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Very High-Dose Intravenous Buprenorphine Dependence A Case Report

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Abstract

Buprenorphine, a mixed agonist-antagonist opioid, was claimed to be a safe opiate analgesic with low abuse potential, but various case reports and studies have shown that buprenorphine too has an appreciable abuse potential. The maximum daily dose of buprenorphine used by patients has been reported to be 7 mg. In therapeutic clinical trials it has been used in doses between 16-32 mg per day sublingually. We here report a case using 24 mg of intravenous buprenorphine daily. The distinctive clinical features of the case and the implications are discussed (German J Psychiatry 2004; 7: 58-59).

Keywords: Buprenorphine; abuse; dependence

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Introduction

Buprenorphine, a mixed agonist-antagonist opioid, available in sublingual, oral and parental preparations has been available for quite some time and has been claimed to be a potent (0.3 mg = 10 mg of morphine on an equianalgesic basis) and safe opiate analgesic with low abuse potential (Jasinski et al., 1978). The US Food and Drug Administration approved buprenorphine and buprenorphine/naloxone combination in 2002 for the treatment of opioid dependence. However, various case reports and studies have challenged the safety claim and have shown that buprenorphine too has an appreciable abuse potential; many such reports have come from India (Singh et al., 1992; Sharma & Mattoo, 1999; Basu et al., 1994, 2000). Till now studies have reported abuse of buprenorphine up to the dose of 7 mg per day (Sharma & Mattoo, 1999). We report a patient who had been using 24 mg of buprenorphine (equivalent to 800 mg of morphine!) per day in a dependent pattern.

Case Report

R.S, a 24-year married unemployed male belonging to a Hindu joint family presented with a history of injecting buprenorphine for 8 years. Initially the patient started using the drug out of curiosity, with friends, in a dose of 0.6 mg (one ampoule) per day intravenously. The quantity kept on increasing over time, till he started injecting 24 mg/day (40 ampoules) in 5-6 divided doses by 24 months. The patient reported that initially he increased the dose to derive pleasure, but later on (approximately after 20-25 ampoules) the pleasure did not increase any further. However, the quantity kept on increasing because of expectation of increase in pleasure and lack of control. In addition to the increase in the dose of buprenorphine he also started mixing it with chlorpheniramine, initially 1 vial (10 ml) with 10 ampoules of buprenorphine, but later on when the effect of buprenorphine plateaued, progressively higher dose. After increasing chlorpheniramine to 60-70 ml/day along with 24 mg of buprenorphine, he started having generalized tonic-clonic seizures, but was not able to control his drug intake and continued to inject the cocktail in large doses. He would have withdrawal features starting after 24-36 hours of last

dose in the form of rhinorrhea, lacrimation, diarrhea, body aches, restlessness, anxiety and intense craving. There was severe socio-occupational dysfunction. He discontinued the injectables for a few months but developed premature ejaculation. He relapsed, but this time would derive the same amount of pleasure with only 1.2 mg of buprenorphine per day. Later this quantity increased to about 2.4-3.6 mg/day. He was very much apprehensive about any further increase and sought treatment. There was no history of any other drug dependence (except nicotine), or any comorbid physical or psychiatric illness. After detoxification using clonidine and symptomatic treatment he was started on naltrexone and was provided relapse prevention counselling, and has since been abstinent on naltrexone.

Discussion

Buprenorphine can be visualized on a continuum between a full agonist and an antagonist, it is described as a partial agonist at the mu receptor, and an antagonist at the kappa–receptor, has high affinity for both the receptors, low intrinsic activity at the mu-receptor and no intrinsic activity at kappa receptor (Johnson et al., 2003). It has been suggested that at, low doses, mu effect predominate, while at higher doses kappa antagonist effect offsets the mu effect (Cowan et al., 1977). Due to the same at low doses buprenorphine demonstrates morphine like agonist effects, but there is only a minimal increase or slight decrease in agonist effects, i.e., both physiologic and subjective effects at higher doses. Consistent with this, it was observed that among patients treated with 16 mg/day of sublingual buprenorphine in a double-blind study and given the opportunity to increase their dose to 32 mg/day during an extension open label phase of the study, approximately 20% requested a dose decrease back to 16 mg/day (Ling, W., personal communication, cited in Johnson et al., 2003). Our patient also demonstrated similar phenomenon in the form of lack of pleasure after the dose of 12-14 mg/day of intravenous buprenorphine. Such a high intravenous dose has not been reported earlier. He also used chlorpheniramine to increase the stimulating effect of buprenorphine, as reported in the past by various studies (Singh et al., 1992).

In the past it has been reported that the usual buprenorphine abuser has been abusing other drugs prior to starting buprenorphine and starts buprenorphine either out of curiosity or as a substitute during treatment for heroin dependence. However, the index case shows that with growing awareness regarding the drug, easy availability and low cost, it may well become the drug of choice among young first-time users' illicit substances. Further, as illustrated by the index case, it may have a potential seizure threshold lowering effect if very high doses are combined with other drugs like chlorpheniramine. This has not been reported earlier.

The approval of buprenorphine-naloxone combination is a welcome addition to the options available for the treatment of opioid dependence. This would certainly benefit those dependent on other opioids. However, one needs to be aware that although this strategy will be useful in countries where it is available, buprenorhine abuse and dependence (especially intravenous) continues to be a major problem in developing countries such as in India where prescription monitoring and control systems are lax.

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