

Treatment of exfoliative cheilitis with Traditional Chinese Medicine: a systematic review

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Abstract

OBJECTIVE: To systematically review treatments of exfoliative cheilitis based on symptom patterns in terms of Traditional Chinese Medicine.

METHODS: PubMed, Cochrane Central Register of Controlled Trials and Wanfang data were screened for case reports, case series or clinical trials that were published in English or Chinese from January, 1973 to September, 2015. The keyword of "exfoliative cheilitis or scaling cheilitis or factitious cheilitis" was used. Effectiveness or ineffectiveness was investigated as outcome for Meta analysis, which is based on effective index in each study. Response to treatment was described for case reports or case series.

RESULTS: From 38 screened studies, 17 were ran-

domized controlled trials (RCTs), 5 were single-arm trials, and 16 were case reports or case series. Three RCTs were eligible for Meta analysis and all of them compared managements between Traditional Chinese Medicine and corticosteroids for exfoliative cheilitis, which involved 223 participants. Interestingly, data of Meta analysis showed similar effect of Traditional Chinese Medicine and corticosteroids for patients with exfoliative cheilitis [relative risk ratio: 1.10; 95% *CI* (1.00-1.21), *P* = 0.06].

CONCLUSION: Traditional Chinese Medicine might be a substitute for corticosteroids on exfoliative cheilitis. However, the evidence and recommendation of exfoliative cheilitis managements need to be taken with caution because of the low quality of evidence in the studies obtained.

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Keywords: Evidence-based medicine; Dentistry; Exfoliative syndrome; Cheilitis; Therapeutics; Medicine, Chinese traditional; Adrenal cortex hormone; Review

INTRODUCTION

Exfoliative cheilitis (EC) is a chronic condition that affects the vermilion zone of the upper, lower, or, more commonly, both lips by the more or less continuous, excessive production and subsequent desquamation of thick keratin scales.¹ Epidemiologically, EC is more likely to affect young women and children.² The etiology of EC remains unknown. It may result from abnormal psychological status, bad oral habits,²⁻⁵ human immunodeficiency virus and fungal infection,^{6,7} or poor oral hygiene.⁸ Further, EC can be a manifestation of

systemic disease such as vitamin B6 deficiency⁹ or a side-effect of chemotherapy for leukemia or lymphoma, peeling disease,¹⁰ and retinoic acid intake.¹¹ Clinical manifestations vary from person to person. Patients can feel pain, itchiness, dryness, chapping, desquamation, crusting, or swelling on the lips. Lip biopsies are sometimes performed, but the results are usually negative.

The treatment for EC remains a clinical challenge. The utilization of topical and systemic corticosteroids has been reported, but the response varies from case to case.¹⁵ Antifungal therapy, which is etiological treatment, can be administered to patients with secondary fungal infection.² Antidepressant therapy such as diazepam or amitriptyline hydrochloride has traditionally been applied for improvement of EC.^{3,12} Improvement in patients with EC has also been shown from treatment with tacrolimus, an immunosuppressive macrolide that was approved in the last decade for the treatment of atopic dermatitis.¹³

In addition to the above, Lu¹⁴ successfully treated 32 cases of EC with Jianpi Chushi Tang, a Traditional Chinese Medicine (TCM) that is said to invigorate the spleen and remove moisture. Roveroni-Favaretto *et al*¹⁵ reported a case of an 18-year-old man who had not responded to triamcinolone cream and sunscreen and in whom a 10% topical *Calendula officinalis* ointment successfully cleared lip lesions in 15 days, contributing to clinicians' insight into the treatment of this disease with TCM.

Symptom pattern identification and holism are the fundamental concepts of TCM among others. Eight principles of symptom pattern identification include *Yin* and *Yang*, internal and external aspects, cold and heat as well as deficiency and excessiveness.¹⁶ The phenomena that bear the properties of being warm, bright, active, rising and dispersing pertain to *Yang*; while what bear the properties of being cold, dim, static, descending and astringing pertain to *Yin*. In the theory of TCM, *Yin* and *Yang* explain the histological structure of the human body, the relationship between structure and function, pathogenesis, diagnose and guide clinical treatment.¹⁷ The common symptoms of deficiency include fatigue, shortness of breath, night sweating, dry mouth and throat, thirst with desire to drink, dry skin, scanty urine and dry feces. In contrast, the common symptoms of excessiveness include fever, restlessness, chest oppression, retention of dry feces and inhibited urination.¹⁶ In ancient Chinese medical literature, EC is known as "lip wind", which excessive "heat" of the stomach and/or spleen induces sores on the lips in the early stages of EC; while, in later stages, yin deficiency in the whole body is the dominant local pathology.¹⁸

The purpose of this study was to systematically review currently available case reports, case series and clinical trials involving EC treatment and to provide an optimal treatment plan for dentists or dermatologists to treat patients with EC.

MATERIALS AND METHODS

This study followed the Preferred Reporting Items for Systematic Reviews and Meta analysis (PRISMA) statement guidelines.¹⁹ The evidence level and recommendation grade were evaluated by evidence criteria from the Oxford Centre for Evidence-based Medicine.

Search strategy

We used 1# "exfoliative cheilitis or scaling cheilitis or factitious cheilitis" as keywords, 2# species were limited to "human", 3# publish date from 1973/01/01 to 2015/09/30, 4# language was limited to "Chinese" or "English" as search terms to retrieve case report, case series and clinical trials in PubMed, the Cochrane Central Register of Controlled Trials, and the Wanfang data (<http://www.wanfangdata.com.cn>).

Selection criteria

The inclusion criteria for the systematic review were that the study: (a) must be related to EC or a desquamation type of chronic cheilitis (because, in Chinese studies, a subset of chronic cheilitis, called the desquamative type, also refers to what is defined as EC); (b) must be a case report, case series or clinical trial; (c) must show the response to treatment for case report, case series and clinical trial; and (d) must show effective index as a treatment outcome for randomized controlled trials (RCTs) that were enrolled for further Meta analysis (as defined below).

The exclusion criteria were that the study: (a) was not clear in its description of the desquamation type of chronic cheilitis; (b) reported no clinical outcome; (c) the response to treatment was not available; or (d) evaluated severe systematic disease.

Outcome for meta analysis

Based on the existence of desquamation, dryness and chapping, itching and pain, and erosion and scabbing of lips, each patient was rated from mild to severe and scored as 0, 1, 2, and 3. The absence of desquamation scored 0, desquamation less than 1/3 of the vermilion area scored 1, desquamation more than 1/3 but less than 2/3 of the vermilion border scored 2, and desquamation greater than 2/3 of the vermilion area scored 3. The absence of dryness or chapping scored 0, mild dryness scored 1, obvious dryness and longitudinal cracks appearing in lip movement scored 2, and obvious cracks with little leakage scored 3. The absence of itching or pain and free movement scored 0, mild itching or pain scored 1, paroxysmal pain with a sense of tension scored 2, and persistent pain and restricted eating or mouth movements scored 3. The absence of erosion or scabbing scored 0, less than 2 millimeter (mm) of erosion or scabbing scored 1, greater than 2 mm of erosion or scabbing but on less than half of the lip area scored 2, and large areas of erosion or scabbing of the upper or lower lip scored 3.

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