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[Intervention Review]

Supervised dosing with a long-acting opioid medication in the management of opioid dependence

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ABSTRACT

Background

Opioid dependence (OD) is an increasing clinical and public health problem worldwide. International guidelines recommend opioid substitution treatment (OST), such as methadone and buprenorphine, as first-line medication treatment for OD. A negative aspect of OST is that the medication used can be diverted both through sale on the black market, and the unsanctioned use of medications. Daily supervised administration of medications used in OST has the advantage of reducing the risk of diversion, and may promote therapeutic engagement, potentially enhancing the psychosocial aspect of OST, but costs more and is more restrictive on the client than dispensing for off-site consumption.

Objectives

The objective of this systematic review is to compare the effectiveness of OST with supervised dosing relative to dispensing of medication for off-site consumption.

Search methods

We searched in Cochrane Drugs and Alcohol Group Specialised Register and Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL, Web of Science from inception up to April 2016. Ongoing and unpublished studies were searched via ClinicalTrials.gov (www.clinicaltrials.gov) and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/).

All searches included non-English language literature. We handsearched references on topic-related systematic reviews.

Selection criteria

Randomised controlled trials (RCTs), controlled clinical trials (CCTs), and prospective controlled cohort studies, involving people who are receiving OST (methadone, buprenorphine) and comparing supervised dosing with dispensing of medication to be consumed away from the dispensing point, usually without supervision.

Data collection and analysis

We used the standard methodological procedures expected by Cochrane.



Main results

Six studies (four RCTs and two prospective observational cohort studies), involving 7999 participants comparing supervised OST treatment with unsupervised treatment, met the inclusion criteria. The risk of bias was generally moderate across trials, but the results reported on outcomes that we planned to consider were limited. Overall, we judged the quality of the evidence from very low to low for all the outcomes.

We found no difference in retention at any duration with supervised compared to unsupervised dosing (RR 0.99, 95% CI 0.88 to 1.12, 716 participants, four trials, low-quality evidence) or in retention in the shortest follow-up period, three months (RR 0.94; 95% CI 0.84 to 1.05; 472 participants, three trials, low-quality evidence). Additional data at 12 months from one observational study found no difference in retention between groups (RR 0.94, 95% CI 0.77 to 1.14; n = 300). There was no difference in abstinence at the end of treatment (self-reported drug use) (67% versus 60%, P = 0.33, 293 participants, one trial, very low-quality evidence); and in diversion of medication (5% versus 2%, 293 participants, one trial, very low-quality evidence).

Regarding our secondary outcomes, we did not found a difference in the incidence of adverse effects in the supervised compared to unsupervised control group (RR 0.63; 96% CI 0.10 to 3.86; 363 participants, two trials, *very low-quality evidence*). Data on severity of dependence were very limited (244 participants, one trial) and showed no difference between the two approaches. Data on deaths were reported in two studies. One trial reported two deaths in the supervised group (*low-quality evidence*), while in the cohort study all-cause mortality was found lower in regular supervision group (crude mortality rate 0.60 versus 0.81 per 100 person-years), although after adjustment insufficient evidence existed to suggest that regular supervision was protective (mortality rate ratio = 1.23, 95% CI = 0.67 to 2.27).

No studies reported pain symptoms, drug craving, aberrant opioid-related behaviours, days of unsanctioned opioid use and overdose.

Authors' conclusions

Take-home medication strategies are attractive to treatment services due to lower costs, and place less restrictions on clients, but it is unknown whether they may be associated with increased risk of diversion and unsanctioned use of medication. There is uncertainty about the effects of supervised dosing compared with unsupervised medication due to the low and very low quality of the evidence for the primary outcomes of interest for this review. Data on defined secondary outcomes were similarly limited. More research comparing supervised and take-home medication strategies is needed to support decisions on the relative effectiveness of these strategies. The trials should be designed and conducted with high quality and over a longer follow-up period to support comparison of strategies at different stages of treatment. In particular, there is a need for studies assessing in more detail the risk of diversion and safety outcomes of using supervised OST to manage opioid dependence.

PLAIN LANGUAGE SUMMARY

Supervised-dosing strategies versus take-home opioid substitution treatment for people dependent on opioid drugs

Review question

We reviewed the evidence about the effectiveness of supervised dosing strategies in opioid substitution treatment for people dependent on opioid drugs.

Background

Opioid dependence (OD) is a global clinical and public health problem that is associated with significant burden of disease and drug-related deaths. OD represents a complex health condition that usually requires long-term treatment. International guidelines recommend opioid substitution treatment (OST), such as methadone and buprenorphine, as a first-line treatment for OD. OST is a form of health care for people who are dependent on heroin, or who have become dependent after taking prescribed opioids for pain, and involves substitution of the drug that is being used inappropriately with a long-acting opioid. OST gives people who are opioid dependent the opportunity to stabilise their lives, and to address the social and psychological dimensions that tend to accompany opioid dependence. A negative aspect of OST is that the medications used can be diverted, by being sold on the black market or used inappropriately. One strategy for minimising diversion is for OST medications to be administered under supervision (supervised dosing). With supervised dosing, access to unsupervised or take-away doses of medication is then a privilege which can be used as a motivational and reward incentive. Supervised dosing is also associated with more frequent contact between the client and service provider offering more opportunities for therapeutic engagement. However, providing supervised dosing is more expensive for service providers, and more restrictive for clients who have to attend for dosing every day. The purpose of this review was to assess the effectiveness of supervised dosing, compared to dispensing of take-home medication, in terms of reduction in heroin and other unsanctioned opioid use, retention in treatment, diversion of medication and adverse effects.

Search date

The evidence is current to April 2016.

Study characteristics



We identified six studies involving 7999 people receiving treatment with methadone (7786 people) or buprenorphine–naloxone (213 people) for opioid dependence. Four of the studies were randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups), while the other two studies followed groups of people over time. Four of the studies were funded by the National Institutes for Health Research and by the Health Research Board, with one study not reporting the funding source. One study was also funded by the drug company of buprenorphine–naloxone.

Key results

At three or more months follow-up, this review found no evidence on benefit of the supervised dosing with respect to keep people in treatment, or reduce opioid use, mortality reduction and adverse drug events. One study found that supervised dosing led to a reduction of diversion. None of the studies assessed the effect of supervised dosing on pain symptoms, drug craving, days of unsanctioned opioid use, overdose and hospitalisation.

We are unable to make any conclusion about the effectiveness of supervised dosing compared to dispensing of medication as take-home doses, in the context of OST. Further research is required to determine the effectiveness of supervised or take-home dosing in OST.

Quality of the evidence

Overall, the studies were moderately well-conducted, but there was a small number of studies reporting outcomes of interest, therefore insufficient to evaluate the efficacy of intervention such as diversion, opoid use reduction, retention in treatment and frequency of unsanctioned opioid use, Furthermore, low rates of occurrence of some events between studies resulted in the overall quality of the evidence being assessed as low and very low. This indicates that further evidence would be likely to change the estimates of relative effect made in this review.