

# A case of heroin overdose reversed by sublingually administered buprenorphine/naloxone (Suboxone®)

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## ABSTRACT

**Background** Opioid overdose is a major source of morbidity and mortality in injection drug users in the United States and many other countries. **Case description** A case is described in which buprenorphine/naloxone (Suboxone®) was administered sublingually to reverse a heroin overdose. **Conclusions** Sublingually administered buprenorphine/naloxone might be used as a means to reverse opioid overdose.

**Keywords** Addiction, buprenorphine/naloxone, opioids, overdose, Suboxone.

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## INTRODUCTION

Opioid overdose is the single leading cause of death among injection drug users (IDUs) in the United States and in many developed countries. Opioid overdose accounts for more than half the deaths of heroin IDUs [1], far exceeding the proportion of deaths due to human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) [2, 3]. In addition to the burden of overdose mortality, IDUs suffer a high prevalence of non-fatal heroin overdoses. Studies have documented that a high percentage of IDUs have experienced at least one non-fatal overdose in their life-time: 38% in London [4], 41% in Baltimore [5], 48% in San Francisco [6] and 68% in Sydney [7]. Non-fatal opiate overdose is associated with numerous deleterious health outcomes, including pulmonary edema, pneumonia, cardiac arrhythmia, compartment syndrome, necrotizing fasciitis ('gangrene'), rhabdomyolysis, renal failure and cognitive impairment. These morbidities occur in a relatively small but significant proportion (5–10%) of opiate overdose cases [8].

Naloxone (known commonly by its trade name Narcan®) is a *mu* opioid receptor antagonist that is used routinely by emergency medical personnel to reverse the effects of opioid intoxication. In the United States, as in most countries, naloxone is regulated as an unscheduled prescription drug and is not available for broad distribution to opioid users. During the last 15 years, a number of

overdose prevention and naloxone distribution (OPND) programs have emerged in Australia, Europe and the United States [6, 9–11]. These programs have prescribed naloxone to thousands of IDUs and the programs in the United States have reported approximately 1000 overdose reversals [12].

To our knowledge, this is the first report of a case of the sublingual use of buprenorphine/naloxone to reverse a heroin overdose.

## CASE DESCRIPTION

A 28-year-old Caucasian male patient who is prescribed buprenorphine/naloxone (Suboxone®) 16/4 mg per day reported that he had been in a house where an 'acquaintance' overdosed on heroin. The acquaintance, a 24-year-old Caucasian male, had reportedly rapidly injected 'three or four dimes' of heroin and, within several minutes, 'he wasn't breathing and his lips turned blue'. 'He wouldn't wake up even when we rubbed his chest hard'. The individual reportedly had not used any benzodiazepines, prescription opioids or other illicit substances and had not been drinking alcohol.

Although one of the individuals in the room had learned about managing opioid overdose through the Baltimore City 'Staying Alive' (overdose prevention) program, no one present had naloxone. The patient who

was prescribed buprenorphine/naloxone had one of his 8/2 mg pills with him and, remembering that it could precipitate opioid withdrawal if used soon after a full opioid agonist, decided that it might work in this case. After placing the individual on his side (in the 'recovery position'), he rubbed a small amount of water under the individual's tongue 'because he didn't have much saliva'. He reports that, 'to make it work faster', he 'crumbled the pill a little' and placed the pieces under the individual's tongue. Within 'a couple' minutes, the patient began breathing and 'woke up all angry'. 'He didn't throw up but he retched some'. Although 911 (the emergency service) was called, the individual refused to go to the hospital. The patient who had administered the buprenorphine/naloxone remained with the individual for several hours, during which 'he was fine; he never went back out'.

## CONCLUSIONS

Buprenorphine is a semi-synthetic opioid derived from thebaine, a naturally occurring alkaloid of the opium poppy, *Papaver somniferum*. Although developed originally as an analgesic, its potential utility for the management of opioid dependence has been discussed since early research in the 1970s [13]. Buprenorphine exerts the majority of its effects at the *mu* opioid receptor where it acts as a partial agonist. Because of the relatively decreased activation (compared to a full agonist), there is a plateau of receptor activation with no further effect from further increase in dose.

Buprenorphine is absorbed readily through the gastrointestinal and mucosal membranes. However, due to extensive first-pass metabolism, buprenorphine has very poor oral bioavailability (10% of the intravenous route) if swallowed. Its availability is increased significantly with sublingual administration (30–50% of the intravenous route) [14,15], making this a feasible route of administration for the treatment of opioid dependence.

Because of its relatively unique pharmacology as a partial *mu* opioid receptor agonist with a very high binding affinity for the *mu* receptor, buprenorphine can both alleviate opioid withdrawal symptoms and precipitate them, depending upon the timing of when it is administered relative to the opioid. Typically, if administered within several hours following a short-acting opioid such as heroin, withdrawal will be precipitated; if administered once symptoms of withdrawal have occurred (the amount of time is dependent upon the half-life of the opioid, the amount of opioid taken and individual tolerance), withdrawal will be alleviated. These times may be prolonged considerably when administered following a long-acting opioid such as methadone, especially if the methadone has been taken chronically. Because of the

very high binding affinity for the *mu* opioid receptor, buprenorphine readily displaces most other opioids from the receptor and prevents others from binding. It also allows the clinical effects of buprenorphine to last significantly longer than would be expected based solely upon its elimination half-life.

A combination pill, buprenorphine/naloxone, is available in the United States under the trade name Suboxone<sup>®</sup>. Because naloxone is absorbed poorly sublingually, its effect is minimal when the tablet is taken properly. However, if the tablet is dissolved and injected, the naloxone blocks *mu* receptors and prevents receptor activation or precipitates withdrawal in opioid-dependent patients. When taken sublingually, the opioid withdrawal precipitated by buprenorphine/naloxone (Suboxone<sup>®</sup>) appears to be due almost exclusively to the buprenorphine's partial agonist properties and its high *mu* opioid receptor binding capacity, not the naloxone. Because of this, there is no reason that the buprenorphine mono-product available in many countries would not work in a similar manner to buprenorphine/naloxone (Suboxone<sup>®</sup>) in reversing an opioid overdose.

Because of the ceiling effect of *mu* opioid receptor activity, buprenorphine appears to be a very safe medication in overdose. Although there are reports of fatal overdose involving buprenorphine and benzodiazepines [16,17], these reports have all come from Europe (where the buprenorphine/naloxone combination is not used) and generally involved individuals who appear to have injected higher doses of benzodiazepines with dissolved buprenorphine tablets. To the best of our knowledge, there are no reports of life-threatening buprenorphine overdoses when taken orally or sublingually.

Although certainly not approved for this indication, it might be useful for programs concerned with public health issues related to opioid use (such as overdose prevention) to be aware of the potential use of buprenorphine and buprenorphine/naloxone for the reversal of opioid overdose in life-threatening situations where no other option is available. Buprenorphine's relatively long duration of action at the *mu* opioid receptor might even provide an advantage over naloxone, which has a relatively short duration of action and must be re-administered often to treat re-emergence of respiratory depression, especially in the case of overdose on longer-acting opioids. Because of the reported cases of fatal overdose when used concurrently with higher dose of intravenous benzodiazepines, caution should be heeded in opioid overdoses where sedative-hypnotic co-ingestion is suspected.

## References

1. Sporer K. A. Acute heroin overdose. *Ann Int Med* 1999; 130: 584–90.

2. Frischer M., Bloor M., Goldberg D., Clark J., Green S., McKeganey N. Mortality among injecting drug users: a critical reappraisal. *J Epidemiol Commun Health* 1993; **47**: 59–63.
3. Tyndall M. W., Craib K. J., Currie S., Li K., O'Shaughnessy M. V., Schechter M. T. Impact of HIV infection on mortality in a cohort of injection drug users. *J Acquir Immune Defic Syndr* 2001; **28**: 351–7.
4. Strang J., Powis B., Best D., Vingoe L., Griffiths P., Taylor C. *et al.* Preventing opiate overdose fatalities with take-home naloxone: pre-launch study of possible impact and acceptability. *Addiction* 1999; **94**: 199–204.
5. Tobin K. E., Latkin C. A. The relationship between depressive symptoms and nonfatal overdose among a sample of drug users in Baltimore, Maryland. *J Urban Health* 2003; **80**: 220–9.
6. Seal K. H., Kral A. H., Gee L., Moore L. D., Bluthenthal R. N., Lorvick J. *et al.* Predictors and prevention of nonfatal overdose among street-recruited injection heroin users in the San Francisco Bay Area, 1998–1999. *Am J Public Health* 2001; **91**: 1842–6.
7. Darke S., Williamson A., Ross J., Mills K. L., Havard A., Teesson M. Patterns of nonfatal heroin overdose over a 3-year period: findings from the Australian treatment outcome study. *J Health* 2007; **84**: 83–91.
8. Warner-Smith M., Darke S., Lynskey M., Hall W. Heroin overdose: causes and consequences. *Addiction* 2001; **96**: 1113–19.
9. Galea S., Worthington N., Piper T. M., Nandi V. V., Curtis M., Rosenthal D. M. Provision of naloxone to injection drug users as an overdose prevention strategy: early evidence from a pilot study in New York City. *Addict Behav* 2006; **31**: 907–12.
10. Maxwell S., Bigg D., Stanczykiewicz K., Carlberg-Racich S. Prescribing naloxone to actively injecting heroin users: a program to reduce heroin overdose deaths. *J Addict Dis* 2006; **25**: 89–96.
11. Piper T. M., Rudenstine S., Stancliff S., Sherman S., Nandi V., Clear A. *et al.* Overdose prevention for injection drug users: lessons learned from naloxone training and distribution programs in New York City. *Harm Reduct J* 2007; **4**: 3.
12. Sporer K., Kral A. Prescription naloxone: a novel approach to heroin overdose prevention. *Ann Emerg Med* 2007; **49**: 172–7.
13. Jasinski D. R., Pevnick J. S., Griffith J. D. Human pharmacology and abuse potential of the analgesic buprenorphine: a potential agent for treating narcotic addiction. *Arch Gen Psychiatry* 1978; **35**: 501–16.
14. Mendelson J., Jones R. T., Welm S., Baggott M., Fernandez I., Melby A. K. *et al.* Bioavailability of sublingual buprenorphine. *J Clin Pharmacol* 1997; **37**: 31–7.
15. Kuhlman J. J., Lalani S., Maglullo J., Levine B., Human Darwin W. D. Pharmacokinetics of intravenous, sublingual, and buccal buprenorphine. *J Clin Pharmacol* 1997; **37**: 31–7.
16. Tracqui A., Kintz P., Ludes B. Buprenorphine-related deaths among drug addicts in France: a report of 20 fatalities. *J Anal Toxicol* 1998; **22**: 430–4.
17. Auriacombe M., Franques P., Tignol J. Deaths attributable to methadone vs. buprenorphine in France. *JAMA* 2001; **285**: 45.