# The Use of Hypertonic Saline In Critical Care

## Essay

Submitted for partial fulfillment of Master Degree *In Intensive Care Medicine* 

By:

**Mohamed Bedeer Ghazy** M.B.B.Ch

Under supervision of

#### **Prof. Bahaa Eldin Eewees**

Professor of Anesthesia and Intensive Care Faculty of Medicine Ain Shams University

## Dr. Amir Kamal Eshak

Lecturer of Anesthesia and Intensive Care Faculty of Medicine Ain Shams University

> Faculty of Medicine Ain Shams University 2012





First and foremost, thanks to **Allah** for giving me the will and the patience to finish this work.

I find it difficult to express my gratitude and sincere feelings to my supervisors and all those who offered me help and advice during laying down the manuscript of this thesis. May Allah reward them all.

I would like to express my thanks to **Prof. Dr. Bahaa Eldin Eewis** Professor of Anesthesia and Intensive Care Faculty of Medicine Ain Shams University for his sound advice and guidance. He kindly offered me his advice and guidance all over the period of my work.

I am also grateful to **Dr. Amir Kamal Eshak** Lecturer of Anesthesia and Intensive Care Faculty of Medicine Ain Shams University for his enthusiasm, keen supervision, and kind help. She kindly assisted me and offered me a lot of her precious time.

I also thank all my professors, seniors and colleagues in Ain Shams University for their sincere encouragement, and help.

Finally, I thank my parents, my wife, my children and my whole family for their support, patience, and forbearance during my work.



Mohamed Bedeer Ghazy

# **Contents**

List of Abbreviations	i
List of Tables	ii
List of Figurs	iii
Introduction and Aim of the Work	1
Relevant fluid and electrolyte physiology & Preparati	ions
of Hypertonic saline	
The mechanism of action of hypertonic saline	42
Clinical uses of hypertonic saline in critical care	49
Potential side effects and complications	86
Summary	93
References	95
Arabic Summary	

# **List of Abbreviations**

ANF : Atrial natriuretic factor

ANG II : Angiotensin II

ANP : Atrial natriuretic peptide

E : Epinephrine

ECF : Extracellular fluid

GFR : Glomerular filtration rate

ICF : Intracellular fluid

ISF : Interstitial fluid

LVP : Lysine vasopressin levels

NE : Norepinephrine

NO : Nitric oxide

TBW : Total body water

## List of tables

Table	Title	Page
1	Summarises the osmolarity and sodium concentrations of the different hypertonic saline solutions used in clinical trials	34

# **List of Figurs**

Fig.	Title	Page
1	Fluid compartments of the body. These are approximate values for a 70 kg person (per cent of total body water (TBW)	5
2	Osmotic movement of water. Water flows across a semi-permeable membrane driven by osmotic pressure.	8
3	Osmotic composition of different body fluids	9
4	Cells activate volume regulatory mechanisms in response to volume perturbations. Volume regulatory solute loss and gain are termed regulatory volume decrease (RVD) and regulatory volume increase (RVI), respectively.	9
5	Volume regulatory electrolyte loss and accumulation is mediated by changes in the activity of membrane carriers and channels.	10
6	The mechanism of organic osmolytes accumulation and loss	12
7	Mechanism whereby renal interstitial hydrostatic pressure reduces sodium reabsorption in response to extracellular fluid volume expansion	18
8	Mechanisms whereby increases in renal perfusion pressure enhance sodium excretion. PT, proximal tubule	20
9	Mechanism whereby activation of sympathetic nervous system reduces sodium excretion in response to extracellular fluid volume contraction	22

## List of Figurs (Cont.)

2150 01 1 1 <b>5</b> 0115 (Cont.)				
Fig.	Title	Page		
10	Mechanism whereby activation of renin-	25		
	angiotensin system reduces sodium excretion			
	in response to extracellular fluid volume contraction			
	Mechanism whereby atrial natriuretic peptide			
	enhances sodium excretion in response to			
	extracellular fluid volume expansion			
11	Mechanism whereby nitric oxide increases	29		
	sodium excretion in response to extracellular			
	fluid volume expansion. GFR, glomerular			
	filtration			
12	Integrated response to increases in dietary	30		
	sodium intake. ANF, atrial natriuretic factor			
13	Hypertonic saline dextran reverses	45		
	endothelial swelling, restoring blood flow to			
	near normal levels			
14	Central pontine demyelination after HTS	88		
	rapid infusion			

#### Introduction

Clinical use of hypertonic solutions dates back to 1926, when Silbert used 5% saline to treat Burger's disease. Moderately hypertonic solutions of 1.5% to 3% have been used to treat patients with burn shock and hypovolemia since the 1970s (**Monafo, 1970**).

The use of isotonic crystalloids for resuscitation has several limitations as large volumes are needed and the fluid rapidly redistributes throughout the extravascular space. Hypertonic solutions, on the contrary, are administered as small-volume boluses and, by mobilizing extravascular water to the intravascular space, result in an immediate restoration of intravascular volume that can last several hours. Additional properties of hypertonic solutions include positive effects on cardiac function, the microvasculature, and the immune system that not only justify their use in shock resuscitation but also suggest the opportunity for other applications (**Kyes and Johnson, 2011**).

Hypertonic saline resuscitation may reduce the inflammatory responses triggered by shock and trauma, decrease susceptibility to post-traumatic sepsis, modulate trauma and sepsis-induced immune dysfunction, inflammatory response and apoptosis. These beneficial effects may be of potential relevance for the management of severe sepsis and septic shock (**Poli de Figueredo, et al 2006**).

Owing to their systemic effects and osmotic effect on the brain, hypertonic saline solutions have been investigated as resuscitative fluid in brain-injured patients with hemorrhagic shock, as therapy for intracranial hypertension resistant to standard therapy, as first line therapy for intracranial hypertension in certain intracranial pathologies, as small volume fluid resuscitation during spinal shock, and as

#### Introduction and Aim of The Essay

maintenance intravenous fluid in neurocritical care (Qureshi and Suarez, 2000).

Hypertonic saline is used in treating symptomatic hyponatraemia. In acute hyponatremia, usually observed in the postoperative period, prompt treatment with hypertonic saline can prevent seizures and respiratory arrest. On the other hand, chronic symptomatic hyponatremia, rapid correction should be avoided to reduce the risk of development of osmotic demyelinating syndromes (**Decaux** *and Soupart*, **2003**).

Nebulised hypertonic saline is a promising treatment in cystic fibrosis as it can enhance mucociliary clearance and lessen the destructive inflammatory process in the airways (*Wark and McDonald*, 2009).

Potential adverse effects of intravenous administration of hypertonic saline include electrolyte abnormalities, cardiac failure, renal failure, bleeding diathesis, and phlebitis. Although unproven, a possibility for central pontine myelinolysis and rebound intracranial hypertension exists with uncontrolled administration (Qureshi and Suarez, 2000).

## Introduction and Aim of The Essay

## **Aim of Essay**

This work aims to provide a comprehensive overview of body fluid and electrolyte physiology, uses and mechanism of possible therapeutic effects of hypertonic saline and the potential adverse effects and complications of its use in the intensive care setting.

## Relevant fluid and electrolyte physiology

The example of homeostasis and homeostatic imbalances shown by acid—base balance is one of many homeostatic systems that act throughout the body to maintain a constant internal environment. A large number of other examples can be used to show how important this balance is and the consequences of its failure, but one of the most critical is the maintenance of the correct fluid balance.

The human body contains large quantities of water in a number of different compartments, and the maintenance of the correct amounts of fluid, of the correct composition in the different compartments is essential for all vital chemical reactions.

#### **Body Fluids And Fluid Compartments**

#### **Body Fluids:**

The total body water (**TBW**) of adult male is about 60%. This percentage varies with age and weight. Babies, at birth, are about 80% water, while an elderly person may only have about 50% water. As the amount of adipose tissue increases, the proportion of body water decreases. The TBW is divided into two main compartments—which have different ionic compositions (Fig. 1-1).

- **Intracellular fluid** (ICF), which is contained inside all cells, is about two-thirds of the TBW (or 40% body weight).
- **Extracellular fluid** (ECF), which surrounds all cells, is about one-third of the TBW (or 20% body weight).

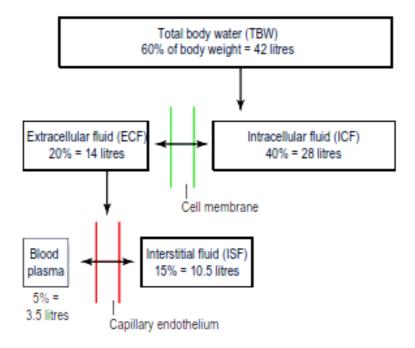


Figure 1 Fluid compartments of the body. These are approximate values for a 70 kg person (per cent of total body water (TBW), (Joe Patlak, 1999).

#### The ECF itself is divided into two main compartments:

- **Interstitial fluid** (ISF). This is about three-quarters of the ECF (or about 15% TBW). The ISF surrounds the cells but is outside the blood vessels. Unlike the blood plasma, it contains very little protein and few cells in suspension.
- **Blood plasma**. This is one-quarter of the ECF (or about 5% TBW). It is the fluid inside the blood vessels and carries the other components of blood, such as red and white blood cells and plasma proteins, in suspension around the body. Fig. (1-1) shows the volume in various compartments in an adult weighing 70 kg. The total blood volume is about 5.5 L for a 70 kg person. Only

3.5 L of this is blood plasma, the remainder is mainly red blood cells. The total blood volume is about 5.5 L for a 70 kg person. Only 3.5 L of this is blood plasma, the remainder is mainly red blood cells.

#### **Fluid Compartments:**

The different fluid compartments are separated by semipermeable barriers with different characteristics. In tissues, the cells are surrounded by membranes which allow water movement in and out of cells, but restrict the movement of the main extracellular ion, sodium. The interstitial fluids are separated from the blood plasma by a layer of cells, the endothelium. Gaps between the cells allow free movement of water and ions, but under normal conditions restrict the blood cells and proteins to the vascular compartment. This means that water can move freely between the compartments but that sodium does not move into cells, and proteins and blood cells are restricted to blood (Joe Patlak, 1999).

#### Fluid movements among fluid compartments:

The movement of water between the compartments is determined by the differences in hydrostatic and osmotic pressure in the different compartments. Hydrostatic pressure is produced by the pumping action of the heart, and osmotic pressure by the concentration of solute particles. Water moves osmotically from dilute to concentrated solutions, moving from a high concentration of water to a low one Fig (1-2).

The more solute particles there are in a solution the greater the 'pull' on the water molecules. Osmolarity is determined by the number of osmotically active particles per litre and the normal osmolarity of body fluids is 290 mOsm/L. The tonicity of a solution is the actual effect of a solution on a living cell. A solution bathing a cell that does not cause the

cell to osmotically take up or lose water is said to be isotonic (Joe Patlak, 1999).

A hypertonic solution, which contains more osmotically active particles than the cell, would cause cells to lose water and shrink. In a hypotonic solution, the cell takes up water until it bursts (lysis). The tonicity of a solution not only depends on the solute concentration but on the nature of the solute. For example, a solution of sodium chloride that has an osmolarity of 290 mOsm/L has no effect on the cells, so it is isotonic. However, a solution of urea of 290 mOsm/L causes cell lysis; it is hypotonic. This is because the cells are impairment to sodium, which does not move into the cells, but urea can cross the cell membrane. So it moves into the cell, increasing the number of osmotically active particles inside the cell, then water follows and the cell swells and bursts. This shows that it is not only the volume of water surrounding the cells that is important but the solutes as well (Joe Patlak, **1999**).

Under normal conditions, while there are large exchanges of fluid between the different fluid compartments over time there are no net changes in the volumes in each compartment. This is because the different compartments have the same tonicity. However, if there was a change in either the water content or solute concentration in a compartment then net changes would occur (Joe Patlak, 1999).

#### **Body fluid osmotically active solutes:**

The three major fluid compartments have different solutes within them. The major extracellular ions are sodium (Na) and chloride (Cl-). The major intracellular ions are potassium (K+) and large anions such as protein and phosphate (Guyton, 1996).