Table 4

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Goldfrank L *et al*, 1986, USA	7 patients attending an ED with symptoms of opioid overdose, given single boluses of naloxone	Observational	Phase one: Serial naloxone levels	Construction of a dosing nomogram from the pharmacokinetic data obtained	Small study with a high drop out rate (20% in phase two). The revised nomogram has not been tested on a repeated phase two study
			Phase two: Serial naloxone levels; Comparing the measured levels with target levels predicted by the nomogram	Levels measured in phase two were consistently higher than those predicted by the nomogram; the nomogram was adjusted and tested with a computer simulation	

Three part question
In [patients acutely intoxicated with opioids] is [intravenous infusion of naloxone better than repeated bolus doses] at reducing [the risk of precipitation of acute withdrawal symptoms]?

Search strategy
Medline 1966–09/01 using the OVID interface. [{exp naloxone OR naloxone.mp} AND {exp infusions, intravenous OR exp injections, intravenous} AND {exp narcotics OR opioid.mp OR opiate.mp OR morphine.mp OR buprenorphine.mp OR codeine.mp OR dextromoramide.mp OR diphenoxylate.mp OR dipipanone.mp OR dextropropoxyphene.mp OR diamorphine.mp OR dihydrocodeine.mp OR alfentanil.mp OR fentanyl.mp OR remifentanil.mp OR meptazinol.mp OR methadone.mp OR nalbuphine.mp OR oxycodone.mp OR pentazocine.mp OR pethidine.mp OR phenazocine.mp OR tramadol.mp}] LIMIT to human AND English.

Search outcome
Altogether 188 studies were found of which five addressed the question directly (table 4).

Comment(s)
It was found that there was large variation in factors determining plasma naloxone concentrations between people, and the nomogram was constructed to ensure that those who eliminate naloxone rapidly would not experience a reduction in levels and thus risk renarcotisation. This leads to an overestimation of the infusion rate for those who eliminate naloxone more slowly with the theoretical risk of precipitation of acute withdrawal symptoms. A practical regimen for titrating naloxone by infusion for opioid overdose has been calculated: (1) titrate the initial bolus of naloxone against clinical effect; (2) start an infusion of naloxone, giving two thirds of the initial bolus per hour; (3) consider a second bolus (at half of the initial dose) after 15 minutes, if there are signs of reduced respiratory rate or conscious levels. Further research is needed to: validate the regimen against clinical criteria; assess whether it is possible in practice to titrate the patient's response to a "safe" level (for example, breathing with a safe airway and a GCS of 14/15 rather than a GCS of 15/15 but agitated and at risk of leaving the ED prematurely) and compare the regimen with other routes of administration.

▸ CLINICAL BOTTOM LINE
A practical regimen for titrating naloxone by infusion for opioid overdose has been calculated.

Goldfrank L, Weisman RS, Errick JK, *et al*. A dosing nomogram for continuous infusion intravenous naloxone. *Ann Emerg Med* 1986;**15**:566–70.

Discharge of patients who have taken an overdose of opioids

Report by Simon Clarke, *Specialist Registrar*
Checked by Paul Dargan, *Specialist Registrar*

Abstract
A short cut review was carried out to establish whether patients with no recurrence of symptoms one hour after receiving naloxone for an opioid overdose can safely be discharged. Altogether 195 papers were found using the reported search, of which five presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
A 30 year old opioid addict is brought to the emergency department having overdosed on heroin. He is successfully treated with a titrated bolus of naloxone. You wonder when it will be safe to discharge the patient.

Three part question
In [patients given naloxone for the treatment of opioid overdose] is [a lack of recurrence of symptoms after one hour] a sensitive predictor for [safe discharge from the department]?

Search strategy
Medline 1966–09/01 using the OVID interface. [{exp narcotics OR opioid.mp OR opiate.mp OR morphine.mp OR buprenorphine.mp OR codeine.mp OR dextromoramide.mp OR diphenoxylate.mp OR dipipanone.mp OR dextropropoxyphene.mp OR diamorphine.mp OR heroin.mp OR alfentanil.mp OR fentanyl.mp OR remifentanil.mp OR meptazinol.mp OR methadone.mp OR nalbuphine.mp OR oxycodone.mp OR pentazocine.mp OR pethidine.mp OR phenazocine.mp OR tramadol.mp} AND {exp overdose OR overdos$.mp OR exp poisons OR poison$.mp OR "acute intoxic$".mp OR "acute toxic$".mp} AND {exp patient admission OR admission.mp OR exp patient discharge OR discharge.mp OR observ$.mp OR monitor$.mp OR predict$.mp}] LIMIT to human AND English.

Table 5

Author, date and country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Smith DA *et al*, 1992, USA	124 patients presenting to an ED with a heroin overdose	Observational	Time to decision	20 min	Treatments given were neither standardised nor randomised so analysis of outcome could not be performed in relation to mode of treatment. Follow up was poor so it is possible that patients who sought further treatment or who died elsewhere would have been missed.
			Further treatment after discharge	None	
Osterwalder JJ, 1995, Switzerland	192 patients attending an ED with clinical suspicion of opioid od	Observational	Time to decision	15 min	No attempt was made to compare the outcomes of different treatment modes The period of observation in the ED was not recorded.
			Reattendance if discharged	1 patient died	
Watson WA *et al*, 1998, USA	84 patients attending an ED who had been given naloxone for a presumed opioid od	Observational	Subsequent recurrence of opioid toxicity	Patients who have taken a longacting opioid are more likely to experience a recurrence of toxicity	No follow up of patients was attempted after admission to hospital/discharge from the ED to assess the incidence of late complications. The period of observation in the ED was not recorded.
Vilke GM *et al*, 1999, USA	317 patients with a clinical suspicion of opioid od who refused to be transported to the ED after being given naloxone by the paramedics	Observational	Death	No patients treated with naloxone died	Variable doses and routes of administration of naloxone were used.
			Reattendence of the ambulance within 12 hours	Nil	No follow up of patients was attempted to ascertain if they received subsequent treatment or died in another area or attended the ED by other means of transport.
Christenson J *et al*, 2000, Canada	573 patients attending an ED with clinical evidence of opioid intoxication who had been given naloxone either in the prehospital setting or ED	Observational	Clinical prediction rule to predict safe discharge	Patients can be safely discharged one hour after administration of naloxone if they have normal mobility, SpO_2 >92%, respiratory rate 10–20/min, heart rate 50–100/min , temperature 35–37.5°C, GCS 15/15	The rule has not been validated yet. The pattern of drug misuse in Vancouver is different from other cities, so there are concerns about whether these results can be applied to different populations (for example, those that misuse a higher proportion of longer acting agents).

Search outcome

Altogether 194 papers found. Of these only five were relevant to the preoperative setting (table 5).

Comment(s)

The evidence consists of observational studies, three of which are retrospective reviews of medical records and thus there are concerns regarding the reliability of the data collected. In addition, only Christenson's study attempts to apply a "rule out" strategy by attempting to identify the clinical variables that predict a low risk of delayed complications from the opioid overdose. Further work is required to validate the rule in different populations by further prospective studies. Also, comparative trials need to be undertaken to assess the validity of the rule for different opioid overdoses.

▸ CLINICAL BOTTOM LINE

The evidence suggests that if a patient remains well one hour after administration of naloxone, then it is safe to discharge them.

Smith DA, Leake L, Loflin JR, *et al*. Is admission after intravenous heroin overdose necessary? *Ann Emerg Med* 1992;**21**:1326–30.
Osterwalder JJ. Patients intoxicated with heroin or heroin mixtures: how long should they be monitored? *Eur J Emerg Med* 1995;**2**:97–101.
Watson WA, Steele MT, Muelleman RL, *et al*. Opioid toxicity recurrence after an initial response to naloxone. *J Toxicol Clin Toxicol* 1998;**36**:11–17.
Vilke GM, Buchanan J, Dunford JV, *et al*. Are heroin overdose deaths related to patient release after prehospital treatment with naloxone? *Prehospital Emerg Care* 1999;**3**:183–6.
Christenson J, Etherington J, Grafstein E, *et al*. Early discharge of patients with presumed opioid overdose: development of a clinical prediction rule. *Acad Emerg Med* 2000;**7**:1110–18.

Gastric lavage in iron overdose

Report by Stuart Teece, *Research Fellow*
Search checked by Ian Crawford, *Research Fellow*

Abstract

A short cut review was carried out to establish whether gastric lavage is of use after an overdose of ionic compounds. Altogether 74 papers were found using the reported search but none answered the question posed.

Clinical scenario

A 29 year old woman presents to the emergency department 30 minutes after swallowing 40 lithium tablets. Given the recent onset and the apparent low efficacy of activated charcoal in ionic compounds you wonder whether she is a candidate for gastric lavage.

Three part question

In [overdose with ionic compounds] is [gastric lavage better than no treatment] at [reducing toxicity]?

Search strategy

Medline 1966–01/02 using the Ovid interface. [exp irrigation OR lavage.mp OR exp gastric lavage OR gastric lavage.mp OR exp gastric emptying OR gastric emptying.mp OR washout.mp] AND [(exp iron OR iron.ar OR exp iron compounds OR exp ferrous compounds OR ferrous.ar OR exp ferric compounds OR ferric.ar)] AND [exp poisoning OR poisons.ar OR