Medical *Education* Network

PRIORITY PRESS

13th World Conference on Tobacco or Health

Washington, DC / July 12-15, 2006

Combining Behavioural Counselling with Pharmacological Therapy: A Viable Formula for Smoking Cessation

Washington, DC - Double-blind controlled trials have demonstrated that the relative specificity of pharmacologic therapies directed at central mediators of tobacco addiction appear to promote longer remission from smoking, according to experts. As well, investigators deemed that when combined with validated concepts about how to free patients from motivational cues to smoke, these strategies begin to produce highly encouraging continuous smoking cessation rates. In Canada, where approximately 50% of smokers attempt to quit each year, combination of these tools has the potential to alleviate a large public health burden.

New data confirm that differences in mechanism of action of currently approved pharmacologic therapies for smoking cessation markedly influence both initial quit rates and the proportion of patients able to maintain smoking cessation a year or more after therapy. While the ultimate benefit of these therapies depends on simultaneous control of the motivational systems that return individuals to tobacco use after biologic signals have been alleviated, progress in identifying the cues for smoking along with better medical therapies indicates new opportunities for durable success.

Pharmacologic Therapy plus Behaviour Counselling

According to Dr. Robert West, Department of Epidemiology and Public Health, University College London, UK, "Control of smoking requires a comprehensive approach that over time keeps the motivation to quit greater than the motivation to smoke. The ultimate goal is not just to quit but to achieve a permanent remission. That is where we get the health benefits."

Based on clinical trial data, Dr. West described the impulse to smoke as a product of a series of biological and psychological cues. The biological signals are strongest in the earliest stages of quitting. These signals produce a drive to smoke that Dr. West compared to the desire for food when hungry. There is now compelling evidence that these can be controlled pharmacologically by targeting the receptors that produce these signals. However, even with control of the biological mechanisms of addiction, there must also be control of the behavioural cues that can also be powerful precipitators of smoking even months or years after quitting. That is why combination therapies are essential to avoid the powerful cues that return patients to their habit.

"Individuals attempting to become non-smokers experience an array of unpleasant physical and psychological symptoms that overwhelm and undermine their resolve," Dr. West explained. While pharmacological therapy can address the physical symptoms, some type of support system is usually required to allow even highly motivated individuals to remain smoke-free after biologic signals to smoke have been controlled.

Targeting Central Mediators of Nicotine Addiction

Therapy aimed at the biological signals of smoking may be essential for some individuals to traverse the acute stage when urges are strongest.

Recently, the novel nicotinic acetylcholine receptor (nAChR) partial agonist varenicline has demonstrated greater efficacy than sustained-release bupropion, the only other pharmacotherapy besides nicotine replacement approved for smoking cessation. The reduction in the desire to smoke on buproprion, which was initially developed for control of depression, is attributed to its ability to inhibit dopamine reuptake in the mesolimbic dopamine system. Developed for smoking cessation, varenicline targets the $\alpha 4\beta 2$ subtype of the nAChR in the ventral tegmental area of the brain. The $\alpha 4\beta 2$ receptor is believed to play a major role in mediating the effects of nicotine and on nicotine dependence. As a partial agonist, it is thought to relieve symptoms of nicotine withdrawal and cigarette craving while preventing nicotine from occupying the receptor and producing its biologic effects.

NOT FOR DISTRIBUTION

Continued

Study Results

"The efficacy of varenicline relative to bupropion confirms its specificity of action and greatly expands the evidence that addictions are controllable by targeting central mediators," reported Dr. Mitchell Nides, Los Angeles Clinical Trials Group, California. Presenting pooled data of two recently published trials that analyzed the two agents for smoking cessation (Gonzalez et al. *JAMA* 2006;296:47-55, Jorenby et al. *JAMA* 2006;296:55-63), he observed that "the odds of quitting were nearly doubled compared with bupropion."

Both of the studies randomized approximately 1000 patients (2052 patients total) to either compound or placebo. All patients were required to be motivated to quit and to be smoking an average of ≥10 cigarettes/day. About 80% of patients were Caucasian. Women represented just under half of the study population. On average, patients were approximately 43 years of age, had been smoking for 25 years and consumed 21 cigarettes/day. Most patients had attempted to quit previously. All groups received similar counselling and support.

At 12 weeks, bupropion was shown to be highly effective, producing a quit rate almost double that of placebo (29.7% vs. 17.7%; $P<0.0001$) and varenicline achieved a 44.2% quit rate. Relative to bupropion, the odds ratio (OR) of successfully quitting with varenicline almost doubled (OR 1.87; 95% CI, 1.50–2.34; $P<0.0001$) and was almost four times greater than placebo (OR 3.69; 95% CI, 2.88–4.72; $P<0.0001$).

The discontinuation rates for adverse events were 8.2% for placebo, 9.5% for varenicline and 13.9% for bupropion. While most cases were mild, nausea was the most common adverse event on varenicline and occurred more often than on bupropion (28.8% vs. 9.9%), causing discontinuation rates of 2.5% and 1.0%, respectively.

Extended Treatment to Reach Long-term Cessation

The effect of both pharmacological therapies is to control the acute cravings during the initial period of smoking cessation, when the physical component of addiction is strongest. While a typical course of all smoking cessation treatments is 12 weeks, another study published in the same issue of *JAMA* (Tonstad et al. *JAMA* 2006;296:64-71) has demonstrated that longer periods of treatment further increase quit rates and are associated with greater protection against the resumption of smoking over one year.

In this maintenance therapy trial, 1927 smokers were treated with open-label varenicline for 12 weeks. Of those who did not smoke or use nicotine replacement therapy during the last week of treatment, 1210 patients were then randomized to a further 12 weeks of varenicline 1 mg b.i.d. or placebo. Abstinence from smoking was confirmed using carbon monoxide monitoring over the period of the active trial and then from week 12 to week 52. At the end of the placebo-controlled 12 weeks of treatment (weeks 13-24), the quit rates were 70.5% in the active treatment groups vs. 49.6% in the placebo group, producing an OR >2.48 than placebo (95% CI, 1.95–3.16; $P<0.001$). From weeks 13 to 52, the quit rates were 43.6% vs. 36.9%, producing an OR >1.34 than placebo (95% CI, 1.06-1.69; $P=0.02$).

Dr. Serena Tonstad, Department of Preventive Cardiology, Ullevål University Hospital, and Professor, Institute for Nutrition Research, University of Oslo, Norway, told the audience, "This study is not a comparison of the efficacy of 12 weeks vs. 24 weeks of treatment. This is a study to determine whether if you have successfully stopped smoking at 12 weeks, does another 12 weeks of treatment help in the long-term ability to remain off cigarettes, and the results demonstrate that it does." She noted that like the earlier bupropion-controlled trials, the benefit of varenicline relative to controls was similar when patients were stratified by gender, age or baseline cigarette consumption. While nausea was again the most common adverse event during the open-label phase, it was an uncommon event in the placebo-controlled phase, observed in just 1.2% of patients.

Summary

A large proportion of individuals who smoke would like to stop. In Canada, half of all smokers attempt to quit each year. Even with counselling, only a small proportion succeeds. Quit rates can be improved substantially with pharmacologic therapy to control the acute biologic signals for seeking nicotine when combined with counselling. The relative efficacy of varenicline and bupropion demonstrates that cigarette addiction can be pharmacologically controlled. These therapies should be employed to allow patients to reduce their urge while adjusting to a non-smoker lifestyle that includes avoiding cues to smoking. The critical goal is not just quitting but permanent cessation. □

Note: At the time of printing, varenicline is not available in Canada.

© 2006 Medical Education Network Canada Inc. All rights reserved. Priority Press™ is an independent medical news reporting service providing educational updates reflecting peer opinion from scientific and clinical meetings worldwide. Views expressed are those of the participants and do not necessarily reflect those of the publisher or the sponsor. Support for distribution of this report was provided by Pfizer Canada Inc. through an unrestricted grant and under written agreement that ensures independence. Any therapies mentioned in this report should be used in accordance with the recognized prescribing information in Canada. No claims or endorsements are made for any products, uses or doses presently under investigation. No part of this newsletter may be reproduced in any form or distributed without written consent of the publisher. Information provided herein is not intended to serve as the sole basis for individual care. Our objective is to facilitate physicians' and allied health care providers' understanding of current trends in medicine. Your comments are encouraged.

Medical Education Network Canada Inc. 132 chemin de l'Anse, Vaudreuil, Quebec J7V 8P3
E-mail: mednet@mednet.ca / Web site: www.mednet.ca **Please e-mail us at our address to receive reports on-line.**

NOT FOR DISTRIBUTION