TITLE: Naltrexone for Opioid Dependence: Clinical Effectiveness

DATE: 13 October 2009

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of naltrexone, alone or in combination with other therapies, for treatment of opioid dependence?

2. What is the evidence for how long to treat with naltrexone for opioid dependence?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including OVID Medline, the Cochrane Library (Issue 3, 2009), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between 2004 and September 2009. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, and randomized controlled trials. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

RESULTS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials.

One health technology assessment, six systematic reviews and meta-analyses, and six randomized controlled trials were identified regarding the clinical effectiveness of naltrexone.
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alone or in combination with other therapies, for treatment of opioid dependence. An additional article that may be of interest can be found in the appendix.

OVERALL SUMMARY OF FINDINGS:

One systematic review⁴ and one RCT⁹ assessed the ability of NTX to induce opioid withdrawal. The systematic review was undertaken to assess the effectiveness of opioid antagonists along with minimal sedation to induce opioid withdrawal.⁴ The authors reported that patients may experience delirium after the first dose of an opioid antagonist, especially with higher doses (eg. >25 mg of NTX).⁴ The authors stated that it was not clear if the combination of NTX and sedation reduces the length of withdrawal or makes the transition to NTX maintenance treatment easier for the patient.⁴ A double-blind RCT evaluated the safety and effectiveness of very low dose naltrexone (VLNTX) combined with methadone treatment, to reduce withdrawal systems during opioid detoxification.⁹ Patients received tapering doses of methadone and were randomized to receive 0.125 mg NTX, 0.250 mg NTX, or placebo for six days.⁹ Patients treated with VLNTX in addition to methadone reported weakened withdrawal symptoms and reduced craving.⁹ The authors concluded more study is needed before a definitive conclusion about this treatment can be made.⁹

Seven reports¹,³,⁵-⁷,¹¹,¹² were identified regarding the effectiveness of NTX, with or without other therapies, for opioid relapse prevention.

One HTA examined the effectiveness of NTX treatment for relapse prevention compared to interventions without naltrexone.¹ Though not statistically significant, the results of the included studies suggested NTX is more effective than placebo for treatment retention. The risk of drug abuse and the relapse-free rates were statistically significantly improved with NTX treatment compared to placebo, Although the evidence is poor, the authors concluded NTX may provide some benefit to maintaining abstinence for opioid-dependent individuals.¹ A meta-analysis looked at studies examining NTX versus control and psychopharmaceuticals with or without psychosocial interventions.⁵ NTX was significantly better than control for reducing observed opioid-positive urine tests.⁵ A systematic review examined effectiveness of NTX combined with psychosocial therapy for maintenance treatment of opioid and alcohol dependence.⁷ While cognitive behavioral therapy in combination with NTX therapy appeared to be effective for alcohol dependence, there was not enough evidence to support this treatment for opioid dependence.⁷ Another systematic review examined treatment with NTX versus placebo or other treatments after opioid detoxification for relapse prevention and maintenance.⁶ The results showed NTX therapy alone, or in combination with psychosocial therapy, was more effective than treatment with placebo alone.⁶ However, the authors concluded that the evidence available could not provide an objective evaluation.⁶

Two Russian RCTs examined the effectiveness of NTX in preventing opioid relapse.¹¹,¹² In the first study,¹² 52 patients were randomized to receive biweekly counseling and NTX or counseling alone for six months. At the end of the study, there were significantly more patients remaining in treatment without relapse in the NTX and counseling group (44%) compared with the control group (16%).¹² In the second study,¹¹ the effectiveness of oral NTX, with or without fluoxetine, was studied. Patients recovering from heroin dependence were randomized to receive NTX or placebo, with and without fluoxetine.¹¹ After six months, two to three times more patients
receiving NTX remained in treatment without relapse than patients receiving placebo. The addition of fluoxetine appeared to have no impact on patient outcomes.

One systematic review was included in this report regarding relapse prevention in people with opioid dependence. Information about the safety and effectiveness of NTX was included in the systematic review, but no results or conclusions were presented in the abstract.

Four studies investigated the effectiveness of different doses of NTX for relapse prevention and maintenance. A double-blind RCT was conducted to evaluate the effectiveness of low dose NTX for relapse prevention. After one week of detoxification treatment, patients were randomized to receive NTX doses of 50 mg/day, 0.5 mg/day, or 0.05 mg/day and were also offered counseling. After six months, the mean days in treatment were 58.9, 46.6, and 47.8 days, respectively. There were no significant differences in retention between groups. The authors observed no relation between ability to maintain heroin abstinence and NTX dose. They concluded there was no obvious advantage to low dose NTX and participants preferred a dose of 50 mg/d.

One systematic review and one RCT compared depot injection NTX to placebo. Patients were assigned to receive 192 mg or 384 mg depot NTX, or placebo. The systematic review showed patients receiving the higher dose NTX showed a significant increase in treatment days when compared to the placebo group, and when compared to the lower dose NTX group. The RCT results showed patient retention in treatment 39% for placebo, 60% for 194 mg NTX, and 68% for 384 NTX at the end of two months. The systematic review authors stated that there was not enough evidence to draw a conclusion about the effectiveness of depot NTX.

Patients were randomized in an open-label design to receive a sustained release NTX implant or usual care after completing initial inpatient treatment for opioid dependence. Patients who received the implant showed a significant reduction of 45 days less heroin use and 60 days less opioid use than those in the control group. The study determined the NTX implant to be save and effective in a motivated patient population.

Many studies were unable to provide a definite conclusion regarding the clinical effectiveness of NTX, alone or in combination with other therapies, for treatment of opioid dependence. High dose injection therapy and NTX implant may provide benefit to some patients. Low dose therapy appears to have no benefit or increased patient satisfaction when compared to standard dosages. Psychosocial therapy may be a valuable addition to NTX treatment. No evidence about how long to treat with NTX for opioid dependence was identified. Overall, the available evidence may not be sufficient for a definite conclusion regarding the clinical effectiveness of NTX, alone or in combination with other therapies, for treatment of opioid dependence.
REFERENCES SUMMARIZED:

Health technology assessments


Systematic reviews and meta-analyses


Randomized controlled trials


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APPENDIX – FURTHER INFORMATION:

Randomized controlled trials