

TITLE PAGE

Title:

DOES APPLICATION OF TOPICAL STEROIDS FOR LICHEN SCLEROSUS (BALANITIS XEROTICA OBLITERANS) AFFECT THE RATE OF CIRCUMCISION? - A SYSTEMATIC REVIEW.

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ABSTRACT

Purpose:

To determine whether treatment of Lichen Sclerosus et atrophicus (LS), with topical steroids reduces the rate of circumcision.

Methods:

Two independent reviewers performed a literature search of studies reporting treatment of LS with topical steroids using EMBASE and MEDLINE database(s). Inclusion criteria: boys aged 0-18 yrs, clinical diagnosis of LS, treatment with topical steroids. Literature reviews, studies of phimosis without LS and adult patients were excluded. Data analysed for each paper included age, duration of treatment, length of follow up and outcome, notably circumcision or no surgery.

Results:

The original search identified 26 titles. Application of exclusion criteria left 6 articles for inclusion in the study. Eighty nine patients with LS were treated with topical corticosteroids. Circumcision was avoided in 31/89 (35% ; range 0% - 100%). Median patient age was 6.5 yrs (1month - 15 yrs). Median duration of treatment was 2 months (1 - 23 months); median follow-up 4 months (6 weeks – 5 yrs).

Conclusions:

Treatment of LS with topical steroids reportedly avoided circumcision in 35% of boys. Duration of medical therapy and patient follow up in analysed studies were, however, short. A prospective randomised trial would provide a definitive answer.

Key Words

Lichen Sclerosus (LS), Balanitis Xerotica Obliterans (BXO), Topical Steroids, Circumcision

Type of Study

Systematic review

Level of Evidence

III

MAIN TEXT

INTRODUCTION

Lichen Sclerosus et atrophicus (LS, also known as Balanitis Xerotica Obliterans, BXO) is a chronic atrophic dermatitis of unknown aetiology. It is uncommon before the age of 5 and has an incidence in boys of 0.4 cases/1000 boys per year [1]. LS is characterised by white atrophic plaques that may affect the foreskin, glans penis, frenulum and meatus or urethra in males [2]. Histologically LS is characterised by epidermal atrophy, oedema and hyalini-sation of the dermis, with a deep dermal band of lymphocytes [3].

Most surgeons consider that definitive treatment of LS to be circumcision [4, 5, 6, 7], but there have been a number of studies that have advocated the use of medical therapy including topical corticosteroids [8], topical male sex hormone (testosterone propionate ointment) [9] and long-term antibiotics [10].

The aim of this systematic review was to determine whether or not there is a good evidence base to support medical treatment of LS with topical application of corticosteroids by determining the proportion of male patients that avoid a circumcision.

MATERIALS AND METHODS

Two independent reviewers(SF, HC) performed a literature search of studies reporting the treatment of LS with topical steroids using EMBASE and MEDLINE. The search terms used were (balanitis xerotica obliterans, lichen sclerosus et atrophicus , lichen sclerosus, lichen sclerosus, corticosteroid, steroid, topical steroids, circumcision, preputioplasty, pre-pucioplasty, dorsal slit). Search limits were 'Human', 'English Language', 'Subjects under 18 years'. No publication date limits were applied. All retrieved articles were evaluated manually for additional relevant studies. Literature reviews, studies of phimosis without LS and adult studies were excluded. The inclusion of publications was agreed by study authors (SF, HC) and the data were then extracted independently. Data collected from each

paper included age, duration of treatment with topical steroids, length of follow up and outcome (proportion of patients that avoided a circumcision).

THEORY

Lichen sclerosus is a chronic inflammatory dermatosis characterised by altered fibroblast function in the papillary dermis leading to fibrosis of the upper dermis. The aetiology of this condition is not fully understood and the its reversibility by topical steroids is not unproven and not universally accepted.

RESULTS

The initial search retrieved 18 titles with one duplicate record, leaving 17 titles that were assessed for eligibility (Fig. 1). Nine of the 17 titles were excluded following initial application of the exclusion criteria to the abstracts, leaving 8 titles for full text review. An additional 7 papers were identified for full text review on screening the references of the original 8 full text articles. After carefully reading the full length text manuscripts, 9 of the 15 papers were then excluded based on exclusion criteria leaving 6 papers for inclusion in the final review.

Eighty-nine patients with LS were treated with topical corticosteroids. Circumcision was avoided in 31/89 cases (34.8%, range 0% - 100%). The median age of the patients was 6.5 years (range 1 month - 15 years). The median duration of treatment was 2 months (range 1 - 23 months) and the median period of follow-up was 4 months (6 weeks - 5 years).

DISCUSSION

Lichen sclerosus et atrophicus (LS) is a chronic inflammatory disease of unknown aetiology affecting the foreskin, underlying glans, glandular meatus and urethra in males. The traditional treatment of this disease has been complete excision of the foreskin notably circumcision, however others have proposed alternate measures to preserve the foreskin. These include preputioplasty and triamcinolone injection into the prepuce [11], and the application of topical corticosteroids as an adjuvant, neo-adjuvant and stand alone therapy [2, 12, 13].

The papers included in the systematic review addressed the proposal of topical corticosteroid as an alternative to circumcision in the management of LS. The range of successful response rate(s) to the topical application of corticosteroids were 0% to 100%, with an average success of 35% based on a median follow up time period of 4 months.

Prior to comparing and contrasting the papers included in the final analysis of this systematic review, it is worth mentioning a notable omission, the study by Kiss *et al.* [2]. This was a double-blind randomised controlled trial in which 40 boys with LS were randomised to receive topical application of 0.05% mometasone furoate or placebo. All of the patients included in the study ultimately underwent a circumcision with histological analysis of the foreskin after 5 weeks of treatment irrespective of whether or not there was a response to topical steroids. Therefore it was not possible to fully confirm whether or not topical steroids would have averted the need for circumcision in this study.

With regards to the papers included for final review the lowest response rates to topical steroids were demonstrated in the studies that had the longest complete period of follow-up; Vincent *et al.* [12] 27% response rate (14 months follow-up), and Lindhagen *et al.* [14] 0% response rate (6 months follow-up). Zavras *et al.* [8] reported a 100% response rate to topical steroids but the follow-up period was just 8 weeks. One could hypothesise that a

longer period of follow-up by Zavras *et al.* [8] may have yielded a cadre of patients with ongoing or recurrent LS ultimately requiring surgical intervention.

It is worth also noting that in the only prospective double blind randomised controlled trial [14], no single patient with LS responded to topical corticosteroids and all required circumcision.

It proved challenging to ascertain the duration and severity of LS in all of the patients included in this current systematic review. To this end we found no robust data reporting the response rates of LS to topical corticosteroids based on disease severity. Additionally there is not a universally agreed classification system for the severity of LS. Kiss *et al.* [2] showed application of topical corticosteroids can affect improvement in LS particularly with the histologically 'early' and 'intermediate' milder stages of disease. A limitation here in this study was that however all patients ultimately underwent circumcision.

In summary treatment of LS with topical steroids reportedly avoided circumcision in 35% of boys. This systematic review has shown that the duration of medical therapy and patient follow up in analysed studies were however short. Long term follow up would seem advisable to monitor patients for LS recurrence in those that may ultimately require circumcision. A prospective randomised trial would usefully provide a definitive answer.

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