Prevention of esophageal cancer: the nutrition intervention trials in Linxian, China. Linxian Nutrition Intervention Trials Study Group

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Abstract: In Linxian China, the esophageal/gastric cardia cancer mortality rates are among the highest in the world. There is suspicion that the population's chronic deficiencies of multiple micronutrients are etiologically involved. We conducted two randomized, placebo-controlled nutrition intervention trials to test the effects of vitamin and mineral supplements in lowering the rates of esophageal/gastric cancer. In the first trial, the dysplasia trial, 3318 adults with a cytological diagnosis of esophageal dysplasia received daily supplementation with 26 vitamins and minerals in doses typically 2-3 times the United States Recommended Daily Allowances, or placebos, for 6 years. The second trial, the general population trial, involved 29,584 adults and used a one-half replicate of a 2(4) factorial experimental design which tested the effects of four combinations of nutrients: A, retinol and zinc; B, riboflavin and niacin; C, vitamin C and molybdenum; and D, beta-carotene, vitamin E, and selenium. Doses for these daily supplements ranged from 1 to 2imes the United States Recommended Daily Allowances, and the different vitamin/mineral combinations or placebos were taken for a period of 5.25 years. As part of the general population trial, and end-of-intervention endoscopy survey was carried out in a small (1.3%) sample of subjects to see if supplementation affected the prevalence of dysplasia and early cancer. Herein we review the methods of these trials and the results of the endoscopic survey. Fifteen esophageal and 16 gastric cancers were identified in endoscopic biopsies from the 391 subjects evaluated from two villages, and nearly all were asymptomatic. No significant reductions in the prevalence of esophageal or gastric dysplasia or cancer were seen with any of the four supplement groups. However, the prevalence of gastric cancer among participants receiving retinol and zinc was 62% lower than those not receiving those supplements (P = 0.09), while participants receiving beta-carotene, vitamin E, and selenium had a 42% reduction in esophageal cancer prevalence (0.34). We have reported separately that cancer mortality over the entire 5.25-year period was significantly reduced among those receiving beta-carotene, vitamin E, and selenium. The findings from the overall trial and the endoscopic sample offer a hopeful sign and should encourage additional studies with these agents in larger numbers of subjects.