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Medicina Clínica xxx (xxxx) xxx–xxx

MEDICINA CLINICA

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Letter to the Editor

Use of insulin and heparin in the management of severe hypertriglyceridemia in a critically ill patient

Insulina y heparina en el tratamiento de la hipertrigliciridemia grave en un paciente crítico

Dear Editor,

Severe hypertriglyceridemia, which is characterized by serum triglyceride (TG) concentrations above 1000 mg/dL, can lead to acute pancreatitis and cardiovascular complications.[1] Critically ill patients have certain clinical characteristics that make them susceptible to the development of hypertriglyceridemia.

Firstly, they may require invasive mechanical ventilation and sedation with high doses and during a long time of propofol, which has high lipid content (0.1%). A prevalence of 18–45% of propofol-associated hypertriglyceridemia has been reported among patients under this treatment, which usually resolves upon reduction or discontinuation. Other risk factors are the parenteral nutrition if the lipid supply is not properly controlled and SARS-CoV-2 infection.[2]

The current strategies followed to normalize TG concentration, which include a reduction of TG intake and treatment with oral lipid-lowering drugs (fibrates and omega-3 fatty acids), may be insufficient for critically ill patients with severe hypertriglyceridemia.[1,3]

In these cases, the combined use of insulin and heparin has been described as effective in several case series of patients. Both treatments enhance the lipoprotein lipase activity, an essential enzyme to eliminate circulating TG.[1]

Here, we present our experience of a patient admitted to the intensive care unit (ICU) for SARS-CoV-2 pneumonia who experienced severe hypertriglyceridemia and was treated with insulin and heparin, achieving a rapid reduction in TG.

A 39-year-old white male, 77 kg, was admitted to the hospital for SARS-CoV-2 pneumonia. Despite the treatment received, he presented with an increasing oxygen requirement, so he was transferred to the ICU, where invasive mechanical ventilation was started. Within 24 h of admission, he presented refractory hypoxemic respiratory failure secondary to acute respiratory distress syndrome and pulmonary thromboembolism (PT). Therefore, veno-venous extracorporeal membrane oxygenation (ECMO-VV) and anticoagulant treatment with an intravenous continuous infusion of unfractionated heparin were started. Sedoanalgesia with propofol and remifentanil were maintained, as well as total parenteral nutrition.

During admission, TG increased up to 1.215 mg/dL (values at admission were 379 mg/dL). Then, propofol dose was optimized from 4.7 mg/kg/h to 2 mg/kg/h, adding midazolam to ensure patient comfort; and gemfibrozil (600 mg q12 h by nasogastric tube) was initiated, both strategies allowing a reduction of TG to 659 mg/dL.

However, one month after ICU admission, a new increase in TG up to 1.655 mg/dL was observed. By then, he was not receiving propofol, he was on enteral nutrition, ECMO-VV had been withdrawn and heparin treatment had been discontinued 4 days before because of bleeding. Omega-3 fatty acids (1 g q12h by nasogastric tube) and intravenous continuous infusions of rapid insulin at 0.01 IU/h and unfractionated heparin at 13.5 IU/kg/h were started, achieving TG values of 653 mg/dL in 24 h. Insulin dose was increased according to the patient tolerance to 0.4 IU/h for 7 days. Heparin infusion was replaced 2 days after initiation by subcutaneous enoxaparin (1 mg/kg q12h) to complete 6 months of anticoagulation treatment for PT, which also allowed a TG concentrations control around 500 mg/dL. Given the clinical improvement of the patient, after ten weeks at the ICU, he was transferred to the ward and discharged one month later with TG values of 225 mg/dL.

The patient experienced an increase in TG despite receiving anticoagulation with heparin, associated with high propofol requirements that decreased when propofol dose was reduced. Once propofol infusion had been withdrawn, a second increase in TG concentrations related to the discontinuation of heparin infusion occurred. The normalization of TG in 24 h was achieved with the combined therapy of insulin and heparin. Insulin was used at lower doses than those previously reported to avoid hypoglycemia, and it was maintained for a longer period until normalization of TG. The dose of heparin used in our patient agrees with those described in literature.[4]

In line with literature, we did not report any adverse effects secondary to the treatment. However, insulin and heparin can lead to hypoglycemia and bleeding, respectively. Since non-diabetic patients are susceptible to present hypoglycemia with insulin administration, close monitoring and glucose solution administration is recommended.[5]

This case supports the combined use of insulin and heparin as an effective and safe strategy for the treatment of severe hypertriglyceridemia in critically ill patients. Further studies are needed to determine their optimal regimen.

Ethical responsibilities

The authors declare that the protocols and procedures of our institutional centers related with the patient's data publication have been followed, as well as the subject privacy.

Funding

The authors received no financial support for the research and publication of this article.

https://doi.org/10.1016/j.medcli.2022.08.003

Please cite this article as: N. Arranz, S. Fernández and C. Bastida, Use of insulin and heparin in the management of severe hypertriglyceridemia in a critically ill patient, Med Clin (Barc)., https://doi.org/10.1016/j.medcli.2022.08.003

Conflict of interests

None.

References

1. Rawla P, Sunkara T, Thandra KC, Gaduputi V. Hypertriglyceridemia-induced pancreatitis: updated review of current treatment and preventive strategies. Clin J Gastroenterol. 2018;11:441–8, http://dx.doi.org/10.1007/s12328-018-0881-1.
2. Kovacevic MP, Dube KM, Lupi KE, Szumita PM, DeGrado JR. Evaluation of hypertriglyceridemia in critically ill patients with coronavirus disease 2019 receiving propofol. Crit Care Explor. 2021;3:e0330, http://dx.doi.org/10.1097/CCE.0000000000000330.
3. Balfour JA, McTavish D, Heel RC. Fenofibrate: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in dyslipidaemia. Drugs. 1990;40:260–90, http://dx.doi.org/10.2165/00003495-199040020-00007.
4. Kuchay MS, Farooqui KJ, Bano T, Khandelwal M, Gill H, Mithal A. Heparin and insulin in the management of hypertriglyceridemia-associated pancreatitis: case series and literature review. Arch Endocrinol Metab. 2017;61:198–201, http://dx.doi.org/10.1590/2359-3997000000244.
5. Coskun A, Erkan N, Yakan S, Yildirim M, Carti E, Ucar D, et al. Treatment of hypertriglyceridemia-induced acute pancreatitis with insulin. Prz Gastroenterol. 2015;10:18–22, http://dx.doi.org/10.5114/pg.2014.45412.

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