Squamous cancer of the oesophagus in Africa: A change of focus for research

Squamous cancer of the oesophagus (SCCO) continues to be a major problem in many parts of East, Central and southern Africa. In 2005, the fruitless nature of the search for a single potent carcinogen responsible for high regional incidences of SCCO was noted.[1]

Research effort continues to be expended on case-control studies, on meta-analyses, and on systematic reviews of these studies, still with nothing essentially new to report: tobacco, alcohol, and nutritional deficiencies remain important.[2-4] Polycyclic aromatic hydrocarbons (PAHs) currently receive regular mention, and many other substances are mentioned in each litany of possible causes,[4-6] none with compelling evidence against them as major factors.[7] Genetic studies have been helpful but not ground-breaking in the move to understand endemic SCCO.[4]

Tobacco, alcohol, PAHs, genetic differences – none of these can logically be the key factor causing the very high incidences of SCCO in some communities, compared with communities that are similarly exposed but have incidences of a lower order of magnitude. They are important, but the evidence so far suggests that they are peripheral to the main reasons behind endemic incidences. In susceptible communities, case-control studies may help to identify reasons for individual cases of SCCO, but do not address community susceptibility.[8,9] This approach of using case-control comparison has been exhaustive and is now producing little in the way of new information. The existence of a single undiscovered potent carcinogen or combination of carcinogens that will be uncovered by case-control study should now be accepted as extremely unlikely. A promising line of research into mechanisms of oesophageal squamous carcinogenesis has opened up with the naming of non-acid reflux as having a strong and probably causative association with SCCO[10] – in contradistinction to the known association of acid reflux with oesophageal adenocarcinoma.

Is it not now time for two changes of focus: firstly to return to the problem of community susceptibility as repeatedly addressed by Van Rensburg,[11,12] rather than individual susceptibility? Comparative study of communities rather than of individuals should clarify reasons for some communities being more susceptible than others.

A second change of focus is to consider factors other than carcinogens, but which predispose to carcinogenesis. Van Rensburg[11] stated in 1981 that the choice of cereal that constitutes the bulk of the diet in those adhering to a simple lifestyle is the main determinant of risk. In Africa, risk is invariably associated with maize. He has maintained that nutritional deficiency is the comprehensive cause of endemic levels of SCCO, and advocates prevention by healthy nutrition that includes all the necessary micronutrients from a young age. Sammon and colleagues[7,9,13] have in addition identified evidence that in communities that depend on maize, there is a strong association with maize meal; the rapid release of free fatty acid starting from the time of milling of maize combines with nutritional deficiency to create population susceptibility. Prevention requires elimination or mitigation of the risk associated with chemical degeneration of maize meal,[9] combined with a diet containing all necessary vitamins and micronutrients.

It is now prudent to abandon the search for an undiscovered potent carcinogen and to address community susceptibility in endemic areas, acknowledging that currently we have no credible candidates for predisposition apart from nutritional deficiencies of a maize-based diet, and chemical degeneration of milled maize. Region-to-region and community-to-community comparisons are appropriate.

Investigation of causal links between SCCO, non-acid reflux, and diet currently offers some promise of explaining mechanisms of predisposition to carcinogenesis.

There is now sufficient evidence to expand the implementation of preventive measures: targeted supplementation of maize meal in countries where this has not yet been enforced, and recognition that maize meal is a rapidly perishable food that requires control of chemical content at point of sale.

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