Cochrane Library

Cochrane Database of Systematic Reviews

Pharmacological therapies for management of opium withdrawal (Review)

Rahimi-Movaghar A, Gholami J, Amato L, Hoseinie L, Yousefi-Nooraie R, Amin-Esmaeili M

Rahimi-Movaghar A, Gholami J, Amato L, Hoseinie L, Yousefi-Nooraie R, Amin-Esmaeili M.
Pharmacological therapies for management of opium withdrawal.
Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD007522.
DOI: 10.1002/14651858.CD007522.pub2.

www.cochranelibrary.com

WILEY

[Intervention Review]

Pharmacological therapies for management of opium withdrawal

Afarin Rahimi-Movaghar[1], Jaleh Gholami[1], Laura Amato[2], Leila Hoseinie[1], Reza Yousefi-Nooraie[3], Masoumeh Amin-Esmaeili[1]

[1]Iranian National Center for Addiction Studies (INCAS), Tehran University of Medical Sciences, Tehran, Iran. [2]Department of Epidemiology, Lazio Regional Health Service, Rome, Italy. [3]Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Canada

Contact address: Afarin Rahimi-Movaghar, Iranian National Center for Addiction Studies (INCAS), Tehran University of Medical Sciences, No. 486, South Karegar Ave., Tehran, Tehran, 1336616357, Iran. rahimia@tums.ac.ir.

Editorial group: Cochrane Drugs and Alcohol Group.
Publication status and date: New, published in Issue 6, 2018.

Citation: Rahimi-Movaghar A, Gholami J, Amato L, Hoseinie L, Yousefi-Nooraie R, Amin-Esmaeili M. Pharmacological therapies for management of opium withdrawal. *Cochrane Database of Systematic Reviews* 2018, Issue 6. Art. No.: CD007522. DOI: 10.1002/14651858.CD007522.pub2.

ABSTRACT

Background

Pharmacologic therapies for management of heroin withdrawal have been studied and reviewed widely. Opium dependence is generally associated with less severe dependence and milder withdrawal symptoms than heroin. The evidence on withdrawal management of heroin might therefore not be exactly applicable for opium.

Objectives

To assess the effectiveness and safety of various pharmacologic therapies for the management of the acute phase of opium withdrawal.

Search methods

We searched the following sources up to September 2017: CENTRAL, MEDLINE, Embase, CINAHL, PsycINFO, regional and national databases (IMEMR, Iranmedex, and IranPsych), main electronic sources of ongoing trials, and reference lists of all relevant papers. In addition, we contacted known investigators to obtain missing data or incomplete trials.

Selection criteria

Controlled clinical trials and randomised controlled trials on pharmacological therapies, compared with no intervention, placebo, other pharmacologic treatments, different doses of the same drug, and psychosocial intervention, to manage acute withdrawal from opium in a maximum duration of 30 days.

Data collection and analysis

We used the standard methodological procedures expected by Cochrane.

Main results

We included 13 trials involving 1096 participants. No pooled analysis was possible. Studies were carried out in three countries, Iran, India, and Thailand, in outpatient and inpatient settings. The quality of the evidence was generally very low.

When the mean of withdrawal symptoms was provided for several days, we mainly focused on day 3. The reason for this was that the highest severity of opium withdrawal is in the second to fourth day.

Comparing different pharmacological treatments with each other, clonidine was twice as good as methadone for completion of treatment (risk ratio (RR) 2.01, 95% confidence interval (CI) 1.69 to 2.38; 361 participants, 1 study, low-quality evidence). All the other results showed

no differences between the considered drugs: baclofen versus clonidine (RR 1.06, 95% CI 0.63 to 1.80; 66 participants, 1 study, very low-quality evidence); clonidine versus clonidine plus amantadine (RR 1.03, 95% CI 0.86 to 1.24; 69 participants, 1 study); clonidine versus buprenorphine in an inpatient setting (RR 1.04, 95% CI 0.90 to 1.20; 1 study, 35 participants, very low-quality evidence); methadone versus tramadol (RR 0.95, 95% CI 0.65 to 1.37; 1 study, 72 participants, very low-quality evidence); methadone versus methadone plus gabapentin (RR 1.17, 95% CI 0.96 to 1.43; 1 study, 40 participants, low-quality evidence), and tincture of opium versus methadone (1 study, 74 participants, low-quality evidence).

Comparing different pharmacological treatments with each other, adding amantadine to clonidine decreased withdrawal scores rated at day 3 (mean difference (MD) -3.56, 95% CI -5.97 to -1.15; 1 study, 60 participants, very low-quality evidence). Comparing clonidine with buprenorphine in an inpatient setting, we found no difference in withdrawal symptoms rated by a physician (MD -1.40, 95% CI -2.93 to 0.13; 1 study, 34 participants, very low-quality evidence), and results in favour of buprenorpine when rated by participants (MD -11.80, 95% CI -15.56 to -8.04). Buprenorphine was superior to clonidine in controlling severe withdrawal symptoms in an outpatient setting (RR 0.35, 95% CI 0.19 to 0.64; 1 study, 76 participants). We found no difference in the comparison of methadone versus tramadol (MD 0.04, 95% CI -2.68 to 2.76; 1 study, 72 participants) and in the comparison of methadone versus methadone plus gabapentin (MD -2.20, 95% CI -6.72 to 2.32; 1 study, 40 participants).

Comparing clonidine versus buprenorphine in an outpatient setting, more adverse effects were reported in the clonidine group (1 study, 76 participants). Higher numbers of participants in the clonidine group experienced hypotension at days 5 to 8, headache at days 1 to 8, sedation at days 5 to 8, dizziness and dry mouth at days 1 to 10, and nausea at days 1 to 9. Sweating was reported in a significantly higher number of participants in the buprenorphine group at days 1 to 10. We found no difference between groups for all the other comparisons considering this outcome.

Comparing different dosages of the same pharmacological detoxification treatment, a high dose of clonidine (1 to 1.2 mg/day) did not differ from a low dose of clonidine (0.5 to 0.6 mg/day) in completion of treatment in an inpatient setting (RR 1.00, 95% CI 0.84 to 1.19; 1 study, 68 participants), however a higher number of participants with hypotension was reported in the high-dose group (RR 3.25, 95% CI 1.77 to 5.98). Gradual reduction of methadone was associated with more adverse effects than abrupt withdrawal of methadone (RR 2.25, 95% CI 1.02 to 4.94; 1 study, 20 participants, very low-quality evidence).

Authors' conclusions

Results did not support using any specific pharmacological approach for the management of opium withdrawal due to generally very low-quality evidence and small or no differences between treatments. However, it seems that opium withdrawal symptoms are significant, especially at days 2 to 4 after discontinuation of opium. All of the assessed medications might be useful in alleviating symptoms. Those who receive clonidine might experience hypotension.

PLAIN LANGUAGE SUMMARY

Medications for the management of opium withdrawal

What was the aim of this review?

The aim of this Cochrane Review was to find out which medications are more effective and safer for the management of opium withdrawal. We collected and analysed all relevant studies to answer this question, and found 13 studies involving 1096 participants.

Key messages

This review included the following 12 comparisons: baclofen versus clonidine, clonidine versus clonidine plus amantadine, clonidine versus buprenorphine, high-dose clonidine versus low-dose clonidine versus symptomatic management, clonidine versus methadone, methadone versus tramadol, methadone versus methadone plus gabapentin, gradual reduction of methadone versus sudden withdrawal of methadone, methadone plus amitriptyline versus methadone, diphenoxylate versus propoxyphene, three different protocols of tincture of opium, and tincture of opium versus methadone. The studies were carried out in three countries, Iran, India, and Thailand. Support from a pharmaceutical company in the form of free provision of medications was reported in only one study.

The evidence is unclear as to whether any of the evaluated medications is more effective than another in the management of opium withdrawal. However, it seems that opium withdrawal symptoms are significant in the first days after discontinuation of opium. All of the assessed medications might be useful in alleviating symptoms. Use of clonidine might result in low blood pressure.

What was studied in this review?

Withdrawal symptoms from opium are similar to those of other opioids such as heroin, but with mild intensity. Patients usually need medications to help alleviate withdrawal symptoms.

What are the main results of the review?

We are uncertain as to whether the effects of clonidine differ from those of baclofen in number of participants who completed treatment (certainty of evidence was very low).

We are uncertain as to whether adding amantadine to clonidine decreases the severity of withdrawal symptoms in days 1 to 3 in an inpatient setting, or whether it has an effect on completion of treatment (certainty of evidence was very low).

We are uncertain as to whether buprenorphine is better than clonidine in controlling withdrawal symptoms in both inpatient and outpatient settings (certainty of evidence was very low). Adverse effects, including hypotension, were reported in higher numbers in the clonidine group.

We are uncertain as to whether a high dose of clonidine differs from a low dose of clonidine in completion of treatment in an inpatient setting (certainty of evidence was very low), however a higher number of cases of low blood pressure was reported with high-dose clonidine.

Clonidine may be better than methadone in keeping patients in treatment in an outpatient setting.

We are uncertain as to whether tramadol differs from methadone in completion of treatment and in alleviating withdrawal symptoms, and whether adverse effects are common with methadone (certainty of evidence was very low).

Adding gabapentin to methadone may make little or no difference in completion of treatment and the severity of withdrawal symptoms.

We are uncertain as to whether abrupt withdrawal of methadone is associated with fewer patient complaints than gradual reduction of methadone (certainty of evidence was very low).

Tincture of opium may make no difference in completion of treatment, severity of withdrawal symptoms, and adverse effects in comparison to methadone.

How up-to-date is this review?

We searched for studies published up to September 2017.