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File: ■ Food for Special Medical Purposes
■ Veisalgia
■ Hangover

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RE: Symptoms of Veisalgia May Be Improved by Use of a Food for Special Medical Purposes

Lieb B, Schmitt P. Randomized double-blind placebo-controlled intervention study on the nutritional efficacy of a food for special medical purposes (FSMP) and a dietary supplement in reducing the symptoms of veisalgia. *BMJ Nutr, Prev, & Health.* Apr 2020;0:1-9. doi: 10.1136/bmjnph-2019-000042.

Veisalgia, or hangover, spans all physical and psychological symptoms experienced the day after one-time ethanol alcohol use, when blood alcohol concentration is 0.0%. Symptom intensity increases as alcohol is metabolized, < 24 hours. Symptoms are due to alcohol ingestion, possible congeners, and metabolic intermediates; most common are exhaustion, thirst, fatigue, headache, dry mouth, and nausea. Individual, gender-independent variables in symptom intensity and frequency occur regardless of amount of alcohol consumed. Dehydration and loss of electrolytes have been cited as causing veisalgia, but one study found no notable change in electrolytes after alcohol use.

Ethanol diffuses into tissues with high blood requirements, e.g., the brain, producing radical oxygen species (ROS) during its catabolism. While antioxidant enzymes help neutralize ROS, one-time alcohol use significantly reduces antioxidant levels in the skin. By inhibiting the superoxide dismutase enzyme in blood and liver tissue, alcohol intake slows ROS elimination and increases oxidative stress in the liver. Such stress is increased by alcohol-related factors such as induction of hepatic enzymes and formation of free radicals in brain tissue leading to mitochondrial dysfunction. Thus, oxidative stress seems to be the main cause of veisalgia. Congeners (e.g., phenols, aldehydes, fusel alcohols, tannins, and methanol) may also cause symptoms, although at a much lower level than alcohol.

Acute hangover is often treated with aspirin or ibuprofen, but nutritional substances may be used prophylactically to avoid or reduce symptoms. Earlier reports of the efficacy of some foods in this regard present only subjective evidence. Jadad scores for most are low. In this randomized, three-armed, double-blind, placebo-controlled clinical trial (RCT), the Acute Hangover Scale (AHS) and Hangover Symptoms Scale (HSS) were used in an effort to improve standardization of hangover intervention studies. The authors hypothesized a correlation between severity of hangover symptoms and amounts of alcohol consumed, considering the contribution of congeners and body fluid loss due to alcohol intake, the latter frequently described in the literature.

A food for special medical purposes (FSMP; Fermenta Biotech GmbH; Hamburg, Germany) included five plant extracts, a variety of vitamins and minerals, and flavorings and

sweeteners. The complete FSMP was given to group 1 (n = 69). A formulation lacking plant extracts was given to group 2 (n = 76). A formulation with only flavoring and sweetening ingredients was given as placebo (group 3; n = 69). Participants were healthy men and women aged 18-65 years. Participants were tested for alcohol consumption via breath analysis, urine and vital parameters, and antioxidative capacity of skin before alcohol intake and after 12 hours, with some measures repeated immediately after consumption. Premixed solutions (7.5 mg randomized group-assigned powdered agents dissolved in 100 mL water) were given 45 minutes before and immediately after alcohol intake. In a relaxed group setting, participants drank as much beer (4.8% alcohol), mixed beer (2.5%), white wine (11%), or white wine spritzer (5.5%) as they liked for four hours. Small meals were offered, and participants could go outside to smoke. Restroom visits and number of drinks consumed by each participant were documented. Participants were instructed to go home after the drinking session, sleep, and return 12 hours later for testing. The AHS and HSS were administered at that time.

With all parameters measured nearly equal among groups, between-group comparisons of 47 symptoms on "the morning after" found significant advantages for the FSMP in less severe headache, nausea, indifference, and restlessness vs. placebo (P = 0.333; 0.036; 0.037; and 0.027, respectively) and no significant differences between placebo and the study agent lacking plant extracts. Other symptoms did not differ notably among groups. Amounts of alcohol consumed relative to dehydration as measured by skin antioxidant content showed no significant correlations, nor were significant effects of congeners, distribution of alcohol within body tissues, or dose-response dependency seen.

The authors mention ten plant species with potential metabolism-enhancing effects for alcohol. Extracts of three of these, ginger (*Zingiber officinale*, Zingiberaceae) root, ginkgo (*Ginkgo biloba*, Ginkgoaceae) leaf, and barbary-fig (*Opuntia ficus-indica*, Cactaceae) fruit, are included in the FSMP used. Previously, *Opuntia* was studied in a rigorous randomized, placebo-controlled study. The study design of this investigation differed from the current study, which could explain the differences in results. The participants in the *Opuntia* study: (1) used the product before ingestion of alcohol, (2) the alcohol was administered to provide 1.75 g per kg body weight, and (3) a uniform pre-meal was given ahead of the alcohol ingestion. *Opuntia* reduced alcohol-related symptoms, which was thought to be related to reducing inflammation. The authors of this current study believed that alcohol-induced symptoms were related to oxidative stress. Two other plant ingredients are not discussed, *escobillo* (*Malpighia glabra*, Malpighiaceae) fruit and white willow (*Salix alba*, Salicaceae) leaf extracts. White willow is the plant source of acetylsalicylic acid, or aspirin, one of the pharmaceutical hangover cures mentioned above. Failure to disclose the possible effect of white willow extract on hangover symptoms weakens this RCT. Also, the provision of both diet and alcohol should have been better controlled. With the mixed results, it is not clear if the FSMP was ever sold. The German courts deemed that hangover was a disease, so a FSMP would be needed to make a claim.

The authors declare no conflicts of interest.

—Mariann Garner-Wizard

Referenced article can be accessed at https://nutrition.bmj.com/content/early/2020/04/01/bmjnph-2019-000042/