Cochrane Corner

Smoking cessation – a cheap medication is now available

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In each study the reviewers used the strictest available criteria to define cessation, so they extracted figures for sustained abstinence in preference to point prevalence where both were presented. In studies that used biochemical validation of cessation, only those subjects meeting the criteria for biochemically confirmed abstinence were regarded as having stopped smoking.

Nortriptyline

All three trials of nortriptyline found a significant increase in quit rates at long term follow-up. The pooled odds ratio was 2.83 (95% CI 1.59-5.03). A past history of depression did not appear to modulate the efficacy of nortriptyline. In one study the presence or absence of behaviour therapy did not influence the active vs placebo odds ratio (Hall 1998).

Moclobemide and SSRIs. None of these studies found a benefit for smoking cessation.

Atypical antidepressants Bupropion (Zyban)

Pooling the results of four trials with twelve month abstinence rates and three with six month rates gave an estimated odds ratio of 2.54 (95% CI 1.90–3.41). Excluding this study reduces the effect estimated by the meta-analysis OR 2.28 (95% CI 1.66–3.15), although it does not change the conclusions about the clinical benefit. Bupropion was also significantly more effective than nicotine patch in one study (Jorenby 1999) (OR 2.07, 95% CI 1.22–3.53). Combined bupropion plus patch also appeared to be more effective than patch alone (OR 2.65, 95% CI 1.58–4.45) but not more than bupropion alone. Bupropion appears to decrease withdrawal symptoms (Shiffman 2000) and post-cessation weight gain while being used (Hurt 1997).

Adverse effects

As with any medication there are side effects. The review details those due to Buproprion which occurred at the rate of 14/1000 in the UK and 0./1000 in Canada. Medsafe in New Zealand recommends the use of nicotine products before using Buproprion. In particular patients with a risk of seizures should not be on Buproprion. The web address for Medsafe is http://www.medsafe.govt.nz/Profs/Datasheet/z/zybantab.htm

Amongst people allocated to bupropion in clinical trials for smoking cessation, the drop out rate due to adverse events ranged from 7% to 12%. Early trials of bupropion in depression suggested it increased the risk of seizures. This led to the development of the slow release preparation now licensed for smoking cessation. Using this preparation in doses of 300mg/day or less, and excluding those at risk of seizures, no seizures were reported in any of the smoking cessation trials. Based on an observational safety surveillance study, the manufacturers report the risk of seizure with the slow release preparation at a maximum dose of 300mg/day to be about 1:1000 patients prescribed the drug (Dunner 1998). Three participants had a seizure considered to be related to the therapeutic use of bupropion. The commonest side effects are insomnia, occurring in 30–40% of patients, dry mouth (10%) and nausea. Although no patient has been reported to have died while taking bupropion in trials for smoking cessation, some people have died whilst taking bupropion prescribed for smoking cessation in routine practice.

Adverse effects of nortriptyline

Drop out rates in the two trials published in full were 4% and 9%. The adverse events reported included the

well known tricyclic effects of dry mouth, drowsiness, lightheadedness and constipation.

Clinical bottom line

The existing evidence is sufficient to endorse the use of bupropion (Zyban) and nortriptyline in clinical practice for smoking cessation. Nicotine replacement therapy has proven efficacy in over 80 studies and has a very benign side-effect profile. The confidence intervals around the efficacy estimates for bupropion, nortriptyline and NRT overlap, which suggests that no treatment is better than another. The numbers needed to treat to stop one person smoking for one year ranges from two to 15 for Bupropion and eight for Nortriptyline. Smokers with a previous history of depression or mild current depression have not been shown to do better with antidepressants than NRT. Patient preferences, cost, availability and side-effect profile will all need to be taken into account. Bupropion is indicated in those who fail nicotine replacement. Nortriptyline may be also be considered a second line therapy after failed nicotine treatment and has the advantage of being fully funded in New Zealand. Both antidepressants can produce clinically significant adverse effects, however, typically <10% of those on antidepressants stop taking the drug due to adverse effects.

References

References are available from B Arroll or from the Cochrane library.

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