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Uses and misuses of albumin during resuscitation and in the neonatal intensive care unit

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A B S T R A C T

Albumin is one of the most abundant proteins in plasma and serves many vital functions. Neonatal concentrations vary greatly with gestational and postnatal age. In critically ill neonates, hypoalbuminemia occurs due to decreased synthesis, increased losses or redistribution of albumin into the extravascular space, and has been associated with increased morbidities and mortality. For that reason, infusion of exogenous albumin as a volume expander has been proposed for various clinical settings including hypotension, delivery room resuscitation, sepsis and postoperative fluid management. Albumin is often prescribed in infants with hypoalbuminemia, hyperbilirubinemia, and protein-losing conditions. However, the evidence of these practices has not been reviewed or validated. Albumin infusion may initiate highly complex processes that vary according to the individual and disease pathophysiology. Indeed, it may be associated with harms when misused. In this review, we critically appraise the scientific evidence for administering albumin in most conditions encountered in the neonatal intensive care unit, while emphasizing the benefits and risks associated with their use.

1. Introduction

In the neonatal intensive care unit (NICU), several therapies are used without convincing physiological plausibility or evidence-based information. Albumin is an important protein that serves many essential functions. Infusion of exogenous albumin has been proposed for several neonatal conditions, including resuscitation, sepsis, asphyxia, hypoalbuminemia and others. In this review, we investigate the appropriateness of such practice and provide the evidence supporting it, if any.

2. Physiology of endogenous albumin

2.1. Molecular composition

Albumin is one of the most abundant proteins in plasma, accounting for about 50–60% of serum proteins and 3% of total body protein [1,2]. It is a relatively small molecule with an approximate molecular weight of 66,500 Da, and is composed of 585 amino acids organized into three repeated homologue domains and two subdomains [1,2].

2.2. Albumin synthesis

The precursor protein of albumin, pre-proalbumin, is mainly produced by hepatocytes in the liver [3,4]. Pre-proalbumin is converted to proalbumin and then to albumin in the Golgi apparatus (Fig. 1). A normal adult liver produces 10–15 g of albumin per day, equivalent to 8.5% of plasma albumin and 4% of total body albumin [2,3].

2.3. Albumin distribution

Once synthesized, almost all albumin is rapidly transferred to the plasma, where it eventually crosses the capillary wall into the extravascular space and returns into circulation through the lymphatic system (Fig. 1) [1,3,4]. Under physiological conditions, the complete distribution of albumin in the extravascular compartment occurs over 7–10 days and depends on the types of capillaries found in different body tissues [1,5]. Tissues with discontinuous capillaries (liver, spleen and gut) have rapidly equilibrating compartments, whereas tissues with continuous

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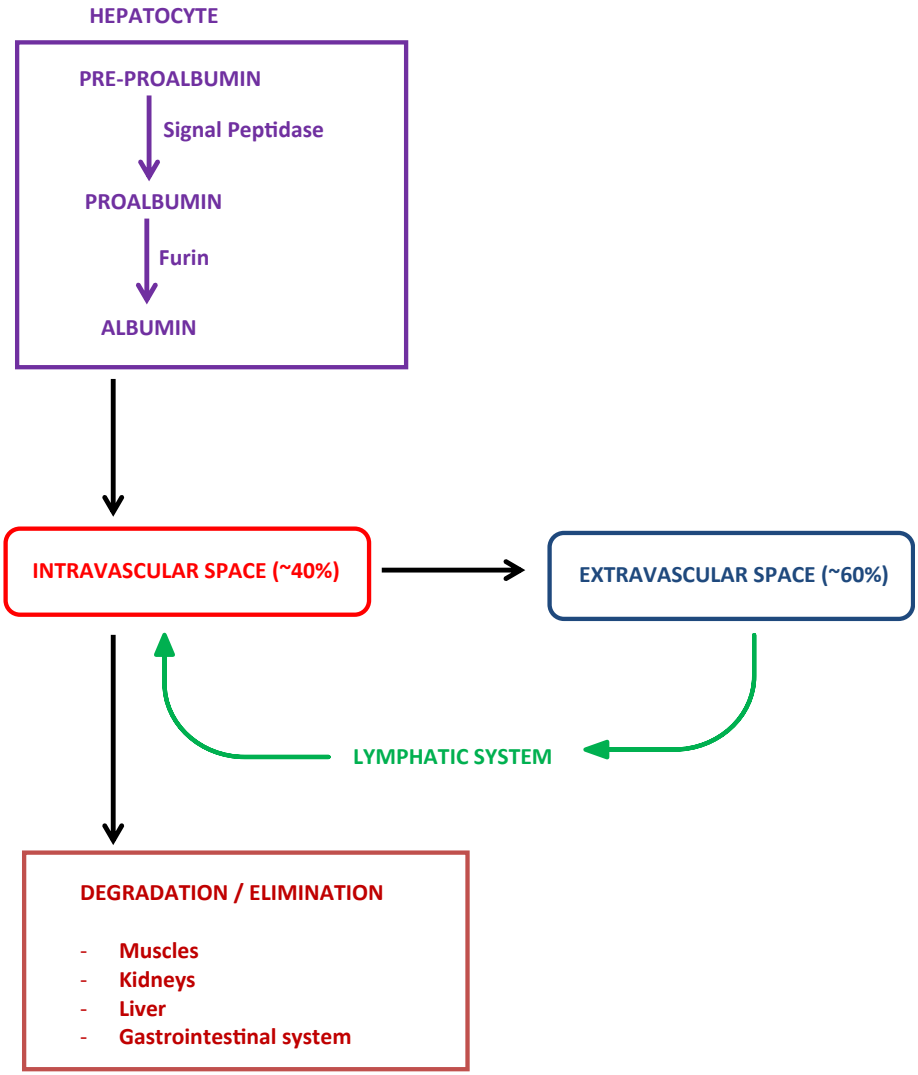

Fig. 1. Albumin synthesis, distribution, and elimination.

capillaries (skeletal muscles and skin) are slower to equilibrate. In the capillary beds, the vascular endothelium barrier is completely permeable to water, impermeable to proteins >70,000 Da, and semi-permeable to albumin, with transcapillary escape rates (TERs) of albumin approximating 4–5% per hour in healthy adults [1].

2.4. Normal newborn albumin concentrations

In contrast to adults and children, where plasma albumin concentrations range between 3.3 and 5.2 g/dL, neonatal concentrations vary immensely with gestational and postnatal age. During fetal life, albumin concentrations correspond to about 30% of the maternal levels at the end of the first trimester and progressively increase to reach maternal values by the third trimester (Table 1).

Table 1
Normative albumin concentrations.

Completed weeks gestation	Albumin concentration (g/L)		
	Maternal	Fetal	Neonatal (birth)
12–15	28	11	–
16–26	34	19	–
26–34	28	26	11–32
35–41	29	34	17–39

At birth, albumin concentrations range from 2.0 g/dL at 27–30 weeks to 3.0 g/dL at term [6]. In preterm infants, albumin concentrations are typically less due to a more rapid turnover of the albumin pool and slower rate of synthesis by the immature liver. Nonetheless, albumin synthesis, and hence albumin concentrations, increase by 15% in the first 3 weeks of life regardless of gestational age [6].

2.5. Albumin degradation

The turnover of albumin is relatively stable under physiological conditions, due to a steady balance between synthesis and metabolism. Albumin is mainly degraded by muscles, liver and kidneys, and is eliminated via catabolic (84%), renal (<6%) and gastrointestinal (<10%) processes (Fig. 1) [2,4]. The serum half-life of albumin averages 17 days in adults, 14–21 days in full-term infants and 5–7 days in the premature neonate [2,3].

2.6. Albumin functions

Albumin serves many essential functions, as listed on Box 1. The two most important functions are described below:

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