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Expert Opinion

Alcohol and Cluster Headaches

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Historically, cluster headache has been known by many names, including erythromelalgia, erythroprosopalgia of Bing, hemicrania periodic neuralgiforms, histamine cephalalgia, Horton headache, migrainous neuralgia, petrosal neuralgia, and sphenopalatine neuralgia. Our patient might simply label his as a margarita and Chardonnay headache.

CASE HISTORY

This 50-year-old white man has a 5-year history of headaches described as an 8/10 in intensity stabbing in the left temple and sometimes around the left ear associated with tearing and redness of the left eye, congestion of the left nares, and light and noise sensitivity but no aura. During a headache, he prefers to sit or lie down. Without treatment, the headache lasts about 2 hours. Since the onset, the headache has been triggered almost all of the time by alcoholic beverages with the onset 30-45 minutes later. Perhaps one time per year the headache occurs spontaneously.

The headaches have been triggered by drinking white or red wine, margaritas, beer, vodka, and grappa. Every evening, he usually drinks 3 margaritas and 2 glasses of Chardonnay and occasionally other alcoholic beverages. He does not drink at other times of the day. About twice a month, he has 6 or more drinks. He scores a 16 on the Alcohol Use Disorders Identification Test (AUDIT). (A score of 8 or more indicates a strong likelihood of hazardous or harmful alcohol consumption in adult populations.) The headaches are invariably triggered by lesser and greater amounts of alcohol intake.

The headache goes away in about 30 minutes if he takes zolmitriptan 5 mg nasal spray or tablet or rizatriptan 10 mg at the onset. A few weeks after starting a triptan, he noticed that if he takes any of these triptans 5 minutes before his first drink, he only gets a headache about once a month. He has been taking one of these triptans on a daily basis for 3.5 years. If he does not take the triptan preemptively before drinking, he will get a headache. One hundred percent oxygen at 12 liters per minute was not effective. Topirimate was not effective for prevention. He was prescribed verapamil on a number of occasions but did not start the medication. Despite multiple recommendations, he did not seek counseling for alcohol abuse. The unknown risk of daily triptan use was discussed with the patient several times.

Past medical history was otherwise negative. He smokes one pack per day. He has a white-collar job working in sales. Neurological examination is normal.

Questions.—How common and what are the triggers in cluster headache? To be considered a trigger, how long after exposure to the trigger should the headache begin? How often is alcohol a trigger and what types? Will greater amounts of alcohol trigger a

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headache as often as lesser amounts? Is it common for cluster headache to occur only after exposure to a trigger such as alcohol and not spontaneously? What is the evidence for efficacy of triptans taken before a trigger to prevent a headache? Is alcohol consumption more in those with episodic or chronic cluster? How might alcohol trigger the headaches?

EXPERT COMMENTARY

This patient combines many interesting aspects of primary headache disorders. The clinical presentation including 8/10 pain intensity located around the left temple with ipsilateral tearing and reddening of the eye as well as nasal congestion lasting for 2 hours suggests the diagnosis of cluster headache (CH) compatible with the International Headache Society criteria from 2004.[1] The presence of attacks for 5 years without remission would classify him as suffering from chronic CH. Although the vast majority of patients experience pain in the orbital/temporal region, it has recently been shown that up to one-fourth of chronic CH sufferers report pain around the ear (like in our patient) and in more distant sites.[2,3] The other symptoms like photo- and phonophobia as well as the desire to lie down have "traditionally" been ascribed to migraine, but are also compatible with CH. Recent studies have shown that photo- and phonophobia occur in about 50-65% of patients during CH attacks.[2-5] I am not aware of any data regarding the desire to rest. Yet, only about 45-90% of CH patients report restlessness[2-5] and this feature seems to be particularly low in chronic CH sufferers.[3] It may well be that some patients with no feeling of restlessness have indeed the desire to rest and a number of my patients have reported this.

Cluster headache attacks typically occur spontaneously, as seen by the circadian and circannual pattern. Furthermore, during active episodes, certain triggers may provoke additional attacks, sometimes even when successful preventive treatment is implemented.[6] However, in between episodes attacks cannot be triggered. Alcohol is a well-known potent trigger for CH attacks, first described by Horton in 1941.[7] It elicits attacks in about 50-80% of patients,[2,4,8] less frequently in chronic (54%) than in episodic CH (65%).[2] Red wine seems to be particularly potent, as it was reported to elicit attacks in about 70% of patients in one study.[4] This may in part be ascribed to certain congeners, byproducts of alcohol fermentation. Our patient, however, experiences attacks following various kinds of alcohol including those without congeners (vodka, grappa). The latency of attack onset after alcohol ingestion (30-45 minutes) is compatible with a previous study.[4] There are early reports that in some patients with chronic CH alcohol consumption may ameliorate attacks[9] or lead to remission for a period of time proportional to the amount consumed.[10] However, the number of patients was too small to draw meaningful conclusions (2 out of 17 patients in the former and 3 out of 5 patients in the latter report). From my experience, there are no thresholds beyond which alcohol either elicits or ameliorates CH attacks. Also, there is no strict rule as to how long after the exposure of a certain "agent" a CH attack has to occur in order to be called a trigger. However, data from studies using the nitroglycerin provocative test (NPT) may be helpful in defining such a rule. Using the NPT, all CH attacks occurred within 3 hours after application, mostly within 45 minutes.[11] In contrast, migraine attacks may occur with a delayed onset after up to 8 hours.[11] This arbitrary "3-hour rule" may be applied to alcohol, which would be compatible with our patient. Yet, 2 aspects should be considered here. First, it is not applicable in a patient with 5 spontaneous CH attacks per day, for instance, as distinguishing between spontaneous and triggered attacks will be impossible. Second, it is questionable if this rule can be applied to other triggers as well. Among those triggers are stress (40%), weather (29%), fatigue (27%), physical activity (17%), tobacco (16%), rest (14%), smells (14%), food (10%), altitudes (9%), and menses (3%).[3]

In our patient, we are facing the rare instance of only one spontaneous attack per year while all the other ones are triggered by alcohol. The patient's history, in particular an AUDIT score of 16, refusing to seek counseling for alcohol abuse, and employing triptans to be able to continue alcohol consumption without getting CH attacks, clearly demonstrates that alcohol consumption as opposed to the CH is the patient's major problem. Early studies have reported that the vast majority of CH sufferers drank alcohol

excessively and patients with chronic CH seemed to drink more than those with episodic CH.[12-14] In addition, in a Swedish study, 67% of CH patients had scores indicative of high alcohol consumption using the Malmö modification of the Michigan Alcoholism Screening Test.[8] However, a large Italian multicenter case–control study did not find a difference in drinking behavior between CH patients and controls,[15] and a German study found a lower alcohol consumption among CH patients compared with controls.[16] In addition, chronic CH patients drank much less frequently than episodic CH patients.[16] Only one-fifth of patients were identified as hazardous alcohol consumers using the AUDIT. Considering the trigger potential of alcohol, this makes intuitive sense and is in line with study results showing that 79% of CH patients decrease their alcohol consumption during headache periods.[8]

Inhaled oxygen and sumatriptan injection are the treatments of choice when it comes to terminating CH attacks.[17] Triptans as nasal sprays and tablets are also effective, yet probably to a lesser degree. Employment of preventive medications like steroids, verapamil, and topiramate may be complicated by a number of factors, including adverse side effect profile, need for slow titration, bradycardia, impaired cognition, etc. As attacks often occur during the night, thus precluding timely application of acute medication, and as some episodes only last 2 or 3 weeks, the idea of time-adjusted and short-term prophylaxis has been introduced. Taking a long-acting triptan like frovatriptan once or twice daily for a limited period of time has been shown to be successful in preventing attacks and to be safe.[18] However, a note of caution must be given here, owing to the possibility of medication overuse headache (MOH) with prolonged use. For a long time, the notion prevailed that CH patients cannot develop MOH; however, it has recently been reported that frequent use of subcutaneous sumatriptan can indeed increase attack frequency in CH.[19] In addition, the risk of prolonged regular triptan use is unknown in CH. It is still not fully understood how triptans work in CH; however, owing to the many similarities between CH and migraine, a related mode of action may be postulated. Pharmacologically, triptans activate 5-HT_{1B} and 5-HT_{1D} receptors on cerebral and peripheral vessels and on peripheral and central neurons.[20] Stimulation of vascular 5-HT_{1B} receptors causes vasoconstriction, which may provoke ischemia, particularly in the presence of other cardiovascular risk factors like smoking, as in our patient.

Another striking aspect about this patient is that he consistently and reliably can prevent alcohol-induced CH attacks with triptans. Despite alcohol being a potent CH attack trigger, as sketched above, it is speculative whether this is due to its vasoactive properties, due to one of its complex central nervous system mechanisms[21] or whether several of these mechanisms act in synergy. It seems unlikely that the effect is solely attributable to congeners, as this patient reports the same effects with red wine and vodka, for instance. It may be hypothesized that alcohol causes attacks through vasodilation, which can be terminated by the vasoconstrictor properties of triptans, and also that the vasoconstrictor properties of triptans taken early may prevent alcohol-induced vasodilation and thus CH attacks. However, owing to the neurovascular theory of CH pathogenesis, which is only marginally understood by now, this view appears rather simplistic and does not account for the involvement of brain structures like the hypothalamus and the brain stem.[22]

In summary, this is a very special case of CH. While the clinical criteria for CH are fulfilled, the patient also presents uncommon symptoms. In addition, he appears to be in a chronic state with a very low spontaneous attack frequency. In contrast, his daily attacks are all triggered by alcohol. As the patient is likely alcohol-dependent, drinking every night, this creates the main problem for him. Apart from the alcohol-associated health hazards, he is willing to accept the unknown risk of daily triptan intake. The only therapy for him appears to stop drinking (with professional help), but he is incompliant. Abstinence from alcohol would likely dramatically reduce his attack frequency, leaving him potentially needless of preventive medication. In addition, he might turn out to be responsive to oxygen after all.

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