

Marked variation in malignant transformation rates of oral leukoplakia

Abstracted from

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Malignant transformation of oral leukoplakia: a systematic review of observational studies. *J Oral Pathol Med* 2015; Jul 20. doi: 10.1111/jop.12339. [Epub ahead of print]

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Question: What is the malignant transformation rate of oral leukoplakia?

Data sources Searches were carried out in the Medline, Embase and PubMed databases in July 2014 with a date range, 1960-2013.

Study selection Observational cohort studies (either prospective or retrospective) were included. Studies following identical cohorts, case control studies, clinical trials, interventional studies, laboratory studies, experimental studies, studies with no follow-up data, studies of pre-leukoplakia or snuff-induced lesions were excluded.

Data extraction and synthesis The databases were searched by one reviewer who also screened the studies and evaluated them against the inclusion criteria. Final decision on both inclusion and exclusion of the papers was agreed upon by both authors.

Results A total of 24 studies were included in this review, involving 12,103 patients. Of the 24 studies included 14 were retrospective. Studies were analysed by subgroup, allowing the authors to identify the rate of malignant transformation as 14.9% with a range of 0.13% to 34%. Only 11 studies gave information on the site of malignant transformation; the most common site was the buccal mucosa. For buccal mucosa the malignant transformation was 3.53%, compared to 24.22% for the tongue. Homogenous oral leukoplakia (OL) was most common, however non-homogenous types showed a higher rate of transformation of 13.1%. There was an increased risk of malignant transformation with age. Most studies demonstrated that there is a higher risk of transformation in the female population.

Conclusions Malignant transformation rate of OL varies from 0.13 to 34% across the 24 studies reviewed here. The authors identified clear risk factors for malignant transformation of oral leukoplakia, including location (tongue), appearance (non-homogenous), increased age and female gender. There was little evidence that surgical intervention had any benefit in reducing the risk of transformation

Commentary

Oral leukoplakia is one of the most common pre-malignant lesions of the mucosa.¹ Due to the prevalence of OL within the population it is important to understand its relationship with malignant transformation. This systematic review was written shortly after the Cochrane group had published a systematic review, which had been based on interventional studies on a similar topic.²

Cochrane reviews provide a highly concentrated source of reports based on randomised controlled trials (RCTs). The reason Cochrane only includes randomised controlled trials is to reduce overall bias (particularly allocation and selection bias). By including only trials which were randomised, the Cochrane review may exclude a number of possibly important studies. In the Cochrane review around this subject only nine studies were included of which only two recorded malignant transformation.

Some would argue that the focus Cochrane has on just including randomised trials is problematic; Anglemeyer for example demonstrated that looking at both observational studies and RCTs³ gives a similar effect to looking at randomised controlled trials alone.

The authors chose to perform a systematic review of observational studies to provide a detailed analysis of the rate of malignant transformation in oral leukoplakia and to give an insight into potential risk factors.

This review highlighted a number of very important risk factors for oral leukoplakia. By compiling studies, which included follow-up data on 12,103 patients, the authors of this systematic review emphasised the common traits among patients with OL, particularly in those who have undergone malignant transformation. Although this paper provides an insight into the rate of malignant transformation, there were some technical evidence based issues that cannot be overlooked.

The authors included studies from 11 different countries including the UK, USA, Japan and India. Whereas the reviewers were careful to exclude snuff-induced leukoplakia it can be problematic to compare transformation rates between countries where there is a difference in prevalence of known carcinogenic habits, such as betel nut chewing, a specific habit common in Indo-asia and China.⁴ It would have been appropriate to have carried out subgroup analysis within countries that have similar 'habits' to understand if these behaviours alter the rate of transformation.

The authors only included studies in the English language, which possibly excluded relevant research. Another limitation, which was highlighted by the authors themselves, is the difficulty

in coming to a consensus as to the definition of oral leukoplakia. Although definitions for oral leukoplakia were provided, the lack of clarity in definition and subsequent diagnosis/inclusion of a lesion in the reviewed studies could have caused bias. Additionally the dates chosen for the included studies may have contributed to this variation as the World Health Organisation did not provide a definition for OL until 1978,⁵ 11 years after one of the studies started.⁶

One of the most important elements of a review is the analysis and interpretation of data. This review summarises 24 studies in considerable detail, however, the authors failed to carry out any analysis to show risk of bias within the studies or across studies. This is disappointing for a review with such important findings as it decreases its validity. The authors should have also quality assessed the included studies perhaps using the GRADE system.⁷

In a similar manner, the reasons for some analysis are unclear. The authors showed several statistics, which highlighted their findings, eg malignant transformation of OL in tongue lesions at 24.22%, n = 78, however, it is unclear how the values were generated and there is no mention of adjustment for multiple comparisons, which would have a strong impact on the P values given.⁸

Although the results are not precise and may contain a high level of bias, it would be foolish to dismiss the importance of this review. With the correct information about the risks for patients with OL, clinicians can make better decisions for treatment. This review indicated a higher rate of malignant transformation in OL lesions on the tongue, in non-homogenous clinical types, in patients with advancing age and in females. The review also highlighted lesions of over 200 mm² as having an increased risk of malignant transformation.⁹

As this review was not looking at intervention studies, there are no clear implications for the outcomes. Despite the lack of statistical

evidence within this review it is useful to accept the conclusions within it as a strong indicator of the innate risk factors for malignant transformation of OL and to understand the importance for clinicians to ensure follow up appointments are attended by patients who display signs of leukoplakia and dysplasia.

Practice points

- When a patient presents with OL, it is essential that clinicians are able to identify and diagnose the condition, state the prognosis and propose a clinical management plan for the patient. This research is useful for the dental team as it highlights several risk factors for patients with OL that will assist clinicians in deciding when intervention is required.

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