

Pharmacotherapy Newsletter

Buprenorphine Diversion: an update

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The uptake of high-dose buprenorphine substitution treatment has been significant in Victoria since the drug was released in 2001, and it now accounts for about 40% of the clients in opioid substitution treatment in the state.

Diversion of the drug for injecting or selling has to some degree offset the therapeutic advantages of buprenorphine, which include its lower toxicity and dose flexibility.

While buprenorphine causes less respiratory depression than methadone, unsupervised availability, injection and concurrent use with other psychoactive drugs have been implicated in fatalities overseas.

In two surveys of pharmacists over 3 years in Victoria, the authors found that community pharmacists estimated 1 to 1.5% of doses were being diverted.

Given that:

- Pharmacists may not suspect all diversions (or necessarily even a majority), and
- Concurrent findings from the Illicit Drug Reporting Surveys have shown an increasing use of diverted and injected buprenorphine, diversion has become an issue of ongoing concern.

The time needed to administer supervised buprenorphine doses has also been highlighted as a potential disincentive to pharmacists providing the service. Indeed, a dozen of the almost 300 pharmacists surveyed had stated that they would no longer provide buprenorphine, or would not take new referrals for it.

Dissolution times for a 16mg dose in whole tablets of over 10 minutes make close supervision of doses difficult in a busy community pharmacy.

The Drugs and Poisons Regulation Group of the Department of Human Services in 2001-2 recommended that all doses of buprenorphine be substantially broken up or crushed by pharmacists prior to administration to reduce chance for diversion.

Crushing of buprenorphine doses, while aimed to reduce diversion, was also requested by clients during the buprenorphine trials due to a perceived benefit in reduced dissolution time.

Potential concerns with crushing have been:

- That crushing the tablets is an unlicensed use of the product.
- It may not reduce dissolution time or diversion
- It may change absorption or activity of the drug
- It may potentially increase risk by mouth contaminants if the drug is still diverted and injected.

Welcome to the June 2007 Pharmacotherapy Newsletter in which we are featuring "Buprenorphine Diversion".

Your feedback and contributions are always welcome, particularly any good news stories about clients and services.

We look forward to developing a forum for the exchange of opinions and information.

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Recently pharmacists at Turning Point Alcohol and Drug Centre conducted a study on the effect of crushing Suboxone® tablets on dissolution time. Preliminary analysis shows a substantial reduction in dissolution time with crushed tablets compared with whole tablets, and that there is a relationship between dose and dissolution time. Notable also is that previous analysis of the dose of buprenorphine required before and after a mandatory crushing policy began did not vary, suggesting that bioavailability of the crushed and uncrushed tablets may not differ significantly.

Research currently being undertaken in Finland on whether crushing buprenorphine has any effect on plasma levels is under way.

The combination buprenorphine-naloxone product (Suboxone®) was released last year. Possible benefits including more flexibility with buprenorphine take home doses, a lemon-lime flavour, and anecdotally quicker absorption have resulted in almost all Turning Point buprenorphine maintenance clients requesting the change voluntarily.

Turning Point pharmacists report a reduction in overtly suspicious behaviour reported compared with mono buprenorphine.

Instances of Suboxone® injection have nevertheless been reported in the community, with drug users being prepared to tolerate unpleasant short-term effects to inject the drug.

Largely, the level of misuse of Suboxone® will be related to the availability and cost of other more preferable drugs for injectors. There are some pharmacological studies suggesting that in buprenorphine-maintained individuals, some level of intravenous naloxone may be tolerated. This means that care still needs to be taken in:

- Assessing suitability for unsupervised Suboxone® doses and
- Monitoring diverting behaviour in the pharmacy setting.

The National Drug and Alcohol Research Centre (NDARC), in association with Turning Point, will be carrying out interviews in the near future with pharmacists and prescribers as part of post-marketing research for Suboxone®. Suspicious behaviour for buprenorphine clients includes:

- Handling the medication
- Rushing out quickly after dose
- Not able to talk clearly (devices in mouth)
- Arriving with a group of friends or having groups of people waiting for them outside the pharmacy

Pharmacy measures to reduce diversion of buprenorphine/buprenorphine / naloxone doses may include:

- Ensure clients understand before commencement that buprenorphine is a supervised treatment and that the pharmacist's responsibility is to do that.
- If possible, provide a comfortable space (ideally a seat visible to the pharmacist) where clients can stay until the pharmacist is satisfied that the dose is dissolved.
- Communicate with the prescriber where concerns exist about possible diversion.
- Don't turn a blind eye to infractions. Addressing suspected diverting behaviour might help identify and resolve treatment issues for the client.
- Crushing doses to granules (even in Suboxone®) speeds up the process significantly. Clients may appreciate that saving to their (and your) time.

Pharmacotherapy Policy for take away doses of methadone and Suboxone®

Who can have take away doses of methadone and buprenorphine: Suboxone®?

After two months in stable treatment, clients who satisfy the requirements specified for medium supervised dosing in the pro forma for assessing level of supervised dosing, Appendix 4, Victorian Policy for Maintenance Pharmacotherapy for Opioid Dependence (referred to as the policy) may have up to two take away doses of methadone or Suboxone® per week.

After six months in stable treatment, clients who satisfy the requirements specified for low supervised dosing in the policy may have up to five take away doses of methadone or Suboxone® per week. NOTE: a maximum of 3 consecutive days supply is allowed. Clients receiving five take-away doses should not receive all five at once. An example of an acceptable pattern would be a supervised dose on Monday, with three take-away doses for Tuesday, Wednesday and Thursday. A supervised dose on Friday, with two take-away doses for the weekend.

How do doctors assess suitability of clients for take away medication?

The policy includes a pro forma for doctors to use to assess stability of clients for supervised dosing. There are three levels of supervised dosing and doctors use the check list to ensure that their clients are suitable to have take away methadone or Suboxone®. NOTE: No take-away doses should be authorised for any client, or any changes made to existing take-away authorisations, unless the prescriber has consulted with the regular dosing point to determine regularity of dosing and incidence of presentation while intoxicated.

How should take away doses be prepared, labelled and packaged?

Take away doses of methadone and Suboxone® should be prepared as single daily doses and labelled as for all dispensed Schedule 8 poisons. In addition the following should be included:

- Contains a single daily dose of (methadone or buprenorphine/naloxone) to be taken on date dose to be taken by name of patient
- May cause death or injury if taken by another person

Methadone should be diluted to 200 millilitres and supplied in a container with a child resistant closure.

Buprenorphine is an unstable compound and should be supplied in the original blister where possible.

Take care when dispensing methadone

Clients who are taking methadone for opioid dependence may sometimes present to a pharmacy twice in one day because they have become confused about when they had their last dose. It is the pharmacist's role to ensure that these clients are protected by ensuring that a second dose is not administered. If a second dose is accidentally administered, it is important that the client is contacted and observed to prevent fatal overdose.

Advise clients and their families to never leave a client to sleep it off, particularly if they are snoring or unable to be aroused as this may be an indication of overdose.

New Pharmacies

Stratford Pharmacy. 48 Tyers St, Stratford.
Tel: 5145 7080

Prince's Pharmacy. 350 Bridge Rd,
Richmond. Tel: 9428 1953

Park Orchards Guardian. 614 Park Rd, Park
Orchards. Tel: 9876 2989

Hartwell Pharmacy. 1142 Toorak Rd,
Hartwell. Tel: 9889 3520

Airey's Inlet Pharmacy. 2/28-30 Great
Ocean Rd, Airey's Inlet. Tel 5289 7434

Priceline Pharmacy Leopold, Shop 1
Gateway Plaza, Bellarine Hwy, Leopold. Tel:
5250 3222

Terry Whites Chemists Town Centre,
Shop 121 Watergardens Shopping Centre,
Melton Hwy, Taylors Lake. Tel: 9449 2999

Sunshine Health Pharmacies, 25
Devonshire Rd, Sunshine. Tel: 9312 0066

Raiu's Pharmacy, Shop 11-13 Gisborne
Village Shopping Centre, Gisborne.
Tel: 5428 2107

Your Pharmacy-Mentone Shop 32/33
Thrift Park Centre, Mentone.
Tel: 9583 6636

Pharmacotherapy prescriber training online

A new website has been launched on the RACGP site introducing doctors to training to prescribe pharmacotherapies for opioid dependence. The site includes the first seven modules of the training manual and allows the doctor to work at his own pace to complete the exercises prior to attending a one day workshop to become authorised to prescribe.

The website is at: www.gplearning.com.au

GP Training Workshop dates for 2007

Saturday 9 June 2007

Saturday 21 July 2007

Saturday 1 September 2007

Saturday 10 November 2007

Contact Mal Doreian at Turning Point
Alcohol and Drug Inc on (03) 8413 8413

Prescribing for clients on opioid substitution pharmacotherapy

Benzodiazepines and pharmacotherapy.

Methadone is seldom the only drug detected in drug toxicity deaths: methadone-related deaths are usually caused by combined drug toxicity involving other CNS depressant drugs.

The most common other drugs involved in these deaths are benzodiazepines, mostly diazepam.

Benzodiazepines contribute to drug toxicity deaths involving both pharmacotherapies - methadone or buprenorphine.

Prevalence of benzodiazepine use and injection by IDU.

Illicit use and injection of benzodiazepines is common¹. In the 2006 IDRS survey of 1914 Australian injecting drug users (IDU), about two thirds (67%) had recently used benzodiazepines and 1 in 8 (12%) had recently injected benzodiazepines. The prevalence of recent benzodiazepine injection in Victoria has decreased from 40% in 2001 to 9% in 2006, after temazepam capsules were removed from the market.

Between one-third and one-half of Australian IDUs reported that the benzodiazepines they used were illicitly obtained, that is prescribed for someone else, suggesting that sharing or trafficking of these pharmaceutical drugs is common.

Diazepam was reported by 38% of IDU as the main benzodiazepine used by them, followed by alprazolam (6%) and oxazepam (6%).

Reason for concern: tissue and vascular injury

Injection of benzodiazepines formulated as tablets is associated with a high risk of injection-related harm to tissue and blood vessels.

Reason for concern: risk of coma and death

Benzodiazepines alone have a less marked effect on respiration than opioids, but significant respiratory depression can occur with high doses. These drugs exert their effects through GABA receptors in the brain stem, where the respiratory centres are located.

Mechanism

Benzodiazepines inhibit respiration by enhancing the effects of GABA, and together with opioids exerting a similar effect through the opioid receptors, act synergistically to depress respiration. Benzodiazepines also decrease the opioid concentration required for loss of consciousness. Combinations of benzodiazepines and opioids can also cause significant and occasionally profound decreases in blood pressure, heart rate and vascular resistance.

Methadone-related deaths

There is now substantial evidence that heroin-related and methadone-related drug deaths are usually due to combined drug toxicity, and the most common drugs other than these opioids are benzodiazepines, usually diazepam.

Buprenorphine-related deaths

A recent paper about deaths associated with buprenorphine reviewed 117 fatalities involving this drug, and found that the major risk factors were concomitant use of benzodiazepines or neuroleptic drugs, and injection of crushed tablets².

Recommendation.

To minimise the risk of drug toxicity death of pharmacotherapy patients:

- A single prescriber should supply CNS depressant drugs, particularly those subject to illicit use, and particularly if the patient is known to engage in illicit drug use. This prescriber should make a careful evaluation of the patient and their drug use, and tightly control supply.
- Use of benzodiazepines during induction into methadone treatment should also be carefully controlled because the first 10 days is the period of greatest risk of drug toxicity during methadone treatment.

1. Illicit Drug Reporting System (IDRS) 2006

2. Kintz P, Deaths involving buprenorphine: a compendium of French cases. *Forensic Sci Int* 2001;121:65-9.