Bupropion: a new treatment for smokers

John Britton and Martin J Jarvis

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quickly among those treated with midazolam when calculated from the time they entered the emergency department; this is because midazolam was administered earlier and the administration of diazepam requires an intravenous line.

What is the clinical significance of a two minute difference in the efficacy of the treatment of a benign condition? There is no question that two minutes of seizures corresponds to 120 long seconds of distress for parents and medical staff. Moreover, the apparent safety of this mode of drug delivery may allow nurse practitioners, nurses, and eventually even parents to administer midazolam intranasally to children with recurrent seizures.

Because of obvious ethical limitations, the authors could not randomly assign children to a placebo group in their study. Thus, theoretically, the similarity in responses to diazepam and midazolam may merely mean that both were not more effective than placebo. It may well be that most children would have stopped seizing spontaneously sometime after 10-15 minutes, and because 10 minutes of seizures was chosen as an entry criterion, the seizures might have gradually resolved even with placebo. However, the survival curves of children treated with diazepam and midazolam were similar, except for the difference in the time of the initial response, which corresponds to the time needed to insert an intravenous line. If this was merely a placebo effect, the two curves should have overlapped completely.

The authors did not define the power of their sample to detect certain differences. Yet it is obvious that the sample size in this study does not have enough power to address the rates and severity of adverse effects. The authors did not specify how blinding was achieved: the research team had to be in the treatment room, and the lack of an intravenous line among those in the midazolam group during the first few minutes is not easy to ignore.

Although Lahat et al defined "delayed seizure control" in their methods section, they did not report the results. Lastly, the duration of a child's seizure before arriving at the study unit was inferred to have been at least 10 minutes, based on the distance of the facility from neighbouring communities; however, it was not measured directly. It could be assumed that randomisation would ensure similar distributions of durations of seizures between the two treatment arms, but randomisation often does not do justice to all confounding variables, especially when the sample size is comparatively small, as was the case here.

However, these limitations are small in view of the step forward these investigators have made in improving drug treatment for a common paediatric condition. This study should be repeated by others before intranasal administration of midazolam becomes the standard of care to address some of the questions alluded to and to ensure the safety of this treatment.

Gideon Koren *professor*

Hospital for Sick Children, 555 University Avenue, Toronto, ON, Canada M5G 1XS

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Bupropion: a new treatment for smokers

Nicotine replacement treatment should also be available on the NHS

Bupropion was licensed in June by the Medicines Control Agency for use in the United Kingdom to help patients stop smoking. Bupropion is the first new pharmacological treatment for smokers to be introduced since nicotine replacement therapy 20 years ago. Bupropion can potentially have a huge impact on public health not only through the efficacy of the drug itself but also by making smoking cessation services more widely available.

There are about 13 million regular smokers in the United Kingdom.[1] One in every two lifelong smokers will die prematurely from tobacco related causes.[2] Interventions to help people stop smoking are cost effective in preventing that premature loss of life, and nicotine replacement products are the most effective treatment available.[3 4] About 20% of those given nicotine replacement with support from specialist counsellors will remain non-smokers for one year and up to about 10% will remain non-smokers if given brief advice from a health professional in addition to nicotine replacement.[3] This latter approach may potentially have a far greater impact on public health because wider coverage of the population can be achieved. It is also cost effective.[5] However, nicotine replacement and counselling services have not been made generally available through the NHS, and nicotine replacement products have been removed from the list of prescribed drugs for which patients can be reimbursed. New services to help people stop smoking, which are being established in England as a result of the recent government white paper on smoking, aim to provide smokers with counselling support

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but still require smokers to pay for most or all of their nicotine replacement.[1] One week of free nicotine replacement is available to those eligible for free prescriptions but the bureaucracy can be daunting. The potential impact of these specialist services at a population level is small, and their declared target is to reduce the number of smokers by only 20 000 each year—less than 0.2% of the current population of smokers.[6]

Bupropion was originally developed as an antidepressant, but it is chemically unrelated to other antidepressant drugs. Its mechanism of action in smoking cessation is not understood but may be mediated by raising the concentration of dopamine in the nucleus accumbens, a process that is also involved in nicotine addiction.[2 7] Two preliminary reports,[8 9] and now two clinical trials funded by the manufacturers, have shown its efficacy in smokers who were also given regular counselling support.[10 11] The first of these studies compared placebo with three different doses of sustained release bupropion given for seven weeks in a parallel group study of 615 smokers: rates of quitting smoking after one year were 12.4% among those who took a placebo, 19.6% for those who took 100 mg bupropion daily, 22.9% for those who took 150 mg, and 23.1% for those who took 300 mg.[10] This effect occurred independently of any evidence of current or previous depression.[12] The second study of 893 smokers compared treatment with 150 mg sustained release bupropion twice daily (once daily for the first three days) either alone or in conjunction with transdermal nicotine, with nicotine alone or placebo.[11] Cessation of smoking was sustained for one year of follow up in 5.6% of participants treated with placebo, 9.8% of those treated with transdermal nicotine, 18.4% of those treated with bupropion alone, and 22.5% of those treated with bupropion and nicotine.[11] Bupropion alone was significantly more effective than placebo or transdermal nicotine and not significantly less effective than bupropion plus transdermal nicotine. Bupropion significantly reduced weight gain during the treatment period, although this effect was subsequently lost. The main adverse effects of bupropion were insomnia and dry mouth. Subsequent evidence has suggested that longer treatment with bupropion may reduce the likelihood of relapse and produce a more sustained reduction in weight gain (unpublished data).

On the evidence of the only comparative study available bupropion seems to be more effective than transdermal nicotine.[12] Although this finding needs to be confirmed and the combined effectiveness of bupropion and nicotine replacement needs to be established, the recent confirmation by the government that bupropion will be available on reimbursable prescriptions provides doctors in this country with a treatment to help patients stop smoking that is effective and, importantly, affordable for smokers. An eight week course of bupropion with support from a telephone helpline will cost the NHS about £86 ($129) (GlaxoWellcome, product information); this is less than the cost of a full course of most nicotine replacement formulations.[4] To the smoker however, bupropion will be provided in four week treatment packs, so eight weeks will cost a maximum of two standard prescription charges (£12), which is less than the cost of one week's supply of transdermal nicotine. Given a choice between bupropion and nicotine replacement, a substantial proportion of smokers are likely to choose bupropion. This choice will be made easier by the fact that bupropion is available from general practitioners while nicotine replacement and counselling services are likely to involve referral elsewhere.

The challenge to health service management is to reform and integrate nicotine replacement and counselling services into primary care to provide widespread accessibility to these and to bupropion. Since nicotine treatment may be preferred by some patients and bupropion may be contraindicated in others it is also essential to end the present irrational and unfair exclusion of nicotine replacement products from the list of reimbursable prescriptions. It is time that helping patients to quit smoking is taken seriously by the NHS, and if the arrival of bupropion is the catalyst that causes this to happen, then the drug might really achieve something.

John Britton *professor of respiratory medicine*

Division of Respiratory Medicine, University of Nottingham, City Hospital, Nottingham NG5 1PB
(j.britton@virgin.net)

Martin J Jarvis *professor of health psychology*

Department of Epidemiology and Public Health, ICRF Health Behaviour Unit, University College London, London WC1E 6BT
(martin.jarvis@ucl.ac.uk)

JB has been reimbursed by GlaxoWellcome, the manufacturer of bupropion, for attending international conferences in respiratory medicine and is participating in a clinical trial of transdermal nicotine funded by Pharmacia and Upjohn. MJJ has received honorariums from GlaxoWellcome for speaking and attending meetings of advisory panels.

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Correction

Isolated systolic hypertension: a radical rethink

An error occurred in this editorial by Wilkinson and colleagues (24 June, p 1685). The second author's name is D J Webb [not D J Webb Christison]. D J Webb is Christison professor of therapeutics and clinical pharmacology at the University of Edinburgh. We apologise for the error.

We ask all editorial writers to sign a declaration of competing interests (bmj.com/guides/confli.shtml#aut). We print the interests only when there are some. When none are shown, the authors have ticked the "None declared" box.