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Re-evaluation of Human Albumin Use in Acute Decompensation of Cirrhosis: From Prescription Practices to Precision Medicine

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Abstract: *This article systematically examines the clinical application status and advancements of human albumin in acute decompensation of cirrhosis. Analysis of prescription audit data from a regional healthcare system demonstrates substantial improvement in the standardization of human albumin utilization in clinical practice. The paper elaborates on the biological characteristics of human albumin, including its roles in acute decompensation of cirrhosis. It comprehensively reviews evidence-based medical data supporting its use in preventing post-paracentesis circulatory dysfunction, treating spontaneous bacterial peritonitis, and managing hepatorenal syndrome. Based on recent research developments and clinical guidelines, standardized application recommendations are proposed, emphasizing strict indication criteria guided by evidence-based medicine to avoid inappropriate use. Finally, the direction for developing personalized precision therapy with human albumin is discussed.*

Keywords: *Human albumin; Acute decompensation of cirrhosis; Clinical application*

1. Introduction

Acute decompensation (AD) of cirrhosis refers to a clinical syndrome in patients with previously compensated cirrhosis who experience acute hepatic decompensation, characterized by new-onset or worsening of major complications such as ascites, hepatic encephalopathy, gastrointestinal bleeding, or infections[1-3]. According to prospective studies by the European Association for the Study of the Liver - Chronic Liver Failure Consortium (EASL-CLIF), approximately 30%-40% of AD patients progress to acute-on-chronic liver failure (ACLF), a syndrome associated with organ failure and high mortality[4]. Human albumin (HA), a blood product derived from healthy human plasma through viral inactivation processes, is commonly used in patients with AD[5]. As the most abundant protein in plasma, HA plays crucial physiological roles[6]. This review integrates prescription audit data from a specific region with current domestic and international research to discuss the biological characteristics of HA and its application in AD, aiming to provide a theoretical basis for clinical practice.

2. Current Clinical Practice Revealed by Hospital Case Data: A Prescription Audit Analysis

A specialized audit of human albumin utilization in patients hospitalized with acute decompensation of cirrhosis in our region from June 1, 2024, to May 31, 2025, revealed a remarkable improvement in prescribing standardization. This study included 66 cases of acute decompensated cirrhosis receiving human albumin. Statistical analysis demonstrated that albumin administration in all cases adhered to relevant domestic and international clinical guidelines, achieving a 100% appropriate usage rate.

These findings reflect significant advancements in prescription quality control and clinical pathway management within regional healthcare institutions. The healthcare team's comprehensive understanding and strict implementation of guideline recommendations signify a successful transition from empirical prescribing to evidence-based practice. We recommend sustaining this standard through continued professional education and quality assurance initiatives to maintain optimal, safe patient care.

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3. Research Advances in Human Albumin Use in Acute Decompensation of Cirrhosis

3.1. Biological Characteristics of Human Albumin

Human albumin is the most abundant protein in human plasma, accounting for approximately 50%–60% of total plasma proteins[6]. Synthesized in the liver and secreted into the circulation, albumin consists of 585 amino acids with a molecular weight of about 66.5 kDa[7]. The HA molecule exhibits a highly conserved "heart-shaped" tertiary structure, divided into three homologous domains (I, II, III), each further subdivided into two subdomains (A and B)[8]. As the primary osmotic regulator in plasma, albumin's relatively small molecular size and negatively charged surface, which attracts sodium ions, allow it to maintain approximately 80% of the plasma colloid osmotic pressure, preventing tissue edema[9].

Albumin possesses multiple ligand-binding sites, enabling reversible binding with endogenous substances (e.g., bilirubin, fatty acids, hormones, metal ions) and exogenous substances (e.g., drugs, toxins), thereby facilitating their transport, distribution, metabolism, and excretion[10].

The free thiol group (Cys-34) of HA can neutralize reactive oxygen species (ROS), conferring antioxidant properties that mitigate oxidative stress-induced tissue damage, which is particularly significant for organ protection in pathological states like end-stage liver disease[11]. Furthermore, albumin can bind certain metal ions (e.g., Cu^{2+}, Fe^{2+}), thereby reducing metal ion-catalyzed peroxidation damage[12].

Albumin can bind pro-inflammatory cytokines such as TNF-α and IL-6, participating in the regulation of inflammatory responses and microcirculatory function, and maintaining endothelial stability. This property is especially crucial in cirrhosis complicated by systemic inflammatory response[13-14].

3.2. Application of Human Albumin in Acute Decompensation of Cirrhosis

Patients with end-stage liver disease often develop hypoalbuminemia due to severely impaired hepatic synthesis, leading to decreased plasma colloid osmotic pressure, exacerbated systemic inflammation, and multiple organ dysfunction[15]. In recent years, exogenous human albumin infusion has evolved from traditional volume replacement therapy to targeted management of specific complications. Its role extends beyond correcting hypoalbuminemia to encompass multiple mechanisms, including immunomodulation, microcirculatory improvement, and organ protection. Clinical studies have demonstrated the significant value of HA infusion in preventing and treating complications associated with end-stage liver disease, such as refractory ascites, spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), and hepatic encephalopathy[16-17]. Consequently, HA is widely used in these patients.

Acute decompensation of cirrhosis represents a state of acute progression, characterized by one or more major complications of cirrhosis[18-19]. It is a primary reason for hospitalization in cirrhotic patients, associated with high mortality and poor predictability. Patients typically present with ascites, hepatic encephalopathy, or gastrointestinal bleeding, accompanied by severe hypoalbuminemia and systemic inflammation[20]. The use of HA in these patients has progressed from merely maintaining colloid osmotic pressure to modulating systemic inflammation and organ dysfunction.

A multicenter randomized controlled trial involving 440 cirrhotic patients with refractory ascites found that long-term HA infusion (40 g/week for 18 months) significantly improved 18-month survival and reduced the rate of ascites recurrence by 38% compared to standard care, demonstrating the value of long-term HA therapy in improving outcomes in decompensated cirrhosis[21]. An Italian cohort study of 70 cirrhotic patients with refractory ascites found that, in addition to standard therapy, long-term administration of 20g HA twice weekly significantly reduced the 24-month cumulative mortality rate (41.6% vs. 65.5%) and markedly extended the interval free of emergency hospitalizations[22]. Another study evaluated the efficacy of HA combined with terlipressin in cirrhotic patients with AD and acute kidney injury. Results showed a significantly higher renal function recovery rate in the combination therapy group compared to the terlipressin-alone group, suggesting synergistic effects of HA through improved renal perfusion[23]. Furthermore, Caraceni et al. found that long-term albumin supplementation plus standard therapy was more effective in reducing recurrences of ascites, HRS, hepatic encephalopathy, infections, and hospitalizations in patients with AD, and also improved survival. The benefits of long-term albumin therapy are likely mediated by improved circulatory function and reduced secretion of pro-inflammatory cytokines[24].

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4. Recommendations for Human Albumin Use in Acute Decompensation of Cirrhosis

HA has broad pharmacological effects, but its approved indications are described generally in package inserts, with variations among manufacturers. Off-label and inappropriate use of HA are common globally. Using the UHC Guidelines for the Use of Albumin, Nonprotein Colloid, and Crystalloid Solutions as an evaluation standard, the inappropriate use rate of HA in adults is as high as 57.8%. The Chinese Expert Consensus on the Clinical Application and Management of Human Albumin (2024) states that human albumin should not be used for: treating non-SBP infections (except for septic shock); preventing or treating gastrointestinal bleeding in cirrhotic patients; or improving malnutrition in patients with end-stage liver disease.

Based on the current situation and the latest evidence, we recommend clearly defining the core indications for HA use in clinical practice: prevention of post-paracentesis circulatory dysfunction (PICD), treatment of spontaneous bacterial peritonitis (SBP), management of hepatorenal syndrome (HRS), and selected cases of refractory ascites. Figure 1 illustrates the therapeutic rationale for HA in acute decompensation of cirrhosis, tracing the pathway from clinical presentation through the drug's multifaceted mechanisms of action to these evidence-based applications. The color-coded connections highlight how specific pharmacological properties, including volume expansion, immunomodulation, molecular transport, and antioxidant activity, correspond to targeted clinical indications. Common misconceptions should be avoided: HA is not recommended for correcting isolated hypoalbuminemia as an independent indication, nor should it be used solely as a nutritional supplement. Routine use of HA in non-SBP infections is not recommended.

4.1.1. Figures

This schematic illustrates the rationale for human albumin use in acute decompensation of cirrhosis. The pathway begins with the characteristic clinical presentations , proceeds through albumin's multifaceted mechanisms of action , and culminates in specific evidence-based clinical applications. The color-coded arrows demonstrate the connection between primary pharmacological properties and their corresponding therapeutic indications, highlighting the targeted nature of albumin therapy in this population.

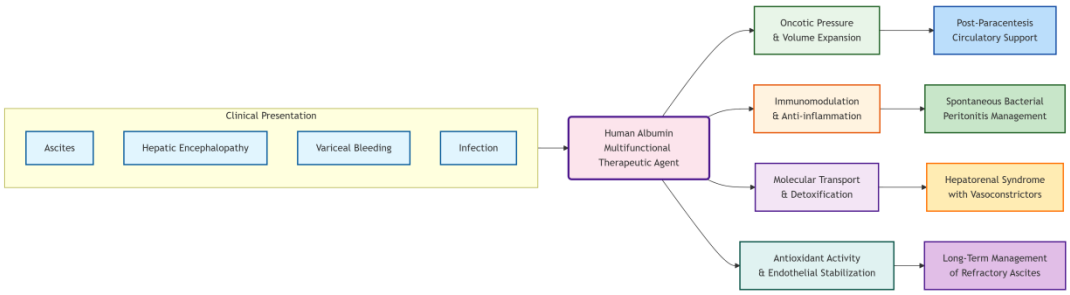

Figure 1: Therapeutic Pathway of Human Albumin in Acute Decompensation of Cirrhosis.

5. Conclusions

Human albumin demonstrates multifaceted therapeutic value in end-stage liver disease. Its mechanisms of action have expanded beyond maintaining colloid osmotic pressure to include immunomodulation, antioxidant effects, microcirculatory improvement, and organ protection[21,25,26]. In patients with AD, long-term HA therapy significantly improves survival in those with refractory ascites, and its combination with terlipressin enhances the reversal rate of HRS[27,28].

Notably, the clinical efficacy of HA varies significantly across disease types and individual patients. The optimal candidate population, dosing, and treatment duration require further clarification. Heterogeneity in results across studies underscores the need for more precise biomarkers to guide individualized therapy. With advancements in precision medicine and biotechnology, the application of HA in AD will become increasingly personalized and precise. Future efforts should involve multidisciplinary collaboration, high-quality clinical research, and translational exploration to further elucidate HA's therapeutic value, optimize clinical practice, and ultimately improve the prognosis and quality of life for patients with acute decompensation of cirrhosis.

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As the pathophysiological mechanisms of AD are further elucidated and understanding of HA's biological characteristics deepens, our appreciation of its value in treating AD and its complications continues to grow. Substantial clinical research data provide hepatologists with evidence-based guidance for HA use in AD. It is believed that with ongoing research, the application of HA in the treatment of patients with acute decompensation of cirrhosis will become increasingly rational and widespread.

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