

KEY MESSAGES

- The management of calcium channel blocker overdose often requires a multitude of pharmacological agents with scarce evidence for their use
- Patients can deteriorate quickly and prompt administration of medications is vital to achieve cardiovascular stability and a good neurological outcome
- In cases where pharmacological management has failed, consideration should be given to emergency extracorporeal life support as a resuscitative tool

CASE PRESENTATION

- 64 male
- Intentional overdose of 840 mg nimodipine
- Past medical history of hypertension, type 2 diabetes mellitus, depression, psychosis and gastro-oesophageal reflux disease
- On arrival,
 - A: patent
 - B: tachypnoeic
 - C: extreme cardiogenic shock, bradycardia at 54 beats per minute and systolic blood pressure of 46 mmHg
 - D: Glasgow Coma Scale was 15, pupils equal and reactive, glucose 11.9
 - E: rectal temperature of 32.4 degrees Celsius

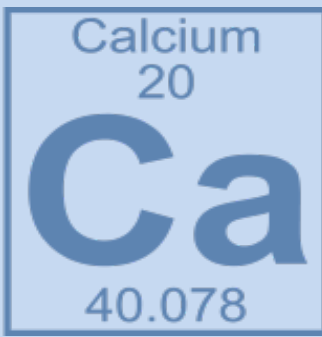


GASTRIC DECONTAMINATION

- Buckley et al (1993): 1 survived, 1 haemodynamic instability
- Belson et al (2000): no major adverse effects (retrospective review of 174 patients)
- Cumpston et al (2010): hyperemesis and haemodynamic instability (2 patients)
- Lo et al (2012): no major adverse effects (retrospective review of 57 patients)

CALCIUM

- Mechanism: overcome competitive blockade
- 7 animal studies: short-lived improvement in cardiac output and blood pressure, little to no effect on heart rate
- 3 observational human studies: inconsistent results, but all show some temporising inotropic benefits
- Reasonable starting regime: 0.6 mL/kg 10% calcium gluconate followed by infusion at 0.6-1.5 mL/kg/hour



GLUCAGON

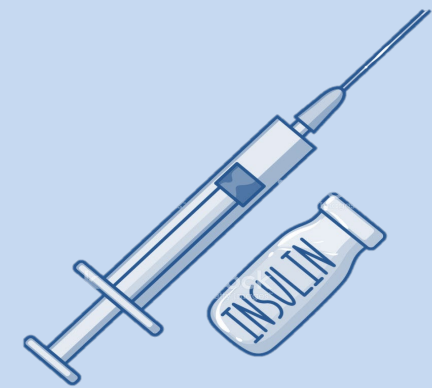
- Mechanism: positive inotropic and chronotropic effects (via cAMP)
- In-vivo: direct reversal of myocardial depression
- Experimental animal studies: improvements in heart rate and cardiac output
- 4 case reports/series: inconsistent results, with no dose-response relationship observed



INTRALIPID

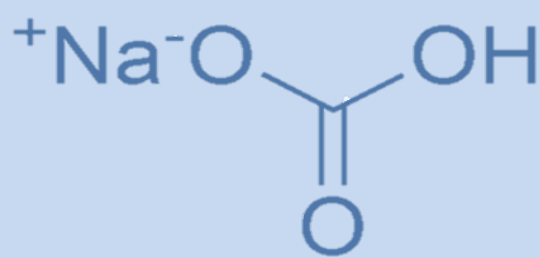
- Mechanism: halt redistribution of lipophilic drug
- 5 case reports showed positive effects on heart rate and blood pressure
- 1 case report showed no improvement, but instead caused interference in biochemical assays and blood gas oxygenation status

EVIDENCE FOR USE



HIGH-DOSE INSULIN (EUGLYCAEMIC) THERAPY

- Mechanism: In haemodynamic shock, glucose is preferred metabolic source for myocardium. Facilitation of glucose transport into myocardial cells improves oxygenation and hence activity. Additionally, it has positive inotropic effects (via phosphatidylinositol-3-kinase) and vasodilates terminal arterioles
- 4 animal studies, 5 human case series and 2 observational studies show improvements in cardiovascular status and survivability
- Reasonable starting regime: 1 U/kg insulin followed by an infusion of 1 U/kg/hr, euglycaemia maintained with a dextrose infusion



SODIUM BICARBONATE

- Mechanism: reduces the affinity of calcium channel blockers to L-type calcium channels and reverses sodium channel blockade in severe overdose
- No convincing data available
- Reasonable starting regime: 1 to 2 mEq/kg aliquots followed by an infusion

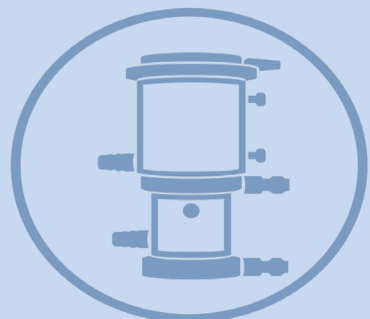
CATECHOLAMINE ADRENERGIC RECEPTOR AGONISTS

- No one agent superior to the other
- Noradrenaline and adrenaline (α - and β -adrenergic properties) for depressed myocardial contractility and decreased peripheral resistance
- Dobutamine (predominantly β_1 -agonist) for cardiac decompensation secondary to depressed contractility
- Isoprenaline (non-selective β -agonist) showed improvement in haemodynamic status in 1 case report and 3 patients in 1 case series, but can worsen peripheral resistance and cause hypotension
- Vasopressin: 2 experimental animal studies show worsened survival; 2 case series (involving 4 patients) show blood pressure improvement



METHYLENE BLUE

- Mechanism: inhibit nitric oxide-cGMP pathway
- 2 case studies report improvement within 1 hour and rapid weaning of vasopressors
- Reasonable starting regime: 1-2 mg/kg/h



EXTRACORPOREAL LIFE SUPPORT

- At least one case showing good survival outcome
- Three observational studies report similar findings following overdoses of other cardiotoxic drugs

“five days following presentation, he was decannulated from ECMO and extubated 11 days later. He sustained hypoxic brain injury with a Cerebral Performance Category 3 and renal failure requiring dialysis ”

“he is able to perform some activities of daily living independently and communicate his thoughts and needs. He has no respiratory or cardiovascular support, is undergoing physical rehabilitation and is awaiting placement”

MANAGEMENT

Time (24 hours)		1400	1415	1430	1445	1500	1515	1530	1545	1600	1615	1630	1645	1700	1715	1730	1745	1800
Respiratory rate		30	32	32	33	26	224	22	26	25	25	25	27	37	20	22	24	24
Saturations (%)		91.6	94.6	94	100	100	100	100	100	100	100	100	100	92.6	93.6	96	100	100
Oxygen delivery		Facemask	-->	-->	-->	-->	-->	-->	-->	-->	-->	-->	-->	-->	intubated	-->	-->	-->
FiO2		15 litres	-->	-->	-->	-->	-->	-->	-->	-->	-->	-->	-->	-->	100%	80%	-->	-->
Blood pressure (mmHg)	Systolic	46	65	58	54	94	39	44	41	42	58	46	62	47	45	49	36	42
	Diastolic	35	37	38	37	72	23	35	24	20	37	26	35	28	27	31	26	35
Heart rate (beats per minute)		54	52	53	62	61	54	61	53	58	60	64	62	62	83	56	58	64
Ephedrine (mg) Metaraminol (mg) Adrenaline (250 µg) Dobutamine (250 µg in 50 mls normal saline) Atropine (µg) Glucagon (mg) Calcium gluconate 10% (mls) Intralipid (mls) Sodium bicarbonate 8.4% (mls) Normal saline (mls) Potassium (mmol) High-dose insulin therapy Fentanyl (µg)		6+3 1 100 100 100 900 infusion --> --																