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Review

Hypocalcaemia, hyperkalaemia and massive haemorrhage in liver transplantation☆

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ABSTRACT

Rapid transfusion of blood products and the presence of ionic changes as hypocalcaemia and hyperkalaemia are common in liver transplantation. The objective of this paper is to give the reader a clear and practical description of the etiological factors, biochemical mechanisms, diagnosis and treatment of the calcium and potassium plasmatic disorders associated with massive transfusion. The peculiarities that arise in the clinical setting of liver transplant surgery and citrate intoxication are highlighted. A non-systematic review of literature was conducted in MEDLINE, OVID and Cochrane databases. Correct and early anaesthetic management of calcium and potassium disorders prevents serious complications in intraoperative bleeding risk surgeries such as liver transplantation.

Hipocalcemia, hiperpotasemia y hemorragia masiva en el trasplante de hígado

Palabras clave:
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RESUMEN

La transfusión rápida de hematocomponentes y la presencia de alteraciones iónicas como la hipocalcemia y la hiperpotasemia son frecuentes en el trasplante hepático. El objetivo de este trabajo es brindar al lector una descripción ordenada y práctica de los factores etiológicos, mecanismos bioquímicos, diagnóstico y tratamiento de las alteraciones del calcio y del potasio asociadas a la transfusión masiva. Se destacan las particularidades del contexto clínico de la cirugía de trasplante hepático y se describe la intoxicación por citrato y sus factores predisponentes. Se realizó una revisión no sistemática de la literatura en las

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bases de datos MEDLINE, OVID y Cochrane. El manejo anestésico correcto y precoz de las alteraciones del calcio y del potasio evita complicaciones graves en el intraoperatorio de las cirugías con riesgo de hemorragia, como el trasplante de hígado.

Introduction

Liver transplant is one of the surgical procedures that often requires transfusion of large volumes of blood products. This gives rise to complex alterations of the internal milieu that may result in life-threatening intraoperative events. Immediate identification and anticipation of these disorders is a mainstay in anaesthetic management. The objective of this review is to provide an overview of the mechanisms and treatment of the most frequent serum calcium and potassium abnormalities occurring as a result of using large volumes of blood products for replacement. Particular details on citrate intoxication, hypocalcaemia and hyperkalaemia will be provided in the context of acute massive haemorrhage during liver transplant surgery.

Methodology

Non-systematic review of the literature was conducted in the MEDLINE, OVID and Cochrane databases using words such as: "hypocalcaemia", "hyperkalaemia", "massive transfusion", "acidosis" and "liver transplantation". Relevant articles and associated references that help understand the aetiology, diagnosis and treatment of calcium and potassium disorders during massive haemorrhage were selected. Relevant articles for the interpretation of those disorders during liver transplant surgery were also included.

Massive haemorrhage

Massive haemorrhage is one of the main causes of death and intraoperative cardiac arrest in adults as well as children.[1–4] It is usually defined in relation to the volume of blood products transfused over 24 h by kilograms of body weight: 10 volumes of red blood cells (RBCs) in a patient weighing 60 kg,[5] replacement of more than 50% of the blood volume in 3 h, or transfusion of more than 4 volumes of RBCs in 1 h.

However, in cases of acute haemorrhage happening within a period of minutes, immediate identification is required in order not to delay therapeutic action. For that reason, in anaesthesia we prefer to consider millilitres of blood lost in a few minutes: 150 ml/min or more than 1.5 ml/kg/min over a period of more than 20 min.[6] Mortality is associated with the presence of acidosis (pH < 7.1), hypothermia, coagulopathy, number of concentrated blood products transfused and volume ratios between the different blood products given.[7] The acute complications of massive haemorrhage are related with shock and transfusion therapy.[8,9] We will focus on two of these, namely, citrate toxicity[7,10,11] and hyperkalaemia.[4,7,12]

Hypomagnesaemia is another frequent ionic abnormality in patients with massive haemorrhage, although it does not seem to be significantly associated with mortality.[13]

Hypocalcaemia

Although it is defined as a total serum calcium concentration of less than 8.5 mg/dl (4.5 mEq/l, 2.10 mmol/L),[14] clinical hypocalcaemia may occur even with normal total calcium values when serum ionized calcium concentrations are lower than 4.5 mg/dl. In surgery, the most common causes of hypocalcaemia are hyperventilation and citrated blood infusion at a rate of more than 1.5 ml/kg/min. Acute respiratory alkalosis reduces ionized calcium by lowering hydrogen ion concentrations, freeing albumin binding sites and leading to increased ionized calcium protein binding. The clinical manifestations of hypocalcaemia are due to the lowering of ionized calcium, because it is this free fraction which acts on membrane potentials.[15] That is why it manifests in excitable tissues: changes in mental status (central nervous system), tetany (skeletal muscles), hypotension (smooth muscle) and arrhythmias, prolonged QT interval or pulseless electrical activity (myocardium).[9,14] Plasma calcium levels are a poor surrogate indicator for total body calcium, accounting for only 0.1–0.2% of the extracellular calcium and 1% of total body calcium. Ionized calcium, in turn, usually represents 40–50% of plasma calcium. Total serum calcium concentrations must be interpreted in relation to serum albumin. In the presence of hypoalbuminemia, there is less substrate for calcium binding, allowing for a larger percentage of free calcium, ionized calcium. In this situation, plasma calcium values may underestimate ionized calcium values.[16] Serum calcium concentrations are corrected in relation to a concentration of albumin of 40 g/L; for every 1 g/L of albumin above or below this value, calcium is adjusted by lowering or increasing it by 0.02 mmol/L. This estimate may not be accurate in critically ill patients.[17] The use of 5% albumin and of blood products during liver transplant determines protein binding of calcium ions.[18] On the other hand, in critically ill inpatients with hypoalbuminemia there may be a lower value of total calcium without lowering of ionized calcium.[16] In these cases, there is no need for acute calcaemia correction, but improving nutrition is required.[14]

During blood transfusion, the degree of hypocalcaemia depends of the patient's volemia, the volume of blood products administered, the transfusion rate, and liver function.[2]

Hypocalcaemia during massive haemorrhage is a predictor for mortality, and there is a linear relationship between calcaemia values and mortality. Lower plasma calcium is a better indicator of hospital mortality than minimum fibrinogen concentration, acidosis or low platelet counts.[19]