Opioid antagonists for alcohol dependence (Cochrane Review)

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ABSTRACT

A substantive amendment to this systematic review was last made on 07 February 2002. Cochrane reviews are regularly checked and updated if necessary.

Background: The results from animal studies suggest that opioid antagonists may prevent the reinforcing effects of alcohol consumption. Based on the results of those animal studies, some opioid antagonists, such as, naltrexone, nalmefene, have been studied for their benefits in treating alcohol dependence.

Objectives: To determine the effectiveness of opioid antagonists in attenuating or preventing the recommencement of alcohol consumption in patients with alcohol dependence in comparison to placebo, other medications and psychosocial treatments. In addition, discontinuation rate, death, patient satisfaction, functioning, health-related quality of life and economic outcomes were also evaluated.

Search strategy: Electronic searches of Cochrane Controlled Trials Register (Cochrane Library 2001, issue 4), MEDLINE (1966 - October 2001), EMBASE (1980 - December 2001), and CINHAL (1982 - December 2001) were undertaken. Du Pont Pharmaceutical and Ivax Corporation were contacted for information regarding unpublished trials. The reference lists of the obtained papers were also examined. The specialised register of the Cochrane Group on Drugs and Alcohol was searched until February 2003.

Selection criteria: All relevant randomised controlled trials (RCTs) and controlled clinical trials (CCTs) were included. Participants were people with alcohol dependence. Naltrexone (NTX), nalmefene (NMF) and other opioid antagonists with/without other biological or psychosocial treatments were examined. Four primary outcomes of interest were number of patients who return to drinking, percentage or number of drinking days, number of standard drinks of alcohol and amount of alcohol consumed. A number of secondary outcomes were also considered.

Data collection and analysis: Two reviewers evaluated and extracted the data independently. The dichotomous data were extracted on an intention-to-treat basis. The Relative Risk with the 95% confidence interval was used to assess the dichotomous data. Weighted (or Standardised) Mean Difference with 95% confidence interval was used to assess the continuous data.

Main results: The review included 19 RCTs or CCTs presented in 26 articles. In comparison to placebo, two of four short-term primary outcomes were significantly in favour of NTX. Those were number of patients who return to drinking (61% in NTX group vs 69% in placebo group) [RR (95% CI) = 0.88 (0.80 to 0.98), NNT = 14] and percentage or number of drinking days [WMD

(95% CI) = -4.52 (-5.29 to -3.75)]. However, the short-term discontinuation rates were high and not different between NTX and placebo groups [RR (95% CI) = 0.96 (0.81 to 1.13)]. No medium-term outcomes of NTX and placebo groups showed any significant difference after the completion of NTX treatment for three to six months. However, those who were regularly treated with NTX treatment in both short and medium terms consumed smaller amounts of alcohol than placebo-treated patients. Because of the small sample sizes, there were few significant differences for other comparisons.

Reviewers' conclusions: NTX at the dose of 50 mg/day is effective for alcohol dependence in short-term treatment. The optimal duration of NTX treatment may be longer than 3 months. The evidence so far may be too little to support the superiority of NTX to acamprosate and the inferiority of NTX to disulfiram. NTX treatment should be concurrently given with a psychosocial intervention. Other patterns of NTX administration should not be used at present, e.g., a dose of three times a week, combined NTX with other biological treatments. NMF has no role for the treatment of alcohol dependence in clinical practice. Randomised, double-blind, placebo-controlled trials of NTX treatment in patients with alcohol dependence are still needed. Some issues should be concerned in further studies. Firstly, further trials should be conducted in larger sample sizes and over longer periods of time. Secondly, other than the outcomes relevant to alcohol use, some important outcomes should also be measured, e.g., functioning, health-related quality of life, economic cost. Thirdly, the comparisons between NTX and other treatments for alcohol dependence, both biological and psychosocial, should be investigated. Fourthly, combined treatments of NTX and other biological treatments for alcohol dependence may be in issue of interest. Lastly, high discontinuation rate in both treatment and control groups should be concerned.

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