Treatment of lichen planus: an evidence-based medicine analysis of efficacy
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Authors' objectives
To critically appraise the body of literature concerning treatment of lichen planus (LP).

Searching
MEDLINE and BIOSIS Previews were searched from inception to March 1998 using the keywords 'lichen' and 'treatment' or 'therapy', and each treatment modality was combined with 'lichen'.

Study selection
Study designs of evaluations included in the review
No specific study designs were detailed in the inclusion criteria. Eighty-three clinical trials (of various designs) that contained specific data on LP and its treatment were included. Case reports, anecdotal reports of drug efficacy and review articles containing therapeutic data were also analysed.

Specific interventions included in the review
Treatments for cutaneous LP: psoralen plus UV-A therapy (conventional and bath); etretinate; acetretin; oral tretinoin; corticosteroids; griseofulvin; oral cyclosporine; dapsone; phenytoin.

Treatments for mucous LP: topical corticosteroids; systemic corticosteroids; etretinate; oral tretinoin; topical tretinoin; topical isotretinoin; topical cyclosporine; oral psoralen plus UV-A therapy; extracorporeal photochemotherapy; griseofulvin; hydroxychloroquine.

Participants included in the review
Participants were individuals who had received treatment (or placebo) for either cutaneous or mucosal LP. Other participant characteristics were not reported.

Outcomes assessed in the review
No specific outcome measures were detailed in the inclusion criteria. All trials or series of patients which reported clinical data were included.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
When possible, the validity of retrieved studies was assessed according to the criteria defined by Sackett (see Other Publications of Related Interest no.1). The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
Studies were combined by narrative review and study findings were discussed with reference to methodological quality.
How were differences between studies investigated?
The authors acknowledged the differences between the studies in terms of participants, interventions, outcomes (particularly the lack of a consistent definition of ‘cured’ LP) and methodological quality. Studies were broadly grouped as evaluations of treatment of cutaneous or mucosal LP. These groups were further subdivided into studies looking at particular types of intervention.

Results of the review
Eighty-three clinical trials were included in the review. Three of these were small-scale randomised trials, while the remainder of the published trials were controlled trials with imprecise methods or extremely small populations, uncontrolled studies, or observational studies, some of which were retrospective.

The majority of studies included in the review were of poor quality, 80 being categorised as ‘level C’ according to Sackett's criteria. Only three studies were categorised as ‘level B’ and there were no high quality ‘level A’ studies.

Cutaneous LP:

1. Of all systemic retinoids, only acitretin has shown a relatively good level of evidence of its efficacy in the treatment of cutaneous LP.

2. The level of evidence of PUVA efficacy in the treatment of cutaneous LP is weak. In some cases, PUVA is able to decrease pruritus during the first weeks of treatment or to rapidly cure patients with resistant long-standing LP. Bath PUVA could be more effective than oral PUVA, but the possibility of exacerbation of the disease induced by PUVA or after the treatment has been raised; thus the results must be interpreted cautiously.

3. Although unpublished clinical experience has suggested that short-course systemic therapy can be effective in reducing the duration of cutaneous LP, the level of evidence of corticosteroid efficacy is low. The frequency and level of relapse of LP after withdrawal have also never been established.

4. One trial reported griseofulvin to be superior to placebo in terms of “complete regression” (71% vs 30%). Another reported “complete improvement” in 82% and “partial remission” in 18% of patients receiving griseofulvin, compared to partial remission in only 23% of patients receiving placebo. The methods used in both studies do not allow definitive conclusions.

5. Four small uncontrolled case series and one isolated case provided some weak evidence to suggest that oral cyclosporine is an effective treatment for patients with severe cutaneous LP resistant to retinoids or systemic corticosteroid therapy.

6. Various other drugs, such as dapsone, hydroxychloroquine sulphate and metronidazole have been examined in small trials with weak study designs.

Mucous LP:

1. The efficacy of topical corticosteroids in oral LP is supported by a higher level of evidence than are other drugs. This was shown in two small controlled ('level B') trials, examining the efficacy of fluocinonide and fluocinolone.

2. The efficacy of systemic corticosteroids in mucous LP has not been demonstrated by rigorous trials, and the level of evidence for their efficacy is poor, despite widespread use based on clinical experience.

3. Etretinate seems to be effective in reducing the lesions in oral LP. Both 0.1% tretinoin and 0.1% isotretinoin seem to be effective when applied topically to oral LP. The efficacy of 0.05% tretinoin is poor. After withdrawal of systemic or topical retinoids, recurrences are common.

4. Topical cyclosporine washes seem to be effective against oral LP, especially the severe erosive forms, but they do not appear to better than local corticosteroid therapy.
5. A number of small studies found oral PUVA therapy with low-dose UV-A to be effective in treating oral LP of various forms (erosive, atrophic, or reticular). This treatment remains experimental and can cause side effects, mainly nausea, related to oral ingestion of psoralen.

6. As with cutaneous LP, there is a limited amount of evidence for the use of various other drugs in the treatment of mucous LP.

The authors note the difficulty in comparing all the studies, because different criteria were used to define a cure or attenuation. They also note that most of the reports include favourable responses to the studied treatment, which may suggest publication bias.

Authors’ conclusions
Although LP may be associated with substantial morbidity and altered quality of life, especially the erosive mucosal LP, definitive clinical trials have not been performed. Acitretin is the first-line therapy in cutaneous LP. The efficacy of systemic corticosteroids and psoralen plus UV-A therapy has not been established with a high level of proof. Topical corticosteroids are the first-line of therapy in mucosal erosive LP. Other treatments, such as topical cyclosporine and extracorporeal photochemotherapy, remain to be evaluated. European-US co-operation is warranted to perform large randomised controlled trials in cutaneous and mucosal LP.

CRD commentary
On the whole, this is a good summary of the existing literature on the treatment of LP. An attempt was made to identify all the relevant literature and the validity of all papers were assessed according to predefined criteria. Sufficient details of included studies were given and the studies were appropriately grouped in a narrative review. The authors emphasised that there were no high quality studies, but highlighted the results of the better quality evidence. The authors discussed the potential impact of publication bias, made appropriate recommendations for future research and noted that recommendations for practice could not be confidently made on the basis of the existing evidence. The authors’ conclusions are supported by the evidence presented.

Implications of the review for practice and research
Practice: The authors state that the first-line therapy in cutaneous LP is acitretin. All other methods or drugs are of uncertain efficacy. Based on clinical experience worldwide, systemic corticosteroid therapy is recommended by many authors and could be classified as second-line treatment in cutaneous LP. The first-line therapy in oral LP is topical corticosteroid therapy. The authors state that no treatment has convincingly demonstrated its superiority over topical corticosteroids and that second-line therapy in plaque like LP should be topical retinoids or etretinate, but strong evidence of efficacy is lacking.

Research: The authors state that their review shows the lack of clear-cut results in the treatment of LP, even for those drugs considered to be classical standards. For future studies, oral and cutaneous LP should be clearly separated since the modalities of clinical evaluation and treatment are different. The duration of disease before inclusion, the type of lesion and the involved body surface should be detailed. The major criteria for efficacy should be based on objective criteria, and global evaluation should be considered only as an accessory criteria. Erosive and reticular mucous membrane LP must be separated and research concerning topical adapted treatments continued. The new promising treatments, such as topical cyclosporine, extracorporeal photochemotherapy, or even retinoids plus PUVA therapy, should be tested in large controlled trials. Quality-of-life studies could be helpful in the evaluation of oral LP therapy.

Bibliographic details

PubMedID
9875189
Original Paper URL
http://archderm.ama-assn.org

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Evidence-Based Medicine; Humans; Lichen Planus /therapy; Randomized Controlled Trials as Topic

AccessionNumber
11999000129

Date bibliographic record published
31/08/2001

Date abstract record published
31/08/2001

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.