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Short Communication

RAPID HEROIN DETOXIFICATION USING A SINGLE HIGH DOSE OF BUPRENORPHINE

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Abstract—To test the effect of 32 mg of buprenorphine on the withdrawal process from heroin, 10 street-heroin using subjects were given 32 mg of sublingual buprenorphine, following heroin abstinence of 24 hours. Withdrawal symptoms were monitored during the first few hours, and followed for six days after buprenorphine administration, after which naltrexone (50 mg) was introduced to prevent future heroin use. Nine subjects completed detoxification with negligible withdrawal symptoms and a smooth transition to naltrexone. One subject was excluded from the study due to methadone ingestion prior to experiment. These results strongly suggest that painless detoxification from heroin can be obtained by a single high dose of buprenorphine.

Keywords—buprenorphine, heroin detoxification, naltrexone

In the past two decades the approach to rapid opiate detoxification has been mainly based on clonidine-naltrexone detoxification (O'Connor & Kosten 1998 ; Simon 1997 ; Loimer et al. 1991; Brewer, Rezae & Baily 1988) a complex, costly process, mostly involving anesthesia or sedation, and accompanied by residual withdrawal symptoms that last at least one week after detoxification (Albanese et al. 2000; Scherbaum et al. 1998).

Buprenorphine is a high-affinity, m-receptor partial agonist (Cowan, Lewis & MacFarlane 1977), and also a potent k-opioid receptor antagonist (Negus & Dykstra 1988). As a partial agonist, buprenorphine has a ceiling effect, that is, there are no added excessive μ-like effects as the dose is raised. Thus, dangerous effects like decreased blood pressure and more importantly, respiratory depression, do not occur when doses are raised from .02 to 32 mg (up to 70 times the recommended analgesic dose) in nondependent humans (Walsh et al. 1994).

To date, buprenorphine has been used as a potent analgesic, and as a substitution agent for heroin or methadone (Bickel et al. 1999; O'Connor et al 1998; Amass et al. 1994). For detoxification it has only been used in daily doses of 3 to 8 mg, tapered over several (10 to 30) days, with or without transition to naltrexone (Vignau 1998; O'Connor et al. 1997).

In this study the authors attempted a novel approach for rapid detoxification from heroin, utilizing only a single, very high dose of sublingual buprenorphine (32 mg). We hypothesized that the unique pharmacokinetic and pharmacodynamic properties of buprenorphine would enable the subjects to complete the entire withdrawal period, over seven days, without significant discomfort.

SUBJECTS AND METHODS

Patient Population

At the study site (Psychiatric Services at Meir General Hospital, Kfar-Saba, Israel) 10 physically healthy male street-heroin dependent volunteers, accompanied by an adult caretaker, gave their written informed consent after the procedure had been fully explained. Seven of the 10 were undercover police informers placed in safe-houses, and monitored diurnally by two policemen. For these police collaborators, the detoxification treatment was part of the obligation undertaken by the police as part of their agreement with these individuals. Exclusion criteria included recent use of methadone, and refusal to be available for daily evaluation during the seven days of follow-up.

Pretreatment Phase

All subjects were asked to abstain from heroin for 24 hours prior to the intervention, to prevent precipitated withdrawal by buprenorphine. Patients who did not exhibit clear withdrawal symptoms after 24 hours of declared abstinence were excluded from the study.

Buprenorphine Administration

Eight milligrams of buprenorphine (dissolved in 1ml of 40% aqueous ethanol solution) was administered

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sublingually every five minutes. The total amount administered was 32 mg over the first 20 minutes.

Measurements and Monitoring

Pulse (HR) and blood pressure (BP) were monitored continuously during the first hour. Withdrawal symptoms were documented for several hours using the Wang-Scale scoring system (Wang et al. 1974) following buprenorphine administration. Subjects were discharged after five hours that day, but continued to report daily for evaluation of symptoms and signs for the next six days. Naltrexone treatment (50 mg/day) was commenced on day seven, pending a negative naloxone challenge test, to avoid naltrexone-precipitated withdrawal.

Successful detoxification was measured by intensity of withdrawal symptoms, treatment retention, and smooth transition to 50mg naltrexone on the seventh day of treatment.

RESULTS

Subjects ages ranged from 22 years to 40 years. Mean age was 29. Mean length of heroin use was nine years. Mean age of commencement of heroin use was 20, with one subject starting as early as age 13. Range of daily dose of crude street-heroin consumed was 0.5-3.0 gm. Mean street-heroin dose was 2.1 gm/day. All subjects ingested heroin by inhalation of fumes of heated heroin.

Nine subjects completed the seven-day trial. One subject was excluded from the study for having ingested methadone minutes before buprenorphine administration.

Response to Buprenorphine during the First Hour

During the first 20 minutes of buprenorphine administration, the withdrawal symptoms abated, and the mean Wang-Scale score dropped from 25 to 14 points. Four of the nine patients exhibited mild exacerbation of their autonomic symptoms in the midst of the first hour that lasted only a few minutes. By the end of the first hour, the Wang-Scale score dropped to insignificant levels (less than four points) and the subjects were symptom free.

Mean HR dropped from 80.3 to 66.4 beats per minute. Mean systolic BP dropped from 130 to 110 mm Hg, and mean diastolic BP dropped from 76 to 65 mm Hg. Over the next several hours there were no further changes in HR and BP.

Eight subjects responded with visible mild euphoria, and all subjects were relieved of their initial withdrawal distress and became energetic and talkative.

Seven-Day Monitoring

The almost complete attenuation of withdrawal symptoms that was observed during the first hour continued throughout the six days of follow-up. During the third or fourth day, six subjects reported mild restlessness that lasted several hours and disappeared spontaneously. On day seven, all nine subjects showed no withdrawal response to a naloxone challenge test. Commencement of oral naltrexone treatment (50mg) was uneventful.

DISCUSSION

The results of this study strongly suggest that a single high dose of 32 mg buprenorphine produces almost complete abolition of the withdrawal syndrome in heroin addicts. The uneventful response to naltrexone treatment on the seventh day proves that by that time, all subjects were physically detoxified.

This rapid heroin detoxification may be explained by buprenorphine's unique pharmacology: (a) its slow dissociation receptor-kinetics (Hambrook & Rance 1976) and hence its long duration of action; and (b) its mixed partial agonist and antagonist properties that produce a ceiling effect at very high doses. The plasma levels attained at 32 mg during the first hours are high, and even after 96 hours are "comparable to those produced by therapeutic maintenance doses" (Walsh et al. 1994). Thus, the slow decline of buprenorphine plasma levels over the first few days presumably affords a gradual, progressive withdrawal that is better tolerated by subjects than abrupt withdrawal.

Certain precautions should be kept in mind while attempting this method:

1. Our clinical experience suggests that heroin-dependent subjects should abstain from heroin for about 24 hours, until an visible withdrawal syndrome is apparent. The use of buprenorphine immediately following heroin use may lead to a precipitated withdrawal, due to buprenorphine's antagonist properties.
2. Methadone users are not appropriate candidates for this detoxification method. Transition from 60 mg of methadone to buprenorphine elicits a dose-related antagonist effect that may produce considerable discomfort to the patient (Walsh et al. 1995). This antagonist response has not been demonstrated in subjects addicted to short-acting opioids like morphine (Schuh et al. 1994). Transition to short-acting opioids, or gradual tapering of methadone prior to use of buprenorphine is recommended whether for maintenance or detoxification purposes.

The limitations of this study are: (a) the small population sample; and (b) blood levels of buprenorphine and their correlation with withdrawal symptoms were not obtained.

Finally, while this study strongly suggests that heroin detoxification by a single high dose of buprenorphine is simple, safe, and affordable, any conclusion regarding its effects on long-term abstinence from heroin should be

deferred. Opiate abstinence is a more complex, long-term process, and highly dependent on psychosocial variables. While eight of the nine study subjects continued to be abstinent after six months, no correlation can or should be drawn to the method of detoxification. Further studies are needed to clarify the pharmacological and psychological effects of such "one touch" interventions.

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