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Intravenous insulin therapy as a therapeutic option for severe hypertriglyceridaemia in a non-diabetes patient

Severe hypertriglyceridaemia (SH) refers to a group of endocrine diseases characterized by blood triglycerides (TGs) permanently raised to > 4 g/L after 12 h of fasting [1,2]. In patients with SH, the risks of acute pancreatitis (AP) and premature atherosclerosis are also greater.

The overall prevalence of SH is not precisely known. The main causes of hypertriglyceridaemia (HTG) are either familial ones (hyperchylomicronaemia) or secondary HTG (excessive alcohol consumption, uncontrolled diabetes, kidney disease, endocrine disease, medications).

There are no clinical guidelines for SH, but treatment with insulin is predominantly used in diabetes patients, whereas heparin, plasmapheresis or a combination of the two has been successfully tested in non-diabetes patients. In the medical literature, however, the use of insulin infusions to treat SH in non-diabetes patients has not been particularly highlighted.

Case report

Our report is of a 38-year-old patient, with a history of alcohol abuse (8 cans of beer/day) and no other medical history, who presented the day before admission to our establishment with epigastric pain and asthenia, which had prompted a consultation with his general practitioner. The requested laboratory tests showed major HTG at 71 g/L, resulting in the patient's admission to the emergency department. He was later admitted to our department of endocrinology.

Clinical examination showed that the patient weighed 74 kg (body mass index: 24 kg/m^2). He was afebrile; his blood pressure was 120/65 mmHg and his pulse was 78 beats/min. Examination of the abdomen revealed mild epigastric tenderness with no rigidity. Cutaneous xanthomas and lipaemia retinalis were absent. After 12 h of fasting, the patient's serum TG was 81 g/L with lipaemic plasma. In 2014, his TGs were 1.4 g/L. Screening for blood alcohol was positive. All of his laboratory results are summarized in Table 1.

Abdominal ultrasound revealed a fatty liver, but computed tomography (CT) of the abdomen was normal, with no signs of pancreatitis. Nevertheless, given the high risk of acute pancreatitis, emergency therapeutic options [plasmapheresis, intravenous (IV) infusion of heparin or insulin] were considered, and insulin infusions were chosen because of our experience in the field.

An IV analogue insulin infusion was started and continued at 1 IU/h, while the patient was kept fasting for the first 24 h. After this time, a low-fat diet was started. To prevent hypoglycaemia, 10% dextrose was titrated to an average flow rate of 30 mL/h to maintain blood glucose within the normal range. Blood glucose

Table 1
Laboratory test results for a 38-year-old male patient with a history of alcohol abuse.

Laboratory test	Reference range	At admission	Day 1	Day 2	Day 3
Total cholesterol	100–200 mg/dL	1005	966	812	618
Serum triglycerides	20–150 mg/dL	8100	2200	830	380
High-density lipoprotein	40–59 mg/dL	77	38	30	34
Very low-density lipoprotein	28–43 mg/dL	657			
Lipase	13–60 IU/L	72	61		47
Creatinine	62–106 μmol/L	84	73		80
Blood alcohol	< 0.10	0.5			
Free thyroxine (T4)	12–22 pmol/L	16			
Thyroid-stimulating hormone	0.270–4.20 μU/mL	2.37			
Insulin-like growth factor 1	103–221 ng/mL	123			
Free urinary cortisol/24 h	11–73 μg/24 h		23		
Aspartate aminotransferase	< 40 IU/L	86	68		61
Alanine aminotransferase	< 41 IU/L	50	42		36
Total alkaline phosphatase	40–129 IU/L	144	114	127	130
Gamma-glutamyl transpeptidase	10–71 IU/L	2862			2084
HIV serology			Negative		
Haemoglobin A1c	4.3–6.1%	4.4			
Random blood glucose	4.1–6.05 mmol/L	4.5	5	4.3	5.1
Serum potassium	3.6–5.5 mmol/L	3.8	3.7	3.6	4.3

HIV: human immunodeficiency virus.

was monitored hourly. To avoid hypokalaemia secondary to IV insulin infusion, potassium supplementation per os was initiated; the daily dose of potassium chloride was 24 mmol. No hypokalaemia was reported.

Within 24 h, the patient's epigastric pain resolved. In addition, his TGs decreased to 22 g/L after 24 h, to 8.3 g/L after 48 h and to 3.8 g/L after 72 h. When TG levels were at 3.8 g/L, the IV insulin infusion was stopped and fenofibrate was started.

At day 5, the patient was discharged. His evolution was marked by a good clinical outcome, as insulin treatment had dramatically decreased his serum TG levels from 81 g/L to 3.8 g/L in three days, with no hypoglycaemia or hypokalaemia (Table 1). Two months later, the patient's TG levels were 1.7 g/L with fenofibrate, a low-fat diet and alcohol abstinence.

HGT may be inherited, or arise secondarily to uncontrolled diabetes, obesity, alcohol consumption or oestrogen therapy. Other forms of secondary HGT can develop with hypothyroidism, Cushing's disease, acromegaly, end-stage renal disease, nephrotic syndrome, human immunodeficiency virus (HIV) infection and a number of anti-HIV drugs [3].

The main risk of SH is related to the occurrence of acute pancreatitis. It is estimated that HGT accounts for 1–7% of all cases of acute pancreatitis [4]. Another risk of SH is atherosclerosis, although atherogenicity is a matter of debate and varies from one patient to another, depending on the presence of cardiovascular risk cofactors and associated comorbidities that, in themselves, can influence the occurrence of HGT.

SH treatment is not standardized. Plasmapheresis is a therapeutic option in the acute phase, as it can decrease TG levels by as much as 70% within just a few hours [5]. Through plasmapheresis, TG-rich plasma is replaced by fresh-frozen plasma, thus substantially reducing TG levels.

Another therapeutic option is heparin infusion. Heparin increases the release and translocation of tissue-bound lipoprotein lipase (LPL) in capillary endothelium. LPL is a high-affinity heparin-binding protein that hydrolyzes circulating TGs into free fatty acids (FFAs), thereby reducing TG levels [6]. LPL is an important enzyme essential for the removal of TG from plasma, while insulin is a fast and powerful activator of LPL synthesis that, in turn, hydrolyzes TG into FFAs and glycerol, and also helps in the rapid storage of FFAs in adipocytes [2].

IV insulin infusions to treat SH are predominantly used in patients with diabetes. However, in the medical literature, the use of insulin infusions to treat SH in non-diabetes patients has not been sufficiently highlighted. In one adolescent, non-diabetes patient with SH, a subcutaneous bolus dose of regular insulin (0.1 IU/kg) decreased serum TG by 46% after 4 h [7].

Our present patient had SH secondary to alcohol abuse and was not a diabetic. In his case, the combination of fasting and IV insulin infusions decreased serum TGs by 80% in the first 24 h. Thereafter, a low-fat diet and IV insulin decreased serum TGs by 96% by day 3.

In our opinion, the IV insulin infusions contributed significantly to this rapid decline in TGs. In fact, the insulin treatment presented in this case report achieved comparable results to those reported with plasmapheresis, but at a relatively lower cost and in a minimally invasive way. It was also a safe treatment with no reported hypoglycaemia or hypokalaemia.

SH may be associated with significant morbidity and mortality. However, IV insulin infusions appear to be an effective, safe and minimally invasive treatment for SH in patients without diabetes.

Disclosure of interest

The authors declare that they have no competing interest.

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