BUPRENORPHINE ABUSE IN INDIA: AN UPDATE

YOGESH SHARMA
& S.K. MATTOO

ABSTRACT

This study reviews the available Indian literature on buprenorphine abuse. Buprenorphine was introduced in 1986; the abuse, first noticed in 1987, increased rapidly till 1994, and then decreased gradually. Initiated through other addicts and medical practitioners, the abuse was mostly as a cheap, easily and legally available substitute for opioids. The typical young adult male abuser used an intravenous cocktail with diazepam, pheneramine or promethazine for a better kick. The withdrawal syndrome was typical of the opioids and without an expected delayed onset. Complications of pseudoaneurysm and recurrent koro in repeated withdrawal were reported. Buprenorphine as a detoxifying agent for opioids reportedly gave better symptom control in the first week but high rates of dependence induction were reported. The Indian data tends to caution against the Western enthusiasm to use buprenorphine for detoxification or maintenance of opioid abusers.

Key words: Buprenorphine, substance abuse, India.

Buprenorphine is a mixed agonist antagonist opioid, available in sublingual/oral and parenteral form. Developed in mid-seventies, in comparison to morphine, it was reported to be 25-40 times more potent analgesic, to have lower over dose lethality; to give euphoria which is less, and limited by a ceiling effect of higher doses; and to have a mild and delayed withdrawal. Hence, it was claimed to be a safe opioid with low abuse potential, and was recommended not only as an analgesic, but also as a drug for detoxification and maintenance treatment of opioid dependence (Jasinski et al., 1978; Banks, 1979; Mello & Mendelson, 1980; Robertson et al., 1986).

Beginning in 1983, a number of reports have highlighted the abuse of buprenorphine in oral as well as parenteral forms and alone as well as in combination with benzodiazepines or antihistamines (Harper, 1983; Strang, 1985; Stark et al., 1987; O'Connor et al., 1988; Hammerseley et al., 1990). All the studies reported buprenorphine abuse primarily as a substitute abuse in heroin abusers.

In India buprenorphine was introduced in 1986. According to the published data, the first cases of buprenorphine abuse were registered in 1987 (Singh et al., 1992), presented in professional forums in 1989 (Basu et al., 1990) and published in 1990 (Basu et al., 1990; Chowdhury & Chowdhury, 1990; Nizamie & Sharma, 1990). Till date more than a dozen reports have been published covering various aspects of buprenorphine abuse. The present study aims to summarize the Indian research on the abuse of buprenorphine and its use in the treatment of opioid abusers.

MATERIAL & METHOD

The material for this study comprised of i) the published Indian studies on abuse of buprenorphine and its use in the treatment of opioid abusers, ii) the data on 145 cases of buprenorphine abuse seen in the Drug
BUPRENORPHINE ABUSE IN INDIA

De-addiction and Treatment Centre, Department of Psychiatry, Post Graduate Institute of Medical Education and Research, Chandigarh (Sharma & Mattoo, 1998) & iii) the data available from the Drug Controller of India on the production of buprenorphine.

RESULTS

Availability: Buprenorphine was introduced as a Schedule-H drug and listed in the Narcotic Drugs and Psychotropic Substances Act (NDPSA, 1985). As a Schedule-H drug it was to be dispensed only on the prescription of a registered medical practitioner. As a drug under the NDPS Act, it invited severe punishment for unauthorized possession or dealings. But, as with most other scheduled drugs, these provisions have never been effectively implemented. Thus, buprenorphine is almost freely available without a prescription. There have been no prosecutions for buprenorphine under the NDPS Act.

Production: The only data available, provided by the Drug Controller of India, New Delhi (personal communication) listed the production, and presumably the sale, of 8.18 Kg in 1993-1994, 7.2 Kg in 1994-1995, 25.56 Kg in 1995-1996 and 8.28 Kg in 1996-November 97 periods. There is no explanation available for the sudden increase in production in 1995-1996; if some of it was exported or all consumed in the country.

Prevalence of Abuse: The early publications covered 54, 7, and 18 cases respectively, comprising 7%, 10% and 17% of opioid, mostly heroin abusers seen over 2 years, 6 months and 3 years respectively (Chowdhury & Chowdhury, 1990; Lal, 1991; Singh et al., 1992). More recently, series of 90 cases (51% of opioid abusers seen over 3 years) and 100 cases have been reported (Umesh Babu & Chaturvedi, 1995; Vinay Kumar & Singh, 1996). Between 1987 and 1997, out of 687 cases of opioid abuse registered in our centre, 145 cases (20%) reported buprenorphine abuse - the percentage varying from 6 to 34 in different years, with the highest percentages being recorded between 1990 and 1994 and a slow decline being recorded since then (Sharma & Mattoo, 1998).

Profile of Abuser: The typical profile of a buprenorphine abuser is of an urban, young to middle age (19-42 years) male, who has had some school or college education and, has a low to middle level occupation (Basu et al., 1990; Nizamie & Sharma, 1990; Singh et al., 1992; Tripathi et al., 1995; Sharma & Mattoo, 1998).

Onset of Abuse: Most cases had graduated to buprenorphine abuse from the abuse of other opioids, heroin in up to 84% cases, which had preceded for a usual of 3-5 years and a maximum of 2-12 years (Basu et al., 1990; Chowdhury & Chowdhury, 1990; Nizamie & Sharma, 1990; Singh et al., 1992; Chavan et al., 1995; Umesh Babu & Chaturvedi, 1995; Vinay Kumar & Singh, 1996; Sharma & Mattoo, 1998).

Reasons for Initiation: The common reasons given for changing over to buprenorphine abuse were - initially, non-availability, and purity of the drug. The initiation was predominantly through fellow addicts and less often, by medical professionals for detoxification from other opioids (Basu et al., 1990; Chowdhury & Chowdhury, 1990; Lal, 1991; Singh et al., 1992; Umesh Babu & Chaturvedi, 1995; Vinay Kumar & Singh, 1996; Sharma & Mattoo, 1998).

Pattern of Use: The reported duration of buprenorphine abuse has ranged from 4-36 months, with a mean of 14 months, while the daily dose ranged from 1-7 mg, with a mean of 3 mg (Singh et al., 1992). Except for two reports of abuse by mainly intramuscular and less often oral route (Chowdhury & Chowdhury, 1990; Nizamie & Sharma, 1990), all others have reported intravenous abuse in up to 86% cases (Sharma & Mattoo, 1998). Abuse of buprenorphine alone was reported in 13-54% cases (Chowdhury & Chowdhury, 1990; Gupta et al., 1996; Vinay Kumar & Singh, 1996; Sharma & Mattoo, 1998). The common and interesting co-abuse was of an intravenous cocktail of 0.8
mg of buprenorphine with 10-20 mg of diazepam or 45-90 mg of pheneramine or 100-200 mg of promethazine taken 2-4 times daily. Reportedly, compared to buprenorphine alone, the cocktail provide a more intense and prolonged kick (1-3 hours instead of 1/2-1 hour) and in some cases also helped to suppress side-effects like nausea. This co-abuse was reported in 55% and 78% cases in one series (Singh et al., 1992; Sharma & Mattoo, 1998). The concurrent abuse of heroin was reported in 17%, 56% and 48-71% cases respectively (Singh et al., 1992; Vinay Kumar & Singh, 1996; Chowdhury & Chowdhury, 1990).

An interesting finding reported by 2 out of 3 concurrent heroin abusers was of a decrease in euphoria induced by heroin (Singh et al., 1992). Other reported co-abused substances were alcohol, cannabis and carisoprodol (Singh et al., 1992; Sharma & Mattoo, 1998).

Withdrawal Syndrome: By self-reports as well as observation in hospitalized patients, buprenorphine withdrawal was reported to start in 1-2 days, peak after 2-4 days and last for 2-3 weeks (Lal, 1991; Singh et al., 1992; Tripathi et al., 1995). Corresponding findings were reported for naloxone induced buprenorphine withdrawal (Nigam et al., 1994). The aches and pain reportedly tapered off over a longer period of up to 6 weeks and the withdrawal severity was subjectively one half of that of heroin (Singh et al., 1992).

Risk Behaviours and Complications: A higher prevalence of high risk behaviours like unprotected sex, sex with multiple partners and commercial sex workers, homosexuality and inadequate cleaning and sharing of injection material with multiple partners have all been reported for buprenorphine abusers (Mahotra et al., 1993). A case of recurrent koro in repeated intravenous buprenorphine withdrawal has also been reported (Chowdhury & Banerjee, 1996).

Treatment Outcome: One study reported that by 3 visits or one year, 75% cases had dropped out of follow up and 68% cases had relapsed to heroin or buprenorphine abuse (Singh et al., 1992).

Buprenorphine for detoxifying heroin abusers: Two studies reported using buprenorphine to detoxify heroin and other opioid abusers (Chowdhury & Chowdhury, 1990; Nigam et al., 1993). But, with a regime of 0.3 mg intramuscular thrice, twice and once daily, dependence on injectable & oral buprenorphine were found to develop in 18% and 6% cases respectively (Chowdhury & Chowdhury, 1990).
promethazine, which gives a more intense and prolonged kick than buprenorphine alone - a pattern similar to that noted in West (Strang, 1985; Stark et al., 1987; O'Connor et al., 1988; Hammerseley et al., 1990). The daily doses may range from 1-7 mg, much less than the doses at which opioid antagonist ceiling effects on euphoria become manifest; the ceiling effect may still be manifested as decreased concurrent heroin abuse (Jasinski et al., 1978; Mello & Mendelson, 1980; Walsh et al., 1994).

The finding that buprenorphine withdrawal syndrome is of lesser severity than of heroin, but its course in typical of other opioids, is similar to that reported from the West (San et al., 1992). Thus, there is no substantiation of the initial expectations of the withdrawal being delayed by two weeks or so (Jasinski et al., 1978; Mello & Mendelson, 1980).

Detoxification can be successfully completed in most cases by using clonidine and other symptomatic medications. But, as with other opioids, the treatment outcome remains poor, with high rates of drop out and relapse.

Compared to clonidine, the use of buprenorphine to detoxify opioid abusers is marginally advantageous in providing better symptom control in the first week of the withdrawal (Cheskin et al., 1994; Janiri et al., 1994). But, it carries a high risk of introducing the patients to abuse of a new opioid. This is borne out by the onset of buprenorphine abuse following exposure to buprenorphine as a detoxifying agent in as many as 24% cases by clinical observation (Chowdhury & Chowdhury, 1990) and in 33% cases by self-report (Singh et al., 1992).

The dose of abuse reported in India is within the limits of the ceiling effect of high doses on buprenorphine induced euphoria (Walsh et al., 1994). Thus, the inherent antagonistic effect may reduce the risk of high dose morbidity and mortality (Banks, 1979; Robertson et al., 1986), but does not decrease the abuse potential of buprenorphine. The Indian data shows that the health risks and social consequences of buprenorphine abuse are in no measure milder compared to the abuse of other opioids (Singh et al., 1992; Malhotra et al., 1993; Basu et al., 1994).

In the West, more so in the USA, buprenorphine is being promoted as a detoxification and maintenance agent in opioid abuse (Ling et al., 1996). The Indian research findings suggest a need for caution in prescribing buprenorphine in opioid abuse as a detoxifying agent and may be also as a maintenance agent.

REFERENCES

Banks, C.D. (1979) Overdose of buprenorphine - a case report. New Zealand Medical Journal, 89, 255.

Basu, D., Varma, V.K. & Malhotra, A.K. (1990) Buprenorphine dependence: a new addiction in India. Disabilities and Impairments, 3, 142-146.

Basu, D., Mattoo, S.K., Arora, A., Malhotra, A. & Varma, V.K. (1994) Pseudoaneurysm in injecting drug abusers: cases from India. Addiction, 89, 1697-1699.

Chavan B.S., Tripathi, B.M. & Lal, R. (1995) Outcome of parenteral buprenorphine abuse. Indian Journal of Psychiatry, 37(Suppl), 24.

Cheskin, L.J., Fudala, P.J. & Johnson, R.E. (1994) A controlled comparison of buprenorphine and clonidine for acute detoxification from opioids. Drug and Alcohol Dependence, 36, 115-121.

Chowdhury, A.N. & Chowdhury, S. (1990) Buprenorphine abuse: report from India. British Journal of Addiction, 85, 1349-1350.

Chowdhury, A.N. & Banerjee, G. (1996) Recurrent koro in repeated intravenous buprenorphine withdrawal. Addiction, 91, 145-147.

Gupta, D.K., Desai, N.G., Chandiramani, K. & Chaudhary, G. (1996)
YOGESH SHARMA & S.K. MATTOO

Pattern of multiple substance use in heroin dependent individuals. Indian Journal of Psychiatry, 38(Suppl), 82.

Hammerseley, R., Lavell, T. & Forsyth, A. (1990) Buprenorphine and temazepam abuse. British Journal of Addiction, 85, 301-303.

Harper, I. (1983) Temgesic abuse. New Zealand Medical Journal, 96, 777.

Janiri, L., Mannelli, P., Persco, A.M., Serretti, A. & Tempesta, E. (1994) Opiate detoxification of methadone maintenance patients using lefetamine, clonidine and buprenorphine. Drug and Alcohol Dependence, 36, 139-145.

Jasinski, D.R., Pevnick, J.S. & Griffith, J.D. (1978) Human pharmacology and abuse potential of the analgesic buprenorphine-a potential agent for treating narcotic addiction. Archives of General Psychiatry, 35, 501-516.

Lai, R. (1991) Buprenorphine dependence - analysis of seven cases. Indian Journal of Psychiatry, 33, 62-65.

Ling, W., Wesson, D.R., Charuvastra, C. & Klett, C.J. (1996) A controlled trial comparing buprenorphine and methadone maintenance in opioid dependence. Archives of General Psychiatry, 53, 401-407.

Malhotra, A., Balsej, M., Basu, D., Mattoo, S.K., Varma, V.K. & Sehgal, B. (1983) HIV screening & risk behaviour in psychoactive substance users. Indian Journal of Medical Research (A), 97, 231-233.

Mello, K. & Mendelson, J.H. (1980) Buprenorphine suppresses heroin use by heroin addicts. Science, 207, 657-659.

Narcotic Drugs and Psychotropic Substances Act (1985) Government of India, New Delhi.

Nigam, A.K., Ray, R. & Tripathi, B.M. (1993) Buprenorphine in opiate withdrawal: a comparison with clonidine. Journal of Substance Abuse Treatment, 10, 391-394.

Nigam, A.K., Srivastava, R.P., Saxena, S., Chevan, B.B. & Sundaram, K.R. (1994) Naloxone induced withdrawal in patients with buprenorphine dependence. Addiction, 89, 317-320.

Nizame, S.H. & Sharma, L.N. (1980) Buprenorphine abuse: a case report. Indian Journal of Psychiatry, 32, 98-200.

O'Connor, J.J., Maloney, E., Travers, R. & Campbell, A. (1988) Buprenorphine abuse among opiate addicts. British Journal of Addiction, 83, 1085-1087.

Robertson, J.R., Aidan, V. & Bucknall, V. (1986) Buprenorphine: dangerous drug or overlooked therapy? British Medical Journal, 292, 1485.

San, L., Cami, J., Fernandez, T., Olle, J.M., Peri, J.M. & Torrens, M. (1992) Assessment and management of opioid withdrawal symptoms in buprenorphine dependent subjects. British Journal of Addiction, 87, 55-62.

Sharma, Y. & Mattoo, S.K. (1998) A review of 145 cases of buprenorphine abuse seen in Drug De-addiction and Treatment Centre, Department of Psychiatry, PGIMER, Chandigarh (Unpublished).

Singh, R.A., Mattoo, S.K., Malhotra, A. & Varma, V.K. (1992) Cases of buprenorphine abuse in India. Acta Psychiatrica Scandinavica, 37, 23-25.

Stark, C.R., Skyes, R. & Mullin, P.J. (1987) Temazepam abuse. Lancet, 11, 802-803.
BUPRENORPHINE ABUSE IN INDIA

Strang, J. (1985) Abuse of buprenorphine. Lancet, 2, 725.

Umesh Babu, S.B. & Chaturvedi, S.K. (1995) Changing patterns of opiate abuse with a focus on buprenorphine. Indian Journal of Psychiatry, 37(Suppl), 23.

Vinay Kumar & Singh, B.K. (1996) Reasons behind increasing buprenorphine abuse. Indian Journal of Psychiatry, 38(Suppl), 82.

Walsh, S.L., Preston, K.L., Stitzer, M.L., Cone, E.J. & Bigelow, G.E. (1994) Clinical pharmacology of buprenorphine: ceiling effects at high doses. Clinical Pharmacology and Therapeutics, 55, 569-580.

YOGESH SHARMA, MBBS, Junior Resident. S.K. MATTOO*, MD, Associate Professor, Department of Psychiatry, Post Graduate Institute of Medical Education & Research, Chandigarh-160 012.

*Correspondence