

MONITORING BUPRENORPHINE WITHDRAWAL PROTOCOLS

S.A. George, C.F.E. George, M. Chauhan. Regional Laboratory for Toxicology, Birmingham, West Midlands, England

INTRODUCTION

Opiate addiction remains a national problem with a reported lifetime prevalence of opiate use among the 16-59 age range in England and Wales of around 1.1% overall. In addition, data suggests that around 1% of 15 year olds in England had tried opiates (1).

There are several drug therapies that can be used to treat opiate abuse. One such treatment is the combined agonist/antagonist drug buprenorphine.

As with all long-term treatments, there is a requirement for monitoring in individuals prescribed the drug to ensure compliance and to negate therapeutic failures.

This study was performed to determine the concentrations of buprenorphine and its metabolite in individuals undergoing rapid buprenorphine detoxification for opiate dependency.

METHOD

A total of 11 subjects were prescribed reducing buprenorphine doses starting at 10 mg/day and declining to 0.4 mg/day over a period of 4 weeks.

Buprenorphine together with its primary metabolite (norbuprenorphine) were quantified in urine specimens using a gas chromatography-mass spectrometry (GCMS) technique.

Following enzymatic hydrolysis and the addition of a deuterated internal standard, both drug and metabolite were extracted at alkaline pH into chloroform:isopropanol and subsequently analysed as TMS derivatives.

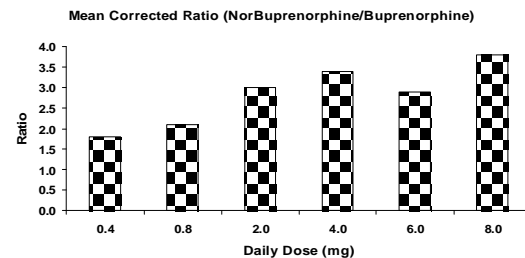
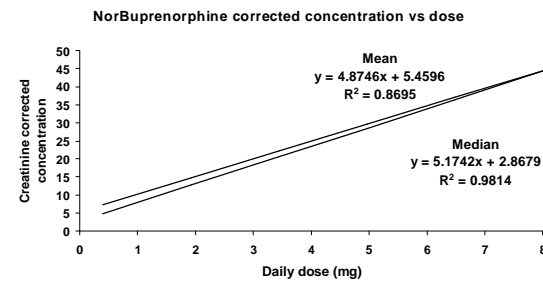
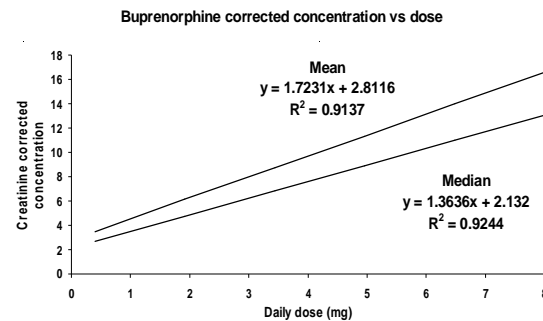
The assay was found to have a limit of detection of 1 ng/mL for buprenorphine and 4 ng/mL for norbuprenorphine.

The assay was linear up to 1,000 ng/mL, and the reproducibility was determined to be 5% at 5 ng/mL and 9% at 800 ng/mL for buprenorphine.

RESULTS

The analytical data supports a linear relationship, once the patient has been stabilised, between the administered daily dose and the mean concentration for both buprenorphine and norbuprenorphine in urine.

This relationship was improved when the data was corrected for creatinine excretion to account for differences in urine dilution. There was also found to be a relatively stable parent:metabolite concentration ratio across the dose range (see figures below).



DISCUSSION

In addition to therapeutic uses, buprenorphine has found favour with opiate abusers usually in conjunction with benzodiazepines as an alternative to heroin (2,3). However, taking high dose buprenorphine with benzodiazepines has been associated with fatalities (4).

It is for these reasons (compliance to treatment regimens and the potential for abuse) that a rapid and sensitive method for buprenorphine monitoring was developed.

The data derived from this study demonstrates the ability of this assay to monitor both buprenorphine and its metabolite even in those prescribed low dose treatment regimens.

Once that data has been corrected for specimen dilution, there is a relatively stable relationship between the concentrations of the parent drug and its metabolite.

The derivation of this relationship should facilitate the detection of any deviation from prescribed treatments in individuals, and aid in the interpretation of therapeutic failures.

REFERENCES

- 1) UK Drug Report 2000 – The drug situation in the UK. (<http://www.drugscope.org.uk>)
- 2) R. Hammersley, T.Lavelle and A. Forsyth. Buprenorphine and temazepam – abuse. *Br. J. Addict.*; 85: 301-303 (1990).
- 3) R.A. Singh, S.K. Mattoo, A. Malhotra, and V.K. Varma. Cases of buprenorphine abuse in India. *Acta. Psychiatr. Scand.*; 86: 46-48 (1992).
- 4) A. Tracqui, P. Kintz and B. Ludes. Buprenorphine-related deaths among drug addicts in France: A report on 20 fatalities. *J. Anal. Toxicol.*; 22: 430-434 (1998).