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EDITORIAL

Antidepressants for smoking cessation: a promising new approach?

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People who smoke find it difficult to stop. Of the smokers in USA who try to quit, only 2–5% succeeds without any smoking cessation intervention [1]. In Europe, these figures are even lower. Smoking cessation is an overall health concern in the general population, for healthy smokers but especially for patients who suffer from diseases associated with smoking like cancer, COPD, diabetes and heart disease. For years now, research has been conducted to find out which intervention is most efficacious in facilitating smoking cessation. The success of these interventions has been moderate [2].

In December 1999, the antidepressant bupropion (Zyban^{TM}) was introduced in Europe as a smoking cessation aid, pioneering in the Netherlands where the drug received a smoking cessation indication. Earlier, in 1997, bupropion was approved as a smoking cessation stimulant by the Food and Drug Administration in the USA. Until today, bupropion is the only nonnicotine drug world-wide registered for smoking cessation [3]. As could be expected, the introduction of bupropion drew a lot of media attention in the Netherlands. Dutch consumers could hear and read about this new drug that helps one in three smokers to quit, a revolutionary improvement compared to other smoking cessation strategies. This drug is one of the first drugs for which antismoking properties have been undoubtedly documented. But exactly how effective is the use of bupropion as a smoking cessation stimulant?

The enthusiasm accompanying the introduction of bupropion is based on the results of two randomized clinical trials, published in the *New England Journal of Medicine* in 1997 [4] and 1999 [5]. These findings suggest that the use of bupropion can increase the chance of successful smoking cessation to 23 and 30% in healthy smokers. Although this is good news indeed, especially for COPD patients, several remarks should be made about these studies.

First, there is the matter of the unobtrusive, but highly relevant difference between point prevalences of smoking cessation and continued smoking cessation rates. At 12-month follow up, the point prevalences of smoking cessation were 23.1% in the 1997 bupropion group (placebo: 12.4%) and 30.3% in the 1999 bupropion group (placebo: 15.6%). However, interest should not only be in the percentage of quitters at a certain point in time, but particularly in the percentage of quitters who have not smoked since the date they quit. A single point prevalence presents merely a cross-sectional quit rate that tells us little about the previous smoking status or relapse since the initial smoking cessation. The fact that point prevalences of smoking cessation can rise over time illustrates this. Therefore, it is important to review continued smoking cessation rates in order to assess the most relevant effect of a smoking cessation intervention. Although continued smoking cessation rates are announced in the methods section of the 1997 studies [4], the authors fail to show the rates at follow-up. In the 1999 studies [5], the continued smoking cessation rate in the bupropion group at 12-month follow-up is 18.4% (placebo: 5.6%).

Second, what is only briefly mentioned in both the 1997 and the 1999 studies is that it is not just the use of bupropion that accounts for the observed effects. In all study groups, subjects were exposed to a very intensive support programme (consisting of at least eleven relapse prevention counselling sessions during visits and additional telephone calls) that continued during follow-up, which explains the relatively favourable effects in the placebo groups. This is an approach daily practice in primary care can hardly live up to.

What is an important result for daily practice is that the effects of the antidepressant bupropion are almost twice as strong as those of more conventional smoking cessation strategies [2]: the editors critical remarks are not intended to alter that fact. However, since bupropion is the only antidepressant registered as a smoking cessation stimulant, one could wonder whether there are no alternatives to consider. A literature search was carried out on the subject of smoking cessation and antidepressant therapy and found that there are indeed other (less costly) antidepressants that might also have effects on smoking cessation. Especially nortriptyline, a generic antidepressant that is frequently prescribed in primary care, which seems to be a promising equivalent of bupropion. To illustrate, continued smoking cessation rates in two randomized clinical trials in which nortriptyline was tested for smoking cessation were respectively 14% (placebo: 3%) in one study at six months [6], and 24% (placebo: 12%) in the second study at fifteen months [7].

It is hypothesized that the use of antidepressants enables quitters to sustain their self-efficacy and positive attitude with regard to smoking cessation, because antidepressants (used as smoking cessation stimulants) may suppress the symptoms of nicotine withdrawal [6], and prevent increases in poor mood [7]. No studies were found in which the efficacy of bupropion and nortriptyline on smoking cessation was compared. Use of both drugs in the same study population would make a valid head-to-head comparison possible, something the editors would endorse.

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So, bupropion is effective, and it is thus far the only antidepressant that has a smoking cessation registration. What has not been emphasized is that bupropion is very expensive: ironically the daily costs almost amount to the price of a package of cigarettes. All the more reason to at least consider the use of other antidepressants. It is difficult to compare results from the bupropion studies [4, 5] and the nortriptyline studies [6, 7] since different study designs (*e.g.* patient characteristics at entry, types of support programme) were used. However, arguing that bupropion is the only effective antidepressant might be a little premature.

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