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Buprenorphine for managing opioid withdrawal.

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Abstract

BACKGROUND: Managed withdrawal is a necessary step prior to drug-free treatment or as the endpoint of substitution treatment.

OBJECTIVES: To assess the effects of buprenorphine versus tapered doses of methadone, alpha$_2$-adrenergic agonists, symptomatic medications or placebo, or different buprenorphine regimens for managing opioid withdrawal, in terms of the intensity of the withdrawal syndrome experienced, duration and completion of treatment, and adverse effects.

SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 11, 2016), MEDLINE (1946 to December week 1, 2016), Embase (to 22 December 2016), PsycINFO (1806 to December week 3, 2016), and the Web of Science (to 22 December 2016) and handsearched the reference lists of articles.

SELECTION CRITERIA: Randomised controlled trials of interventions using buprenorphine to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent. Comparison interventions involved reducing doses of methadone, alpha$_2$-adrenergic agonists (clonidine or lofexidine), symptomatic medications or placebo, and different buprenorphine-based regimens.

DATA COLLECTION AND ANALYSIS: We used standard methodological procedures expected by Cochrane.

MAIN RESULTS: We included 27 studies involving 3048 participants. The main comparators were clonidine or lofexidine (14 studies). Six studies compared buprenorphine versus methadone, and seven compared different rates of buprenorphine dose reduction. We assessed 12 studies as being at high risk of bias in at least one of seven domains of methodological quality. Six of these studies compared buprenorphine with clonidine or lofexidine and two with methadone; the other four studies compared different rates of buprenorphine dose reduction.For the comparison of buprenorphine and methadone in tapered doses, meta-analysis was not possible for the outcomes of intensity of withdrawal or adverse effects. However, information reported by the individual studies was suggestive of buprenorphine and methadone having similar capacity to ameliorate opioid withdrawal, without clinically significant adverse effects. The meta-analyses that were possible support a conclusion of no difference between buprenorphine and methadone in terms of average treatment duration (mean difference (MD) 1.30 days, 95% confidence interval (CI) -8.11 to 10.72; N = 82; studies = 2; low quality) or treatment completion rates (risk ratio (RR) 1.04, 95% CI 0.91 to 1.20; N = 457; studies = 5; moderate quality).Relative to clonidine or lofexidine, buprenorphine was associated with a lower average withdrawal score (indicating less severe withdrawal) during the treatment episode, with an effect size that is considered to be small to moderate (standardised mean difference (SMD) -0.43, 95% CI -0.58 to -0.28; N = 902; studies = 7; moderate quality). Patients receiving buprenorphine stayed in treatment for longer, with an effect size that is considered to be large (SMD 0.92, 95% CI 0.57 to 1.27; N = 558; studies = 5; moderate quality) and were more likely to complete withdrawal treatment (RR 1.59, 95% CI 1.23 to 2.06; N = 1264; studies = 12; moderate quality). At the same time there was no significant difference in the incidence of adverse effects, but dropout due to adverse effects may be more likely with clonidine (RR 0.20, 95% CI 0.04 to 1.15; N = 134; studies = 3; low quality). The difference in treatment completion rates translates to a number needed to treat for an additional beneficial outcome of 4 (95% CI 3 to 6), indicating that for every four people treated with buprenorphine, we can expect that one additional person will complete treatment than with clonidine or lofexidine.For studies comparing different rates of reduction of the buprenorphine dose, meta-analysis was possible only for treatment

completion, with separate analyses for inpatient and outpatient settings. The results were diverse, and we assessed the quality of evidence as being very low. It remains very uncertain what effect the rate of dose taper has on treatment outcome.

AUTHORS' CONCLUSIONS: Buprenorphine is more effective than clonidine or lofexidine for managing opioid withdrawal in terms of severity of withdrawal, duration of withdrawal treatment, and the likelihood of treatment completion.Buprenorphine and methadone appear to be equally effective, but data are limited. It remains possible that the pattern of withdrawal experienced may differ and that withdrawal symptoms may resolve more quickly with buprenorphine.It is not possible to draw any conclusions from the available evidence on the relative effectiveness of different rates of tapering the buprenorphine dose. The divergent findings of studies included in this review suggest that there may be multiple factors affecting the response to the rate of dose taper. One such factor could be whether or not the initial treatment plan includes a transition to subsequent relapse prevention treatment with naltrexone. Indeed, the use of buprenorphine to support transition to naltrexone treatment is an aspect worthy of further research.Most participants in the studies included in this review were male. None of the studies reported outcomes on the basis of sex, preventing any exploration of differences related to this variable. Consideration of sex as a factor influencing response to withdrawal treatment would be relevant research for selecting the most appropriate type of intervention for each individual.

Update of

Buprenorphine for the management of opioid withdrawal. [Cochrane Database Syst Rev. 2009]

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