

BUPRENORPHINE WITHDRAWAL SYNDROME

B.M. TRIPATHI, P. HEMRAJ, N.K. DHAR

The increasing use of buprenorphine among drug dependent subjects demands systematic enquiry into the clinical profile of buprenorphine withdrawal. Six male buprenorphine dependent (parenteral) subjects were observed for opiate withdrawal over a two week period. The onset of withdrawal occurred 48 hours after the last dose, peaked around the third day and lasted up to ten days. The withdrawals were similar to morphine type drugs and moderate in intensity.

Key words: buprenorphine, morphine, opiate withdrawal.

INTRODUCTION

The use of buprenorphine, a narcotic analgesic, has increased in drug using populations all over the world. Since early reports of buprenorphine abuse, its abuse liability and dependence potential have been demonstrated (Quigley et al, 1984; O'Connor et al, 1988; Lal, 1992). The risk of buprenorphine abuse is magnified in heroin users because of its use as a detoxifying agent (Kosten, 1988; Bickel, 1988) and maintenance agent (Seow et al, 1986; Reisinger, 1985). Though a buprenorphine withdrawal syndrome has been described, it needs to be delineated further (Fudala et al, 1990; San et al, 1992). The withdrawal profile in buprenorphine dependent persons has been examined in the current study.

MATERIALS AND METHODS

Six male patients who were hospitalized for the treatment of buprenorphine dependence syndrome, diagnosed using DSM III-R (APA, 1987) criteria and who had used buprenorphine within the last 48 hours were included in the study, after obtaining consent. Patients who had used other morphine type drugs during the previous month were excluded. Urinary screening by thin layer chromatography was done at the time of admission as well as during the stay in hospital for identification of drugs used. The patients were given benzodiazepines (nitrazepam) and/or non-narcotics analgesics (diclofenac sodium or ibuprofen) when needed during hospitalization.

The opioid withdrawal symptoms were recorded for a fortnight between 9 and 10 a.m. using the Opiate Withdrawal Rating Scale (Handelsman et al, 1987). This has two sub-scales, viz, subjective (SOWS) and objective (OOWS) withdrawal scales for recording subjective and objective opiate withdrawal symptoms. Subjective referred to those symptoms that were either reported in the past 24 hours or at the time of examination. Objective

symptoms were present at the time of examination. The resident in charge of the patients rated the withdrawal profile. Since the scale had been used routinely in clinical practice, the raters were familiar with the rating method.

RESULTS

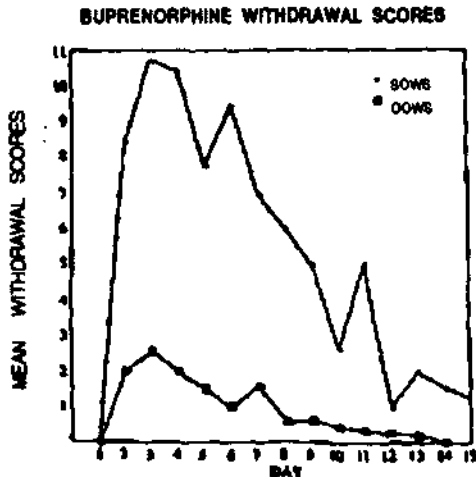
The patients were between 24 and 51 years of age (36.16 ± 9.9 years). The duration of buprenorphine use was 3.16 ± 1.55 years. Out of the six patients, four had been heroin users and started buprenorphine in an attempt to give up heroin; one had used pentazocine prior to buprenorphine and the other patient started buprenorphine use due to a physical ailment. All of them were primarily parenteral users and had used the sublingual mode of administration only rarely. Two patients used promethazine (25-50 mg/day) and one used diazepam (10 mg/day) in addition to buprenorphine. The daily does of buprenorphine was 2.55 ± 1.22 mg parenterally.

None of them were HIV positive in a pre-admission screening using ELISA. Diclofenac sodium (50 mg) or ibuprofen (400 to 600 mg) were used when necessary; these were needed till the second week in four patients. Nitrazepam (10 to 40mg) was given to all patients until the second week.

The withdrawal profile as indicated by the Opiate Withdrawal Rating Scale (Handelsman et al, 1987) shows that predominant subjective complaints were anxiety, yawning, bone and muscle aches and restlessness. These complaints started on the second day after the last dose of buprenorphine, peaked on the third and fourth days and lasted up to a fortnight (Fig 1). The SOWS scores on the first, third and fourteenth day were 8.33 ± 6.34 , 10.4 ± 5.7 and 1.5 ± 0.12 respectively.

Common objective withdrawal features were yawning, rhinorrhoea, lacrimation, mydriasis, restlessness and anxiety. These started on the second day, peaked on the third day and lasted till the twelfth day (Fig. 1). Anxiety and restlessness lasted

for a week. Mydriasis and lacrimation persisted till the tenth day. The OOWS on the first, third and twelfth days were 2.0 ± 2.34 , 2.5 ± 1.6 and 0.3 ± 0.5 respectively.



DISCUSSION

Though buprenorphine was considered to be an opioid analgesic with low abuse potential and dependence liability, its dependence potential has been established. Dependent use of buprenorphine has been documented in heroin users (Quigley et al, 1984; Rainey, 1986; O'Connor et al, 1988; Lal, 1992).

Buprenorphine withdrawal appears within 48 hours after the last dose, peaks around the third or fourth day and lasts for ten days. These withdrawal symptoms are moderate in severity. These findings are similar to the reports by San et al (1992) and Fudala et al (1990), and contrary to the earlier reports of later onset and mild intensity of buprenorphine withdrawal. The withdrawal profile is similar to other morphine type drugs. The subjective scores were higher in comparison to the objective scores, which means that the reported subjective distress is much more than the objective signs of withdrawal.

Buprenorphine should be cautiously used as a detoxifying and maintenance agent in heroin dependent subjects. It is also suggested that the patients undergoing withdrawal from buprenorphine may need medication because of moderately severe symptoms.

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