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[Intervention Review]

Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence

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ABSTRACT

Background

Buprenorphine maintenance treatment has been evaluated in randomised controlled trials against placebo medication, and separately as an alternative to methadone for management of opioid dependence.

Objectives

To evaluate buprenorphine maintenance compared to placebo and to methadone maintenance in the management of opioid dependence, including its ability to retain people in treatment, suppress illicit drug use, reduce criminal activity, and mortality.

Search methods

We searched the following databases to January 2013: Cochrane Drugs and Alcohol Review Group Specialised Register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, Current Contents, PsycLIT, CORK, Alcohol and Drug Council of Australia, Australian Drug Foundation, Centre for Education and Information on Drugs and Alcohol, Library of Congress, reference lists of identified studies and reviews. We sought published/unpublished randomised controlled trials (RCTs) from authors.

Selection criteria

Randomised controlled trials of buprenorphine maintenance treatment versus placebo or methadone in management of opioid-dependent persons.

Data collection and analysis

We used Cochrane Collaboration methodology.

Main results

We include 31 trials (5430 participants), the quality of evidence varied from high to moderate quality.

There is high quality of evidence that buprenorphine was superior to placebo medication in retention of participants in treatment at all doses examined. Specifically, buprenorphine retained participants better than placebo: at low doses (2 - 6 mg), 5 studies, 1131 participants, risk ratio (RR) 1.50; 95% confidence interval (CI) 1.19 to 1.88; at medium doses (7 - 15 mg), 4 studies, 887 participants, RR 1.74; 95% CI 1.06 to 2.87; and at high doses (\geq 16 mg), 5 studies, 1001 participants, RR 1.82; 95% CI 1.15 to 2.90. However,

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there is moderate quality of evidence that only high-dose buprenorphine (≥ 16 mg) was more effective than placebo in suppressing illicit opioid use measured by urinalysis in the trials, 3 studies, 729 participants, standardised mean difference (SMD) -1.17; 95% CI -1.85 to -0.49. Notably, low-dose, (2 studies, 487 participants, SMD 0.10; 95% CI -0.80 to 1.01), and medium-dose, (2 studies, 463 participants, SMD -0.08; 95% CI -0.78 to 0.62) buprenorphine did not suppress illicit opioid use measured by urinalysis better than placebo.

There is high quality of evidence that buprenorphine in flexible doses adjusted to participant need, was less effective than methadone in retaining participants, 5 studies, 788 participants, RR 0.83; 95% CI 0.72 to 0.95. For those retained in treatment, no difference was observed in suppression of opioid use as measured by urinalysis, 8 studies, 1027 participants, SMD -0.11; 95% CI -0.23 to 0.02 or self report, 4 studies, 501 participants, SMD -0.11; 95% CI -0.28 to 0.07, with moderate quality of evidence.

Consistent with the results in the flexible-dose studies, in low fixed-dose studies, methadone (≤ 40 mg) was more likely to retain participants than low-dose buprenorphine (2 - 6 mg), (3 studies, 253 participants, RR 0.67; 95% CI: 0.52 to 0.87). However, we found contrary results at medium dose and high dose: there was no difference between medium-dose buprenorphine (7 - 15 mg) and medium-dose methadone (40 - 85 mg) in retention, (7 studies, 780 participants, RR 0.87; 95% CI 0.69 to 1.10) or in suppression of illicit opioid use as measured by urines, (4 studies, 476 participants, SMD 0.25; 95% CI -0.08 to 0.58) or self report of illicit opioid use, (2 studies, 174 participants, SMD -0.82; 95% CI -1.83 to 0.19). Similarly, there was no difference between high-dose buprenorphine (≥ 16 mg) and high-dose methadone (≥ 85 mg) in retention (RR 0.79; 95% CI 0.20 to 3.16) or suppression of self-reported heroin use (SMD -0.73; 95% CI -1.08 to -0.37) (1 study, 134 participants).

Few studies reported adverse events; two studies compared adverse events statistically, finding no difference between methadone and buprenorphine, except for a single result indicating more sedation among those using methadone.

Authors' conclusions

Buprenorphine is an effective medication in the maintenance treatment of heroin dependence, retaining people in treatment at any dose above 2 mg, and suppressing illicit opioid use (at doses 16 mg or greater) based on placebo-controlled trials.

However, compared to methadone, buprenorphine retains fewer people when doses are flexibly delivered and at low fixed doses. If fixed medium or high doses are used, buprenorphine and methadone appear no different in effectiveness (retention in treatment and suppression of illicit opioid use); however, fixed doses are rarely used in clinical practice so the flexible dose results are more relevant to patient care. Methadone is superior to buprenorphine in retaining people in treatment, and methadone equally suppresses illicit opioid use.

PLAIN LANGUAGE SUMMARY

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Background

Methadone is widely used as a replacement for illicit opioid use such as heroin in medically-supported opioid substitution maintenance programmes. Two other drugs have been used to help reduce illicit opioid use, specifically buprenorphine and LAAM (levo-alpha-acetylmethadol). LAAM is not used in current clinical practice. Buprenorphine is currently used and can reduce illicit opioid use compared with placebo, although it is less effective than methadone. Buprenorphine is an opioid drug that is not as potent as heroin and methadone, although the effects of buprenorphine may last longer. Buprenorphine can be taken once every two days. The trials include different formulations of buprenorphine: sublingual solution, sublingual tablets, combined buprenorphine/naloxone sublingual tablet and an implant.

Key results

The review of trials found that buprenorphine at high doses (16 mg) can reduce illicit opioid use effectively compared with placebo, and buprenorphine at any dose studied retains people in treatment better than placebo.

Buprenorphine appears to be less effective than methadone in retaining people in treatment, if prescribed in a flexible dose regimen or at a fixed and low dose (2 - 6 mg per day). Buprenorphine prescribed at fixed doses (above 7 mg per day) was not different from methadone prescribed at fixed doses (40 mg or more per day) in retaining people in treatment or in suppression of illicit opioid use.