

Smokeless tobacco – a substantial risk for oral potentially malignant disorders in South Asia

Abstracted from

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Question: What is the risk of developing oral potentially malignant disorders (OPMDs) in users of smokeless tobacco (SLT)?

Data sources Medline, the Science Citation Index (SCI) via Web of Science, Scopus, CINAHL, Global Index Medicus, Google Scholar and SLT-related reports of the International Agency for Research on Cancer and the National Cancer Institute of the United States.

Study selection Observational studies on the use of SLT and the risk of developing OPMDs in South Asian Populations.

Data extraction and synthesis Duplicate selection of studies was undertaken with two reviewers undertaking data abstraction and quality assessment independently. Risk and odds ratios were extracted or calculated for studies where possible. Meta odds ratios (mOR) were calculated using a random effects analysis.

Results Fifteen papers reporting 18 studies were included. The majority (12) were from India. All the studies were case-control designs. MOR for any OPMD with the use of any SLT product was 15.5 (95% CI; 9.9-24.2). Risk was higher in women; mOR = 22.2 (95% CI, 9.1-54.1) than men; mOR = 8.7 (95% CI, 2.1-34.8). Betel quid with tobacco carried the highest risk for OPMD, mOR = 16.1 (95% CI, 7.8-33.5).

Conclusions The findings of our study point towards a strong association between some forms of OPMDs and SLT use in South Asia. The risk estimates are high, irrespective of controlling for confounders such as smoking and alcohol or stratification by sex, country or source of controls. There is also an exposure-response relationship between OPMDs and SLT use.

Commentary

Oral cancer is ranked as the sixth most common malignancy in South Asia – with nearly 300,000 new cases diagnosed each year, accounting for one third of the total cancer burden in India.¹ Tobacco and alcohol consumption are the most significant risk factors for oral cancer world-wide, however, in South Asia smokeless tobacco (SLT) accounts for a greater attributable risk.² Smokeless tobacco is any form of tobacco consumed through the mouth or nose that does not involve burning the product - this includes betel quid, paan, gutkha, chewing tobacco and other such products. While only 1.6% of men and 0.5% of women in the United Kingdom use SLT,³ 90% of SLT use is concentrated in South Asia³ with the practice viewed as being socially and culturally acceptable.⁴

Oral potentially malignant disorders (OPMDs) are clearly defined in this study as any chronic lesions/conditions found in the mouth that have the potential to transform into oral cancer;⁵ this includes: leukoplakia, erythroplakia, oral sub-mucous fibrosis (OSMF), lichen planus, actinic keratosis, discoid lupus erythematosus and palatal lesions among reverse smokers.⁶ The prevalence of OPMDs worldwide ranges from 1 to 5%;⁷ and their potential for them to undergo malignant transformation ranges from 1 to 36%, depending on the subtype of OPMD.⁸ This study seeks to quantify the risk associated with SLT use and the development of OPMDs in South Asia.⁶

Fifteen articles corresponding to eighteen studies, pertaining to three of the seven countries in South Asia, were included in the meta-analysis. A substantial risk association between SLT use and OPMDs was estimated from the pooled data (meta odds ratio, mOR = 15.5; 95% CI, 9.9-24.2). The challenge in meta-analysis of published studies is taking into account confounders – analysis of the subgroup of studies here that had adjusted for smoking and alcohol found limited attenuation with a high-risk association remaining (mOR 13.1; 95% CI 8.3-20.7). OSMF was found to have the highest risk association with SLT use (mOR = 20.0; 95% CI, 12.3-32.5), and leukoplakia the lowest (mOR 4.33; 95% CI 1.4-13.2). Of the range of SLT products included, betel quid with tobacco carried the highest risk association for developing OPMDs (mOR = 16.1; 95% CI, 7.8-33.5); and women were found to have a higher risk association (mOR = 22.2; 95% CI, 9.1-54.1) than men (mOR = 8.7; 95% CI, 2.1-34.8).

Overall, this was a well conducted systematic review and meta-analysis conforming to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.⁹ The search

strategy was thorough, but perhaps could also have included seeking unpublished data or contacting authors. The reviewers assessed the quality of the included studies using the National Collaborating Centre for Methods and Tools, McMaster University's 'Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies',⁶ and this identified one of the major limitations of this meta-analysis – ie the quality of included studies were either of moderate (n = 12) or weak (n = 6) quality;⁶ no studies were found to have strong qualities when assessed. Moreover, the quantification of SLT exposure in these studies was also identified by the authors as a problem and limitation – particularly the lack of a clear definition for 'ever' exposure may cause overestimation of the true risk, as an individual who has used SLT once was categorised in the same group as someone who used SLT for 20 years.⁷

This review is a good baseline description of the extent of epidemiological research into SLT and OPMD risk in South Asia. It points to the need for further research into this risk association, and indeed for the risk associations between SLT, OPMD and oral cancer. However, more importantly, it highlights the importance for research into SLT cessation in Asian populations and communities as a means to prevent oral cancer worldwide.

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