

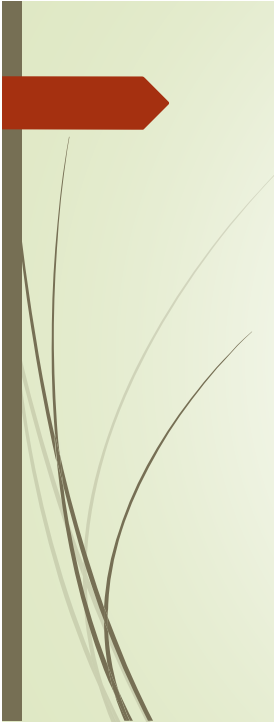
Sustained-release preparations of naltrexone for the treatment of alcohol and opioid dependence: current status

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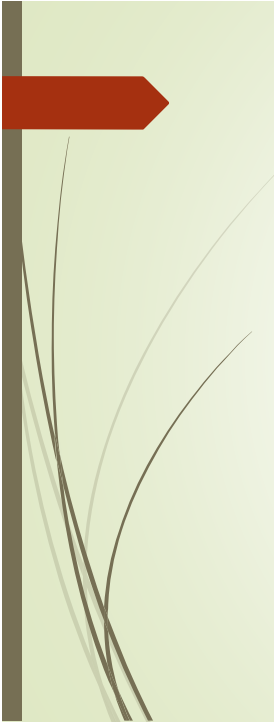
About this presentation

- Overview of current status of sustained-release naltrexone preparations
- Current evidence on commencement in people who are opioid dependent
 - Focus on transition to sustained-release naltrexone
 - Evidence on effectiveness of naltrexone in treatment of opioid dependence is not considered in detail



Rationale for sustained-release preparations

- Effectiveness of oral naltrexone in the treatment of alcohol or opioid dependence has been limited by low rates of adherence to treatment
- Sustained-release preparations overcome need to take medication daily and hence may increase adherence
- Two main types:
 - Depot preparations administered by injection, active for about 1 month, less invasive, unable to be removed
 - Surgical implants, active for at least 2 months depending on amount of naltrexone implanted, inserted through abdominal incision, can be removed



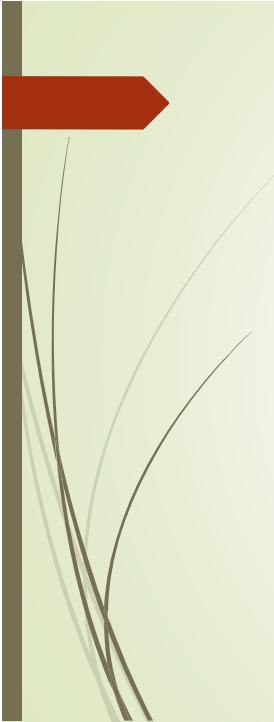
Current status

- Depot formulations
 - Vivitrol, injected im, approved in USA
 - Depotrex, injected sc, development stopped when Vivitrol approved, no longer available
 - Chinese product, injected im
- Implant preparations
 - Prodetoxon has regulatory approval in Russia
 - Go-Medical, manufactured in Western Australia, does not have regulatory approval



Use in treatment of alcohol dependence

- Strong evidence that oral naltrexone is moderately effective in the treatment of alcohol dependence
 - Rosner et al, Cochrane Review, 2010
- Rosner et al found treatment effects of sustained-release preparations comparable to oral naltrexone, from small number of trials
- Commencement relatively easy with alcohol dependence
 - Some side effects, but no induced withdrawal



Naltrexone in treatment of opioid dependence

- Oral naltrexone no more effective than placebo, but evidence poor quality and limited by low adherence to treatment
 - Minozzi et al, 2011 (Cochrane review)
- Depot and implant preparations more effective than placebo (or no medication) in preventing relapse
 - Based on 4 studies of implant, 3 studies of depot (Larney et al, 2014, Drug Alc Rev 33(2), 115-128)
- No direct comparisons with oral naltrexone, limited comparisons with opioid substitution treatment
- Target groups include those committed to abstinence, with appropriate support mechanisms, also prisoners (pre-release)

Commencing naltrexone treatment for opioid dependence

- Induced withdrawal remains a barrier to commencement
 - Example: Hamilton et al 2002, Acad Emerg Med 9(1):63-8
- Several recent studies involved prisoners with history of opioid dependence
 - Transition straightforward when not actively using opioids
- Commencement of naltrexone maintenance treatment was rationale for so-called rapid detoxification techniques that were promoted more than 10 years ago
 - Effectiveness not demonstrated, poor acceptability to clients
- Use of buprenorphine to manage transition appears to be most promising approach for transition from active opioid use but evidence remains sparse

Buprenorphine transition

- Buprenorphine 4mg, commenced on emergence of withdrawal symptoms, tapered over 3 days
- 1 day washout
- Oral naltrexone commenced at low dose and dose increased over 3-4 days
- Sustained-release preparation administered when maintenance dose of oral naltrexone (50mg) is tolerated
- Based on:
 - Mogali et al 2015, Am J Addict 24(3): 258-64
 - Dakwar & Kleber 2015, J Subst Abuse Treat 53: 60-3
- No current evidence on transition from buprenorphine maintenance to sustained-release naltrexone



Disclaimer

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