

4. Brivet FG, Kleinknecht DJ, Loirat P, Landais P, French Study Group on acute renal failure (1996) Acute renal failure in intensive care units. Causes, outcome, and prognosis factors of hospital mortality: a prospective, multicenter study. *Crit Care Med* 24:192-198
5. Lang S, Kuchle C, Fricke H, Schiffel H (1995) Biocompatible intermittent hemodialysis. *New Horiz* 3:680-687

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Hypertriglyceridaemia associated with propofol sedation in critically ill patients

Received: 28 April 1995

Accepted: 11 April 1996

Sir: Propofol is a short-acting anaesthetic, formulated as a 10% soybean oil emulsion. Currently, it is administered in intensive care units (ICUs) in long-term infusions as a sedative agent. We report on 5 cases in which hyperlipaemia is attributed to propofol infusion. All 5 were collected in our 14-bed general ICU over 2 months from among 12 patients who had been sedated with propofol.

The 5 patients (details in Table 1) who presented with hypertriglyceridaemia received propofol doses of 3-8 mg/kg per h, with infusions lasting between 10 and 187 h. Patient number 4 received two separate infusions. The propofol emulsion was the only source of lipids. They also received a moderate intake of glucose.

The remaining 7 patients had not presented hypertriglyceridaemia (values from 0.69 to 1.60 mmol/l). They were 5 men and 2 women, aged between 53 and 69 years, weighing between 55 and 105 kg. There were 3 cases of respiratory failure, 2 cases of peritonitis, 1 case of post-operative gastric surgery and 1 case of multiple injuries. Propofol doses ranged from 1 to 3 mg/kg per h and infusions lasted between 24 and 94 h. This corresponded to a lipid intake of 30-50 g daily.

All 12 patients were discharged home.

Triglyceridaemia was determined in all cases by an enzymatic colorimetric test using the glycerol-phosphate oxidase method. Hypertriglyceridaemia has not been accurately evaluated in long-term infusions of propofol. Gottardis et al. [1] concluded from their study that lipaemia was not significantly influenced by propofol after a 3-day infusion. However, they used moderate doses (about 2 mg/kg per h), corresponding to low doses of lipids (less than 0.7 g of lipids/kg per day). Moreover, the only patient with hypertriglyceridaemia (lipids > 5.6 mmol/l) was excluded from the study because he had inadvertently received 20 g of lipids. Carrasco et al. [2], with mean doses of 2.36 mg/kg per h, found that triglyceridaemia had doubled from baseline values in 10 of 22 patients monitored

Table 1 Characteristics of five patients who presented hypertriglyceridaemia post-propofol infusion

	Patient no.				
	1	2	3	4	5
Age (years)	25	22	18	36	29
Sex	Male	Female	Male	Male	Male
Weight (kg)	55	60	65	100	60
Diagnosics	Status epilepticus secondary to cerebral toxoplasmosis (HIV+)	Multiple injuries (haemothorax, rib and pelvic fractures)	Cranial trauma brain oedema and multiple fractures	Heatstroke, shock and acute renal failure	Brain oedema, lung contusion, pneumothorax
Glucose intake (g/day)	75	75	175	150	100
Propofol dose (mg/kg per h)	6	6-8	5	1st infusion: 3 2nd infusion: 3	5
Propofol infusion duration (h)	10	106	96	1st infusion: 187 2nd infusion: 18	120
Lipid intake (g/day)	33	100	78	72	72
Triglyceridaemia (mmol/l) ^a /glucaemia (mmol/l) ^b					
Before propofol	2.13/8.7	-/-	-/-	0.47/7.2	-/-
During propofol	-/-	4.37/3.5 (54 h) ^c	-/-	-/-	9.54/7.0 (86 h) ^c
2 h post-propofol	3.46/5.4	-/-	3.86/6.2	1st infusion: 8.07/7.2 2nd infusion: 5.69/6.0	-/-
24 h post-propofol	3.52/8.0	1.32/6.8	1.53/6.7	3.88/5.1	-/-
48 h post-propofol	3.64/10.0	1.40/8.8	1.17/6.5	-/-	2.40/5.4
> 48 h post-propofol	2.09/4.9 (3 weeks)	1.15/4.7 (2 weeks) ^c	1.06/5.0 (1 week) ^c	3.37/6.5 (5 days) ^c 1.77/4.9 (4 weeks) ^c	-/-

^a Normal values of triglyceridaemia: 0.34-1.7 mmol/l

^b Normal values of glucaemia: 3.5-5.5 mmol/l

^c Time of measurement

for blood lipids. Eddleston and Shelly [3] presented a patient who needed up to 6.4 mg/kg per h of propofol. His triglyceridaemia reached 5.6 mmol/l.

The evolution of lipaemia in our patients suggests a relationship with propofol. Although patient number 1 possibly had a prior alteration in fat metabolism, his baseline lipaemia was abnormal. The propofol doses we used are relatively high, but the emulsion furnished a moderate load of triglycerides (from 0.6 to 1.5 g lipids/kg per day), far from the maximum recommended dose for parenteral nutrition in critically ill patients, assumed [4] to be 2.5 g of fat/kg per day. Hypertriglyceridaemia has been reported with doses corresponding to 1.8–3.6 g of fat/kg per day [5], but not with infusions of 100 g lipids/day [6], similar to ours. Therefore, the hypertriglyceridaemia in our patients does not seem directly correlated to the quantity of lipids received. Rather, it could be hypothesized that propofol per se somehow alters triglyceridaemia. This would occur when propofol doses approach 5–6 mg/kg per h and the infusion lasts about 100 h – the situation for most our patients. This agrees with some prior observations [7].

Complementary studies are needed of extended, high-dose infusions of propofol to evaluate the incidence of hypertriglyceridaemia [7]. It is advised to monitor lipaemia in patients receiving propofol of over 5–6 mg/kg per h or in long-term infusion.

References

- Gottardis M, Khünl-Brady KS, Koller W, Sigl G, Hackl JM (1989) Effects of prolonged sedation with propofol on serum triglyceride and cholesterol concentrations. *Br J Anaesth* 62:393–396
- Carrasco G, Molina R, Costa J, Soler JM, Cabré L (1993) Propofol vs midazolam in short-, medium-, and long-term sedation of critically ill patients. A cost-benefit analysis. *Chest* 103:557–564
- Eddleston JM, Shelly MP (1991) The effect on serum lipid concentrations of a prolonged infusion of propofol – hypertriglyceridaemia associated with propofol administration. *Intensive Care Med* 17:424–426
- Franke WL, Evans NJ, Rombeau JL (1993) Scientific rationale and clinical application of parenteral nutrition in critically ill patients. In: Rombeau JL, Caldwell MD (eds) *Clinical nutrition. Parenteral nutrition*, 2nd. edn. Saunders, Philadelphia, London, Montreal, pp 597–616
- Gottardis M, Hackl JM, Gruber E, Wieser C, Adelsmayr E, Seyr M, Zadravec M, Pfeiffer KP (1994) Fettinfusion bei polytraumatisierten Intensivpatienten in der Frühphase der Behandlung (abstract). *Infusionsther Transfusionsmed* 21:150–158
- Ball MJ (1993) Parenteral nutrition in the critically ill: use of a medium chain triglyceride emulsion. *Intensive Care Med* 19:89–95
- Haberer JP (1994) L'émulsion lipidique du Diprivan explique-t-elle certains effets pharmacologiques? *Ann Fr Anest Réanim* 13:460–464

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Respiratory distress syndrome and septic shock due to varicella in an HIV-infected adult

Received: 29 September 1995
Accepted: 15 March 1996

Sir: In patients infected with the human immunodeficiency virus (HIV), varicella is rare. As in the general population, its incidence is higher in children than in adults [1–3]. In a retrospective study of 421 patients with HIV (including two children), only 15 (3.5%) had a diagnosis of varicella [1]. Leibovitz et al. [2] reported an incidence of 9.7% among HIV positive Romanian children, with a mortality of 5%, mostly due to respiratory failure. In children as in adults, incidence and outcome were not correlated with the CD₄⁺ cell count [1, 2].

A 37-year-old African man was admitted with hepatalgia, fever and generalized vesicular eruption which had appeared 10 days after his daughter was ill with chickenpox. Chest X-ray studies showed

bilateral interstitial pneumonitis, though the patient denied any dyspnea. Laboratory findings on admission showed normal white blood cell count (WBC) and mild hepatitis. Therapy with intravenous acyclovir 10 mg/kg per 8 h was begun.

The next day, respiratory failure, collapse, disseminated intravascular coagulation (DIC), and acute renal failure with anuria developed. Chest X-ray studies showed massive bilateral pneumonitis. The patient was intubated and dobutamine treatment was begun. Blood gas analysis showed: partial pressure of oxygen in arterial blood/fractional inspired oxygen = 74. Bronchoalveolar lavage (BAL) examination did not yield any bacterial, viral, fungal, or parasitic pathogen.

One week later, physical examination did not show any improvement. Antibodies to HIV were positive, CD₄⁺ cells were 255/mm³. Laboratory findings were: WBC 20900/mm³; amylase 274 IU/l ($n < 115$); lipase 382 IU/l ($n < 190$); creatinine 669 mmol/l. Cultures of BAL and blood were negative. Acyclovir was discontinued for suspicion of acyclovir-induced nephropathy; however, renal biopsy failed to show acyclovir-crystalline precipitation.

Ten days after admission, *Klebsiella pneumoniae* septicemia and *Pseudomonas aeruginosa* pneumonia developed. Despite antibiotic and inotropic treatment the patient progressively worsened and died 1 month after admission. Immunoglobulin G titers for varicella had increased from 700 IU/l 5 days after admission to 2250 IU/l 2 weeks later. Titers for cytomegalovirus, respiratory syncytial virus, influenza virus, Epstein-Barr virus, herpes simplex virus, and toxoplasmosis remained negative.

In HIV-infected patients, varicella often is atypical, prolonged, and recurrent [1, 4]. The duration of the appearance of new lesions frequently is longer than in immunocompetent patients [4]. Reactivated cases have been reported and serologic immunity thus does not provide complete protection [1, 3, 4]. Even if mortality remains low [1, 2], serious complications may occur, with death mostly due to bacterial superinfection [4], respiratory failure [2] and DIC [1].

In our case, the patient deteriorated rapidly with the adult respiratory distress syndrome (ARDS), septic shock, and subsequent multiple organ failure (MOF), despite early initiation of acyclovir therapy. The absence of any other infectious pathogen suggests the direct responsibility of varicella for these complications.

Even if hepatitis [1, 3, 4], pancreatitis [4], pneumonia [5] and DIC [1] have already been described in varicella, their association with ARDS, MOF, and septic