**The Use of Antagonists to the Opioid and GABA\textsubscript{A} Receptors in the Management of Alcohol and Poly Drug Use**

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**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 placebo.
  - 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**


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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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**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.
Patients were treated for problematic alcohol use with

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.

**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.

**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: Vivitol FDA approval for alcohol,
- 2010: Vivitol FDA approval for opiates
- 2015: GMP O’Neil implants used in alcohol, amphetamines and opiates

**Pharmacokinetic Data On 2 Formulations Of OLANI Implants 2006-2011**

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

<table>
<thead>
<tr>
<th>Author</th>
<th>Design</th>
<th>Treatment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lader &amp; Morton</td>
<td>Design Pilot Study n = 32</td>
<td>3.0 mg bolus doses every 6 h</td>
<td>Flumazenil successful in alleviating long term symptoms of benzodiazepine withdrawal</td>
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<tr>
<td>Basset et al.</td>
<td>Double-blind trial n = 20</td>
<td>4.0 mg/day for 8 days with taper</td>
<td>Flumazenil successful in alleviating long term symptoms of benzodiazepine withdrawal</td>
</tr>
<tr>
<td>Saxon et al.</td>
<td>Case series n = 10</td>
<td>Oxazepam infusion twice daily for 8 days with taper</td>
<td>Flumazenil group had significantly reduced withdrawal symptoms, especially among a comparison and induced absence rates</td>
</tr>
<tr>
<td>Hood et al.</td>
<td>Case series n = 10</td>
<td>Oxazepam continuous i.v. infusion over 1 h</td>
<td>Patients had reduced withdrawal symptoms, successfully tapered and withdrawn, less infusion problems</td>
</tr>
<tr>
<td>Doggett et al.</td>
<td>Case series n = 20</td>
<td>Oxazepam 1.25 mg/day for 7 days</td>
<td>All patients completed the withdrawal programme with 95% abstinence at 4 months</td>
</tr>
<tr>
<td>Hacker et al.</td>
<td>Case series n = 20</td>
<td>Oxazepam 1.25 mg/day for 7 days</td>
<td>Subjective withdrawal symptoms well managed. High patient acceptance. Improvement in measures of post-addiction adverse symptoms and QoL</td>
</tr>
</tbody>
</table>

**Hospital Admission Costs Halved with the Fresh Start Alcohol Treatment Program**

**Observation**
- 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.
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.


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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