

Rapid detoxification of heroin dependence by buprenorphine¹

LIU Zhi-Min, CAI Zhi-Ji, WANG Xiao-Ping², GE Yun, LI Chun-Mei²

¹National Institute on Drug Dependence, Beijing Medical University, Beijing 100083;

²Xi'an Berlin Detoxification Center, Xi'an 710061, China)

KEY WORDS substance withdrawal syndrome; buprenorphine; sublingual administration; heroin dependence

AIM: To evaluate the clinical efficacy of buprenorphine (Bup) in treatment of acute heroin withdrawal. **METHODS:** Bup was given sublingually daily to 60 cases of heroin addicts in 3 groups: low, medium, and high doses. Withdrawal signs and symptoms of heroin were rated by Clinical Institute Narcotic Assessment. Craving for heroin during detoxification was assessed by Visual Analogue Scale. The side effects of Bup was assessed by Treatment Emergent Symptom Scale. **RESULTS:** The mean daily consumption of Bup in low, medium, and high group was 2.0, 2.9, and 3.6 mg, respectively. Bup not only suppressed objective signs and withdrawal symptoms for heroin withdrawal, but also reduced the duration for heroin detoxification over 7-8 d. **CONCLUSION:** Bup is an effective and rapid detoxification agent with fewer side effects for treatment of acute heroin withdrawal.

Buprenorphine hydrochloride (Bup) is a mixed opiate agonist-antagonist. The analgesic action is 25-50 times more potent than morphine and has a long duration action. Bup had utility in treating opiate addiction^[1]. Bup is an effective withdrawal agent and has significant advantage over pure opiate agonist such as methadone which are widely used currently for opiate detoxification^[2-4]. The aim of this study was to evaluate the clinical efficacy of Bup in the treatment of heroin withdrawal in Chinese.

SUBJECTS AND METHODS

Subjects Sixty smoking heroin addicts were consecutively admitted to a detoxification center in Xi'an city.

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Each patient had a complete medical examination including blood, urine, X-ray, and ECG. They were required to meet the following criteria: 1) No major physical or psychiatric disorder; 2) No dependence on other drugs; 3) Length of present heroin addiction was at least 6 months; and 4) Met for the criteria of opiate dependence based on DSM-III-R⁵.

They were divided into 3 groups based on the duration of drug abuse, dosage of heroin abuse, and severity of drug dependence.

Mild Group 17 M and 3 F, age 29 ± 6 a, mean duration of heroin abuse 11 months, and mean heroin daily dose before admission 0.6 ± 0.4 g (impure heroin of street dose).

Medium Group 16 M and 4 F, age 27 ± 9 a, mean duration of heroin abuse 26 months, and heroin daily dose before admission 1.7 ± 0.8 g.

Heavy Group 15 M and 5 F, age 28 ± 9 a, mean duration of heroin abuse 44 months, and heroin daily dose before admission 3.1 ± 1.1 g.

Bup (Qinghai Pharmaceutical Co, China) was given sublingually in full dose during the first three days and in the next 4 or 5 d by gradually reduced doses (Tab 1).

Tab 1. Bup dosage schedule ($\text{mg} \cdot \text{d}^{-1}$).

	Mild group	Moderate group	Heavy group
Day 1-3	3.0	4.5	6.0
4	2.0	3.0	4.5
5	2.0	2.0	3.0
6	1.0	1.0	2.0
7	0.5	0.5	1.0
8	-	-	0.5
Mean daily consumption	2.0	2.9	3.6
Total consumption	14.5	20.0	29.0

Ratings Heroin withdrawal signs and symptoms were rated daily on the Clinical Institute Narcotic Assessment (CINA)^[6] which contains 10 items of opiate withdrawal signs and 3 opiate withdrawal symptoms and the range of total scale is 0-30 points.

The patient's craving for heroin was assessed daily by using Visual Analogue Scale (VAS)^[7], which is a self-assessment rating scale: "extremely," "obviously," "moderately," "slightly," and "not at all."

The side effects of Bup were assessed by using Treatment

Emergent Symptom Scale (TESS)^[11], on d 2, 4, 6, and 8.

The criteria for a successful detoxification were: 1) Completion of detoxification without evident withdrawal signs and symptoms; and 2) Minimal craving for heroin and/or without evident symptoms of discomfort.

RESULTS

Bup treatment of acute withdrawal from heroin dependence was successful in all of 60 patients completing within 7-8 d. No significant difference in treatment efficiency was found between the 3 groups (F value = 1.52, $P > 0.05$). The Bup markedly suppressed heroin withdrawal during detoxification, and only mild withdrawal symptoms and signs were found during gradual reduction of Bup. The mean scale of abstinence of signs and symptoms of CINA was gradually reduced and no significant difference was found among the 3 groups during Bup administration (Tab 2, Fig 1).

Tab 2. CINA during Bup administration. $n = 20$, $\bar{x} \pm s$. No significant difference between the 3 groups ($P > 0.05$).

Day	Mild group	Moderate group	Heavy group	F
1	5.0 ± 3.9	7.2 ± 4.1	6.3 ± 3.7	1.1
2	5.3 ± 2.8	5.5 ± 2.9	5.6 ± 3.7	0.1
3	3.5 ± 2.1	4.4 ± 2.7	3.9 ± 2.1	0.9
4	2.7 ± 1.8	3.2 ± 1.9	2.9 ± 2.3	0.3
5	2.6 ± 1.7	2.5 ± 1.7	3.4 ± 2.0	1.4
6	2.3 ± 1.9	2.4 ± 1.6	2.6 ± 1.3	0.2
7	2.4 ± 2.0	1.5 ± 1.0	1.8 ± 1.0	1.9
8	1.5 ± 1.2	1.1 ± 1.1	1.5 ± 1.1	0.6

VAS indicated that 51/60 (85 %) patients complained of extreme discomfort at heroin withdrawal before Bup treatment. The frequencies of patients craving for heroin were different between the phases before and after Bup administration (F -test of multiple regression, F value = 19.45, $P < 0.01$, Tab 3).

All of the 60 patients complained of dry mouth, 22 patients (37 %) experienced nausea, 6 patients (10 %) had mild anxiety and aching bones and muscles respectively, 2 patients (3 %) had insomnia that required treatment, 2 patients (3 %) had withdrawal symptoms that demanded to continue Bup administration following the protocol.

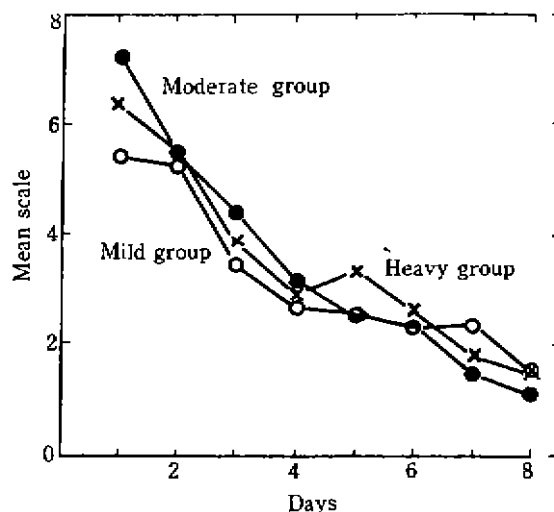


Fig 1. CINA during Bup administration.

Tab 3. The patient frequencies on VAS. $n = 60$. * before Bup administration (base-line level). † after Bup administration.

Day	Craving degrees for heroin				
	Extreme	Obvious	Moderate	Slight	None
1*	51	3	4	2	-
2†	3	23	12	16	6
3†	-	7	25	22	6
4†	-	1	16	29	14
5†	-	1	11	22	26
6†	-	-	11	19	30
7†	-	-	6	15	39
8†	-	-	-	10	50

DISCUSSION

This study supported the general findings from previous studies that Bup was an effective pharmacotherapy for heroin detoxification, not only in suppressing objective signs and reducing subjective symptoms during acute heroin withdrawal phase, but also reduced the duration of heroin withdrawal. Completing detoxification in such a short period was a treatment feature of the present study. Theoretically, the length of time for detoxification from opiate dependence usually requires at least 14 - 21 d^[9]. However, the "peak" of withdrawal syndromes was on d 2 and d 3 after the opiate withdrawal^[10]. The result of this protocol suggested that this schedule might

effectively shorten the phase of detoxification. Unlike pure opiate agonist, Bup has specific pharmacological properties which have a mixed action: a partial μ opiate agonist but also has an antagonist activity at the κ receptor. It can be postulated that the opiate antagonist effect would reverse the hypothesized opiate agonist induced deficiency in central endogenous opiate peptide function during initial detoxification.

Bup has at least other 2 advantages: 1) it has a good therapeutic ratio, presumably because its antagonist action prevent lethal overdose and significant respiratory depression by the agonist opioid actions of the drugs; 2) it has an easier discontinuation than opiate pure agonist because it does not induce significant drug dependence even with chronic administration^[11,12].

Bup dependence and abuse has been reported in patients treated for pain and opiate addicts respectively^[13]. Therefore, the problems of dependent and abuse potential of Bup need to be emphasized.

Limitations of this study: The present study did not observe the signs and symptoms in the prolonged phase following withdrawal of Bup and other dosage levels of Bup. It should be further studied.

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REFERENCES

- 1 Jasinski DR, Pevnick JS, Griffith S. Human pharmacology and abuse potential of the analgesic buprenorphine. *Arch Gen Psychiatry* 1978; **35**: 501-16.
- 2 Kosten TR, Kleber HD. Buprenorphine detoxification from opioid dependence: a pilot study. *Life Sci* 1988; **42**: 635-41.
- 3 Johnson RE, Jaffe JH. A controlled trial of buprenorphine treatment for opioid dependence. *J Am Med Assoc* 1992; **267**: 2750-5.
- 4 Mello NK, Mendelson JH, Kuehnle JC. Buprenorphine effects on human heroin self-administration: an operant analysis.

- J Pharmacol Exp Ther 1982; **223**: 30-9.
- 5 American Psychiatric Association (APA): Diagnostic and statistical manual of mental disorders, 3rd ed rev (DSM-III-R). Washington DC: APA, 1987: 167-8.
- 6 Peachey JE, Lei H. Assessment of opioid dependence with naloxon. *Br J Addict* 1988; **83**: 193-7.
- 7 Littlejohns DW, Vere DW. The clinical assessment of analgesic drugs. *Br J Clin Pharmacol* 1981; **11**: 319-32.
- 8 Guy W. Assessment manual for psychopharmacology, revised. Rockville: DEW, 1976: 341-50.
- 9 Kosten TR. Neurobiology of abused drugs. *J Nerv Ment Dis* 1990; **178**: 217-27.
- 10 Madden S. Effects of drugs of dependence. In: Ghodse H, Maxwell D, editors. Substance abuse and dependence. London: Macmillan, 1990: 30.
- 11 Blaine J. Recent development in pharmacological treatment for drug abuse. *Psychopharmacol Bull* 1990; **26**: 69-73.
- 12 Schuster CR. Implications of laboratory research for the treatment of drug dependence. In: Goldberg SR, Stolerman IP, editors. Behavioral analysis of drug dependence. Orlando: Academic Press, 1986: 357-85.
- 13 O'Connor JJ. Buprenorphine abuse among opiate addicts. *Br J Addict* 1988; **83**: 1085-7.

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丁丙诺啡用于海洛因依赖的快速戒毒¹

刘志民, 蔡志基, 王小平², 葛云, 李春梅²
 (北京医科大学中国药物依赖性研究所, 北京 100083;
 西安市碑林戒毒治疗中心, 西安 710061, 中国)

关键词 物质撤除综合征; 丁丙诺啡; 舌下投药; 海洛因依赖

目的: 评价丁丙诺啡 7-8 d 递减法治疗海洛因戒断症状(戒毒)的临床疗效。 **方法:** 60 例海洛因成瘾者根据依赖程度分为三组, 分别给予低、中、高三种剂量丁丙诺啡舌下含服片剂治疗。 治疗期间患者戒断症状采用“美国临床研究所麻醉药品评价量表”评价; 对海洛因的心理渴求采用“视觉类比量表”自评; 丁丙诺啡副作用采用“副反应量表”评价。 **结果:** 三组戒毒患者丁丙诺啡平均日消耗量分别为 2.0, 2.9 和 3.6 mg。 此剂量的丁丙诺啡不仅可有效地控制海洛因戒断症状, 且可缩短戒毒时程。 **结论:** 丁丙诺啡是一个有希望替代纯阿片受体激动剂的有效、快速戒毒药物。