Investigation vignette

A 22 Year old Man Admitted to Intensive Care with Hyperthermia and Seizures

CASE REPORT

A 22 year old man was admitted to the intensive care unit following ingestion of an unknown amount of alcohol and 3,4 methylene dioxymethamphetamine ('ecstasy'). In the accident and emergency department he began to have seizures and was promptly intubated with an 8.0 mm endotracheal tube, 10 mg of midazolam and 8 mg of vecuronium, and mechanically ventilated. His vital signs revealed sinus tachycardia with a pulse rate of 170 beats per minute, a blood pressure 90/50 mmHg and a temperature of 41.1°C.

The patient was admitted to the intensive care unit and a venovenous extracoproreal circulation was established to allow direct circulatory cooling. He remained sedated with intravenous morphine (2 mg/hr), midazolam (2 mg/hr) and a 1% propofol infusion. The plasma biochemical profile performed immediately on arrival (9.11) is shown in figure 1.

Following 4 hours of extracoporeal cooling his vital signs improved with his pulse slowing to 118 beats per minute, blood pressure increasing to 115/60 mmHg and temperature decreasing to 36.5°C. However, throughout the next 5 days he remained mechanically ventilated, requiring intermittent vecuronium, morphine, midazolam and propofol as he became agitated and hypoxic when these agents were withdrawn. The plasma biochemical profile performed on the fifth day following admission (14.11) is also shown in figure1.

Name	Age	Sex
Mr. J. T.	22	M

	9.11	**14.11**		
Sodium	145	136	mmol/L	(135 - 145)
Potassium	4.5	3.8	mmol/L	(3.2 - 4.3)
Chloride	111	97	mmol/L	(99 - 109)
Bicarbonate	27	30	mmol/L	(21 - 32)
Glucose	5.8	9.6	mmol/L	(3.0 - 6.0)
Urea	10.2	10.6	mmol/L	(3.0 - 8.0)
Creatinine	0.148	0.078	mmol/L	(0.05 - 0.10)
Phosphate	0.91	1.01	mmol/L	(0.75 - 1.40)
Total Calcium	1.95	2.32	mmol/L	(2.00 - 2.55)
Albumin	35	34	g/L	(31 - 44)
Globulins	28	37	g/L	(21 - 49)
CK	4495	582	U/L	(< 150)
ALT	543	153	U/L	(10 - 50)
AST	462	76	U/L	(10 - 40)
GGT	44	131	U/L	(< 40)
ALP	63	139	U/L	(30 - 110)
Total bilirubin	20	20	µmol/L	(4 - 20)
Amylase	68	39	U/L	(< 100)
Triglycerides	0.4	10.7	mmol/L	(< 2.0)

Figure 1. Plasma biochemical profiles performed on arterial blood taken from the patient on admission and 5 days later.

Diagnosis: Ecstasy induced rhabdomyolysis and propofol induced hypertriglyceridaemia

Ecstasy or 3,4 methylene dioxymethamphetamine (MDMA) is chemically related to amphetamine, and has both stimulant and hallucinogenic effects. Although it is often perceived by adolescents as being a 'safe' drug, MDMA is associated with significant morbidity and mortality, largely due to the disturbances it causes in thermoregulation. The acute adverse effects range from a mild disorder of tremor, headache, excessive sweating, blurred vision and muscle cramps (especially jaw muscles), to the severe and potentially fatal effects of hyperthermia, seizures, rhabdomyolysis, disseminated intravascular coagulation, multiorgan failure and death.[1,2]

Treatment for the life threatening effects of hyperthermia and seizures usually requires intubation and ventilation using benzodiazepines to control the seizures and methods for surface and core cooling to correct the hyperthermia. Continuous venovenous haemodialysis or haemofiltration with cold replacement fluids is effective when rapid core cooling is required and was successfully used in this case. While intubation and sedation was required to manage the seizures it was also beneficial in reducing the heat generated by the excessive skeletal muscle activity. The rhabdomyolysis that developed (plasma creatine phosphokinase on admission 4495 U/L) responded to resuscitation and cooling (plasma creatine phosphokinase 5 days later 582 U/L), averting the development of acute renal failure.

The patient required prolonged sedation and relaxation as he became tachypnoeic, hypoxic and agitated during the first five days when the sedation was discontinued. Propofol 1% was used in amounts that varied between 3 - 20 mL/hr (0.5 - 3.0 mg/kg/hr) to supplement the morphine, midazolam and vecuronium, causing severe hypertriglyceridaemia (10.2 mmol/L) by the 5th day of his admission.

Propofol (2,6, diisopropylphenol) is commonly formulated as a 10 mg/mL soya bean oil in water emulsion identical to that of Intralipid 10% (i.e. 100 mg/mL). It is generally accepted that intravascular metabolism of the artificial chylomicrons in Intralipid, closely resembles that of chylomicrons.[3] Intralipid side-effects include thrombocytopenia, urticaria, diarrhoea, confusion, enhanced bacterial virulence (due to reduced neutrophil chemotaxis, phagocytosis, and impaired reticuloendothelial system function), pancreatitis, sinus bradycardia and hypoxia.[4-9] A severe fat overload syndrome (e.g. hyperchylomicronaemia, fever, hepatosplenomegaly, coagulopathy, pancreatitis) has also been reported following an intravenous lipid infusion, requiring plasmapheresis to reduce the plasma chylomicron levels.[10]

The total amount of lipid administered in our patient during the five day period was 112 gm (1.5 gm/kg/5days) and well below the maximum clearance rate of chylomicrons reported in health (2.9 gm/kg/24 hr),[11] and below the maximum recommended rate of infusion of Intralipid (2.5 gm/kg/24 hr).[12] However, the plasma triglyceride level remained > 2.0 mmol/L for the next three days, reducing to 1.8 mmol/L on the fourth day after propofol had been discontinued.

Propofol as a single sedative agent used for 3 or more days has been associated with metabolic acidosis, bradycardia, progressive and unresponsive myocardial failure, lipaemic serum (due to an impaired fatty acid oxidation[13]) and death, in five paediatric intensive care patients.[14] There have also been numerous reports of hypertriglyceridaemia when propofol was used for a prolonged period in critically ill patients,[15-17] two of whom had pancreatitis.[18,19] Unexplained cardiac arrest has also been reported in mechanically ventilated head injured patients who were sedated with high doses of propofol (> 5 mg/kg/hr) for 4 - 5 days.[20,21] In one report of five patients, rhabdomyolysis, acidosis and ventricular arrhythmias preceeded the cardiac arrest,[20] whereas in another report of three patients the increase in creatine phosphokinase, hyperkalaemia and metabolic acidosis did not preceed the cardiac arrest.[21]

While propofol has the advantage of being a rapid onset/offset sedative agent in the management of the critically ill patient, it is not without hazard. It should be used at a rate no greater than 5 mg/kg/hr and daily triglyceride estimations should be performed. If the plasma triglyceride levels are consistently > 5.0 mmol/L, the infusion should be discontinued.

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