Medical treatment of alcohol dependence: a systematic review

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CRD summary
The authors concluded that although the impacts of pharmacological interventions for alcohol dependence were often modest, they can have a positive impact. A lack of clarity on inclusion criteria and a lack of detail provided on outcome data suggest that the authors’ conclusions may not be reliable.

Authors' objectives
To examine the efficacy of pharmacological interventions alone or in combination with brief psychosocial interventions for the treatment of alcohol dependence in primary care and specialist medical settings.

Searching
MEDLINE, EMBASE, SCOPUS, CINAHL and PsycINFO were searched to August 2010 for published studies in English; search terms were reported. Checking references in reviews, internet searches and contacting experts in the field were used to supplement the electronic search.

Study selection
Eligible studies had to be randomised controlled trials (RCTs) of adults (at least 18 years) with alcohol dependence using standard diagnostic criteria. Pharmacological interventions alone or in combination with brief psychosocial interventions were eligible for inclusion. Brief adjunctive interventions had to be less than 30 minutes and applicable to general or specialist settings. Trials that examined only one medication had to include a placebo control. Alcohol consumption was the primary outcome. Studies were excluded if there was only one eligible study on the drug and where there were fewer than 30 participants per study group measuring a continuous outcome.

Very few participant characteristics were provided for individual studies. Most studies considered pharmacological interventions with only brief support. Around one fifth of studies included a pharmacological intervention (usually naltrexone) in combination with a formal psychosocial intervention. Most studies included a placebo control an around one fifth of studies included an active pharmacological intervention as comparator.

Two reviewers independently selected studies. Any disagreements were resolved through re-review and discussion with the primary author acting as final arbiter.

Assessment of study quality
Study quality was assessed using the five-point Jadad scale of randomisation, blinding and withdrawals. Scores of 4 or 5 were considered to have lower risk of bias. Scores below 4 were at higher risk of bias.

Two reviewers assessed quality. Any disagreements were resolved through re-review and discussion with the primary author acting as final arbiter.

Data extraction
Two reviewers independently extracted data on alcohol consumption. Any disagreements were resolved through re-review and discussion with the primary author acting as final arbiter.

Methods of synthesis
A narrative synthesis was used to summarise results of the included studies. The methods used to conduct the synthesis were not reported.

Results of the review
Eighty-five RCTs (18,937 participants) were included in the review. Follow-up ranged from 12 weeks to 15 months.

Disulfiram (11 RCTs): Nine trials were used to draw conclusions as two used a method of administration without proven efficacy. One of the nine trials had lower potential for bias.
It was unclear whether disulfiram was an effective intervention. There were mixed findings for all comparisons with placebo and active interventions. Some outcome measures showed a statistically significant benefit and others did not.

**Topiramate (four RCTs):** Three RCTs were judged to have a lower potential for bias.

There was a statistically significant reduction in alcohol consumption for topiramate compared with placebo (three trials; lower potential for bias). There did not appear to be a difference with naltrexone on most outcomes (two trials) but one trial found differences on some outcomes.

**Naltrexone (31 RCTs):** Seventeen trials were judged to have a lower potential for bias.

Naltrexone was superior to placebo in most trials (25 trials), but no difference or mixed findings were found in some (five trials). Naltrexone combined with sertraline (an antidepressant) was effective in one trial that included participants with alcohol dependence and depression but not in another trial where the participants were not depressed.

The two trials included depot injections and both found statistically significant benefit compared to placebo injections.

**Antidepressants (10 RCTs):** Seven trials examined the use of selective serotonin reuptake inhibitors (SSRI) and all were judged to have low potential for bias.

Four trials compared sertraline (an SSRI) with placebo in people with depression or PTSD. There was no difference with sertraline in three trials and mixed findings in another.

Sertraline combined with naltrexone was not associated with benefit in one trial but there was a statistically significant benefit in another trial that included people with comorbid depression.

For desipramine (a tricyclic antidepressant) there was some evidence of benefit compared with placebo (one trial). Quetiapine (an antipsychotic) was not associated with benefit when used in combination with lithium and divalproex.

**Acamprosate (24 RCTs):** Fifteen trials were rated as having a low potential for bias.

There were mixed findings in 11 trials that compared acamprosate with placebo. Six of these trials found some benefits for acamprosate and five trials found either no significant differences or mixed findings.

There were mixed findings for the combination of acamprosate and naltrexone (two trials). One trial found no difference with naltrexone compared with other medications. The other trials found acamprosate to be less effective than naltrexone (one trial) and disulfiram (two trials).

**Adjunctive psychosocial interventions (11 RCTs):** Most studies of pharmacological interventions summarised above included adjunctive psychosocial interventions. Eleven trials examined this separately and seven were judged to be of low risk of bias. There were mixed findings concerning the benefits of adjunctive psychosocial treatment.

**Authors’ conclusions**

Although effects are modest, pharmacological treatment for alcohol dependence with brief support or more intensive psychosocial interventions can be effective in primary care and specialist settings.

**CRD commentary**

The review question was clear. Inclusion criteria were less clear. For example, although the authors stated that only brief psychosocial interventions would be included it seemed that more intensive psychosocial interventions were used in some studies. The search provided good coverage of electronic databases and this was supplemented by other methods such as contacting experts. Only published studies in English were included so relevant studies may have been missed. Appropriate methods were used to minimise error and bias in the review processes.

Very limited outcome data was provided on the effectiveness of interventions (mostly whether the outcome was statistically significant) so it was not possible to evaluate the size and precision of these reported effects. The number of included trials was unclear for some comparisons (for example, topiramate) as there were discrepancies between the
The lack of clarity for the inclusion criteria and the lack of detail provided for outcome data mean that the authors' conclusions may not be reliable.

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

**Practice:** The authors stated that pharmacological interventions appeared feasible and had potential to improve patient outcomes.

**Research:** The authors stated that further research was needed to identify: patients who were more likely to respond to particular medications; whether medication alone (without brief interventions) was effective; and how to improve problems with compliance and implementation of these interventions in clinical practice.

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