Review: naltrexone reduces alcohol consumption (in the short-term) in patients with alcohol dependence

Srisurapanont M, Jarusuraisin N. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev* 2005;(1):CD001867.

Clinical impact ratings GP/GP/Primary care ★★★★★★☆ Mental health ★★★★★★☆

Q In patients with alcohol dependence, are opioid antagonists effective for attenuating or preventing the recommencement of alcohol consumption?

METHODS

Data sources: Medline (1966 to October 2001), EMBASE/Excerpta Medica (1980 to December 2001), CINAHL (1982 to December 2001), Cochrane Controlled Trials Register (*Cochrane Library* 2001, issue 4), Du Pont Pharmaceutical (Letchworth, UK), Ivax Corporation (Miami, FL, USA), and bibliographies of relevant articles.

Study selection and assessment: randomised controlled trials (RCTs) (published in any language) that evaluated opioid antagonists (mainly naltrexone [NTX] and nalmefene [NMF]) with or without other biological or psychosocial treatments (PST) in people with alcohol dependence and measured relevant outcomes. Study quality was assessed using criteria in the Cochrane Collaboration Handbook of Systematic Reviews.

Outcomes: alcohol dependence relapse (including a return to heavy drinking), a return to drinking (including any drinking at all), and discontinuation of medication. Outcomes were reported for the short term (⩽3 mo), medium term (>3 mo but ⩽12 mo), and long term (>1 y).

MAIN RESULTS

27 RCTs (n = 3048) of NTX and 2 RCTs (n = 126) of NMF met the selection criteria. Meta-analyses were done using a random effects model. *(1) NTX v placebo (short-term outcomes, 18 RCTs)*. Rates of relapse, return to drinking, and withdrawal were lower in the NTX group than in the placebo group (table). *(2) NTX v placebo (medium term outcomes with short term treatment only, 3 RCTs)*. The NTX group were less likely to relapse than the placebo group (relative risk reduction [RRR] 25%, 95% CI 5 to 41), but the groups did not differ for rate of return to drinking (p>0.05). *(3) NTX v placebo (medium term outcomes with both short and medium term treatment, 4 RCTs)*. The groups did not differ for rate of relapse (p>0.05). *(4) NTX v acomprosate (medium term outcomes, 1 RCT)*. Rates of relapse (RRR 29%, CI 12 to 43) and withdrawal (RRR 54%, CI 0 to 79) were lower in the NTX group than in the acomprosate group. *(5) NTX plus an intensive PST v an intensive PST alone (medium and long term outcomes, 1 RCT)*. Rates of relapse (RRR 40%, CI 9 to 60) and return to drinking (RRR 40%, CI 9 to 60) were lower in the combination group than in the PST alone group in the long term, and this was also true for return to drinking (RRR 67%, CI 20 to 86) but not relapses (p>0.05) in the medium term. *(6) NMF v placebo (short term outcomes, 2 RCTs)*. Rate of relapse was lower in the NMF group than in the placebo group (RRR 38%, CI 7 to 59).

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Source of funding: World Health Organization.

CONCLUSIONS

In patients with alcohol dependence, treatment with naltrexone is effective for preventing the recommencement of alcohol consumption and may reduce the risk of treatment withdrawal in the short-term. In conjunction with intensive psychosocial treatment, naltrexone may be beneficial in the medium and long term.

Commentary

The review by Srisurapanont and Jarusuraisin provides convincing evidence that NTX is effective for treating alcoholism, when used in conjunction with psychosocial treatments. This fact, established in 1992,[12] won US Food and Drug Administration approval for NTX in 1994 for alcoholism treatment.

The 3 primary outcomes reported all support the routine use of naltrexone. Significant improvements are expected when treating even a small number of patients: preventing relapse, number needed to treat (NNT) = 7; preventing any drinking, NNT = 10; and avoiding treatment withdrawal, NNT = 13. These treatment effects are compelling. Notable limitations of the published trials include lack of data on optimal lengths of treatment, cost-benefit analysis, and changes in quality of life measures.

Actualising NTX treatment in routine patient care presents problems inherent with innovations. Firstly, prescribing physicians need to accept that these results are significant and decide that they will make changes in their practice routines. Secondly, physicians must overcome the reluctance of their therapist counsellor colleagues that NTX represents a significant enhancement to their current psychosocial treatments. Thirdly, all providers collectively need to develop plans for implementing NTX use and for monitoring adherence to those plans. A case registry and case manager may improve adherence to the plans, as with diabetes and asthma. Fourthly, and most importantly, patients need to believe that NTX will help them achieve their treatment goals in an affordable fashion.

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1 Volpicelli JR, Alterman AI, Hayashida M, *et al*. Naltrexone in the treatment of alcohol dependence. *Arch Gen Psychiatry* 1992;**49**:876–80.
2 O'Malley SS, Jaffe AJ, Chang G, *et al*. Naltrexone and coping skills therapy for alcohol dependence. A controlled study. *Arch Gen Psychiatry* 1992;**49**:881–7.

Naltrexone *v* placebo in alcohol dependence at ⩽3 months*

		Weighted event rates			
Outcomes at ⩽3 months	Number of trials (n)	Naltrexone	Control	RRR (95% CI)	NNT (CI)
Had a relapse or returned to heavy drinking	7 (822)	28%	43%	36% (18 to 49)	7 (5 to 13)
Returned to drinking	10 (1014)	55%	65%	13% (0 to 24)	10 (6 to 100)
Discontinued the medication	18 (1776)	35%	43%	18% (3 to 30)	13 (7 to 100)

*Abbreviations defined in glossary; weighted event rates, RRR, and CI calculated from data in article using a random effects model.