



Letter

Smokeless Tobacco Use and Oral Cancer

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THIS LETTER refers to the review paper by T.E. Axell in the October issue of *Oral Oncology* [1]. The paper provides an account of oral mucosal changes due to the use of oral snuff in Scandinavia.

In the first part of the paper, the author quotes the evaluation from an IARC monograph [2], "There is *sufficient evidence* that oral use of snuff of the types commonly used in North America and western Europe is carcinogenic to humans" and "There is *limited evidence* that chewing tobacco commonly used in these areas is carcinogenic". The author then questions these evaluations with the statement "It seems highly doubtful whether this statement is valid for the present situation in Scandinavia. Opinions thus differ . . .".

In the body of the paper, however, we were not able to locate a single scientific result or finding that was contrary to the quoted evaluations. The paper reviewed findings from small case series and cross-sectional studies of snuff-induced oral mucosal changes (maximum sample size 252 snuff users), sometimes with a short-term follow-up (maximum 6 months). The author discussed histopathological findings in these lesions, including epithelial dysplasia, and claimed that most of the clinical and histopathological changes were reversible.

Axell contrasted these findings with the Indian findings as very different and commented that results of Indian studies cannot be applied to Scandinavia as the type of chewing quid was different. It should be pointed out that in Indian material also [3] the rates of spontaneous regression of clinical lesions as well as epithelial dysplasia without any intervention to normal mucosa were high (over 40 and 13%). Axell found a report of only one oral cancer developing or diagnosed in the studies he reviewed but based on the size of the reviewed material of snuff users and the incidence rate of oral cancer in Scandinavia, finding even one case was significant (using Poisson probability distribution).

A finding that in a large series of 545 cancers of oral cavity, pharynx, larynx or oesophagus during 1931-1937 in a hospital in Sweden, 91% were daily chewers, and 70% of 68 cases of 'outer oral cavity' cancers used snuff [4], was contrasted by Axell with a later finding in 1957 that there was a lack of 'preponderance' of smokeless tobacco users in a series of 36 cases of gingival cancers and 8 cases of buccal cancers (misquoted, actually 18 buccal cancers, 8 men and 10 women)

from the same hospital [5]. The authors, however, described their findings differently, "Nearly half of the patients with cancers in these areas were habitual chewers and had chewed for many years. It seems of particular significance that in the majority of the cases the cancer appeared in the area in which the chewed tobacco was held".

Axell did not mention that this was a case-control study in which authors concluded that (among men) "chewing of this type of tobacco was found, perhaps because of small number of cases, to be suggestively (rather than significantly as the relative risk was less than 2) related to cancer of the gum and buccal cavity". The association was found using ridit analysis by the authors and the information given in the paper is not enough for a re-analysis of the data although this is not a justification for the opposite, unqualified statement that "They did not find any convincing association between tobacco chewing and the tumours".

Another example of somewhat selective quoting mentioned only pancreatic cancer from an abstract [6], "In rapsodic (sic) and unconfirmed reports it has been claimed that there is an increased risk of smokeless tobacco users to contract pancreas cancer". It was not mentioned that this was a cohort study of 12 945 Norwegian and 16 930 American men with 10 years of follow-up in which the authors stated, "... Our findings suggest that men with this habit have an increased risk of cancer of the mouth, pharynx, esophagus and pancreas" (analysis stratified for age, residence characteristics and cigarette smoking). In fact, for cancer of the pancreas, the Norwegian group later published a detailed analysis [7] and reported a clear positive association with chewing of tobacco or use of snuff that was weaker than the association for alcohol drinking but stronger than that for cigarette smoking.

The findings that could perhaps be construed as supportive of the author's assertion were: (1) identification of only 33 cases of oral cancers from the Swedish Cancer Registry over a 10-year period (1962-1971) possibly associated with snuff dipping, that gave an estimated annual incidence rate of 0.5 per 100 000 among daily users of snuff; and (2) an inquiry to all University ENT clinics in Sweden during 1990 that indicated even lower figures of intraoral cancers possibly associated with the use of snuff and developed at the site where the quid was regularly placed. The first finding was from a paper published in Swedish by the author and co-workers [8] and the second finding was from unpublished data of the author and co-workers. It was thus difficult to find out details of methodology

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of these rather unorthodox approaches. It is obvious that if one takes a subset of the numerator of incidence rate (presumably exposed to a risk factor of interest assessed retrospectively), it will result in a small fraction of the original incidence rate. Considering that any such retrospective assessment is not likely to be complete, the bias will be unidirectional, and the result will be an underestimate even if a fraction of original denominator is used as the exposed population. Unless one estimates the incidence rate of the same sites among the non-exposed using similar methods, it is impossible to draw any conclusion about the aetiology.

In the paper there was no report of any case series, case-control or cohort study demonstrating a lack of association between snuff use and oral cancer. The author concluded the paper with a recommendation that case-control and follow-up studies were needed but then he also made a statement in the concluding paragraph, "The question whether smokeless tobacco usage is carcinogenic to humans is perhaps the most important one and it seems to be a matter of dispute". In the English abstract of his Swedish paper [8] Axell stated that "... snuff dipping apparently increases the risk of cancer at the site where snuff is placed five- to six-fold". It is clear that Axell's opinion about carcinogenicity of smokeless tobacco use has undergone a change but he has not presented any credible scientific evidence for it.

The evaluations in the IARC monograph were based on the epidemiological as well as laboratory findings identified from the literature available to the IARC at that time (1984) and to a group of 20 international invited experts including two scientists from Scandinavia. This literature included case-control and cohort studies reported from various parts of the world including Scandinavia. The invited experts arrived at unanimous evaluations which have not been questioned by

scientists anywhere, excepting those connected with tobacco industry.

Thus it appeared that the paper made an attempt to create a dispute when scientifically, none really exists except, of course, in the eyes of tobacco industry.

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