both urobilins and porphyrins can be attributed to the coextraction of urobilins and porphyrins by solid-phase chromatography and the fluorescence characteristics of the presumed zinc–urobilinogen complex. This mild solid-phase extraction condition did not remove all of the zinc cations from our fecal and urine samples, compared with the traditional treatment of using strong acids to release zinc from zinc–porphyrin complexes in biological samples [6].

In conclusion, we have developed a simple and convenient method in which simultaneous identification of urobilins and porphyrins can be achieved. This chromatographic technique for fecal urobilin detection is potentially applicable in investigating clinical problems.

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References


Despite its structural similarity to opiates, the effect of therapeutic nalmefene hydrochloride use on subsequent urine toxicologic screening has not been reported. We undertook a prospective double-blinded trial to determine if a single intravenous dose of nalmefene would produce a falsely positive urine opiate screen.

Nalmefene hydrochloride (Revex®, Baker Norton Pharmaceuticals) received FDA approval as an opiate reversal agent on April 17, 1995. Like naloxone, it has no opiate agonist properties and, therefore, no abuse potential [1, 2]. Both medications work by antagonizing opiate receptors, although nalmefene has a slower clearance and a longer duration of action [1, 3–6].

Nalmefene, like naloxone, is structurally similar to...
Urine samples were tested with the Emit II assay and the Syva ETS® (Emit Testing System) automated analyzer system. The manufacturer’s instructions [11] were followed. Although the Emit II screen is primarily qualitative, the absorbance change value ($\Delta A$) provides semiquantitative numerical results. A $\Delta A$ of zero was the calibrator cutoff to distinguish between a morphine concentration of $\geq 300 \mu g/L$ (positive sample) and $< 300 \mu g/L$ (negative sample). A negative sample is interpreted as not containing morphine, or containing morphine in a concentration below the assay’s cutoff concentration [11]. Testing was done on nine separate days in October and November of 1996. All initially positive opiate screens were repeated by a second Emit II test from another urine sample aliquot.

Data were analyzed by Excel (Microsoft, version 5.0c) and reported descriptively. The mean semiquantitative numerical absorbance changes from the four time periods associated with nalmefene administration were compared with repeated-measures ANOVA involving NCSS statistical software (NCSS, version 6.0.13). Significance was at $\alpha = 0.05$.

Twenty of 25 volunteers completed the protocol. The five subjects dropped from the protocol were those who did not obtain urine samples at all time points. Four subjects missed urine collection at 24 h and one subject missed urine collection at 8 h. The data from these subjects were eliminated from the final analysis.

All urine screens after nalmefene were negative for opiates at all time points. All 30-min, 16 8-h, and five 24-h screens after morphine were opiate positive. There was no discrepancy in the opiate-positive samples during repeat testing. The eliminated data from the five subjects not completing the protocol were consistent with these results.

The absorbance changes for all samples are presented in Table 1. The means and SDs for the $\Delta A$ associated with time periods after nalmefene administration (pretest, 30 min, 8 h, and 24 h) were not significantly different by repeated-measures ANOVA ($F = 0.384$).

A post hoc power analysis was based on the means of negative and positive controls determined at the start of each testing day. For the variability between negative controls and the calibrator cutoff for a positive sample, $n = 20$ provides a power of $>0.99$ at 95% confidence to separate a positive from a negative sample.

Nalmefene’s long duration of action may be an advantage for reversing longer-acting opiates, by requiring less frequent dosing and by reducing the likelihood of renarcotization [4–6].

The 2-mg nalmefene dose was chosen to represent the maximum amount that might be generally considered for management of known or suspected opiate overdose in non-opiate-dependent patients. For this indication, the manufacturer’s recommendation is 0.5 mg/70 kg, followed by, if needed, 1.0 mg/70 kg [11]. Morphine was used as a control to show that our subjects would indeed have positive screening if given a known opiate. Four milligrams was chosen as an intravenous dose likely to be
positive at 30 min. As expected, the screens after morphine were not all positive at 8 and 24 h. Intravenous morphine has a half-life of 1.5–2 h and would only be consistently positive at 30 min.

Unchanged naloxone, at a concentration of 150 mg/L, has been tested by the manufacturer and shown not to cross-react with the Emit II assay [11]. Naloxone metabolites, after intravenous doses of 2 mg and 4 mg, were not associated with positive Emit II screens in a human study [8]. Despite its structural similarity to opiates, neither naloxene nor its metabolites found in human urine have ever been reported to cause falsely positive drug screens (Medline 1986–present). This information would be useful to a patient’s medical caretaker, or to personnel who might administer a urine drug screen after nalmefene use. The military has been using random urine drug screens for many years. Such screening is now common in the civilian workplace, for both preemployment and postaccident information.

This study was limited by the use of a single testing assay. Although the Emit II system is commonly used worldwide, there are other systems used to evaluate drugs in urine. For instance, the Abbott ADX system (Abbott Labs.) lists naloxone as a possible cross-reactant with opiates. This study only investigated a single 2-mg dose of nalmefene in healthy volunteers. Urine concentrations can vary extensively with fluid intake and other metabolic variables. Although the chosen nalmefene dose was high, no conclusions on larger doses, multiple doses, or in patients with hepatic impairment can be made.

Because nalmefene is structurally similar to opiates, and its metabolites are excreted in the urine, the potential to cause false-positive urine drug screens is of concern. Our data suggest that a 2-mg intravenous dose of nalmefene is unlikely to cause falsely positive urine opiate screens up to 24 h after administration.

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References