Critical Care Management of Acute Decompensation of Cirrhosis

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ON DAY 2 of the European Association for the Study of the Liver (EASL) International Liver Congress (ILC) 2022, which took place on 22nd–26th June 2022 in London, UK, there was a session featuring specialist insights from researchers in the field. There were discussions that focused on the critical management of acute decompensation of cirrhosis.

ILC 2022

MULTIDRUG-RESISTANT BACTERIAL INFECTIONS IN CANDIDATES FOR A LIVER TRANSPLANT

Emmanuel Weiss, Department of Intensive Care and Perioperative Medicine, Beaujon Hospital, Paris Cité University, France, opened the session on multidrug-resistant (MDR) bacterial infection in candidates for a liver transplant by emphasising that bacterial infections are a growing global healthcare problem. He presented data that demonstrated an increase in the prevalence of bacterial infection in patients with cirrhosis in Europe, from 29% in 2011 to 38% in 2018. Weiss explained that there are different types of common bacterial infections: Gram-negative *bacilli* and Gram-positive *cocci*. The most common infection is Gram-negative *bacilli* extended-spectrum β-lactamase-producing *enterobacterales*, which has a resistance mechanism of β-lactam hydrolysis. For Gram-positive *cocci*, the most common infections were from vancomycin-resistant *enterococcus* and methicillin-resistant *Staphylococcus aureus*. MDR bacterial-related infections are associated with a lower resolution rate, higher incidence of septic shock and acute-on-chronic liver failure (ACLF), and higher mortality. Weiss explained the variability in MDR rates across the world and explained that the differences between the trends of antimicrobial resistance between the north and south of Europe, detailing the importance of knowing the epidemiology of your centres as a clinician and regularly revise these analyses.

Weiss presented a study of 635 patients with cirrhosis, which demonstrated that each hour of delay in the time to introduce an effective antibiotic therapy was crucial and could increase the adjusted odds ratio of mortality in the patients due to septic shock. Weiss emphasised that clinicians should request the colonisation data in liver transplant candidates, and they should use a negative predictive value to avoid broad-spectrum antimicrobial overconsumption and use it in combination with other risk factors to have a good positive predictive value.

Weiss emphasised the importance of the specialist collaboration with a microbiologist team or infection control team to find the most appropriate treatment for the patient. The optimisation of antimicrobial treatment includes avoiding underdosing and toxicity, as well as increasing the probability of target attainment. In order to do this, the dosage should be adapted using therapeutic drug monitoring or using continuous or prolonged perfusion of β-lactams. In addition, attention should be paid to source control.

Prevention of the spread of antibiotic resistance remains the best treatment. This can be done through the promotion of antimicrobial stewardship programmes, which can limit the prescription of antibiotics. Additionally, the use of infection control policies, such as hand washing, barrier or contact precautions, and isolation of patients with cirrhosis and methicillin-resistant *S. aureus*, can also be effective strategies.

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In his concluding remarks, Weiss stated that in order to use the most appropriate antibiotic treatment, clinicians need to know the new molecules and emerging data in the pipeline but also optimise the pharmacokinetic–pharmacodynamic parameters, control the source, and collaborate with specialists in this field. However, the best treatment remains to prevent the spread of MDR bacteria.

BALANCING ANTICOAGULATION AND GASTROINTESTINAL BLEEDING IN DECOMPENSATED CIRRHOSIS

Annabel Blasi, Anaesthesia Department, Hospital Clinic of Barcelona, Spain, started by defining the rationale for administering anticoagulation (ACO) treatment in patients with cirrhosis. Patients with cirrhosis have a higher chance of developing deep vein thrombosis and/or pulmonary embolism compared with the general population, and the treatment of ACO is advised. In patients with cirrhosis and portal vein thrombosis, ACO treatment could assist in reducing the risk of portal hypertension and ischaemia in the superior mesenteric vein and could help avoid exclusion from a liver transplant list.

Blasi went on to outline some blind spots when it comes to ACO. According to Blasi, only 50–60% of patients with portal vein thrombosis would respond to ACO. Additionally, the efficacy of thromboprophylaxis for deep vein thrombosis or pulmonary embolism in patients with cirrhosis has not been

proved in this population, nor has the safety profile, dosing, and timing. Acute variceal bleeding accounts for 70% of all upper gastrointestinal bleeding events in cirrhosis. Blasi presented a study that showed gastrointestinal bleeding was more frequent in patients with ACLF, compared with patients with a less advanced stage of the disease.

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Some contributing factors for thrombosis or bleeding in patients with cirrhosis include anaemia, low haematocrit, bacterial infection, and renal injury. Infection can act as a risk factor both for anaemia and thrombosis as it can promote thrombotic complications via increasing platelet response to the agonists in patients with cirrhosis. Patients with acute kidney injury (AKI) show lower platelet aggregation, higher thrombin generation, and higher hyperfibrinolysis.

Clinicians can identify patients at high risk of thrombotic complications by analysing the clinical status of the patients to identify infections or AKIs. Additionally, a coagulation test can be carried out to identify the number of platelets and levels of fibrinogen. A low level of fibrinogen and ACLF is a high-risk factor in bleeding and thrombosis in decompensated cirrhosis.

Blasi concluded by emphasising the importance of addressing all the contributing factors for bleeding patients with cirrhosis. Additionally, the decision to administer anticoagulant treatment should be considered case-by-case, based on expected benefits and risk of bleeding, particularly in patients with higher risk factors associated with bleeding. However, further research is required to identify factors associated with a favourable response to ACO treatment in different settings in patients with cirrhosis.

PREOPERATIVE MANAGEMENT OF RENAL FAILURE AND HYPONATRAEMIA IN DECOMPENSATED CIRRHOSIS

Raj Mookerjee, Institute of Liver and Digestive Health, University College London, UK, emphasised the importance of early identification of kidney failure in order to intervene and modulate management. As Mookerjee explained,

there are three types of kidney dysfunction in cirrhosis: AKI, chronic kidney disease, and acute-on-chronic kidney disease, whereby one has repeated episodes of AKI compounding a chronic status.

Mookerjee presented studies showing that a major cause of renal failure in cirrhosis is due to precipitating factors such as bacterial infections, hypovolaemia, hepatorenal, and parenchymal nephropathy. However, the study showed that patients with bacterial infections as well as a hepatorenal syndrome prognosis had the worst outcomes and survival rates compared with patients without bacterial infections. Mookerjee stated that the presence of infection further increases portal hypertension and reduces renal perfusion, thus leading to microvascular dysfunction. Additionally, the infection promotes oxidative stress and tubular damage.

The general management of AKI in decompensated cirrhosis is to assess and confirm the AKI diagnosis by ruling out proteinuria, stopping the administration of nephrotoxins and β-blockers, withdrawal of diuretics, and correct hypovolaemia in the patient. Additionally, any underlying infection should be treated with antibiotics.

In the case of AKI including hepatorenal syndrome, Mookerjee listed some vasoconstrictors that could be useful. Terlipressin with albumin, as used in Europe, is more effective than albumin alone. Although terlipressin could be effective, he advised discontinuation after 14 days when no response or partial response is observed in the patient. Other vasoconstrictors include noradrenaline and midodrine plus octreotide, with emerging data from other countries with no access to terlipressin.

In his closing remarks, Mookerjee explained that AKI is common in acute decompensation in cirrhosis and is often associated with infections and bad outcomes. He emphasised the need for renal biomarkers other than creatinine and glomerular filtration rate values, which could precisely reflect the pathophysiology of the disease. The treatment consists of removing causative factors, volume correction, and vasoconstrictors; however, renal replacement therapy could be considered in unresponsive patients. ●

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