of the different therapies. Additionally, few studies included qualitative data to describe the biopsychosocial aspects of disease management. Mixed-methods analysis with key personnel interviews followed by objective data collection by a multi-institutional group would likely be helpful to fill this knowledge gap.

There is also the risk of negative publication bias. Studies showing no treatment affect may be less likely to be published, leading to an overestimation of the efficacy of some of these treatments. Additionally, we limited our search to the English language and we may have missed data published in other languages. Despite these potential weaknesses, our study has several strengths. It is the first of its kind systematic review on all of the available conservative therapies for genital LS. In addition, despite the small size of many of the studies, most have good quality per the Newcastle-Ottawa Scale.

CONCLUSIONS

Due to its chronic and recurring nature, LS can present significant challenges in treatment to both the clinician and patient. Undertreatment in men can lead to significantly reduced QoL due to decreased urinary and sexual function, and thus, understanding the availability and safety of current therapies is paramount in providing tailored care based on clinical presentation and patient preferences. By presenting the evidence behind the efficacy and safety of current conservative management options for LS, this review provides a clearer picture of available treatments and provides guidance on the therapies which can be offered. This review also exposed the limitations of current literature, most notably the lack of controlled clinical trials for several existing therapies. Future research in the form of controlled clinical trials and long-term follow-up is needed to fully understand the effectiveness and safety of newer therapies.

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EDITORIAL COMMENT

In this article by Shieh et al, the authors performed a systematic review of the available options for conservative management of penile and urethral lichen sclerosus.[1] Taken as a whole, this manuscript serves as a valuable resource for all of us who manage this difficult disease entity in men. However, despite providing an excellent roadmap of treatment options based on the available data, several questions remain.

As the authors rightfully point out, defining "success" with conservative management has been subjective and inconsistent among studies. Where some evaluated patient-reported quality of life measures, others assessed the visible appearance of the penis, urinary symptom scores, or even subjective improvement alone. This heterogeneity makes it difficult to compare studies in terms of efficacy and limits our ability to draw broad conclusions for our patients. Furthermore, the lack of head-to-head trials leads to even more unknowns regarding optimal treatment strategies. Lastly, variabilities in treatment regimens, duration of treatment, and need for maintenance therapies after initial treatments further cloud the picture regarding optimal treatment routines.

Male genital lichen sclerosus is a very poorly understood disease process, and the irregularity in our management choices reflects this. This article does show us that, at present, the best evidence is for topical clobetasol 0.05%; but there are numerous other potential options that have shown promise and should be considered, especially for those who fail initial topical corticosteroid courses. Specifically, CO_2 laser vaporization and platelet-rich plasma infiltration appear to be the most effective potential candidates with relatively low side-effect profiles. However, the feasibility of these treatments in routine practice remains unclear. What we do know, as the authors point out, is that more work is required to create a reliable, evidence-based treatment algorithm based on randomized trials to better standardize and optimize the care of these patients.

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