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Article type : Letters to the Editor

Migraines appear more likely to be caused by histamine rather than ethanol

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Keywords: Headache, Migraine, Alcohol, Histamine intolerance, Diamine oxidase

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ene.14003

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We read with interest the manuscript by Onderwater *et al.* that reported on alcoholic beverages as a trigger factor for migraines [1]. Although, epidemiological studies have found a correlation between alcohol intake and headaches, a specific pathophysiologic mechanism of this headache remains unidentified [2]. Particularly red wine was documented as the most common trigger for migraines in this evaluated population [1]. Most commonly found biogenic amines in wine - histamine, tyramine, phenylethylamine, putrescine, cadaverine, spermidine, serotonin, tryptamine, agmatine - and, flavonoids have suspected relevance for migraines and this implies that ethanol seems not to be the main culprit for the headaches [2].

An unbalanced and elevated quantity of histamine in histamine intolerance (HIT) is assumed to be the consequence of ingesting histamine-containing food or drinks, and mainly the enzyme diamine oxidase's (DAO) reduced ability to metabolize histamine. Generally, red wines reportedly contain clearly more than double the concentrations of biogenic amines, including histamine with $>2.200\mu\text{g/L}$, than white wines ($\sim 900\mu\text{g/L}$ histamine) [3]. Vodka is a clear, distilled alcoholic beverage, made by distilling fermented potatoes or grains that originally have low histamine content [4]. The consumption of vodka was also shown to induce fewer migraines than red wine [1].

DAO genotypes and allelic variants have already shown association with the increased risk for migraines [5]. Recently, a randomized double-blind trial demonstrated that oral ingestion of capsules with DAO reduces headaches in migraine patients [6]. Then, headaches in HIT patients - as one of the many symptoms in HIT - also were, in combination with all other HIT-related symptoms, significantly reduced due to oral supplementation of DAO [7].

In conclusion, the culprit triggers of migraines via consumption of alcoholic beverages are still unknown. However, the histamine content of alcoholic beverages, especially red wine, and possibly parallel consumed food, e.g. mature cheese [4], may play a key role in triggering migraines and headaches.

Disclosure of conflicts of interest:

Wolfgang J. Schnedl received speaking honoraria from Sciotec. Robert Queissner declares no competing interests.

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