Extended Release Naltrexone
XR-NTX

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Learning Objectives

• Describe the research evidence behind medication-assisted treatments used for opioid use disorders.

• Discuss the practical approach to the initiation of and maintenance on medication-assisted treatments in opioid use disorders.

• Evaluate common challenges related to medication-assisted treatments for opioid use disorders.
Oral Naltrexone

- Naltrexone blocks the opiate receptor
- Oral Naltrexone produces a reduction in days of heavy drinking
- Helps severe alcoholics to reduce their drinking
- Oral Naltrexone is easy to simply stop taking
- May be only marginally more effective than placebo for opiate use disorder (because it is so easy to stop)
Oral Naltrexone reduces drinking through extinction.

http://cthreeeurope.com/2014/10/16/how-opioid-antagonists-reduce-the-craving-for-alcohol-part-one/

How Opioid Antagonists Reduce The Craving for Alcohol – Part One (of two)

by Dr David J Sinclair with Dr Roy Eskapa and Michael Sinclair

October 2014
Naltrexone is an opiate receptor blocker

• Opiate receptors are up-regulated and double in number with Naltrexone
• The opiate receptors decrease to normal after about a week without Naltrexone

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How Opioid Antagonists Reduce The Craving for Alcohol – Part One (of two)

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October 2014
Oral Naltrexone

• The findings of this review suggest that oral naltrexone did not perform better than treatment with placebo or no pharmacological agent


Oral naltrexone maintenance treatment for opioid dependence.

Minozzi S¹, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A.
Extended Release Naltrexone
XR-NTX

1. How well does it work?
2. Who does it work for?
3. Pragmatic aspects of use
1. How Well does it work?

- More XR-NTX patients achieved 90% abstinence
- XR-NTX 51% abstinence versus placebo 31%


Treating Opioid Dependence With Injectable Extended-Release Naltrexone (XR-NTX): Who Will Respond?
Nunes EV¹, Krupitsky E, Ling W, Zummo J, Memisoglu A, Silverman BL, Gastfriend DR.
2. How Well does it work?

• XR-NTX averaged 90 weeks of confirmed abstinence
• Placebo averaged only 30 weeks of confirmed abstinence
• Median retention was over 168 days in the XR-NTX group compared with 96 days in the placebo group
• Naloxone challenge confirmed relapse in 17 patients in the placebo group compared with one in the XR-NTX group


Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial.

*Krupitsky E*, *Nunes EV*, *Ling W*, *Illeperuma A*, *Gastfriend DR*, *Silverman BL*. 
3. How well Does it work?

- Treatment with XR-NTX resulted in abstinence lasting twice as long as participants not given naltrexone.
- Treatment with XR-NTX were 1/3 less likely to relapse with 74% of urine samples being negative for opiates.


**Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders.**


1. Who does it work for?

- no patient-treatment matching variables could be identified. This suggests that XR-NTX was effective in promoting abstinence from opioids across a range of demographic and severity characteristics.
- It works for patients that want to try it
- It works for patients that keep using it


**Treating Opioid Dependence With Injectable Extended-Release Naltrexone (XR-NTX): Who Will Respond?**

*Nunes EV*, *Krupitsky E*, *Ling W*, *Zummo J*, *Memisoglu A*, *Silverman BL*, *Gastfriend DR*. 
2. Who does it work for?

- It is as effective in lower and higher addiction severity
- Placebo is less effective with higher addiction severity


Treating Opioid Dependence With Injectable Extended-Release Naltrexone (XR-NTX): Who Will Respond?

Nunes EV¹, Krupitsky E, Ling W, Zimmio J, Memisoglu A, Silverman BL, Gastfriend DR.
1. Pragmatic aspects of XR-NTX use

Opiates leave the body slowly over several days (weeks with methadone and buprenorphine)
XR-NTX blocks the opiate receptor
This can push the opiate off the receptor and speed up the onset of withdrawal.
A precipitated withdrawal can be more severe due to there being less time to adapt to the absence of opiates
Precipitated withdrawal can be highly aversive and increases the chances a patient will drop out of treatment
2. Pragmatic aspects of XR-NTX use

• Results are best after the patient’s acute withdrawal is subsiding
• Results are even better when the worst of the post acute withdrawal is over (after about 4 weeks of abstinence)
• A patient’s quality of life usually continues to improve 90 to 120 days after the last use of the opiate as the post-acute withdrawal fades away
• Discomfort after injection decreases with subsequent injections
• The end of dose failure decreases with subsequent injections
XR-NTX How long to wait after the last opiate use

• Patients should be opioid-free (including tramadol) for a minimum of 7-10 days

• Patients transitioning from buprenorphine or methadone may be vulnerable to precipitation of withdrawal symptoms for as long as 2 weeks.

• Use of naltrexone does not eliminate or diminish withdrawal symptoms.
• **Contraindications**
  • Hypersensitivity to naltrexone or any component of the formulation; opioid dependence or current use of opioid analgesics (including partial opioid agonists); acute opioid withdrawal; failure to pass naloxone challenge or positive urine screen for opioids

• **Warnings/Precautions**
  • Emergency pain management: In naltrexone-treated patients requiring emergency pain management, consider alternatives to opioid therapy (eg, regional analgesia, nonopioid analgesics, general anesthesia). If opioid therapy is required for pain therapy, patients should be under the direct care of a trained anesthesia provider.
  • Surgery: In patients treated with naltrexone for opioid addiction who requiring surgery, discontinue oral naltrexone at least 72 hours before scheduled elective surgery if opioid use is anticipated; extended-release IM naltrexone should be discontinued at least 30 days prior to scheduled surgery (oral naltrexone may be used temporarily) (Kampman [ASAM 2015]).

• Monitoring Parameters
  • Liver function tests (baseline and periodic); monitor for opioid withdrawal, injection site reactions with IM administration, and depression and/or suicidal thinking
Pregnancy

• Pregnancy Risk Factor C

• Adverse events were observed in animal reproduction studies. Information related to the use of naltrexone during pregnancy is limited (Farid 2008). Clinical practice guidelines recommend that if a woman being treated with naltrexone for the treatment of opioid use disorder becomes pregnant, naltrexone should be discontinued if the patient and physician agree that the risk of relapse is low. If patient is concerned about relapse and wishes to continue naltrexone, the patient should be informed of the potential risks of continuing treatment and consent for ongoing treatment should be obtained. If naltrexone is discontinued and the patient subsequently relapses, consideration should be given for treatment with methadone or buprenorphine (Kampman [ASAM 2015]).

• Breast-Feeding Considerations

• Naltrexone is excreted into breast milk. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer recommends a decision be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of treatment to the mother.
Overdose after treatment

• Patients dropping out of treatment face increased risk of overdose death.
• Studies about treatment failures come from various countries and are conducted using different methods and the following must be considered a rough approximation.
  • Methadone 9 times baseline
  • Buprenorphine 15.5 times baseline
  • Naltrexone 22 times baseline
  • Simple abstinence following rehab or incarceration 75-144 times baseline
  • XR-Naltrexone is 3-5 times safer than simple abstinence
XR-NTX Conclusions

• XR-NTX is 2-3 times more effective than placebo
• XR-NTX reduces opiate use; behavioral extinction
• XR-NTX is 3-5 times safer than simple abstinence

• Outpatient treatment dropout with placebo are twice that of XR-NTX
• Residential treatment dropout rates are 6 times higher without XR-NTX
• Works 4 times better than placebo in severe cases