Published in final edited form as:

J Clin Psychopharmacol. 2009 April ; 29(2): 193–194. doi:10.1097/JCP.0b013e31819c57d4.

Effects of Topiramate on Smoking in Patients with Schizoaffective Disorder, Bipolar Type: Response to Khazaal and Zullino

Andrea H. Weinberger, Ph.D.,

Yale University School of Medicine, Department of Psychiatry, New Haven, CT, USA

Tony P. George, M.D.,

Centre for Addiction and Mental Health, Department of Psychiatry, University of Toronto Faculty of Medicine, Toronto, Ontario, Canada

Kenneth A. Perkins, Ph.D., and

Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

K.N. Roy Chengappa, M.D.

Western Psychiatric Institute and Clinic, University of Pittsburgh School of Medicine, and Mayview State Hospital, Pittsburgh, PA, USA

To the Editors:

We recently published a secondary analysis of expired breath carbon monoxide (CO) levels (a measure of smoking exposure) in patients with schizoaffective disorder, bipolar subtype, participating in a clinical trial of topiramate for treating psychiatric symptoms (1). Our analysis found that CO levels remained generally unchanged for participants on topiramate and placebo during the course of the trial. In our discussion, we noted that one limitation of the study was the assessment of smoking by CO level only. Khazaal and Zullino (this issue) further discuss concerns about the suitability of CO as a measure of changes in smoking. Khazaal and Zullino suggest that CO may be a poor indicator of smoking reduction because decreases may be attenuated through increased intensity with which those cigarettes are smoked (i.e. compensation).

Because it is highly dependent on the recency of smoking, we agree that CO is a more labile measure of smoking exposure than other biochemical measures (e.g., cotinine). However, a significant change in smoking consumption (cigarettes per day, CPD) should still result in a

Address for Correspondence: Andrea H. Weinberger, Ph.D., Department of Psychiatry, Yale University School of Medicine, 34 Park Street, SAC Room S-211, New Haven, CT 06519 USA, Tel: (203) 974-7598, Fax: (203) 974-5711, andrea.weinberger@yale.edu.

Author Disclosures:

Dr. George has received consultant and speakers' fees from Pfizer and consultant fees from Evotec, and from Lilly and Janssen for development of smoking cessation medications.

Dr. Perkins has received consultant fees from GlaxoSmithKline regarding development of smoking cessation medications.

Dr. Chengappa has been a past consultant for OrthoMcNeil (before 2004) and received grant support from the OrthoMcNeil Neurologics for the study itself. He has no stock or other arrangements to report.

Dr. Weinberger has no disclosures to report.

noticeable change in CO levels, even with some change in the intensity of smoking. Studies of the efficacy of transdermal nicotine patch (2) and bupropion (3) for smoking cessation in smokers with schizophrenia have shown parallel decreases in CO level consistent with decreases in CPD. It is possible that topiramate was associated with small changes in CPD that were masked through smoking compensation, our small sample size, or the infrequent CO assessments. However, small changes in smoking consumption that do not result in decreases in CO levels may not be clinically significant in terms of beneficial health outcomes for patients. In other words, it is overall smoke exposure, as indicated by CO, that is the more valid marker of health risk, rather than cigarettes per day, regardless of how they may be smoked.

In order to clarify the usefulness of topiramate for smoking cessation with smokers with psychiatric disorders, further research is needed. Clinical trials comparing topiramate to placebo should be conducted in larger samples of smokers with psychiatric disorders using multiple assessments of smoking at frequent time points. Patient-reported changes in smoking consumption (CPD) should be confirmed using CO and cotinine levels. Questions about changes in smoking intensity with topiramate can be assessed through smoking topography techniques. One study (4) has examined changes in smoking topography for topiramate (75mg/day) compared to placebo in nonpsychiatric smokers. Topiramate resulted in decreased puff volume and enhanced reward from smoking, but also no differences in total puffs per cigarette and increased withdrawal during smoking abstinence. Topiramate-induced changes in smoking topography have not been examined for smokers with psychiatric disorders. Finally, the main purpose of the clinical trial was to examine the efficacy of topiramate for mood and psychotic symptoms in patients with schizoaffective disorder. Patients were not necessarily motivated to quit smoking and were not provided with smoking cessation counseling. Future studies should examine the efficacy of topiramate in conjunction to behavioral smoking cessation counseling in patients with current motivation to quit smoking. While our data does not suggest spontaneous decreases in smoking or CO levels for smokers with schizoaffective disorder, future studies that address the limitations of our analysis would provide a clearer picture of the clinical usefulness of topiramate for smoking cessation in this population.

Acknowledgements

This work was supported by an investigator-initiated grant from Ortho-McNeil Neurologics, Inc (to Dr. Chengappa). Ortho-McNeil Neurologics, Inc provided financial support and study medication for this study. The work was also supported in part by National Institute on Drug Abuse (NIDA) grant K12-DA-00167 (to Dr. Weinberger).

References

1. Weinberger AH, George TP, Perkins KA, Chengappa KN. Effects of topiramate on smoking in patients with schizoaffective disorder. *J Clin Psychopharmacol*. 2008; 28(2):247–248. [PubMed: 18344743]
2. George TP, Ziedonis DM, Feingold A, Pepper WT, Satterburg CA, Winkel J, Rounsaville BJ, Kosten TR. Nicotine transdermal patch and atypical antipsychotic medications for smoking cessation in schizophrenia. *Am J Psychiatry*. 2000; 157(11):1835–1842. [PubMed: 11058482]

3. George TP, Vessicchio JC, Termine A, Bregartner TA, Feingold A, Rounsaville BJ, Kosten TR. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. *Biol Psychiatry*. 2002; 52:53–61. [PubMed: 12079730]
4. Reid MS, Palamar J, Raghavan S, Flammio F. Effects of topiramate on cue-induced cigarette craving and the response to a smoked cigarette in briefly abstinent smokers. *Psychopharmacology*. 2007; 192(1):147–158. [PubMed: 17345064]