

Case Study: The highest case of Nefopam overdose

Malgorzata Puchnarewicz BSc
(mpuchnar@sgul.ac.uk)

Presented by Jennifer Button BSc

IATDMCT Nice 2007

Case study

On 7th May 2005, a 33 year old man, a prison inmate, fell from his top bunk and landed on the floor following convulsions. Attempts to resuscitate him at the scene were unsuccessful.

The autopsy examination revealed swelling of the brain, bite marks on the tongue and bruising to the face. The pathologist concluded that these injuries did not contribute to his death.

Case study

The deceased was prescribed:

- Diclofenac, nefopam and co-codamol for back pain
- Venlafaxine for depression
- Cetirizine for hay fever

He held in-possession the nefopam and diclofenac

Immediately after the mans death, 65 tablets were found in the cell, the majority of which were Acupan, containing nefopam

Toxicological Findings

Femoral Blood:

Nefopam: 35.8mg/L (*Therap: 0.01-0.2mg/L, Tox: 4-12mg/L*)

Paracetamol: 64mg/L (*Therap: 10-20mg/L, Tox: >150mg/L*)

Codeine: 0.3mg/L (*Therap: 0.01-0.25mg/L, Tox 0.3-1.6mg/L*)

Morphine: 0.02mg/L (*Therap: 0.01-0.12mg/L, Tox: 0.15-0.5mg/L*)

Venlafaxine: 0.68mg/L (*Therap: 0.25-0.75mg/L, Tox: 1-6.6mg/L*)

Methodology

Internal standard, 1M sodium hydroxide (0.5mL) and MTBE (4mL) were added to the sample (0.1mL)

The nefopam was back extracted into of 0.1M phosphoric acid (0.25mL)

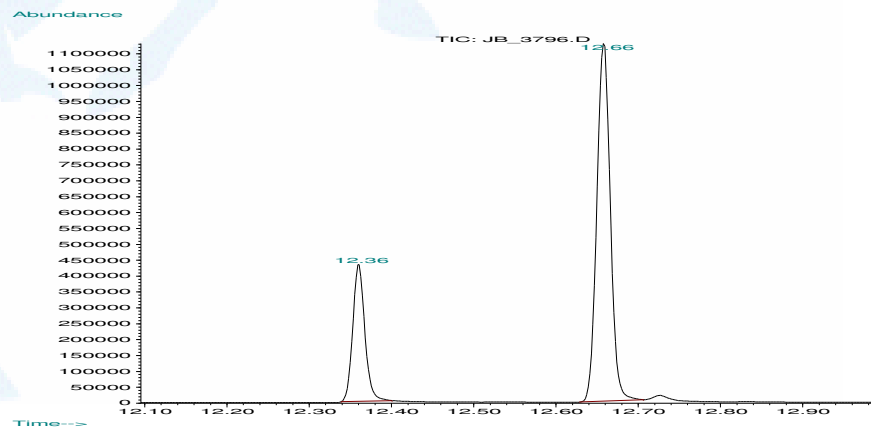
The samples were re-extracted into MTBE (0.2mL) after the addition of 1M sodium hydroxide (0.1mL)

Analysed using GC-MS

Analytical Details

GC-MS

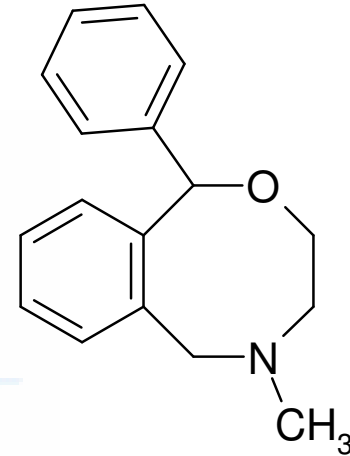
- System: HP 5890 GC interfaced to an HP 5973 MS
- Column: HP-5MS (30m x 0.25mm i.d 0.5 μ m film thickness)
- Ionisation: Electron impact ionisation
- Carrier gas: Helium
- Initial column temperature: 80°C for 4mins, ramped at 25°C/min to 280°C and held for 1min
- Total run time: 13mins
- SIM: 91 (IS) 179, 225 (nefopam)



1 in 5 dilution
(7.2mg/L)

Nefopam

- Trade names: Acupan and Ajan
- A centrally acting non-opioid analgesic
- 10 times more potent than aspirin
- 2 to 3 times less potent than morphine
- Typical dosage is 30-90mg (1-3 tablets) three times daily (p.o)
- It is structurally related to diphenhydramine and orphenadrine
- Low toxicity and potential for dependence
- Adverse reactions include: confusion, hallucinations, dizziness, convulsions, nausea, tachycardia and urinary retention.



Fatalities Involving Nefopam: A Review of the Literature

Year	Age; gender	Circumstance of death	Nefopam (mg/L)	Other drugs
1981	30; F	Suicidal ingestion; death 19 hours later	Post mortem serum 11.9 ⁶	None
1999	38; F	Suicidal ingestion; death 3 days later	Plasma 4.3 (admission) Plasma 0.6 (day one) ⁷	Dihydrocodeine (5.9mg/L)
2001	37; F	Voluntary i.v injection; found dead at home	Post mortem heart blood 4.38 ⁸	None
2005	33; M	Suicidal ingestion	Post mortem femoral blood 35.8	Co-codamol Venlafaxine

⁶ Piercy DM. et al. *Br. Med. J.* **283**:1508-1509 (1981)

⁷ Urwin SC & Smith HS. *Br. J. Anaesth.* **83**:501-502 (1999)

⁸ Tracqui A, et al. *J. of Anal Tox.* **26**:239-243 (2002)

Prisons and Probation Ombudsman's Investigation

Family's Concerns

- Staff should have been more aware of the fact that the deceased was suffering from depression
- Concerns as to how he had been able to hoard his medication

Health Care in Prisons

Generally, prisoners tend to have much poorer physical and mental health than the wider population

90% of prisoners have a diagnosable mental health problem and/or substance misuse problem requiring treatment¹

The prison service spends in the order of £7 million (€10 million) per annum on medicines²

In 2000 the average annual cost per prisoner was between £78 (€115) (male category C training prison) and £273 (€402) (male local prison)²

Medication In-Possession, National Prescribing Centre, August 2005¹

A Pharmacy Service for Prisoners, DOH, June 2003²

Medication In-Possession

Recommendation 5:

....Medicines in use, together with associated monitoring and administration devices, should normally, as a matter of principle, be held in the possession of prisoners. Each prison establishment should have a policy and risk assessment criteria...for determining on an individual basis when medicines and related devices may not be held in the possession of a prisoner.

A Pharmacy Service for Prisoners, DOH, June 2003

Self harm incidents in Her Majesty's Prison Service (HMPS)

2003

4.6% (n=746) of all reported self harm incidents were due to poisoning with own / others medication.

2004

2.1% (n=2) of reported self inflicted deaths were attributed to overdoses of prescribed medication.

Tunde Adeniji, Safer Custody Group, HM Prison Service

Medications NOT to be given 'in-possession'

- All controlled drugs
- All benzodiazepines
- All hypnotics
- All antipsychotics
- Some antidepressants (TCA)
- Opioid analgesics, i.e. tramadol
- All tablets containing codeine and dihydrocodeine
- All medicines containing paracetamol (some exceptions)

Assessment of Self Harm Risk

- On reception the man had denied any incidences or thoughts of self harm.
- He was treated for depression from Oct 2004 through to his death.
- The dosage of his anti-depressant medication was doubled in April.
- He began to see a counsellor at this time and discussions about suicide, including revelations about past attempts were made.
- It was the counsellors professional judgement that the man was not a suicide risk.
- The man's suitability for in possession medication was never formally assessed.

Local recommendation 2:

The Governor and Primary Care Trust should review the procedures in place to ensure that every decision about in possession medication to prisoners is properly risk assessed, authorised and fully documented.

Risk assessment should take into account the effect a large amount of a particular drug would have on a person's health if they were to take a large quantity of tablets together.

Local recommendation 3:

The Governor and Primary Care Trust should review procedures to ensure that the issuing of in possession medication is properly documented and then monitored to prevent the hoarding of prescribed drugs.

Report by the Prisons and Probation Ombudsman for England and Wales Jan 06

Coroner's Narrative Verdict

"At about 10.45 on May 7th 2005 in his cell at Wandsworth Prison, London, he had a fit, fell from his bunk onto the floor and in spite of resuscitation efforts, he died. The cause of death was an overdose of nefopam."

"The recommended prison procedures regarding "in-possession medication" were over elaborate, which might be a reason why they were not followed. However, in this instance it did not have a bearing upon the death."

HM Coroner, Dr Paul Knapman, Inner West London

Conclusions

- The blood concentration of nefopam in this case (35.8mg/L) exceeds the highest therapeutic range by more than 170 times.
- Post mortem redistribution may have been a contributing factor.
- This is only the fourth reported death due to a nefopam overdose and the concentration of the drug is the highest recorded so far.
- The adverse effects attributed to nefopam overdose, such as convulsions, are common to all published cases.



Questions?