

Would Adding an Anesthetic to Nicotine Mouth Spray Increase Smoking Cessation Rates? Would this Justify Starting a Research Project?

¿Añadir un anestésico al spray bucal de nicotina aumentaría las tasas de abstinencia tabáquica? ¿Se justifica por ello iniciar un proyecto de investigación?

JOSÉ IGNACIO DE GRANDA-ORIVE, SEGISMUNDO SOLANO-REINA*, CARLOS A. JIMÉNEZ-RUIZ**

Servicio de Neumología, Hospital Universitario 12 de Octubre, Madrid. * Servicio de Neumología, Hospital Universitario Gregorio Marañón, Madrid. ** Unidad Especializada en Tabaquismo de la Comunidad de Madrid, Madrid.

Dear Sir: Although the addictive properties of tobacco depend on nicotine, this addictive power reflects complex interactions between the drug and the context in which it is released. It is known that there are sensory components that contribute towards the satisfaction felt by the smoker, there being a sensory cue associated with the drug that makes it a conditioned replenisher associated with tobacco. There are nicotine-associated cues with each puff such as, for example, visual, olfactory and gustatory stimuli, that provoke subjective states that can in turn trigger off the search for the drug and thus lead to relapse (Dani and Balfour, 2011). Recently, Liu (2014) has shown the role of cholinergic neurotransmission, via the activation of the acetylcholine receptor alpha7, in the mediation of the conditioned incentive properties of external nicotine cues, for which reason manipulating the activity of the acetylcholine receptor alpha7 could be a target in the development of drugs to prevent relapse brought on by outward cues.

Until such time as neuroscientific research clears up the matter, it has to be said that when cigarette smoke enters the smoker's mouth and passes the pharynx, the larynx and the lower respiratory tract a series of sensations are provoked, it having been hypothesized that these chemosensory signals become powerful conditioned reinforcement stimuli owing to their being associated with the replenishing effect of the nicotine on the central nervous system (Smolka et al., 2006).

Indeed, it has even been shown that sensory factors may be as important in the sensation of satisfaction after smoking, the acceptance of the product and on the desire to smoke as the pharmacological factors of nicotine on a cerebral level (Pritchard, Robinson, Guy, Davis y Stiles, 1996). Rose, Zinsler, Tashkin, Newcomb y Ertle (1984) showed that anesthetizing the upper and lower respiratory tracts reduced the craving for nicotine and the number of puffs desired. The satisfaction experienced by smokers who inhale diminishes if the upper and lower areas are anesthetized (Rose, Tashkin, Ertle, Zinsler y Lafer, 1985). As far as we know, this line of research was not continued afterwards.

We currently have available the nicotine mouth spray to help smokers stop and it has shown its efficacy in increasing the smoker's chances of remaining abstinent (Tønnesen, Lauri, Perfekt, Mann, and Batra, 2012). There is evidence that fast-acting nicotine replacement therapy prescriptions work quickly to alleviate craving and thus calm the discomfort caused by abstinence (Hansson, Hajek, Perfekt and Kraiczi, 2012). Reducing the temptation to smoke, by alleviating the craving, will diminish the number of relapses. Nicotine mouth spray has shown that it alleviates craving rapidly (Hansson et al., 2012).

However, as far as we know, there are no studies that have measured smoking abstinence after adding an anesthetic to the nicotine replacement therapy habitually employed and the question at this point would be: would adding an anes-

Send correspondence to:

Dr. José Ignacio de Granda-Orive. C/ Cavanilles 43, 7º E, Madrid 28007. E-mail: igo01m@gmail.com

thetic to nicotine mouth spray increase smoking abstinence rates? With this we would add two effects at the same time as maintaining abstinence; on the one hand the proven rapid absorption of nicotine via the mouth spray (Hansson et al., 2012) which quickly alleviates craving and, on the other, the anesthetic would equally diminish the craving and the satisfaction that the smoker experiences when inhaling tobacco smoke thus lessening the sensory effects of the nicotine and, therefore, diminishing the conditioned reinforcement stimulus that it leads to. Logically, the key is in the duration of the anesthetic effect. Although we have no answer to the above, possibly what we have expounded in this letter would justify a research project to find such a response.

References

- Dani, J. A. & Balfour, D. J. K. (2011). Historical and current perspective on tobacco use and nicotine addiction. *Trends in Neuroscience*, *34*, 383–392. doi: 10.1016/j.tins.2011.05.001
- Hansson, A., Hajek, P., Perfekt, R., & Kraiczi, H. (2012). Effects of nicotine mouth spray on urges to smoke, a randomised clinical trial. *BMJ Open*, *2*, pii: e001618. doi: 10.1136/bmjopen-2012-001618.
- Liu, X. (2014). Effects of blockade of $\alpha 4\beta 2$ and $\alpha 7$ nicotinic acetylcholine receptors on cue-induced reinstatement of nicotine-seeking behaviour in rats. *International Journal of Neuropsychopharmacology*, *17*, 105–116. doi: 10.1017/S1461145713000874
- Pritchard, W. S., Robinson, J. H., Guy, T. D., Davis, R. A., & Stiles, M. F. (1996). Assessing the sensory role of nicotine cigarette smoking. *Psychopharmacology (Berl)*, *127*, 55–62.
- Rose J. E., Tashkin, D. P., Ertle, A., Zinser, M. C., & Lafer, R. (1985). Sensory blockade of smoking satisfaction. *Pharmacology Biochemistry and Behavior*, *23*, 289-293.
- Rose, J. E., Zinser, M. D., Tashkin, D. P., Newcomb, R., & Ertle, A. (1984). Subjective response to cigarette smoking following airway anesthetization. *Addictive Behaviors*, *9*, 211-215.
- Smolka, M. N., Bühler, M., Klein, S., Zimmermann, U., Mann, K., Heinz, A.,... Braus, D. F. (2006). Severity of nicotine dependence modulates cue-induced brain activity in regions involved in motor preparation and imagery. *Psychopharmacology (Berl)*, *184*, 577–588.
- Tønnesen, P., Lauri, H., Perfekt, R., Mann, K., & Bøtra, A. (2012). Efficacy of a nicotine mouth spray in smoking cessation: a randomised, double-blind trial. *European Respiratory Journal*, *40*, 548 - 554. doi: 10.1183/09031936.00155811.