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Review

Malignant transformation of oral lichen planus and oral lichenoid lesions: A meta-analysis of 20095 patient data

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ABSTRACT

Objectives: For over a century, a heated debate existed over the possibility of malignant transformation of oral lichen planus (OLP). We performed this meta-analysis to evaluate the malignant potential of OLP and oral lichenoid lesions (OLL) and investigate the possible risk factors for OLP malignant transformation into oral squamous cell carcinoma (OSCC).

Materials and methods: We searched Medline, Scopus, and Web of Knowledge for relevant observational studies. Data on OLP malignant transformation were calculated as a pooled proportion (PP), using the Der-Simonian Liard method. We performed subgroup analyses by OLP diagnostic criteria, site, and clinical type, using Open Meta[Analyst] software. Data on possible risk factors for malignant transformation were pooled as odds ratios (ORs), using Comprehensive Meta-Analysis software.

Results: Pooling data for OLP malignant transformation from 57 studies (19,676 patients) resulted in an overall PP of 1.1% [95% CI: 0.9%, 1.4%], while pooling data from 14 recent studies that used the World Health Organization-2003 diagnostic criteria resulted in an overall-PP of 0.9% [95% CI: 0.5%, 1.3%]. The risk of malignant transformation was higher (PP = 2.5%, 95% CI [1%, 4%]) in OLL patients (419 patients). A significant increase of malignant transformation risk was noted among smokers (OR = 2, 95% CI [1.25, 3.22]), alcoholics (OR = 3.52, 95% CI [1.54, 8.03]), and HCV-infected patients (OR = 5, 95% CI [1.56, 16.07]), compared to patients without these risk factors.

Conclusion: A small subset of OLP patients (1.1%) develop OSCC; therefore, regular follow-up for these patients is recommended. A higher incidence of malignant transformation was found among smokers, alcoholics, and HCV-infected patients; however, these associations should be further investigated.

Introduction

Oral Lichen Planus (OLP) is an oral subtype of Lichen Planus, affecting 1–4% of the worldwide population with a higher frequency in middle aged and elderly women [1]. It is a chronic inflammatory disease, characterized by a T-cell mediated response against epithelial basal cells, leading to basal cell degeneration and subepithelial band like infiltration by T-lymphocytes [2,3]. Clinically, there are six different subtypes, classified into two groups: Non-erosive-atrophic forms [including reticular, papular and plaque like] and erosive-atrophic forms [including atrophic (erythematous), erosive (ulcerative) and bullous] [4].

Oral squamous cell carcinoma (OSCC) is the most common form (90%) of oral cancer, with increasing prevalence on a global scale [5]. The first report of OLP malignant transformation was published

Abbreviations: HCV, hepatitis C virus; OLL, oral lichenoid lesions; OLP, oral lichen planus; OSCC, oral squamous cell carcinoma; PP, pooled proportion.

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in 1910 by Hallopeau et al. [6]. Later, several reports were published to investigate the malignant potential of OLP with conflicting results. Several studies [7–13] have reported malignant transformation rates for OLP that ranged between 0.07% and 5.8%, while other studies [14–17] showed no malignant potential for OLP.

The major dilemma that always confused researchers regarding the malignant transformation of OLP was the lack of universal criteria for its diagnosis. In fact, Krutchkoff et al. [18] and Van Der Meij et al. [19] alerted that almost two thirds of published case reports about OLP malignant transformation were not sufficiently documented to be considered. Over decades, several efforts were exerted to overcome this obstacle. In 1978, the World Health Organization (WHO) developed diagnostic criteria for OLP that were based on clinical and histopathological standards [20]. In 2003, Van der Meij and Van der Waal suggested modifying the WHO criteria to differentiate between OLP and other lichenoid lesions, such as lichenoid dysplasia, which has a significantly higher risk of malignant transformation than OLP [21].

We performed this systematic review and meta-analysis to precisely evaluate the malignant potential of OLP and investigate the association between OLP malignant transformation and different related risk factors, such as smoking, alcohol consumption, and hepatitis C infection.

Methods

We followed the guidelines of the (MOOSE statement: meta-analysis of observational studies in epidemiology) during the preparation of this meta-analysis [22].

Literature search strategy

We searched Medline (through PubMed), Scopus, and Web of Knowledge, using the following search strategy [Oral lichen planus OLP OR Oral lichinoid lesion OR OLL AND Malignent OR Cancer OR Oral squamous cell carcinoma OR OSCC]. No restrictions by publication period were used. We also scanned the bibliography of included studies to identify any missed studies that are relevant to our subject.

Eligibility criteria and study selection

We included full length articles of observational studies, published in the English language, in peer reviewed medical journals. All observational studies, providing dichotomous data on the malignant potential of OLP or oral lichenoid lesions (OLL), were included. We excluded conference abstracts, articles published as a whole in a non-English language, case reports/series, and secondary analysis articles. Two independent reviewers applied the selection criteria in two steps [Title and abstract screening, then full text screening] to determine the included studies and disagreements were solved upon the opinion of a third reviewer.

Data extraction

Two independent reviewers extracted the following data from included studies: (I) Characters of study design and length of follow up period, (II) risk of bias assessment domains, (III) characteristics of OLP lesions including the used diagnostic system criteria, site, and clinical type [Atrophic, erosive, reticular, or plaque], (IV) the incidence of malignant transformation in OLP or OLL cases, and (V) the incidence of malignant transformation in different subgroups of OLP patients. Disagreements were resolved upon the opinion of a third reviewer.

Risk of bias assessment

We used the Newcastle-Ottawa scale [23] to assess the risk of bias within the included observational studies. Using this scale, each included study is evaluated based on reporting three essential domains:

(a) Selection of the study subjects i.e. included patients were derived from a representative population, and the exposure (OLP diagnosis) was ascertained based on predefined criteria (preferably including histological examination).
(b) Comparability of groups on demographic characteristics and important potential confounders: which is achieved by adequate control of secondary risk factors, such as smoking and alcohol consumption, as well as adequate separation between OLP and OLL cases (by excluding history of medications or restorations).
(c) Ascertainment of the prespecified outcome (exposure/treatment): based on histological assessment with a sufficient follow up duration.

Due to the design of included studies (lack of non-exposed group), we removed the question about the selection of the non-exposed group (Question No. 2) from the Newcastle-Ottawa Scale; therefore, the total score is out of eight, not nine [24]. Each article was evaluated by two independent reviewers and any disagreements were resolved by consenesus among both reviewers. We assessed for the existence of publication bias, using the Egger's test [25].

Data synthesis

Pooled proportion (PP) of the overall risk of malignant transformation in OLP and OLL was calculated under the random effects model, using Der-Simonian Liard method. We conducted a cumulative meta-analysis to display the trend of malignant transformation over time from 1924 to 2016. Subgroup analysis was conducted to compare the risk of malignant transformation according to the diagnostic criteria, clinical type, and site of OLP. We calculated a pooled odds ratio (OR), along with its 95% confidence interval (CI), to compare the risk of transformation according to patients' gender, smoking, alcohol consumption, infection with hepatitis C virus (HCV), and diabetes mellitus. Comprehensive Meta-Analysis and Open Meta [Analyst] software were used for quantitative data synthesis.

Results

Literature search results

Literature search retrieved 1200 unique records. After title/abstract screening, 197 full text articles were retrieved for further evaluation. Finally, 57 studies that provided data on 19,676 OLP and 419 OLL cases were eligible for inclusion in our analysis (Fig. 1). Of OLP cases, a total of 280 patients developed OSCC. The rate of malignant transformation of OLP in individual studies ranged from 0.3% to 14.3%. Baseline data of enrolled patients in included studies are illustrated in Tables 1. Table 2 displays a comparison between demographic characteristics of OSCC patients in included studies and the reference profile for OSCC patients (from the Surveillance, Epidemiology, and End Results [SEER] database).

Risk of bias assessment

The majority of included studies reported adequately on the representativeness of their cohorts (55 of 57), exposure