The Use of Antagonists to the Opioid and $GABA_A$ Receptors in the Management of Alcohol and Poly Drug Use

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Fresh Start Recovery Programme 2013-2014 Alcohol Assessment

- Naltrexone is an opioid receptor antagonist that blocks the reinforcing effects of opioids and reduces alcohol consumption and craving.
- In alcohol dependence, two large multicenter trials reported alcohol and craving reductions for long acting naltrexone (Vivitrol) and placebo groups, indicating a significant but moderate effect.
- In the first study (Kranzler et al. 2004), the number of patients who achieved total abstinence was 18% compared to 10% in placebos.
- A second study (Garbutt et al. 2005) reported the number of patients who maintained complete abstinence during the trial as 7% compared to 5% in the placebo group.

References

- Garbutt, J.C. et al., 2005. Efficacy and Tolerability of Long-Acting Injectable Naltrexone for Alcohol Dependence. JAMA The Journal of the American Medical Association, 293(13), pp.1617–1625.
- Kranzler, H.R., Wesson, D.R. & Billot, L., 2004. Naltrexone depot for treatment of alcohol dependence: a multicenter, randomized, placebo-controlled clinical trial. Alcoholism, clinical and experimental research, 28(7), pp.1051–1059.

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Fresh Start Recovery Programme

- At the Fresh Start Recovery Programme (FSRP) in Perth, the use of naltrexone implants represents part of the overall treatment for patients with problematic alcohol use.
- At Fresh Start over 150 patients a year are treated with the use of naltrexone implants, with most patients receiving an implant prior to detox. For many patients this represents the main method of treatment.
- Other treatment that is offered includes Antabuse (Disulfiram), Acamprosate, rehabilitation facilities, counselling, GP and specialist support.

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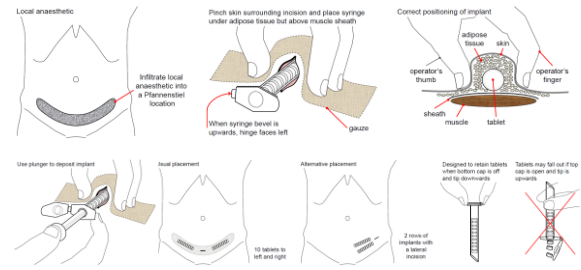
Insertion of Go Medical Implants



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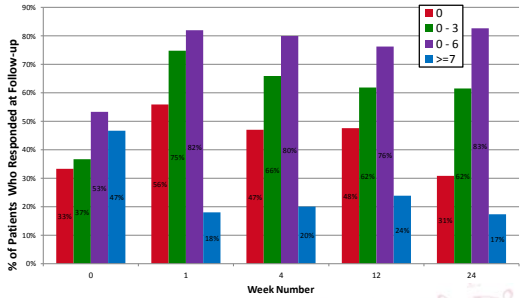
Average Number of Standard Drinks Consumed Per Day in the Last 4 Weeks



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Hospital Admission Costs Halved with the Fresh Start Alcohol Treatment Program

Results

- 94 patients were observed 6 months pre and post implant naltrexone treatment .

Hospital Costs

- In the 6 month prior to treatment 36 patients had 82 hospital admissions, costing $424,605. Following treatment 24 patients were admitted on 43 occasions, costing $203,426.

Emergency Department

- Prior to treatment, 43 patients attended ED costing $74 885. Following treatment, 35 patients attended ED costing $54,712.

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Hospital Admission Costs Halved with the Fresh Start Alcohol Treatment Program

Note: Costs associated with mental health out-patient attendances increased ($9,543 to $11,827).

Treatment Provided

- Patients were treated for problematic alcohol use with a Long Acting Naltrexone Implants at the Fresh Start Recovery Programme Clinic.
- Patients received overall care and follow up, which included counselling, housing support, Antabuse (disulfiram), rehabs, family support and legal support.

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Hospital Admission Costs Halved with the Fresh Start Alcohol Treatment Program

Overview

- Cost Savings averaged at $2,543 per patient, 6 months post treatment.

Method of Study

- Data was collected prospectively by the WA health department.
- Hospital admissions, emergency department attendances and out-patient mental health visits for 6 month pre and post the patient's first naltrexone implant treatment were collated and assigned an approximate cost.

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Hospital Admission Costs Halved with the Fresh Start Alcohol Treatment Program

Limitations of the study

- While the study found significant cost savings in the 6 months following treatment, the study did not examine long term cost savings to determine if the savings were maintained. Additionally the study failed to factor in the influence of multiple implants during the study period or how subsequent implants may affect long term health outcomes. Additionally the study was comprised of a relatively small number of subjects and no separate control or comparison group was utilised.

Conclusion

- The use of implant naltrexone was shown to be associated with a reduction in the utilisation of hospital and ED services and associate costs.

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Overview of Naltrexone Development Program

1964: Development of naltrexone
1974: Intense R&D program
1984: Oral naltrexone registration in UK & USA
2000: Start of Sustained delivery research
2000: Start of O'Neil implant clinical program
2006: Vivitrol FDA approval for alcohol,
2010: Vivitrol FDA approval for opiates
2015: GMP O'Neil implants used in alcohol, amphetamines and opiates

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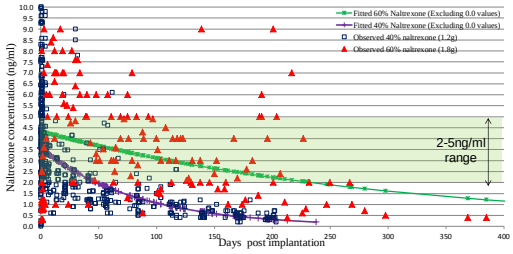
Pharmacokinetic Data On 2 Formulations Of OLANI Implants 2006-2011



Oral naltrexone provides naltrexone for 6 hours only
Implant naltrexone potentially provides naltrexone for 105-300 days

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Summary of reported use of flumazenil in the treatment of long term withdrawal symptoms and management of acute withdrawal

Author	Design	Treatment	Results
Lader & Morton 1992	Design Pilot study n = 11	1–2 mg bolus doses over 3 h	Results Flumazenil successful in alleviating long term symptoms of benzodiazepine withdrawal
Saxon et al 1997	Double-blind pilot n = 10	1.0 mg total in five doses over 1 h X 2	Flumazenil successful in alleviating long term symptoms of benzodiazepine withdrawal
Gerra et al 2002	RCT flumazenil vs. oxazepam taper n = 50	1mg $4h^{-1}$ infusion twice daily for 8 days with oxazepam taper	Flumazenil group had significantly reduced withdrawal symptoms, improved programme completion and reduced relapse rates
Hood et al. 2009	Case series/open trial n = 16	2mg $24h^{-1}$ continuous i.v. infusion with oxazepam. tapering for 4 days	Patients had reduced withdrawal symptoms; successfully completed withdrawal. i.v. infusion problematic
Quaglio et al 2012	Case series n = 29	1.35 mg day^{-1} continuous i.v. infusion with clonazepam for 7 days	All patients completed the withdrawal programme with 51% abstinent at 6 months
Hulse et al 2012	Case series n = 23	4mg $24h^{-1}$ continuous s.c. infusion with oxazepam taper for 4 days	Subjective withdrawal symptoms well managed. High patient acceptance. Improvement on measures of psychological distress over withdrawal period

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Subcutaneous Flumazenil

- At Fresh Start, the standard treatment is to deliver flumazenil subcutaneously at 16mg/30mls over 4 days with the use of a syringe pump (pictured).
- It has been found that the infusion rate that has been most effective for ceasing benzodiazepines is 4mg/24 hour period (±20%) of flumazenil.

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Hulse, G. et al., 2013. Withdrawal and psychological sequelae, and patient satisfaction associated with subcutaneous flumazenil infusion for the management of benzodiazepine withdrawal: a case series. Journal of psychopharmacology (Oxford, England), 27(2), pp.222–70

Flumazenil Implant

Current Practice

- Delivery of flumazenil via S.C. infusion for 1-4 weeks.
- Treatment with implant flumazenil in anxious patients with benzodiazepine, alcohol and amphetamine addiction, if continuing anxiety is troublesome.
- Research trials continuing

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