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NARRATIVE REVIEW **INTENSIVE CARE**

Fluid balance in critically ill: a predictor of death?

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ABSTRACT

In the critically ill patients, fluid therapy may cause fluid overload if it is not based on the indication. The understanding of fluid therapy and precise knowledge of how much fluids a patient might need, is essential to avoid further complications that can lead to morbidity or even mortality. Goal-directed and guided fluid resuscitation is the main concept of fluid therapy, and it must be based on the recorded daily fluid balance. It is a known fact that positive fluid balance during the treatment period may lead to pulmonary edema, hemodynamic instability and can worsen the overall condition of the patient.

Abbreviations: ADH - anti-diuretic hormone; GAG - glycoproteins glycosaminoglycans; RAAS - renin angiotensin aldosterone system;

Keywords: Fluid balance, fluid overload, sepsis, acute kidney injury

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1. INTRODUCTION

Fluid balance is one of the important parameters to be monitored in the emergency room (ER), operating room (OR) as well as in the intensive care unit (ICU). It has been suggested that excessive fluid therapy may increase morbidity and the mortality.[1] Fluid overload often happens if the fluid administration is done without proper monitoring, especially in patients with hemodynamic instability and/or conditions associated with capillary leakage. This situation might commonly be found in critically ill patients. Wikipedia defines fluid balance as; "Fluid balance is an aspect of the homeostasis of organisms in which the amount of water in the organism needs to be controlled, via osmoregulation and behavior, such that the concentrations of electrolytes in the various body fluids are kept within healthy ranges". We have to understand how is the fluid processed in the body physiologically. Our clinical decisions regarding management of complex diseases must take maintenance of the fluid balance into consideration.

2. Physiology of Body Fluids

In the body, the fluids are mainly composed of water and a number of substances. These substances include electrolytes; e.g., sodium, magnesium, chloride and potassium etc. There are also metabolites, such as glucose, oxygen, and carbon dioxide etc. There are non-electrolytes within the body water including proteins; e.g., immunoglobulin, albumin, coagulation factors and hormones. All of the substances mentioned are regulated within the body and maintained in a stable physiological state or homeostasis.[2]

Fluid in the body can be roughly calculated with the rule of three.[2] For example, for an average 70 kg patient, total body water will be for two-thirds of total body weight, means his total body water will be 45 kg (equal to 45 L). Total body water is divided into intracellular and extracellular spaces, and the rule of three is applied, so that 30 kg (equal to 30 L) is in the intracellular and 15 kg (equal 15 L) in the extracellular space. Extracellular fluid is further divided, so that two-thirds of it is in the interstitial compartment and the rest in the intravascular compartment (Figure 1).

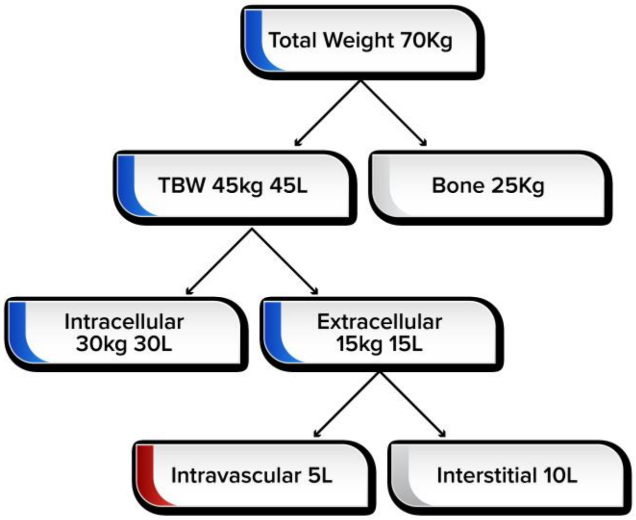

Figure 1: Distribution of body fluids

Fluid movement depends upon hydrostatic and oncotic pressure between blood and tissues as stated in the Starling Principle.[3] Hydrostatic pressure at the arterial end of the capillaries moves fluid out of the capillary, and the oncotic pressure at the venous end of the capillary moves fluid into the capillary, and both are affected by cardiac output. Water, lactic acid, creatinine, oxygen and carbon dioxide can diffuse through the capillary wall. Excess fluid is regulated by the lymphatic system to move back into the intravascular compartment. Fluid in the intravascular compartment depends on water and sodium concentration. Changes in this concentration causes alterations in both plasma volume and its osmolarity. Plasma osmolarity is regulated centrally within the hypothalamus that induces anti-diuretic hormone (ADH) release. Plasma volume is mainly influenced by the renin-angiotensin-aldosterone system (RAAS).[2]

2.1. Revised Starling Principle

Starling's late idea that the movement of fluid between blood and tissues was determined by hydrostatic and oncotic pressures, required revision as stated by Woodcock and Woodcock.[4] The revised Starling Principle discovered that there are micro vessels, which are permeable to macromolecules and pressure balance doesn't stop fluid exchange. The difference of oncotic pressure in the plasma and interstitial space is ruled by low and steady filtration levels, that generally occur in the intestinal mucosa and peritubular capillaries that keeps the interstitial oncotic pressure low. Steady filtration rates are affected by changes of pressure and perfusion. The revised Starling Principle is focused on the oncotic pressure in the microvessels surrounding compartments which are also important in regulation of plasma volume.

2.2. Endothelial Glycocalyx

Glycocalyx layer of vascular endothelium is composed of sugar protein coating that need to be preserved to maintain homeostasis within the body.[5] The glycocalyx contributes up to 2% of the plasma intravascular volume. There are three important constituents form the glycocalyx such as proteoglycans, glycoproteins and glycosaminoglycans (GAGs). GAGs form an active layering in blood and the capillary wall. The glycocalyx layer is a semipermeable membrane that responds to anionic macromolecules such as albumin and plasma proteins. Increased GAGs in plasma are often found in septic shock patients and reduced volume of the glycocalyx layer is also found in diabetes and acute hyperglycemia. Loss of functional glycocalyx has a correlation with edema.[6]

3. Fluid Therapy and its Complications

In the ICU setting, intravenous fluid therapy is frequently used in critically ill patients. Fluid resuscitation is aimed at maintaining homeostasis and preventing fluid imbalance in conditions of impaired tissue perfusion, low cardiac output, abnormal vital signs, low urine output, and skin mottling.[6] The main objective of fluid resuscitation is to increase stroke volume, which in turn augments the cardiac output and an improved tissue oxygenation.

Shock is a common presenting sign in critically ill patients. Shock is a life-threatening manifestation of circulatory failure. Circulatory shock leads to cellular and tissue hypoxia resulting in cellular death and dysfunction of vital organs. Shock is categorized into four types; hypovolemic, distributive, obstructive and cardiogenic shock. The first thing to do in every type of shock is intravenous fluid resuscitation as a first response. Hypovolemic shock is often caused by hemorrhage, loss of body fluids in diarrhea and vomiting, severe burns of skin and it can be mixed with distributive shock in inflammatory states such as sepsis that is preceded by increased vascular permeability. The treatment depends upon the cause of the shock. The main shock sign in sepsis is collapsed neck veins with several clinical features manifested such as hypotension, cold clammy extremities, tachypnoea and tachycardia.

Intravenous fluid therapy is also considered as a drug, which has indications to give, limitation dose and adverse effects. The four Ds principle used in fluid therapy is: 'drug', 'dosing', 'duration' and 'de-escalation'.[7] Before institution of the fluid therapy, the clinician must ask himself the following questions; What type of fluids we should give? How much does the patient need? For how long it should be continued? When do we need to stop? The four phases of fluid management are: 'salvage', 'optimization', 'stabilization' and 'de-escalation'. The first phase is mainly to treat and find the main cause of the shock, reach minimum blood pressure within the range of mean arterial pressure (MAP) 60-65 mmHg, give 500 mL crystalloid solution in 30 min and give vasopressors if needed. The aim of the optimization phase is to improve organ perfusion and mental status with targeted MAP > 65 mmHg, urine output > 0.5 mL/kg/h, and serum lactate < 2 mmol/L. The next phase is stabilization after no further circulatory shock occurs. The de-escalation phase is maintaining hemodynamic stability with parenteral nutrition and eliminating excess unnecessary fluid in the body with diuretics.

The fluids mostly used in resuscitation are either crystalloids or colloids. The crystalloids are the solutions of ions which have a capability to pass through semipermeable membranes. These contain sodium, chloride and ions that affect the efficacy on vascular volume expansion, and thus, can be used for resuscitation as well as for maintenance therapy in critically ill patients. The most popular amongst the crystalloids is normal saline (0.9% NaCl solution), which contains sodium and chloride in equal concentrations. Based on its strong ion difference (SID) is zero, excessive fluid administration will lead to metabolic acidosis. It is thought to activate tubuloglomerular feedback because of its chloride-rich composition, then inducing afferent arteriolar vasoconstriction and decreased glomerular filtration rate.[6] Crystalloid fluids are used as the first line fluids for an acute condition in the ICU. These can be categorized into three types, based upon the different concentrations, e.g., hypotonic, isotonic and hypertonic. Hypotonic solution reduces osmolality of extracellular compartment, then moves fluid to intracellular compartment. Hypertonic solution causes water to shift into the extracellular compartment and it expands the extracellular fluid volume. Hypotonic solutions are usually used for maintenance therapy.

Colloids are also chosen to be an option for fluid management, and theoretically have an advantage over crystalloids since total fluid volume needed is reduced for with volume expansion. The colloids might reduce interstitial edema. Human albumin is one of the appropriate colloids for fluid resuscitation. It acts as a buffer molecule, predominant plasma protein, and the determinant factor of plasma colloid pressure. Human albumin solution also has an advantage for fluid resuscitation in sepsis and other bacterial infections. Normally, albumin ranges between 35-55 g/L within the plasma.

4. Fluid Balance

Keeping the record of daily fluid balance in critically ill patients has a major role in fluid resuscitation. Inability to track down might lead to complications such as fluid deficit or overload. The volume of fluid resuscitation needed depends on the documented fluid balance to achieve an adequate therapy. As Davies et al. discovered in their systematic review of 13 cohort studies, inconsistent recording of daily fluid balance reduces the accuracy of monitoring the changes and may lead to unmeasured risk of fluid overload.[8] Li et al. stated in their retrospective study of 567 critically ill patients that negative fluid balance in post cardiovascular surgery is associated with lower risk of mortality. It further states that the negative fluid balance on day 2 had lower mortality (3.4% vs. 12.2% of the positive fluid balance group).[9]

Fluid overload is defined as a condition in which edema, excessive weight gain and positive fluid balance happen in a patient that has received fluid therapy.[10] The occurrence of fluid overload is characterized by edema, hypervolemia, or in severe conditions such as pulmonary edema, peripheral edema and body cavity effusion. The main effect of fluid overload, beside edema, is hypervolemia, a state of inappropriate high blood volume and increased mean circulatory filling pressure (MCFP), where in a normal condition, increased pressure between the MCFP and central venous pressure by intravenous fluid administration increases the cardiac output. Impaired water excretion by the kidneys and the declined interstitial compartment function contribute to the development of fluid overload. Interstitial pressure is regulated by connection of the collagen matrix in integrin receptors that relate to actin of the cytoskeleton. Under inflammation state, the cytoskeleton is depolymerized and the integrin to collagen link is damaged leading to loosening of the matrix; finally, the interstitial fluid pressure falls. Another situation that can lead to edema in inflammation state is reduced plasma albumin and damaged endothelial barrier to albumin, including the endothelial glycocalyx. Fluid overload can impair gas exchange in the lung, impair oxygen diffusion and damage some vulnerable organs.

Another term that actually used besides fluid overload is positive fluid balance. As Sakr et al. found in his study towards 730 ICUs in 84 countries, there were 1808 patients with sepsis as the diagnosis and higher cumulative positive fluid balance on day 3 was associated with increased risk of mortality.[11] The mechanism of fluid excess that affect the lung can be explained that inadequate intravenous fluid administration makes excessive fluid get into the intravascular compartment, then it increases the hydrostatic pressure within the lungs. The functional lymphatic drainage is also affected and it is overwhelmed by the fluid filtration between the alveoli. It impairs the ability of the diffusion of oxygen and ultimately leads to hypoxia.[12]

Fluid balance monitoring is suggested to be more personalized to help improve patient outcomes. Douglas et al. states that physiology-based guided fluid administration is associated with lower fluid balance and improved vital organs in sepsis when dynamic fluid management protocol is involved during the therapy. When fluid resuscitation is accurately monitored, it may reduce patient's need for diuretics, as Douglas et al. found that patients administered with fluid guided resuscitation and vasopressors had 1.37 L difference fluid balance in 72-hour fluid balance monitoring than usual patients.[13,]

The incidence of positive fluid balance is common in critically ill patients and may lead to another complication such as acute kidney injury, sepsis, and acute respiratory distress syndrome etc. Human albumin is one of the choices of treatment in that case. The human albumin is used for active removal of excess fluid. Wiedermann found in his review that the combination of hyper oncotic human albumin solution with diuretics can be used in some phases of fluid resuscitation to achieve hemodynamic instability by correcting hypoalbuminemia and increasing osmotic colloid pressure, thus reducing the risk of edema formation.[14]

Acute kidney injury can happen as a complication of sepsis and hypovolemia, and is commonly found in critically ill patients. This is linked to another important aspect which must be considered in the fluid resuscitation, - kidney oxygenation. Fluid therapy has several adverse effects on kidney metabolism and perfusion. Montomoli et al. suggest that fluids have a nonoptimal oxygenation together with hemodilution that will decrease blood viscosity.[15] It will lead to decreased oxygenation in cortex and medulla of the kidney.

5. CONCLUSION

Fluid balance must be monitored in critically ill patients to achieve better prognosis and overall hemodynamic instability. The recording of the daily fluid balance is important as it can determine the need of fluid therapy or fluid resuscitation or the need of diuretics. The evidence of positive fluid balance or fluid overload that can increase the risk of mortality is clearly stated in some studies. Further researches on the association of positive fluid balance and increased mortality is needed in order to give an understanding that positive fluid balance may lead to dangerous complications and prevent undesirable effects fluid therapy.

6. Conflict of Interest

The authors declare no conflict of interest in this study and no funding was involved.

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8. Authors contribution

BPS: Concept, conduction of the study work and manuscript editing

MRS: Literature search, concept, illustrator

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