

Bath-related headache induced by varenicline

Cefaleia relacionada ao banho induzida pela vareniclina

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Dear Editors,

The article by Camara Filho et al.¹ reports the case of a woman with recurrent headache attacks which occurred after the use of varenicline. The usual presentation of bath-related headache is a recurrent sudden severe headache attack (*i.e.* thunder-clap headache) typically triggered by bathing or other activities involving body contact with water². The authors commented the possibility of reversible cerebral vasoconstriction as a cause of bath-related headache¹. Interestingly, two cases of thunder-clap headache have recently been reported³ associating reversible segmental vasoconstriction with the use of varenicline. The $\alpha 4\beta 2$ nicotinic receptor partial agonist varenicline is a drug authorized for promoting smoking cessation in the USA and Europe. This receptor mediates the primary effects of nicotine on the mesolimbic system, activating the dopaminergic reward pathway. Thus, by acting as a nicotinic antagonist, it inhibits dopamine release, thereby decreasing the effects of smoking satisfaction often associated with nicotine use. It was developed from cytisine, a natural alkaloid compound widely used to increase the chances of a person successfully giving up smoking. Cytisine is found in the *Baptisia*, *Cytisus*, *Laburnum*, and *Sophora* species, and has nicotine-like effects on the nervous system. These plants may have a recreational purpose when used for smoking because of their stimulant effects and mild hallucinogenic properties. The *Sophora* root, also known as “Ku Shen”, is used in traditional Chinese medicine. The use of such plants by humans, for whatever purpose, may suggest that a particular alimentary/recreational habit might be the reason for a higher prevalence of bath-related headache among Asian populations. Curiously, the usual trigger is hot water, suggesting an imbalance in the thermogenic CNS circuitry. Pharmacological stimulation of $\alpha 4\beta 2$ nicotinic receptors causes changes in body temperature. Indeed, varenicline is able to experimentally modulate hypothermia and antinociception induced by nicotine. This may explain the higher susceptibility (*i.e.* dysfunctions in craniofacial somatosensory processing) to hot water in contact with the head when someone is undergoing treatment with varenicline. Similar phenomenon occurs in a unique form of reflex epilepsy, *i.e.* hot water epilepsy⁴. Ravishankar reported⁵ that migraine attacks were triggered by hair washing in 94 people in a series of 1,500 Indian migraineurs. Some adverse effects may occur soon after the intake of varenicline, and others developed after several weeks of treatment or even after stopping varenicline. Due to the increasing use of smoking cessation drugs, this fascinating form of headache may be more frequent than generally believed.

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