Clinical Evaluation of Hemodynamic Effects of Hypertonic Saline

Thesis Submitted for Partial Fulfillment of the M.D. Degree in Anesthesia

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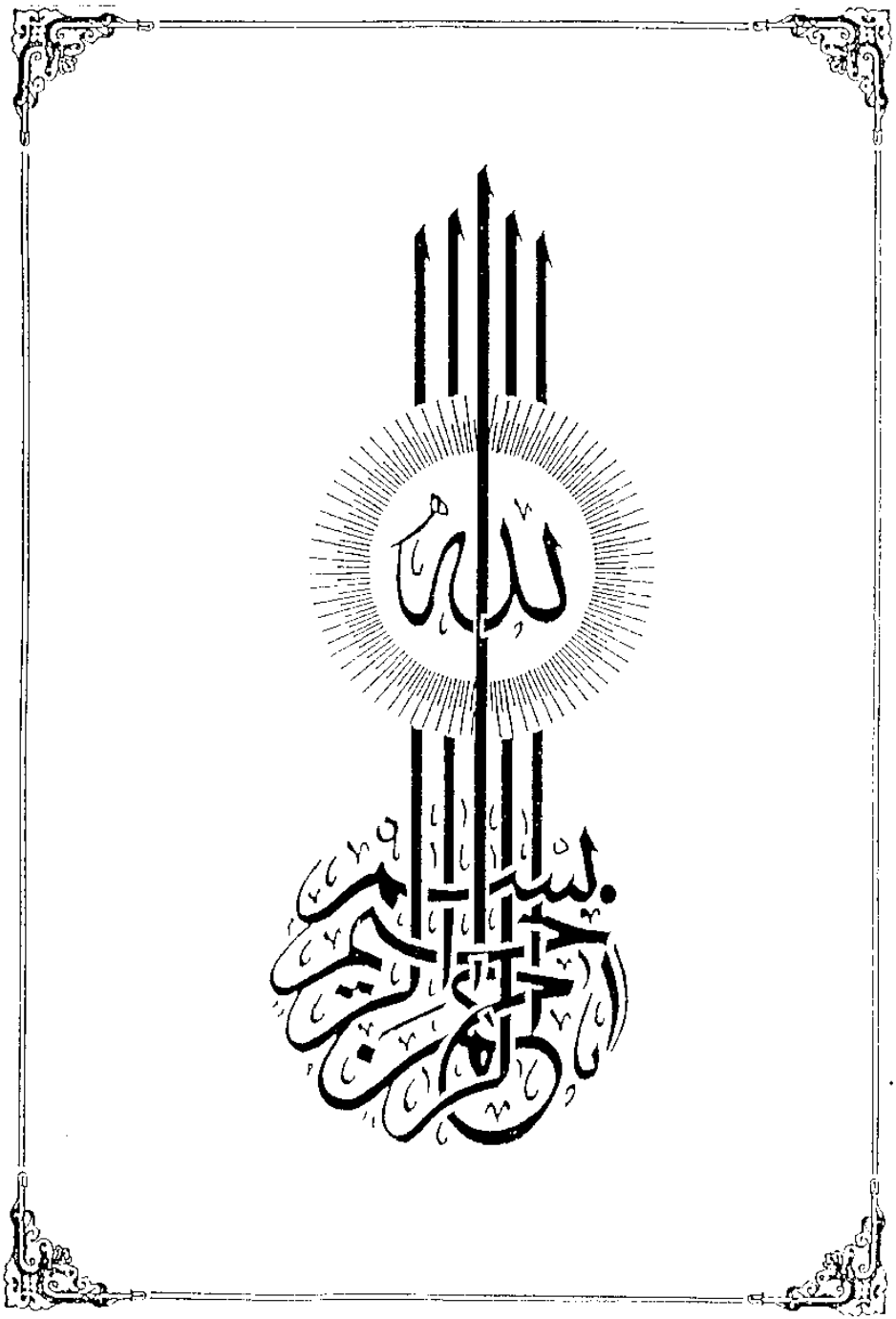
***** 1997 *****

بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

سورة البقرة - الآية ٣٢



To My Family

Acknowledgment

First, thanks are all due to **Holy God** for blessing this work until it has reached its end, as a part of his generous help throughout my life.

I would like to direct special thanks to **Prof. Dr. Mohamed Reda Adel Gawad**, Professor of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, for the great support and encouragement he gave me throughout the whole work. It is a great honor to work under his guidance and supervision.

I would like to express my sincere gratitude to **Dr. Nermin Sadek Nasr**, Assistant Professor of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, for her close supervision, continuous help, and the tremendous effort she has done in the meticulous revision of the whole work.

Also, I am greatly honored to express my utmost thanks to **Dr. Adel Ahmed Fathy Mohamed**, Assistant Professor of Anesthesia and intensive Care, Faculty of Medicine, Ain Shams University, from whom I received faithful supervision, valuable suggestions, and continuous guidance throughout this work.

Mohamed Hosam Eldine

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Introduction

There are different concentrations of hypertonic saline available for clinical use : 2.7%, 3%, 5%, 7.2%, 7.5%, and 10%. Hypertonic saline has been proposed for intraoperative volume replacement ***(Boldt et al., 1991)***. Hypertonic saline may be used to correct hyponatremia ***(Hahn, 1991)***.

The hemodynamic effect of hypertonic saline is based on osmotic translocation of extracellular and intracellular water into the vascular compartment, on peripheral vasodilation and on improvement of regional blood flow ***(Kien et al., 1991)***. In addition to volume expansion, hypertonic saline 7.5% may augment cardiac performance by directly increasing cardiac contractility, reducing afterload, and increasing venous return through a decrease in venous capacitance ***(Axel et al., 1995)***. Hypertonic saline 7.5% has been suggested as a rapid and effective treatment for hypovolemic shock in man ***(Nakayama et al., 1984)***.

For each milliliter of hypertonic saline 7.2% infused, plasma volume is known to increase approximately 3 mL which is the basis of the concept of "small volume resuscitation" ***(Schertel et al., 1990)***.

Aim of the Work :

Clinical evaluation of the uses and hemodynamic effects of hypertonic saline; its effect on the cardiac function, on blood osmolality and indirectly on liver perfusion.

Review of Literature

Homeostasis of Sodium Ion

Alterations of body water and sodium content and distribution can produce multiple organ system dysfunction during the perioperative period. Management of patients with water and sodium disorders requires an understanding of the distribution of water and electrolytes and the electrophysiology of cells *(Schrier, 1992)*.

I. Physiological Role of Sodium Ion :

The electrophysiology of excitable cells is dependent on the intracellular and extracellular concentrations of sodium, potassium, and calcium. An essential characteristic of excitable cells is their ability to maintain concentration gradients for sodium and potassium across their membranes. This unequal distribution of ions (excess potassium inside and sodium outside cells) produces an electrochemical difference across cell membranes, with the interior of cells negative relative to the exterior *(Stoelting and Dierdorf, 1993)*.

At rest, the interior of cells is about -90 mV with respect to the outside of cells. The negative electrical potential of cell interiors is designated the resting membrane potential. The arrival of an appropriate stimulus (electrical, chemical, mechanical) results in altered permeability of cell membranes, such that sodium enters and potassium leaves the cells. The net effect of this change is a decrease in the electrical potential difference (the resting membrane potential becomes less negative) across the cell membrane. When the difference across cell membranes is about -70 mV, a sudden additional influx of

sodium reverses the electrical charge across the cell membranes, producing an action potential *(Stoelting and Dierdorf, 1993)*.

The electrophysiology of cells, and the resulting action potential, are altered by changes in the concentrations of electrolytes **(figure 1)**. Potassium gradients across cell membranes are the key determinants of resting membrane potentials. An increase in the extracellular concentration of potassium results in a less negative resting membrane potential that is close to the threshold potential. Conversely, a reduction in the extracellular concentration of potassium makes the resting membrane potential more negative. Excitability of cells is partly related to the distance between the resting membrane potential and the threshold potential. Since hyperkalemia brings the resting membrane potential close to the threshold potential, a smaller impulse is required to elicit an action potential *(Rose, 1994)*.

The effect of potassium on the rate of spontaneous depolarization and conduction velocity of neural impulses must also be considered when predicting effects of changes in the concentration of this electrolyte on the excitability of cells. For example, hypokalemia increases the rate of spontaneous depolarization, while a high concentration of extracellular potassium slows the conduction velocity of neural impulses. Sodium is also necessary for the cellular depolarization and generation of an action potential. Indeed, the amplitude of the action potential is decreased in the presence of hyponatremia. Calcium ion is also necessary for the maintenance of threshold potentials *(Stoelting and Dierdorf, 1993)*.

Distribution of Body Water

Total body water content is greatest at birth, representing about 70% of the body weight in kilograms. With increasing age, total body water content decreases, constituting about 60% of the

body weight of an average adult male and 50% of the body weight of an adult female. This difference is attributable to the greater fat content of females. Constant total body water content is important for the viability of cells. Indeed, water is the medium in which all metabolic reactions occur. Furthermore, all nutrients and solutes of the body are dissolved or suspended in water *(Rose, 1994)*.

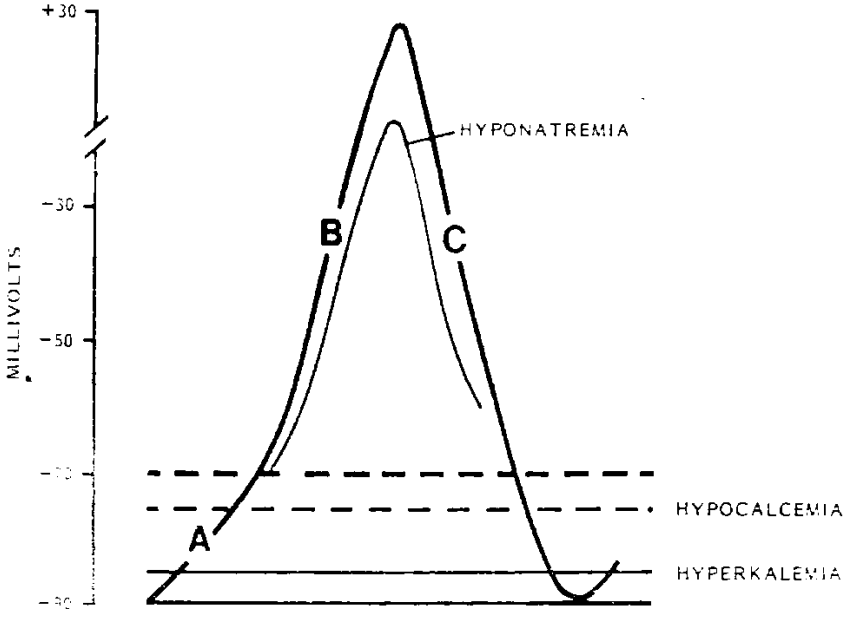

Figure (1) : Schematic diagram of the action potential of an automatic (pacemaker) cell. The resting membrane potential (bottom line) is normally -90 mV. Continuous movement of sodium and potassium ions across the cell membrane results in spontaneous depolarization (A) until the threshold potential (top dashed line) is reached at about -70 mV. When the threshold potential is reached, there is sudden increase in the permeability of the cell membrane to sodium, and rapid depolarization (B) leads to the production of an action potential. After propagation of the action potential, permeability of the cell membrane is restored, sodium is pumped out of the cell, and repolarization occurs (C). Disturbances of electrolyte concentrations alter the electrophysiology of the cell. For example, hyponatremia decreases the amplitude of the action potential. Hyperkalemia results in a less negative resting membrane potential. Hypocalcemia results in a more negative threshold potential.

Total body water content is categorized as intracellular fluid or extracellular fluid, according to the location of water relative to cell membranes. Intracellular fluid represents about 55% of the total body water content; the remaining water is distributed as extracellular fluid. Extracellular fluid is further divided into interstitial and intravascular (plasma) fluid on the basis of the location of water relative to the capillary membranes ***(Stoelting and Dierdorf, 1993)***. The water content of these fluid spaces is calculated in **table (1)**.

Table (1): Calculation of total body water content and distribution in a 70-kg adult.

	Male	Female
Total body water	42 L (70 x 0.6)[a]	35 L (70 x 0.5)[a]
Total intracellular water	23 L (42 x 0.55)[b]	19 L (35 x 0.55)[b]
Total extracellular water	19 L (42 x 0.45)	16 L (35 x 0.45)

[a] Total body water content constitutes 60% of the body weight (kg) of an adult female and 50% of the body weight of an adult female

[b] Intracellular water represents about 55% of the total body water content.

(Cogan, 1991)

The body's main priority is to maintain intravascular fluid volume. Acute reductions in this volume, as occur with fluid deprivation during the preoperative period, blood loss, or surgical trauma that results in tissue edema (third-space) elicit the release of antidiuretic hormone (ADH), renin, and possibly atrial natriuretic factor (ANP). This peptide is released from both right and left atrial

cells following atrial distention and have two major actions: potent arterial vasodilatation and increased urinary sodium and water excretion in the renal collecting tubules. This factor has salutary effect in heart failure. It is potent vasodilator and has properties that antagonize the effects of angiotensin, aldosterone and arginine vasopressin ***(Stoelting and Dierdorf, 1993)***.

These substances subsequently result in responses at renal tubules that lead to the restoration of intravascular fluid volume. Furthermore, interstitial fluid is in dynamic equilibrium with intravascular fluid, serving as an available reservoir from which water and electrolytes can be mobilized into the circulation. Conversely, interstitial fluid spaces can accept water and electrolytes, if these substances are present in excess amounts in the intravascular fluid spaces. Peripheral edema is a manifestation of excess amounts of water in the interstitial fluid spaces ***(Rose, 1994)***.

The pressure necessary to prevent movement of solvent (water) to another fluid space is designated the osmotic pressure. Indeed, osmotic pressure is the principal determinant of the distribution of water among the three major compartments. Sodium is the most important cation for determining plasma osmolarity. In this regard, plasma osmolarity can be predicted clinically by doubling the plasma sodium concentration. Low plasma osmolarity (below 285 mOsm.L-1) means a high concentration of water; a high osmolarity (above 295 mOsm.L-1) means a low concentration of water ***(Rose, 1987)***.

Calculation of Plasma Osmolarity :

The osmolarity of a solution refers to the number of osmotically active particles per liter of solution.

$$\text{Plasma Osmolarity} = 2\ (\text{plasma sodium content}) + \frac{\text{BUN}}{2.8} + \frac{\text{Glucose}}{18}$$

Normal plasma osmolarity is 285 - 295 $mOsm.L^{-1}$. In the presence of a normal blood urea nitrogen concentration (BUN, 10 - 20 $mg.dL^{-1}$) and glucose concentration (60 - 100 $mg.dL^{-1}$), plasma osmolarity can be predicted as twice the plasma sodium concentration. As BUN or blood glucose concentrations increase, a greater impact is exerted by these substances on plasma osmolarity.

In contrast, plasma osmolality of a solution is a measure of the number of osmotically active particles per kilogram of solvent.

$$\text{Osmolality} = ([Na]^{+} \times 2) + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{2.8} \quad (mOsm.kg^{-1})$$

(Stoelting and Dierdorf, 1993)

Intravenous solutions administered to patients are considered isotonic, hypotonic, or hypertonic, according to their effective osmotic pressures relative to plasma. Normal saline have an osmolarity similar to that of body fluids. Therefore, this fluid is classified as isotonic solution. $D_{5\%}$ is hypotonic, so the resulting free water can distribute itself among all fluid compartments, with less than 10% remaining intravascular. Lactated Ringer's solution, containing 5% glucose, is initially hypertonic (about 527 $mOsm.L^{-1}$), but the hypertonicity diminishes as glucose is metabolized and taken up by cells ***(Cogan, 1991)***.

The intravascular pressure produced by the heart results in a hydrostatic pressure gradient of approximately 20 mmHg across capillary membranes. If this pressure gradient is not counterbalanced, it tends to force intravascular water into the interstitial fluid compartment. But since this is not applied for large protein molecules as albumin which can not freely cross capillary membranes, there will be no continuous intravascular fluid volume loss. The concentrations