

Case Report

Benefit of Albumin Infusion in an Elderly Cirrhotic Patient on DOAC

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Introduction

Hypoalbuminemia is frequently observed in decompensated cirrhotic patients, exacerbated by nutritional status, renal insufficiency common that are in elderly patient leading to infectious, hemodynamic, hydroelectrolytic complications and increased bioavailability of certain drugs like DOACs. Albumin perfusion, alone or in combination with other medications, has been suggested for treating various cirrhosis complications [1]. We invite you to look into the case of our patient cirrhotic Child-Pugh A on DOAC that was infused with albumin.

Case Presentation

The patient is an 89-year-old female with a history of type II diabetes on diet control, left partial nephrectomy with moderate chronic renal insufficiency, metabolic cirrhosis (NASH) CHILD-PUGH A on DOAC for atrial fibrillation. Admitted to geriatric FRC (Follow-up and Rehabilitation Care) unit for rehabilitation following Oedema-as-cites decompensation due to urinary sepsis. Clinical presentation on arrival and during hospital stay: Cardiac assessment:

- Atrial fibrillation arrhythmia with CHADS VASC score of 5.
- Dabigatran anticoagulation switched to Eliquis due to worsening renal function with creatinine clearance at 21.5 ml/min.
- Calcified aortic stenosis (TAVI).
- Global cardiac decompensation in the context of SARS-CoV-2 infection. Pulmonary assessment:
- Non-oxygen-requiring SARSCoV2 pneumonia with signs of pulmonary arterial hypertension (PAH). Infectious.

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- Severe sepsis originating from urinary source with ESBL Klebsiella pneumoniae germ. Hepatic side:
- Edematoascitic decompensation cirrhosis, Elastometry at 46.5 kPA. Renal side : Hepatorenal syndrome. Acute renal failure on chronic renal insufficiency with a creatinine elevation of > 50% in one week (creatinine on 30.03.23 at 97 umol/l, creatinine on 05/04/2023 at 163 umol/l). Hemostasis:
- Recurrent macroscopic hematuria, episode of epistaxis under Eliquis with HAS-BLED bleeding score of 4..
- Tibial deep vein thrombosis right posterior. Nutritional side:
- Severe malnutrition with serum albumin at 19.9 mg/l, prealbumin at 0.06mg/l, BMI 24.3kg /m². Treatment on admission: IRBESAR- TAN 150 mg 1 tablet in the morning AMLODIPINE 2 mg 1 tablet in the morning. LANSOPRAZOLE 30 mg 1 gel in the evening. DABIGATRAN 110 mg 1 tablet/day. AUGUMENTIN 1 g x3/day. FUROSEMIDE 250 mg IV.

Discussion

Albumin infusion in cirrhosis is beneficial in correcting hemodynamic complications by increasing oncotic pressure, reducing infectious risk by decreasing prostaglandin bioavailability, and limiting DOAC bioavailability, thus reducing the risk of overdose increased by renal insufficiency and hypoalbuminemia. The decision to use Eliquis in our patient was based on the risk of Cerebrovascular Accident (CVA) complicating rhythmic heart disease with a CHA2DS2-VASc score of 5, there were no absolute contraindications to its use, given our patient's Child-Pugh A Cirrhosis. The choice of a low dose of 2.5mg/12h was aimed at preventing bleeding risk due to age >80 years and low clearance <30ml/min, but was insufficient to prevent epistaxis. Indeed, the patient's clinical characteristics potentially altered Eliquis pharmacokinetics [2], as renal impairment led to Eliquis accumulation because its renal excretion represents 27% of the total renal clearance, furthermore severe multifactorial hypoalbuminemia, related to cirrhosis, protein-energy malnutrition and Renal insufficiency, increased Eliquis bioavailability due to its 90% protein binding, mainly to albumin, posing a higher risk of overdose and bleeding. It is crucial to consider that elderly individuals often have multiple comorbidities, and drug interactions that can potentiate bleeding risk. Nissan and Coll evaluated the concentration of apixaban in octogenarians based on the dose used, among those using the appropriate dose of 5 mgx2/day, 30% had subtherapeutic levels and 40% had levels higher than expected. Huppertz and Coll reported a case of a 75-year-old woman with genetic polymorphisms potentially affecting apixaban elimination, leading to increased exposure. These genetic polymorphisms involve genes encoding proteins responsible for the activation, transport or metabolism (pharmacokinetics and pharmacodynamics) of DOACs, such as CES1, ABCB1, CYP3A4, CYP3A5, resulting in interindividual variability in response to DOACs [3]. In this population, monitoring apixaban plasma levels by high-performance chromatography would be beneficial to anticipate

bleeding risks due to overdose, when the benefit ratio risks is in favor of maintaining anticoagulation; For apixaban (10mg×2/day), the average maximum plasma concentration (C max) was 371.57 ng/mL and the median time to reach C max (T max) was 4 hours [4]. Various factors appear to influence apixaban concentrations, including age, weight, albumin levels, comorbidities such as renal impairment, cirrhosis, the presence of genetic polymorphisms and protein-energy malnutrition [5]. Besides the hemostatic complications for our patient, hypoalbuminemia primarily resulted in decreased oncotic pressure, leading to fluid leakage through blood capillaries causing ascites and relative hypovolemia complicated by HRS (Hepatorenal syndrome), as well as exacerbating cardiac and inflammatory pleural effusion. The infusion of 1g/kg of albumin on Day 1 followed by 0.5g/kg for 2 days corrected the albumin level from 19 g/L to 28 g/L. This correction addressed hemodynamic complications by increasing oncotic pressure, thereby limiting the worsening of pleural effusion. It also reduced the risk of ascites recurrence by combining it with fluid restriction, prevented ascitic fluid infection by decreasing prostaglandin bioavailability and by administering Ofloxacin antibiotic therapy, corrected electrolyte imbalances by addressing dilutional hyponatremia and temporarily reduced the hemorrhagic risk by enhancing albumin binding to Elixquis. No adverse effects related to albumin infusion were observed in our patient, however, it is important to note that adverse effects associated with albumin infusion are rare but potentially serious. The incidence of adverse effects ranges from 1.29 to 4.65 per 10 doses, with 0.05 to 0.185 per 10 doses being fatal. The most common adverse effects include mild skin reactions, fever and nausea, which typically resolve quickly when the infusion rate is

reduced or stopped. Fatal adverse effects may include anaphylactic shock and toxidermia. Caution is advised when using albumin in patients with chronic heart failure and in elderly patients due to the risk of volume overload [1].

Conclusion

Our observation suggests that albumin infusion improves the clinical status of cirrhotic patients with severe hypoalbuminemia on DOACs. However, no studies have yet proven its efficacy in reducing hemorrhagic risk in these patients.

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