Office based treatment with buprenorphine plus naloxone, or buprenorphine alone reduces opiate use and craving


Q How effective is buprenorphine with or without naloxone in reducing opiate use and craving in people addicted to opiates?

**METHODS**

**Design:** Multicentre randomised controlled trial.

**Allocation:** Unclear.

**Blinding:** Double blind.

**Follow up period:** Four weeks.

**Setting:** Eight centres in the United States; October 1996 to September 1999.

**Patients:** Adults aged 18–59 years with opiate dependence (DSM-IV) seeking opiate substitution pharmacotherapy. Exclusions: pregnant or nursing women, primary Axis 1 psychiatric diagnosis (DSM-IV) other than opiate, caffeine, or nicotine dependence, or use of methadone, levomethadyl acetate or naltrexone 14 days before enrolment.

**Intervention:** Sublingual tablets of: buprenorphine (16 mg/day) alone; buprenorphine (16 mg/day) plus naloxone (4 mg/day), and placebo.

**Outcomes:** Proportion of opiate negative urine samples; participant reported cravings for opiates (measured on a visual analogue scale where 0 = no craving and 100 = intense craving).

**Patient follow up:** As both treatments were more effective than placebo, the trial was terminated early. Of 296 people not affected by the early termination, 243 (82.1%) completed the trial.

**MAIN RESULTS**

Both buprenorphine plus naloxone, and buprenorphine alone significantly increased the proportion of people with opiate negative urine samples compared with placebo (17.8% vs 20.7% vs 5.8%, respectively; p<0.001 for both drug treatments compared with placebo). Buprenorphine based treatments, with or without naloxone, significantly reduced the number of cravings for opiates, compared with placebo (p=0.001 for all treatments vs placebo).

**CONCLUSIONS**

Buprenorphine based treatments, with or without naloxone, reduced opiate use and cravings in people with opiate addiction, and were suitable for use in an office based setting.

**Commentary**

The focus of this paper is the efficacy and safety of the buprenorphine-naloxone tablet in office based treatment settings. The finding that buprenorphine alone, and the combination of buprenorphine and naloxone have greater efficacy than placebo, is not new information. Indeed the inclusion of a placebo control could be a point of ethical debate. What is novel about this study is the setting in which it was undertaken, namely office based practice in the USA. Office based substitution treatment for opioid dependence using methadone or buprenorphine is practised in several Western countries, including the UK, Australia, and France, but until recently was restricted to specialist clinic settings in the USA. Politicians and the general public are uncomfortable with the concept of substitution treatment. Despite strong evidence for the public health benefits of methadone maintenance treatment, there is continuing ambivalence towards the prescription of a drug of dependence to treat drug dependence, and medical practitioners are often reluctant to treat drug users. It is this political context that gives importance to this study.

Office based substitution treatment has potential benefits in terms of improved treatment retention rates and attractiveness to users concerned about possible stigma associated with attendance at a specialist addiction clinic. The buprenorphine-naloxone tablet, with its reduced risk of misuse and diversion, may enhance public confidence in substitution treatment. The open label component of the study provides useful data on the adverse effects of the buprenorphine-naloxone combination tablet, and the RCT, together with previous studies, supports the idea that naloxone does not reduce the efficacy of buprenorphine. However, there remains a need for long term effectiveness data—particularly data on retention rates and withdrawal symptoms experienced during six or 12 months of substitution treatment with the combination tablet compared with buprenorphine alone.

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