

Comparison of Corticosteroids VS Multivitamin for the Treatment of Oral Aphthous Ulcer: A Systematic Review

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Abstract

Objectives: The purpose of the study was to compare corticosteroids with a multivitamin for the treatment of recurrent aphthous stomatitis.

Data Sources: An extensive systematic literature search was performed in PubMed, Google Search, using a combination of keywords like Oral Aphthous ulcer, corticosteroids, Multivitamin, recurrent aphthous stomatitis, canker sore, Cortisol, steroid, Nutritional supplement, vitamin.

Study Eligibility Criteria: Inclusion criteria: Studies that provided information for treatment of aphthous ulcer and Primary research data, randomised controlled trials. Exclusion criteria: Studies that provided inadequate information about treatment of the aphthous ulcer.

Participants: Adults having aphthous ulcers were included in the study.

Interventions: Corticosteroids and multivitamin.

Results: Through search strategy 148 articles were yielded. After screening through titles and abstracts, 14 articles remained which were further screened for full text. At the end, 7 articles were included in systematic review according to the eligibility criteria of this review.

Conclusions: Corticosteroids are better for relieving pain, size, number, erythema of the recurrent aphthous ulcer. Multivitamins have least effects or no effects on the aphthous ulcer, these are used as prophylactic medicine, not as a definitive treatment for a recurrent aphthous ulcer.

Implications: Corticosteroids should be used as definitive treatment for the recurrent aphthous ulcer.

Keywords: Oral Aphthous Ulcer; Corticosteroid; Multivitamin

Introduction

Rationale

An aphthous ulcer is an inflammatory condition which has an unknown cause etiology further characterized by painful condition, reoccurring single/multiple ulcerations seen on the oral mucous membrane. It has estimated to affect 2.5 billion people worldwide, such common disease is also known as a canker sore. Initially, the Greek term apthai was used for oral disorders of which Hippocrates is credited. In general population, the frequency of aphthous ulcer is up to 25% with a 3-month re-occurrence rate.

The common factors contributing are local trauma and stress, other related factors include systemic disease, nutritional deficiencies, food allergies, genetic predisposition, immune disorders, medications, and human immune deficiency virus infection. Due to such condition aphthous ulcer may be a marker of underlying systemic disease, like celiac disease, may be a feature of Behcet's disease, in some cases no other body systems are affected and patients remain fit and well. Because etiology is unknown and no any laboratory procedures available to confirm the diagnosis.

Aphthous ulcer usually represented as a single or clusters of painful ulceration which has erythematous borders. 1 - 2 weeks may be required for healing of the lesion but it may reoccur monthly or several times in a year. Patients with immune- suppression shows hematologically decreased a ratio of t-helper (CD4) to T-suppressor/cytotoxic (CD8) cells. Scientifically aphthous ulcers occur due to the accumulation of immune complexes where complement activation and cytokine activity are responsible for an infiltration by neutrophils and cytotoxic T lymphocytes leading to vacuolar degeneration of basal keratinocytes. According to such diagnostic criteria, aphthous ulcer remains poorly understood, ulcers are not preventable and treatments are symptomatic only. Reduction in pain and healing time restores basic functions like eating, swallowing and talking.

Generally, aphthous ulcers are classified as, major, minor and herpetiform. Researchers show some study which is related to cause of ulceration those are vitamin b complex deficiencies, gastrointestinal disease related with malabsorption, immune deficiency, stoppage of smoking, luteal phase of menstrual cycle. In some studies, prophylactic use of multivitamin shows the reduction in a number of aphthous ulcers.

Focused Question

Which is the most efficacious treatment modality in the treatment of aphthous ulcer, systemic steroid vs multivitamin?

Objective

To determine the effectiveness of systemic steroid vs multivitamin in the treatment of aphthous ulcer.

Methods

Eligibility Criteria

Inclusion criteria

- Literature explaining the treatment modalities of aphthous ulcer.
- Literature from 1jan 2006 to 1jan 2016 i-e for 10 Yrs.
- Literature showing follow up results of the treatment modalities
- Literature should be written in English or should have a detailed summary in English.

Exclusion criteria

- Literature which does not mention about the treatment modality of aphthous Ulcer in any other language.
- Literature before 1 January 2006.

PICO:

P- Participants: patients having aphthous ulcers

I- Intervention: corticosteroids

C- Comparison: multivitamins

O- Outcomes: pain release and healing of the ulcer

S- Study design: comparative study

Information Sources

Evidence from the internet sources was used in the satisfactory search of appropriate papers for the study: The National Library of Medicine (MEDLINE-PUBMED) and Clinical trials registry and manual search using DPU college library resources. All cross reference lists of the selected studies were screened for additional papers that could meet the eligibility criteria of the study.

The databases were searched up to and including December 2015 using the search strategy.

Search strategy for PubMed

- Oral aphthous ulcer AND multivitamin AND corticosteroid
- Oral aphthous ulcer AND vitamins
- Oral aphthous ulcer AND corticosteroids
- Oral aphthous ulcer AND nutritional supplement
- Oral aphthous ulcer AND steroids
- Recurrent aphthous stomatitis AND steroid
- Recurrent aphthous stomatitis AND multivitamin
- Recurrent aphthous stomatitis AND nutritional supplement
- Canker sore AND steroid
- Canker sore AND multivitamin

Results for Search strategy

S. No.	Search strategy	Number of articles	Number of selected articles	After Duplicate Removal
1	Oral aphthous ulcer AND multivitamin AND corticosteroid	0	0	0
2	Oral aphthous ulcer AND vitamins	8	5	5
3	Oral aphthous ulcer AND corticosteroids	45	9	9
4	Oral aphthous ulcer AND nutritional supplement	4	0	0
5	Oral aphthous ulcer AND steroids	36	5	0
6	Recurrent aphthous stomatitis AND steroid	15	5	0
7	Recurrent aphthous stomatitis AND multivitamin	1	1	0
8	Recurrent aphthous stomatitis AND nutritional supplement	2	1	0
9	Canker sore AND steroid	36	5	0
10	Canker sore AND multivitamin	1	1	0
Total no of articles		148	32	14

Study Selection

Preliminary screening consisted a total of 148 articles out of which 14 articles were selected. The papers were screened independently by four reviewers (AM and DG). Initially, papers were screened on the basis of its title. Any disagreement between the four reviewers was resolved after additional discussion. Duplicates from 32 screened articles were removed and abstract was then made ready. As the second step, 14 abstract were again screened to remove 07 article which does not fulfill the inclusion criteria. free full text 07 papers were obtained when they fulfill the criteria of the study aim. Finally, a total of 07 articles were included.

Data Collection Process

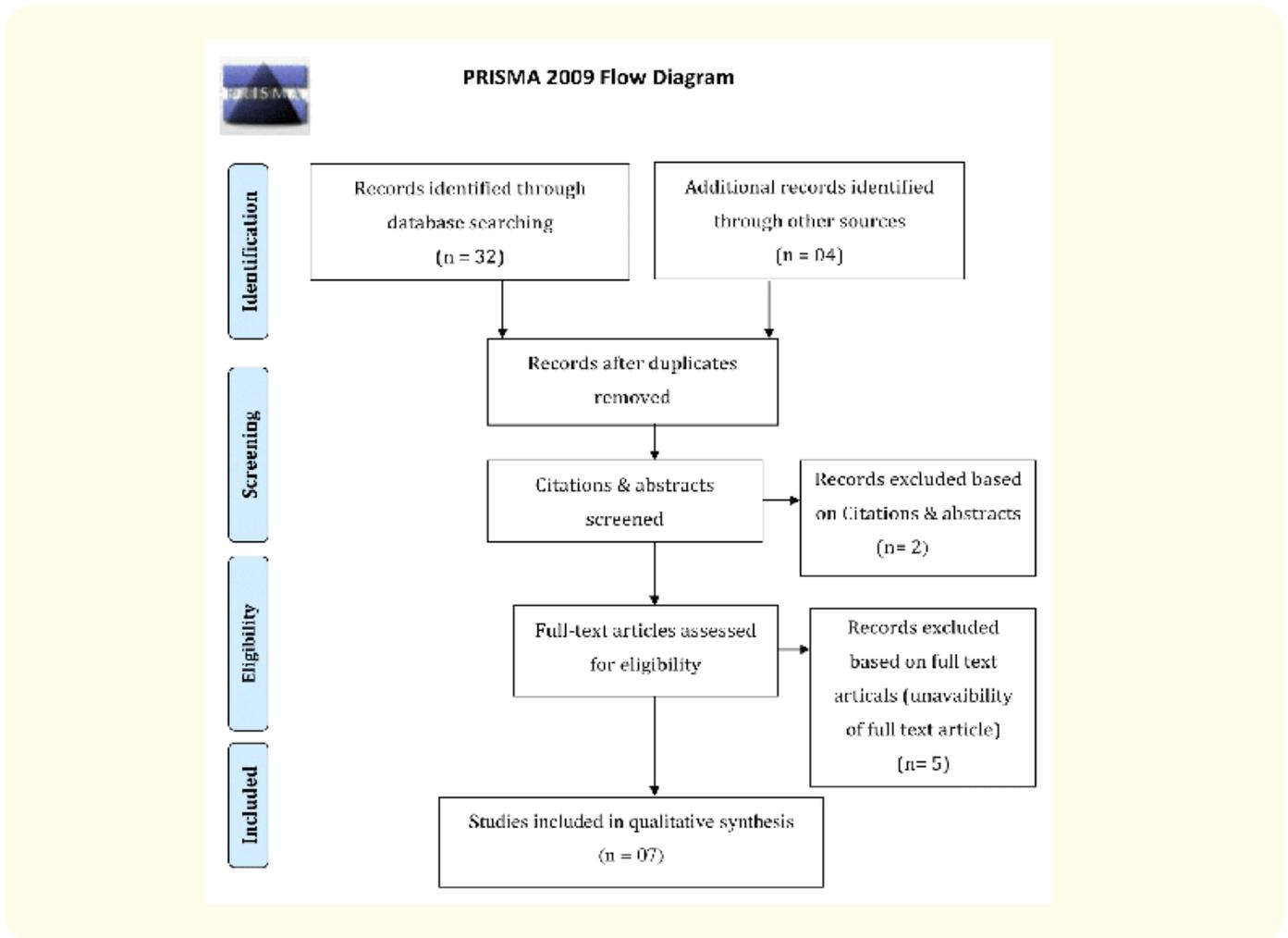
A standard pilot form in excel sheet was initially used and then all those headings not applicable for review were removed. Data extraction was done for one article and this form was reviewed by an expert and finalized. This was followed by data extraction for all the articles.

Data Items

The data items included were

1. Author – The name of the author
2. Location – The country in which the study took place
3. Year of publication – The year in which the study was published
4. Study design – If the study was a control or a clinical trial, blinding
5. Participant description – participant characteristics
6. Sample size – No. of participants included in the study
7. Setting – place where the study was conducted
8. Intervention – corticosteroid and multivitamin
9. Comparison – corticosteroid vs multivitamin
10. Duration – time of evaluation
11. Outcome- Result of the study
12. Remarks – comments of the author (AM and DG)

Results



Discussion

A pathological condition, “aphthous ulcer” is characterized by an onset of painful single or multiple recurring ulcerations on the non-keratinised oral mucosa. The aphthous ulcer appears rarely in a single episode. Patients are affected by this condition representing relapsing ulcerative lesions that differ in quantity and frequency for each episode. Amongst one in five people is affected by the aphthous ulcer, is quietly estimated. The etiology of the disease remains obscure even though the high prevalence and considerable clinical research on aphthous ulcer are done, still, there is no available curative therapy for this common mucosal lesion.

The aphthous ulcer clinically represents typical well-defined round or oval shaped ulcerations surrounded by an inflammatory halo. They are usually less than 1 cm in size(minor aphthae), but some patient represents deeper or larger lesions which last about a week and produce screening (major aphthae). Such lesions can be associated with a deficiency of folic acid, iron, zinc, or vitamin B complex, gastrointestinal disorders related to malabsorption, immunodeficiencies, stress, trauma, stoppage of smoking, luteal phase of the menstrual cycle, and oral health care products containing sodium lauryl sulfate.

In some of the patients, with high radio-sorbent test levels and positive results for the same test to foods, the aphthous ulcer can be considered as allergic reactions to an antigenic stimulus. Patients with ulcer show a depressed ratio of t-helper (CD4) to T-suppressor/ cytotoxic (CD8) cells. of folic acid, iron, zinc, or vitamin B1, B2, B6, or B12, gastrointestinal disorders (Crohn disease, celiac disease, or ulcerative rectocolitis), immunodeficiencies (e.g. human immunodeficiency virus infection), stress, trauma, cessation of smoking, luteal phase of the menstrual cycle, and oral health care products containing sodium lauryl sulphate.

Therapy remains largely palliative for symptomatic cases. Enormous medicaments for the topical application have been used to suppress the pain and duration of ulceration, including chlorhexidine, hyaluronic acid, amlexanox, diclofenac, tetracycline, triamcinolone, and clobetasol, with different and not always reproducible results. Recurrent therapies are largely symptomatic, and their therapeutic

value with respect to the development of adverse effects remains unproven in large clinical trials. Therefore, the use of well tolerated nonsteroidal drugs in individuals who are unresponsive to topical corticosteroids would enhance the therapeutic options for clinicians.

Volkov I., *et al.* [1] studied that use of 1000 mcg of vitamin B12 in 58 patients suffering from recurrent aphthous stomatitis. From these 31 included in the intervention group and 27 in control group. All conditions related to aphthous ulcer were recorded and those compared with the controlled group. Clinical parameters of ulcer reduced with the treatment of vitamin B12 within 5 - 6 months. At last month the significant number of the patient had no aphthous ulcer according to this study. The drawback of this study is initial blood level of vitamin B12 is not considered.

El-Haddad S., *et al.* [2] conducted a comparative study of honey and the topical corticosteroid for the recurrent aphthous ulcer. He found that honey is better than triamcinolone acetonide in ulcer size reduction, shows significant results in pain relieving and healing of the ulcer. According to this study topical corticosteroid especially triamcinolone acetonide 0.1% is one of the frequently used and it effectively improves symptoms of the aphthous ulcer. Besides that, it causes local immunosuppression when in contact with the oral mucosa, further leading to candidiasis. In other cases such as intraoral bacterial or viral infection is contraindicated. Along with this effect on sodium and water retention, anorexia, weight loss, flushing, depression, muscle wasting is noted when topically applied intra orally to large areas or using occlusive dressings. The aim of the study was to identify the highest effective topical agent and the least side effects to treat of aphthous ulcer, which shows an obvious interest in the field of oral medicine.

Zinah M., *et al.* studied comparative effects of dexamethasone and triamcinolone acetonide in Orabase. He observed that faster healing of ulcer and a significant reduction in adverse effect with dexamethasone treatment compared with triamcinolone acetonide, he noticed that there is significant pain reduction with dexamethasone. The conclusion was dexamethasone is equally effective in the treatment of aphthous ulcer with some advantages compared with triamcinolone acetonide.

In the study of Lalla R., *et al.* [3] he found that daily multivitamin supplementation is not effective in the size and reduction in a number of aphthous ulcers, and he suggests that clinician should not recommend multivitamin as routine prophylactic medicine for the aphthous ulcer.

Neelkamal S., *et al.* [4] found that alone levamisole is equal to combination with a low dose of prednisolone in altering the disease course of aphthous ulcer. the combination is slightly better in the reduction of severity of aphthous ulcer.

In the study of Femiano F., *et al.* [5] according to him prednisolone and montelukast were the same effective in reduction of a number of ulcers, pain relief, healing when compared with placebo. While, prednisolone is more effective in case of healing, pain, a number of ulcers compared to montelukast, the Adverse reaction is more common with a prednisolone group than montelukast.

In the study of Rodriguez M., *et al.* [6] he found that 5% amlexanox and 0.05% clobetasol have the same effect on pain and reduction of the size of the aphthous ulcer.

Few articles were found for comparison of corticosteroids and multivitamin. the comparative study was not done in any article so comparison done by taking data from each article separately. On the basis of articles included in this study, out of 7 studies 6 were done in foreign countries while only 1 studies were done in India. All the studies are done recently i.e. last 1 decade. No old literature was found for this comparative study. This shows both corticosteroid and multivitamin therapies are frequently used modalities in the treatment of RAS. 6 case control study and 1 case control study were included in this study. Many review articles were found but were not included in this study due to incomplete information or no standardized comparison of 2 treatment modality. A sample size of studies included varied from 50 to 160. Out of 7 studies included 1 studies were done in medical college and 5 studies were done in dental college and 1 study done in primary health center. This shows more interest of dental professionals in this study. All patient included in all 7 studies were examined for presence of recurrent aphthous ulcer in the oral cavity and studied under following headings

1. Level of pain
2. Number of ulcer
3. Duration
4. Erythema
5. Ulcer size

Keeping corticosteroid as gold standard multivitamin was compared. Out of 7 studies, 5 studies mentioned that corticosteroids are better in healing, pain reduction, duration, reduction in erythema, reduction in size as compare to multivitamin studies in 2 articles. Out of 2 studies on multivitamin therapy 1 study of Lalla R., *et al.* [3] concluded that Daily multivitamin supplementation, with the reference daily intake of essential vitamins, did not result in a reduction in the number or duration of Recurrent Aphthous Stomatitis episodes, another article Volkov I., *et al.* [1] concludes that vitamin B12 treatment is effective in the treatment of RAS.

Less number of articles on multivitamin therapy shows least clinicians interest or as a not definitive treatment for the recurrent aphthous ulcer. Multivitamins used as a prophylactic medicine, not as a drug of choice [7].

Hence, corticosteroid remains the gold standard for the treatment of recurrent aphthous stomatitis.

Limitations of this review were the unavailability of full-text article and inability to take literature from another database. Relevant data found was less in this study.

Conclusions

After studying all the article we conclude that corticosteroids are better for relieving pain, size, number, erythema of the recurrent aphthous ulcer. Multivitamins have least effects or no effects on the aphthous ulcer, these are used as prophylactic medicine, not as a definitive treatment for the recurrent aphthous ulcer.

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