



March 6th, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Brasileiro et al_Reviewed Manuscript).

Title: A Critical Review of Topical Management of Oral Hairy Leukoplakia

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Name of Journal: *World Journal of Clinical Cases*

ESPS Manuscript NO: 9266

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer.

1) **Abstract:** *Add about the results of topical therapy.*

The abstract section was reorganized as follows:

Podophyllin with acyclovir cream was effective and showed regression of lesions and no recurrence.

2) *Include the data on number of publications retrieved on initial search. Add Inclusion and exclusion criteria applied for writing the review.*

The last paragraph of the introduction and the beginning of the review section were rewritten to meet the reviewer suggestions.

The methodology was a search of the literature related to topical treatment of the OHL performed on PubMed from 1966 through December 2013. The search was conducted in English and Portuguese language and the keywords used were "oral hairy leukoplakia", "oral hairy leukoplakia and topical management" and "oral hairy leukoplakia and topical treatment". Additional studies were found in the list of references of the selected articles. Randomized clinical trials, case reports and review articles were included in current paper (Table 1).

Review: The search of the literature showed 16 articles related to OHL topical treatment. All OLH topical management identified in published studies will be presented."

3) *Instead of 'association' use 'combined topical therapy'.*

This change was made in the all manuscript as suggested by the reviewer.

4) *Discussion can be omitted as author already covered it under each drug. However, matter of discussion can be used for conclusion.*

This change was made in the manuscript as suggested by the reviewer. The conclusion was rewritten as follows:

A combined topical therapy of 25% podophyllin and 5% acyclovir cream is effective showing fast healing and no recurrence. In this case, additional multicenter studies are necessary. In relation to other agents, gentian violet (2%) was also used successfully in the OHL treatment, with no recurrence in a year, although only one previous study has evaluated the effectiveness of this therapy. Future double-blind and placebo-controlled trials are needed to support clinical evidences of OHL topical management.

5) *Inconsistencies were observed in writing references.*

References were reorganized and cited in numerical order.

6) *Discuss the surgery and systemic therapy in brief with respect to recurrence of the lesion. Compare it with topical therapy to show its importance.*

This discussion was made in the manuscript as suggested by the reviewer. The recurrence rate section was rewritten as follows:

Systemic antiviral drugs such as desciclovir, valacyclovir, acyclovir and ganciclovir has been used as OHL therapy and recurrence was observed after discontinuation of treatment^[17,18]. The possibility of occurrence of side effects and drug resistance must be carefully evaluated so that the potential harm does not exceed the expected benefits^[18]. Surgical excision as a treatment for OHL has been showed and no recurrence was observed within three months. However, most patients presented new foci of OHL after this time^[19]. Considering this and comparing to systemic therapy and surgery, topical treatment is recommended because does not produce systemic adverse effects, is less invasive and is effective over a long period of time^[4].

7) *Mentioned about the malignant transformation rate of OHL. Compare treated and non-treated cases with respect to transformation.*

According to the literature, oral hairy leukoplakia is a benign lesion and there is no evidence that has the potential for malignant transformation. Therefore, this discussion was not included in the review.

8) *Use ART instead of HAART.*

According to the World Health Organization (WHO), the “antiretroviral therapy (ART) is treatment of people infected with human immunodeficiency virus (HIV) using anti-HIV. The standard treatment consists of a combination of at least three drugs (often called “highly active antiretroviral therapy” or HAART) that suppress HIV replication.” Therefore, the authors believe that the term HAART can be used. (http://www.who.int/topics/antiretroviral_therapy/en/)

3 References and typesetting were corrected. However, few references are due to limitation of the subject in the literature.

Thank you again for publishing our manuscript in the *World Journal of Clinical Cases*.

Sincerely yours,

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