Is subcutaneous or intramuscular naloxone as effective as intravenous naloxone in the treatment of life-threatening heroin overdose?

Clinical question

"Is subcutaneous (SC) or intramuscular (IM) naloxone as effective as intravenous (IV) naloxone in the treatment of life-threatening heroin overdose?" An emergency department clinician was interested in comparing routes of administration of naloxone in light of anecdotal evidence suggesting that various routes may not be equally efficacious in restoring a patient to spontaneous breathing and consciousness.

Search question

Patients presenting to an emergency department for the management of a heroin overdose were the focus of the search strategy. The search question was *"How long does it take for patients to return to consciousness after administration of naloxone by various routes?"*. In order to answer this question, a randomised controlled trial comparing the effects of SC or IM versus IV naloxone would be the ideal study design.

Search

The search terms "heroin", "opioid overdose", "naloxone" and "route of administration" were combined to identify relevant English-language articles published between 1966 and June 2000. Databases and websites searched included the *Cochrane Library*, *Best Evidence*, *PubMed*, *CINAHL* (Cumulative Index to Nursing and Allied Health Literature), *Smart Search* and *Bandolier*. Studies other than those set in the emergency department (ie, those conducted in hospital wards or post-anaesthetic care units) were excluded, as the clinician had specified that we limit the search to pre-hospital or emergency department settings. The search yielded only one study that compared SC with IV naloxone for treating opioid overdose in this setting. No studies were found comparing the use of IM with IV naloxone.

Summary of findings

In a comparative study using historical controls, Wagner et al[1] compared naloxone administered intravenously or subcutaneously to patients in the community with suspected opioid overdose. The two intervention arms were 0.4 mg IV naloxone and 0.8 mg SC naloxone.

The study was conducted sequentially in two phases: the IV phase, from 1 June to 30 June 1996, and the SC phase, from 1 July to 1 September 1996. Ambulance attendants in a regional district of British Columbia, Canada, administered naloxone to people meeting the British Columbia Ambulance Services' criteria for suspected overdose (ie, reduced consciousness, history suggestive of opioid use, and respiratory rate of less than 10 breaths per minute). The protocol also included a second dose of SC or IV naloxone if the first dose was not observed to be physiologically effective.

The primary outcomes of interest included the time interval from arrival at the patient's side until the respiratory rate rose above 10 breaths per minute, the time interval from arrival at patient's side to naloxone administration, and the duration of bag–valve–mask ventilation. Overall, there was no significant difference between the two modes of naloxone administration with regard to the time interval between arrival at the patient's side and attainment of a respiratory rate greater than 10 breaths per minute (9.3 ± 4.2 minutes [IV] v 9.6 ± 4.6 min [SC]; $P = 0.67$). There was also no significant difference in duration of respiratory bag–valve–mask ventilation between administration arms (8.1 ± 6.0 minutes [IV] v 9.1 ± 4.8 minutes [SC]; $P = 0.20$; 95% CI of difference, –2.53 to 0.53).

Outcome

We submitted the report to the emergency physician, stating that the single study in a community setting demonstrated that IV and SC naloxone administration appeared to be equally effective in returning patients suffering from opioid overdose to spontaneous breathing. However, we advised the physician that the study was subject to a number of biases, including the utilisation of historical controls, a lack of clear randomisation, and the recruitment of fewer patients (74) than the 92 required to achieve 90% power. The physician used the information from our report to change the emergency department's policy — the use of IV naloxone was eliminated to reduce the risk of needlestick injury to staff.

Jason Wasiak
Research Officer
Ornella Clavisi
Research Officer
Centre for Clinical Effectiveness
Monash Institute of Health Services Research
Clayton, VIC
cce@med.monash.edu.au

Reference

1. Wagner K, Brough L, MacMillan I, et al. Intravenous vs subcutaneous naloxone for out of hospital management of presumed opioid overdose. *Academy of Emergency Medicine* 1998; 5: 293-299.

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