Alcohol-induced asthma

Alcohol-Induced Asthma

Key words: acetaldehyde, alcoholic beverage, aldehyde dehydrogenase, histamine

Frequency and race-related differences

In a questionnaire-based study Ayres and Clark (1) reported that 54 (32.1%) of 168 patients experienced wheezing after alcohol consumption, while 39 patients (23.2%) showed a reduction of symptoms. Patients whose symptoms were aggravated in response to every type of alcoholic beverage consumed numbered only 3 of the 168 asthmatics. Breslin et al (2) reported that bronchoconstriction was not induced by the oral administration of pure ethanol dissolved in water in any of 3 asthmatics who had shown a decrease in FEV_1 (forced expiratory volume in one second) following consumption of specific alcoholic beverages. Thus, beverage ingredients other than ethanol are thought to aggravate asthma in Western populations.

In Japan, it was shown that 51.4% of asthmatic individuals had alcohol-induced asthma (ALA) (3). Drinking pure ethanol produced a 20% or greater decrease in the FEV_1 in 23 of 42 Japanese patients, indicating that ethanol is responsible for their ALA in Japanese asthmatics (4). Although we cannot be sure that no ingredient other than ethanol is responsible for any ALA among Japanese, evidence points to race-related differences in ALA making ethanol per se the principal cause in Japan.

Metabolism of ethanol and acetaldehyde and race-related factors

Although 2 to 10% of ingested ethanol is eliminated in exhaled air or in the urine, ethanol is metabolized primarily by the liver. In the liver, ethanol is degraded into acetaldehyde, which is degraded by aldehyde dehydrogenase (ALDH) into acetic acid and water. ALDH includes two isozymes, ALDH1 and ALDH2, and the latter plays a more significant role in the metabolism of acetaldehyde. Known genotypes of ALDH2 include: $ALDH2^1/ALDH2^1$ (normal homozygote; an active type), $ALDH2^1/ALDH2^2$ (heterozygote; an incompletely deficient type), and $ALDH2^2/ALDH2^2$ (mutant homozygote; a completely deficient type). ALDH2 deficiency is seldom observed in Caucasians and blacks, while it is present in approximately 50% of the Japanese population (5).

Individuals with ALDH2 deficiency are known to develop facial and systemic flushing due to accumulation of acetaldehyde (6–8), and ALDH2 deficiency also shows links to ALA. In Japan, more than a 20% decrease in FEV_1 was observed after an oral ethanol challenge in 3 of 16 (19%) asthmatics with a normal homozygous ALDH2 genotype, 10 of 14 (71%) asthmatics heterozygous for the mutation, and 2 of 2 (100%) asthmatics homozygous for the mutant ALDH2 gene (9). In Western populations, in whom bronchoconstriction does not develop in response to alcohol, severe asthmatic attacks can follow alcohol intake in chronic alcoholics taking disulfiram to enforce abstinence (10). These observations suggest that accumulation of acetaldehyde due to mutation of the ALDH2 gene is involved in the onset of ALA.

Symptoms of ALA

Patients with ALA become aware of a wheeze and/or dyspnea soon after alcohol ingestion. Usually, these symptoms appear within 30 minutes following alcohol intake (3), often subsiding if β_2-agonists are inhaled. In rare cases, life-threatening attacks can be caused by alcohol intake; an asthmatic patient receiving the disulfiram therapy required mechanical ventilation for a severe attack of ALA (10). In this issue Saito et al (11) also reported a Japanese asthmatic patient who developed severe asthma attacks after taking a small amount of alcohol included in food. Thus, careful attention should be taken to ALA in clinical practice.

See also p 643.

Mechanism of ALA

Blood acetaldehyde and histamine levels following alcohol ingestion have been shown to be higher in patients with ALA than in asthmatics without ALA or in healthy individuals despite equivalent blood ethanol levels (4). Studies in guinea pigs (12) and in patients with asthma (13) have shown that inhalation of acetaldehyde induces bronchoconstriction through the release of histamine. Acetaldehyde causes the release of histamine from leukocytes of patients with asthma (4), particularly from mast cells and basophils. The release of histamine does not differ between patients with and without ALA (4). Thus, it is likely that blood acetaldehyde levels and bronchial hyperresponsiveness determine the extent of bronchoconstriction following alcohol ingestion.

Drug effects on ALA

In 1978, Geppert and Boushey (14) reported that neither atropine nor cromolyn inhibited the decrease in sGaw following alcohol intake in a 28-year-old Asian-American woman who manifested a dry cough, wheezing, and facial flushing immediately after alcohol consumption. In 1981, Gong et al (15) described an Asian patient with alcohol-induced bronchoconstriction in whom cyproheptadine, atropine, acetylsalicylic acid,

and chlorpheniramine, but not cromolyn sodium or isoproterenol, showed partial inhibition of ALA.

Our study (16) has clearly shown that alcoholic beverage-induced bronchoconstriction can be completely prevented by histamine-H_1 antagonists, indicating that histamine is a dominant mediator in alcoholic beverage-induced bronchoconstriction.

Prevention and treatment of ALA

It is possible, as mentioned above, to prevent ALA almost completely by oral dosing of the histamine H1-antagonist, terfenadine, 2 hours before alcohol intake (16). Patients at our outpatient clinic have been satisfied with this preventive measure. ALA also can be prevented by as nonspecific bronchodilators 20 to 30 minutes before alcohol intake. Once it has developed, ALA can be treated similarly to other acute exacerbations of asthma. Generally, severe attacks of ALA are uncommon. Patients with ALA often avoid alcohol intake for fear of exacerbation of their symptoms. While abstinence obviously will prevent ALA, it is reasonable to expect patients with ALA to consume alcohol occasionally at business or social events. Terfenadine taken 2 hours before alcohol ingestion should help to reduce subsequent symptoms.

Masaki FUJIMURA, MD, PhD and Shigeharu MYOU, MD, PhD
The Third Department of Internal Medicine,
Kanazawa University School of Medicine,
13-1 Takara-machi, Kanazawa 920-8641

References

1) Ayres JG, Clark TJ. Alcoholic drinks and asthma: a survey. Br J Dis Chest **77**: 370–375, 1983.
2) Breslin AB, Hendrick DJ, Pepys J. Effect of disodium cromoglycate on asthmatic reactions to alcoholic beverages. Clin Allergy 3: 71–82, 1973.
3) Sakurai S, Kobayashi Y, Okada T, Ohya N. A clinical investigation of acute exacerbation after drinking of alcoholic beverage. Kokyu **11**: 1340–1347, 1992 (English Abstract).
4) Shimoda T, Kohno S, Takao A, et al. Investigation of the mechanism of alcohol-induced bronchial asthma. J Allergy Clin Immunol **97**: 74–84, 1996 (see comments).
5) Goedde HW, Agarwal DP, Harada S, et al. Population genetic studies on aldehyde dehydrogenase isozyme deficiency and alcohol sensitivity. Am J Hum Genet **35**: 769–772, 1983.
6) Wolff PH. Ethnic differences in alcohol sensitivity. Science **175**: 449–450, 1972.
7) Ewing JA, Rouse BA, Pellizzari ED. Alcohol sensitivity and ethnic background. Am J Psychiatry **131**: 206–210, 1974.
8) Harada S, Agarwal DP, Goedde HW. Aldehyde dehydrogenase deficiency as cause of facial flushing reaction to alcohol in Japanese. Lancet **2**: 982, 1981 (letter).
9) Takao A, Shimoda T, Kohno S, Asai S, Harda S. Correlation between alcohol-induced asthma and acetaldehyde dehydrogenase-2 genotype. J Allergy Clin Immunol **101**: 576–580, 1998.
10) Zapata E, Orwin A. Severe hypertension and bronchospasm during disulfiram-ethanol test reaction. BMJ **305**: 870, 1992 (see comments).
11) Saito Y, Sasaki F, Tanaka I, et al. Acute severe alcohol-induced bronchial asthma. Intern Med **40**: 643–645, 2001.
12) Myou S, Fujimura M, Bando T, Saito M, Matsuda T. Aerosolized acetaldehyde, but not ethanol, induces histamine-mediated bronchoconstriction in guinea-pigs. Clin Exp Allergy **24**: 140–143, 1994.
13) Myou S, Fujimura M, Nishi K, Ohka T, Matsuda T. Aerosolized acetaldehyde induces histamine-mediated bronchoconstriction in asthmatics. Am Rev Respir Dis **148**: 940–943, 1993.
14) Geppert EF, Boushey HA. An investigation of the mechanism of ethanol-induced bronchoconstriction. Am Rev Respir Dis **118**: 135–139, 1978.
15) Gong H Jr, Tashkin DP, Calvarese BM. Alcohol-induced bronchospasm in an asthmatic patient: pharmacologic evaluation of the mechanism. Chest **80**: 167–173, 1981.
16) Myou S, Fujimura M, Nishi K, Ohka T, Matsuda T. Inhibitory effect of terfenadine, a selective H1 histamine antagonist, on alcoholic beverage-induced bronchoconstriction in asthmatic patients. Eur Respir J **8**: 619–623, 1995.