Facial flushing after alcohol consumption was not a risk factor for upper aerodigestive tract cancer

Isao Oze[1], Keitaro Matsuo[1], Takeshi Suzuki[2], Takakazu Kawase[1], Satoyo Hosono[1], Hidemi Ito[1], Miki Watanabe[1], Kazuo Tajima[1], Hideo Tanaka[1]

[1]Division of Epidemiology and Prevention, Aichi Cancer Center Research Institute, Japan, [2]Department of Medical Oncology and Immunology, Nagoya City University, Japan

Background: Alcohol intake is one of the most important risk factors for upper aerodigestive tract (UAT) cancer (oral, pharyngeal, laryngeal, and esophageal cancer). After drinking alcoholic beverage, alcohol is promptly oxidized to acetaldehyde, which is considered toxic and carcinogenic agent. Acetaldehyde is oxidized to acetate by aldehyde dehydrogenase (ALDH) enzymes, mainly ALDH2. In East Asians, *ALDH2* is polymorphic (rs671, Glu504Lys). After drinking alcohol, the concentration of acetaldehyde becomes elevated for those with *ALDH2* Lys allele, which had low catalytic activity to eliminate acetaldehyde. Therefore, those with *ALDH2* Lys allele have higher risk for UAT cancer than those with *ALDH2* Glu allele due to their high exposure to acetaldehyde. On the other hand, acetaldehydemia is considered to be associated with flushing response, such as facial flushing, palpitation, drowsiness and other unpleasant symptoms. We hypothesized that the flushing response, considered as a surrogate marker of *ALDH2* genotype, may also be associated with the UAT cancer risk. We conducted a case-control study to elucidate the association between flushing response and UAT cancer.

Methods: The subjects were 961 patients diagnosed with UAT cancer (oral cavity and pharynx cancer in 436, larynx cancer in 91, esophageal cancer in 434) between January 2001 and December 2005 at Aichi Cancer Center Hospital. The controls were 2883 first-visit outpatients at Aichi Cancer Center Hospital during the same period who were confirmed to have no cancer. Information on facial flushing, alcohol consumption, and cumulative smoking was collected via self-administered questionnaire, checked by a trained interviewer. Associations between UAT cancer and facial flushing were assessed by odds ratio (OR) and 95% confidence intervals (CI) using conditional logistic regression models.

Results: Facial flushing was not significantly associated with UAT cancer (OR 1.01, 95%CI 0.86-1.19), while we confirmed alcohol consumption and cumulative smoking were significantly associated with UAT cancer. In addition, no significant association was observed between facial flushing and each cancer site (oropharyngolaryngeal cancer and esophageal cancer). Facial flushing had no significant interaction with alcohol consumption and cumulative smoking (interaction P=0.219 and 0.132, respectively). Similarly, no interaction was observed between facial flushing and alcohol consumption and cumulative smoking. We calculated the population attributable fraction (PAF) for alcohol consumption among flushers, non-flushers, and subjects in total (76.5%, 60.9%, and 73.9%, respectively). Though the PAF among flushers were higher than that among non-flushers, the PAF among total subjects was similar to that among flushers.

Conclusions: In this study, facial flushing was not a risk factor for UAT cancer. In addition, facial flushing was a useless index for

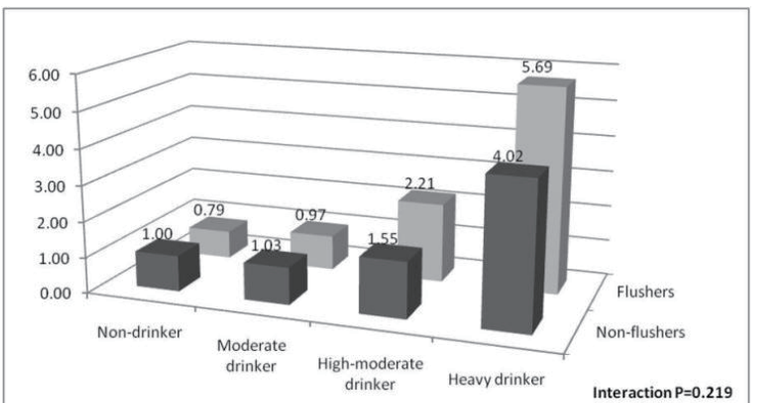

Figure 1. Interaction between facial flushing and alcohol consumption

intervention about alcohol consumption to prevent UAT cancer. Further investigation about the association between facial flushing and *ALDH2* polymorphism is required.