A comparison of methadone, buprenorphine and alpha2 adrenergic agonists for opioid detoxification: a mixed treatment comparison meta-analysis

Meader N

CRD summary
This review found that buprenorphine and methadone were associated with the highest rates of completion of treatment for opioid dependency. A lack of information on the included studies and the methodological quality of the included studies made the reliability of the author's conclusions unclear.

Authors' objectives
To simultaneously compare the efficacy of methadone, buprenorphine, clonidine and lofexidine for opioid detoxification.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, MEDLINE, EMBASE, PsycINFO and HMIC were searched from inception to May 2006 for relevant studies in English; search terms were reported. References of retrieved articles and previous reviews and meta-analyses were checked for additional studies. The authors contacted experts to request studies.

Study selection
Randomised controlled trials (RCTs) that compared methadone, buprenorphine, clonidine and lofexidine treatment for durations of less than 12 weeks in patients with opioid dependency and a mean age of greater than 16 years were eligible for inclusion. Studies with fewer than 10 patients per group and studies in which randomisation was not adequately described were excluded.

The primary outcomes evaluated related to completion of detoxification treatment. Treatment completion was defined as retention in treatment to the final day of the planned duration of treatment, ingestion of the final dose of study medication or reaching the point of zero dose of study medication. Participant age ranged from 17 to 50 years. Drug treatment duration ranged from three to 30 days.

The author did not state how many reviewers performed the study selection.

Assessment of study quality
Methodological quality was assessed using the SIGN checklist for RCTs.

The author did not state how many reviewers performed the quality assessment.

Data extraction
The author and a research assistant independently extracted data on completion of treatment to calculate odds ratios (OR) and corresponding 95% credible intervals (CrI). In trials with three treatment arms, data from two groups were used to avoid double counting.

Methods of synthesis
Pooled odds ratios and 95% CrIs were calculated. Direct and indirect comparisons were made between treatments using a Markov Chain Monte Carlo model. The mixed treatment comparison approach was used to assess the probability of effectiveness of each treatment.

Results of the review
Twenty-three RCTs (n=2,112) were included in the review. Completion of treatment across all drug treatment arms ranged from 11% to 90%. Methadone was compared to clonidine (five trials) lofexidine (two trials) and buprenorphine (three trials). Buprenorphine was compared to clonidine in eight trials and lofexidine in one trial. Four trials evaluated comparisons between clonidine and lofexidine. The methodological quality of the studies was not reported.
There were statistically significant higher rates of completion of detoxification treatment observed with buprenorphine compared to clonidine in mixed treatment meta-analysis (OR 3.95, 95% CrI 2.01 to 7.46) and direct comparison analysis (OR 2.22, 95% CrI 1.10 to 4.26). Methadone was observed to be associated with significantly higher rates of treatment completion than clonidine in the mixed treatment comparison (OR 2.42, 95% CrI 1.07 to 5.37).

Buprenorphine was associated with non-statistically significant trends towards benefits for treatment completion compared to methadone and lofexidine. A non-significant benefit was observed for methadone compared to lofexidine. There were no statistically significant differences between lofexidine and clonidine.

Buprenorphine was found to have the highest probability of being the most effective treatment (0.85), followed by methadone (0.12), lofexidine (0.03) and clonidine (0.0001).

**Authors' conclusions**

Buprenorphine and methadone appeared to be the most effective detoxification treatments for opioid dependency. Lofexidine and clonidine were very unlikely to be the most effective treatment.

**CRD commentary**

The review addressed a clear question. Criteria for inclusion were stipulated. Restriction of the review to studies published in English meant that there was a risk of language bias. Appropriate electronic databases and journals were searched. Attempts were made to identify unpublished studies. Steps were taken to minimise errors and bias in data extraction, but were not reported for study selection and assessment of study quality. An assessment of methodological quality was reported, but the results were not published and so the reliability of the results was unknown.

Non-completion of treatment in some drug treatment arms was nearly 90%; whether the results were assessed using intention-to-treat analyses was unknown. There was little information published about patients, interventions and comparators in the included trials. Various definitions of the primary outcome were used and it was unclear whether pooling of these results was appropriate.

The author's conclusions are based on the evidence presented, but the uncertain quality of the included trials made it difficult to make a judgement on the reliability of the results and the author's conclusions.

**Implications of the review for practice and research**

**Practice:** The author did not state any implications for practice.

**Research:** The author stated that further research was required to determine whether there were significant differences in the effectiveness between buprenorphine and methadone.

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