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Fluid and Electrolytes in Critically Ill Patients

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List of Abbreviations

AAP	American Academy of Pediatrics
AN/AD	Auditory abnormalities include auditory neuropathy /dys-synchrony
B/A	Bilirubin/albumin
BAER	Brainstem auditory evoked response
BBS	Bronze baby syndrome
BIND	Bilirubin-induced neurologic dysfunction
CBE	Chronic bilirubin encephalopathy
CNS	Central nervous system
CT	Computed tomography
ESR	Erythrocyte sedimentation rate
ET	Exchange transfusion
Hb	Hemoglobin
HDN	Hemolytic disease of the neonate
HIDA	Hepatobiliaryimino-diacetic acid
LED	Light-Emitting Diodes
MRI	Magnetic resonance imaging
MRP2	Multidrug-resistance associated protein
NMDA	N-methyl-D-aspartic acid
NNPT	Neonatal phototherapy
OATP	Organic anion transport polypeptide
PAs	Peripheral arteries

PDA	Patent ductus arteriosus
PV	Peripheral vein
RCT	Randomized controlled trial
RE	Reticuloendothelial
ROP	Retinopathy of prematurity
ROS	Reactive oxygen species
TB	Total bilirubin
TcB	Transcutaneous bilirubin
UC	Umbilical cord
UCB	Uncojugated bilirubin
UDPGT	Uridine diphospho glucuronyltransferase
UV	Umbilical vein

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Introduction

Fluids have been widely used in critically ill patients to optimize hemodynamics, to enhance renal protection from contrast, globins, and uric acid, to offercaloric intake and as an adjunct for medication dilution***(Yealyet al., 2014)***. During the first hours of shock syndromes,isotonic fluids can stabilize arterial pressure and perfusion and are lifesaving at times. Furthermore,to reach physiological hemodynamic targets, a large amount of intravenous fluids may be required.Some fasting patients receive infusions of one to three liters of dextrose in water with added electrolytes, mainly sodium, chloride and potassium, to avoid hypoglycemia, dehydration and electrolyte deficiency***(Besenet al., 2015).***

Fluid and electrolyte disorders are among the most common clinical problems encountered in the setting of intensive care. Critical disorders such as severe burns, trauma, sepsis, brain damage, and heart failure lead to disturbances in fluid and electrolyte homeostasis.Possible mechanisms include reduced perfusion to the kidney due to hypovolemia or hypotension; activation of hormonal systems such as renin-angiotensin-aldosterone system and vasopressin; and tubular damage caused by ischemic or nephrotoxic kidney damage, including renal insult caused by a myriad of medications used in the intensive care. In addition, inappropriate administration of fluid and electrolytes should be considered in the diagnosis and treatment of fluid and electrolyte disturbances***(Lee,2010)***.

Fluid and electrolyte abnormalities are common in critical ill patients and often represent complications from underlying disease states or medication therapies. Critically ill patients often experience alteration in absorption, distribution, and excretion of fluids and electrolytes. Changes in hormonal and hemostatic processes and fluid status are also common in intensive care unit patients***(Kaplan and Kellum, 2010).***

Most critically ill patients experience external or internal fluid shifts and hemodynamic instability. In response to these changes,intravenous fluids are frequently administered. However, rapid losses of administered fluids from circulation and the indirect link between the short-lived plasma volume expansion and end points frequently result in transient responses to fluid therapy***(Kellum, 2016)***. Therefore, fluid overload is a common finding in intensive care units. There is evidence of harm associated with fluid overload and the physiologic processes that lead to fluid accumulation in critical illness. The authors then consider methods to prevent fluid accumulation and/or manage its resolution ***(O'Connor and Prowle, 2015).***

Disturbances of body fluid homeostasis are common in major surgery and a range of critical illnesses including sepsis and trauma. Administering appropriate intravenous fluid is a core part of medical care during these episodes***(Myburgh and Mythen, 2013).*** Despite years of research, there is still widespread debate about the best dosing strategy for these fluids and the optimum fluid composition for a given clinical situation. These are still important research questions, as there are clear signs from the current literature that fluid administration strategies have the power to affect clinical outcomes in a variety of areas***(Edwards and Mythen, 2014)***.

Aim of the Work

The aim of this essay is to discuss the importance of adjustment of fluid and electrolytes in critically ill patients and in emergency settings

Body Fluids and Electrolyte Physiological Background

Fluid and electrolyte physiology is central to the clinical management of surgical patients. The composition and regulation of body fluids has been studied for centuries, and the concept of intravenous infusion of fluids was established over a century ago ***(Ritz et al., 2008)***. David Sabiston, one of the premier surgeons of the twentieth century, reviewed Alfred Blalock's landmark work on the pathogenesis of shock, which demonstrated that fluid losses related to injury could be treated with intravascular volume repletion. This work provided the foundation for intravenous therapy in the management of hypovolemia***(Davis and Rosenbaum, 2014).***

Total Body Water and the Fluid Compartments:

Total body water (TBW) is defined as the total volume of water within the body. TBW is a percentage of body weight and is dependent on both the fat content and the chronological age of the individual. TBW as a percentage of body weight decreases with increasing body fat and with increasing age ***(Wait and Alouidor,2011)***. As a general rule, TBW is 60% of the healthy adult human body weight in men and 50 % of body weight in women***(Kaye and Riopelle, 2010).***

TBW is comprised of the intracellular and the extracellular compartments. Intracellular fluid (ICF) makes up two thirds of TBW, and extracellularfluid (ECF) accounts for the remaining one third. ECF is subdivided into the intravascular and interstitial spaces. The intravascular

space accounts for 25 % of the ECF and 8 % of the TBW; this space contains the plasma volume. The interstitial space comprises the remaining 75 % of the ECF and 25 % of the TBW; this space contains a free phase of fully exchangeable water and a bound phase of minimally exchangeable water. The trans cellular compartment is an additional ECF designation this compartment contains cerebrospinal fluid, synovial fluid, the water in cartilage and bone, eye fluids and lubricants of the serous membranes. This type of fluid is poorly exchangeable and comprises approximately 4 % of the TBW. The exchangeable components of the compartments comprising TBW are in dynamic equilibrium ***(Wait and Alouidor, 2011).***

Effective circulating volume is the portion of the ECF that peruses the organs. Under normal physiologic conditions, this corresponds to the intravascular volume. This relationship is altered in some disease states. For example, in congestive heart failure and in patients who have arteriovenous fistulae, the intravascular volume as well as total body salt and water are high, but effective circulating volume is low. However, it is clear that disease processes, warrant aggressive fluid management strategies because the intravascular volume is markedly diminished in these clinical scenarios***(Kasiewicz et al., 2011).*** Hypoperfusion is the end result in these cases and is best managed with restoration of circulating volume and treatment of vasodysregulation with vasoactive press or agents. Even though the intravascular volume is only a small percentage of the TBW, significant decreases in intravascular volume are poorly tolerated when decreased mean arterial pressure occurs ***(Koeppen and Stanton, 2012).***

The ionic composition of the ECF and the ICFis highly defended in the normal physiologic state. The predominant cation in the ECF is sodium. Therefore, the ECF contains most of the sodium content of the body

(60 mEq/kg). The ECF also contains small quantities of other cations, including potassium, calcium, and magnesium. The cations are electrochemically balanced principally by chloride and lactate anions. Bicarbonate, phosphate, sulfate, albumin, and other extracellular proteins also provide negative charge in the ECF. The predominant cation in the ICF is potassium. The ICF contains most of the potassium content of the body (42 mEq/kg). The ICF also contains smaller quantities of other cations, including magnesium and sodium. Phosphates and intracellular proteins are the primary anions of the ICF, and chloride and bicarbonate are present in lower concentrations ***(Wait and Alouidor, 2011)***.

The principles of osmosis dictate the movement of water between fluid compartments. Osmotic equilibrium occurs when two solutions separated by a semipermeable membrane equalize the concentration of osmotically active particles on either side of that membrane as water moves along aconcentration gradient. Osmolarity is measured in milliosmoles per liter, mOsm/L. Osmolality is measured in milliosmoles per kilogramH2O, mOsm/kg H2O. Both define the osmotic activity of particles in solution and are considered equivalent if the concentration of solutesis very low ***(Wait and Alouidor, 2011).*** Indicates total body osmolality. Sodium [Na+] is the predominant extracellular cation, and glucose and blood urea nitrogen (BUN) concentrations are significant in certain disease states. Therefore, the following formula is used for determination of Plasma.osm

$$= 2 \times \text{serum}\left[\text{Na}^{+} \right] + \text{glucose} / 18 + \text{BUN} / 2.8$$

The principles of osmosis as they relate to hypothetical semi permeable membranes are generalizations. The physiologic membranes that separate the body fluid compartments are much more complex. The capillary endothelium serves as the membrane that separates the intravascular and interstitial

compartments. The endothelium exhibits different characteristics in different organs and is more permeable in the lung and liver than in the periphery. The capillary endothelium is very permeable, allowing for rapid equilibration between the intravascular and interstitial spaces. Therefore, the interstitial space can serve as a buffer for the more highly defended intravascular space ***(Macielet al., 2012)***.

Volume Control Mechanisms:

Under normal physiologic circumstances, plasma osmolality is tightly controlled, averaging 289 mOsm/kg H2O. Thirst and antidiuretic hormone (ADH) are the two primary regulators of water balance. Osmoreceptor cells in the paraventricular and supraoptic nuclei of the hypothalamus detect small changes in cell volume and activate the neuronal centers that control thirst and ADH secretion. Therefore, osmoreceptors control the fine-tuning of volume relationships. Stimulants of ADH secretion include nicotine, ether, morphine, barbiturates, and tissue injury (including operative tissue dissection and manipulation). Ethanol inhibits ADH secretion and its water resorption activity in the renal collecting ducts ***(Carbrey and Agre, 2009).***

The relationship of aquaporins to ADH physiology has been the subject of significant investigation over the course of the past two decades. Peter Agre, an American medical doctor and molecular biologist, won the 2003 Nobel Prize in Chemistry for the discovery of aquaporins ***(Davis and Rosenbaum, 2014)***. Aquaporins are integral membrane pore proteins that regulate the flow of water. These water channels are uniquitous in nature, including in the human body. Aquaporin proteins are comprised of six transmembrane alpha-helices arranged in a right-handed bundle, with the amino and the carboxyl termini located on the cytoplasmic surface of the membrane. The specific types of aquaporins differ in their peptide sequences ***(Fenton and Moeller, 2008)***.

The principal cells lining the renal collecting ducts control the fine-tuning of body water homeostasis by regulating water resorption through aquaporin-2 (AQP2) aquaporin-3 (AQP3) and aquaporin-4 (AQP4). AQP3 and AQP4 are embedded in the basolateral plasma membrane. ADH binds to the vasopressin-2 (V2) receptor on the basal membrane of the renal collecting duct. This triggers redistribution of AQP2 from intracellular vesicles into the apical plasma membrane. Water enters into the cells via AQP2 and exits through AQP3 and AQP4 ***(Fenton and Moeller HB, 2008) .***The mechanism of action of ADH with respect to the water permeability of the renal collecting duct has therapeutic implications. A number of nonpeptide V2 antagonists (vaptans) are in development. The mixed V2/V1a antagonist conivaptan has been approved by the US Food and Drug Administration (FDA) for intravenous use in the treatment of euvolemic and hypervolemic hyponatremia. Conivaptan produces aquaresis (solute-free water excretion), resulting in increased serum sodium levels, free water clearance, urine flow, and plasma osmolality ***(Metzger et al 2008; Davis and Rosenbaum, 2014).***

Baroreceptors control volume via sympathetic and parasympathetic connections in a less precise manner than do osmoreceptors. Stretch receptors detect changes in pressure and changes in volume that are manifested by changes in pressure. Volume receptors are located in the intra-thoracic capacitance vessels (vena cava) and the atria. Depending on volume status, these receptors either increase or decrease sympathetic tone to the kidney, which affects renal blood flow and tubular sodium resorption. Pressure receptors of the aortic arch and carotid arteries are important in extreme changes in arterial pressure (such as occurs with hemorrhage). Intra-renal baroreceptors of the afferent arteriole cause variability in release of renin depending on pressure. Hepatic volume receptors and cerebrospinal volume receptors have also been characterized ***(Aditianingsih and George, 2014)***.