THE ROLE OF VASOPRESSIN IN ICU

An Essay Submitted For Partial Fulfillment of
Master Degree in Intensive Care

By

Rania Mamdouh Ahmed
M.B., B. Ch. (2006)
Ain Shams University

Supervised By

Prof.Dr./ Amr Mohamed El-Said
Professor of Anesthesia and Intensive care
Faculty of Medicine, Ain Shams University

Prof. Dr./ Fahmy Saad Latief
Assist. Professor of Anesthesia and Intensive care
Faculty of Medicine, Ain Shams University

Dr./ Rania Maher Hussien
Lecturer of Anesthesia and Intensive care.
Faculty of Medicine, Ain Shams University

Ain Shams University
Faculty of Medicine
2011

دورالفاسوبريسين في الرعاية المركزة

رسالة مقدمة من

الطبيبة / رانيا ممدوح أحمد

بكالوريوس الطب و الجراحة

توطئة للحصول علي درجة الماچستير فى الرعاية المركزة

تحـت إشـــــراف

الأستاذ الدكتور/ عمرو محمد السعيد

أستاذ التخدير و الرعاية المركزة

كلية الطبـ جامعة عين شمس

الدكتور/ فهمي سعد لطيف

أستاذ مساعد التخدير و الرعاية المركزة

كلية الطبـ جامعة عين شمس

الدكتورة / رانيا ماهر حسين

مدرس التخدير و الرعاية المركزة

كلية الطبـ جامعة عين شمس

جامعة عين شمس

كلية الطب

٢٠١١

SUMMARY

Arginine vasopressin (AVP), also known as vasopressin, argipressin or antidiuretic hormone (ADH), It is derived from a preprohormone precursor that is synthesized in the hypothalamus and stored in vesicles at the posterior pituitary to be released into the bloodstream. The vasopressins are peptides consisting of nine amino acids (nonapeptides).

There are three subtypes of vasopressin receptors, V1, V2, and V3, have been identified. V1 receptor is further divided into V1A &V1B. V1 receptors are found on various cells including vascular smooth muscle, and V1 stimulation causes vasoconstriction. Kidney collecting duct cells express V2 receptors, which mediate water retention. V3 receptors are mainly found on cells within the central nervous system, especially in the adenohypophysis; their stimulation modulates corticotropin secretion.

In shock states vasopressin infusion leads to vasoconstriction. low-dose (up to at least 0.03 U/min, and maybe as high as 0.067 U/min) is safe in septic

shock. Vasopressin and corticosteroids are both commonly used in septic shock and they both increase responsiveness to endogenous and infused catecho-lamines.

Vasopressin, a nonadrenergic endogenous peptide that induces peripheral, coronary, and renal vasoconstriction via stimulation of the V1 receptors, and through V2 receptor stimulation, vasopressin may induce vasodilation and therefore lessens the end-organ hypoperfusion thought to occur with epinephrine

Vasopressin antagonists produce an aquaresis leading to increased plasma Na+ concentration in the majority of patients with hyponatremia due to SIADH, CHF, and Liver cirrhosis. Conivaptan is a combined V1aR and V2R antagonist and used for treatment of euvolemic hyponatremia.

Vasopressin causes vasoconstriction and arrests the bleeding in 36-100% of patients. The recurrence rate following completion of vasopressin infusion can be as high as 71%; therefore, vasopressin is used to temporize the acute event and to stabilize patients before surgery.

List of Tables

List of Figures

Contents

CHAPTER ONE

INTRODUCTION

Arginine vasopressin (AVP), also known as vasopressin, argipressin or antidiuretic hormone (ADH), is a peptide hormone that controls the reabsorption of molecules in the tubules of the kidneys by affecting the tissue's permeability. It also increases peripheral vascular resistance, which in turn increases arterial blood pressure. It plays a key role in homeostasis, and the regulation of water, glucose, and salts in the blood. It is derived from a preprohormone precursor that is synthesized in the hypothalamus and stored in vesicles at the posterior pituitary. Most of it is stored in the posterior pituitary to be released into the bloodstream; however, some AVP is also released directly into the brain ***(Vincent, 2008).***

Hypotension is a profound stimulus to increase plasma vasopressin levels. In early shock, increased secretion of vasopressin leads to appropriately high plasma levels of vasopressin to defend organ perfusion. As the shock state progresses, plasma vasopressin levels fall for reasons that are

not entirely clear. Exogenous infusion of low-dose arginine vasopressin increased vasopressin levels, indicating that the low vasopressin levels in septic shock were due to impaired vasopressin secretion, not increased vasopressin metabolism or clearance ***(Russell et al.,2008).***

AVP can be used to treat various conditions in critically ill patients. for example, In Septic shock, Hemorrhagic shock, Cardiac arrest, GIT bleeding and hyponatremia ***(Ghali, 2008).***

CHAPTER TWO

PHYSIOLOGY OF VASOPRESSIN

Arginine vasopressin (AVP), also known as vasopressin, argipressin or antidiuretic hormone (ADH), is a neurohypophyseal hormone found in most mammals, including humans. Vasopressin is a peptide hormone that controls the reabsorption of molecules in the tubules of the kidneys by affecting the tissue's permeability. It also increases peripheral vascular resistance, which in turn increases arterial blood pressure. It plays a key role in homeostasis, and the regulation of water, glucose, and salts in the blood *(Vincent,2008).*

It is derived from a preprohormone precursor that is synthesized in the hypothalamus and stored in vesicles at the posterior pituitary. Most of it is stored in the posterior pituitary to be released into the bloodstream; however, some AVP is also released directly into the brain, where it plays an important role in social behavior and bonding*(Vincent, 2008)*.

Two different types of hypothalamic neurons, magnocellular and parvocellular, synthesize AVP. The magnocellular neurons are mainly located in the supraoptic and paraventricular nucleus. Each neuron gives rise to a single axon into the posterior pituitary gland, where its neurosecretory endings release AVP. Because the capillaries within the pituitary gland do not have a blood-brain barrier, AVP released in close proximity to the capillaries easily enters the bloodstream. Similarly, neurons from the parvo-cellular division of the paraventricular nucleus send axons to the external zone of the median eminence of the pituitary gland, where AVP is secreted into the pituitary portal circulation. AVP is also released within the nuclei of its origin to regularize the phasic firing pattern of the neurons (Fig. 1) *(Leng et al.,1999) (Gouzenes et al.,1998).*

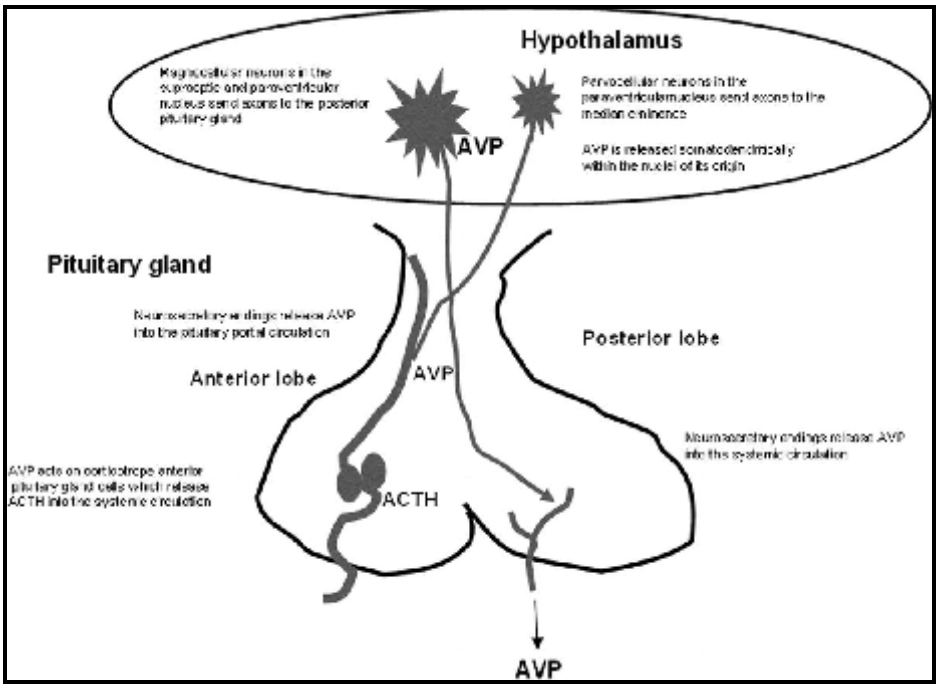

Fig. (1): Scheme of vasopressin release within the central nervous system (CNS) quoted from Leng et al 1999.

Structure of vasopressin:

The vasopressins are peptides consisting of nine amino acids (nonapeptides). The amino acid sequence of arginine vasopressin is Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly, with the cysteine residues forming a sulfur bridge. Lysine vasopressin has a lysine in place of the arginine *(Vincent, 2008)*.

The structure of oxytocin is very similar to that of the vasopressin: It is also a nonapeptide with a disulfide

bridge and its amino acid sequence differs at only two positions. The two genes are located on the same chromosome separated by a relatively small distance of less than 15,000 bases in most species. The magnocellular neurons that make vasopressin are adjacent to magnocellular neurons that make oxytocin, and are similar in many respects. The similarity of the two peptides can cause some cross-reactions: oxytocin has a slight antidiuretic function, and high levels of AVP can cause uterine contractions *(Li et al., 2008)*.

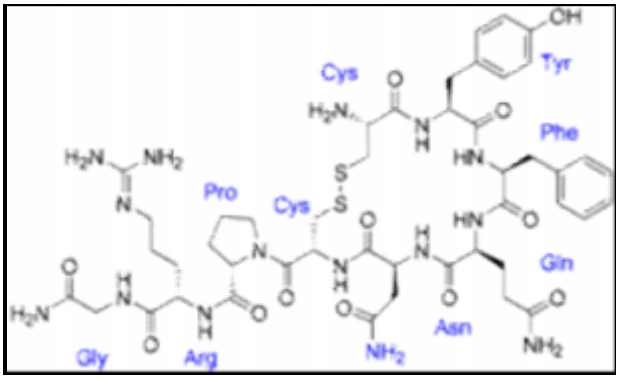

Fig. (2): Chemical structure of vasopressin quoted from vincent 2008.

AVP Receptors and Signal Transduction

Three subtypes of vasopressin receptors, V1 which is further subdivided into V1A and V1B (also called V3) and V2, have been identified. V1 receptors are found on various cells including vascular smooth muscle, and V1 stimulation causes vasoconstriction. Kidney collecting duct cells express V2 receptors, which mediate water retention. V3 receptors are mainly found on cells within the central nervous system, especially in the adenohypophysis; their stimulation modulates corticotropin secretion. Vasopressin receptors are heptahelical membrane proteins coupled to specific G-proteins for intracellular signal transduction *(Maybauer et al., 2008)*.

A variety of signaling pathways have been shown to be associated with the AVP receptor. Activation of V1 and V3 receptors stimulates phospholipase C, which mediates the hydrolysis of inositol 4,5-bisphosphate to inositol 1,4,5-trisphosphate and diacylglycerol. These second messengers activate enzymes, such as protein kinase C, and mobilize intracellular calcium stored in the endoplasmic reticulum. Emptying of calcium stores activates cationic channels that allows extracellular calcium to enter the cells *(Thibonnier et al., 1998).*

V2 receptors interact with adenyl cyclase and generate cyclic adenosine monophosphate as a second messenger, which stimu-lates protein kinase and causes insertion of aquaporin-2 into the luminal wall of collecting duct cells in the kidney. Binding of AVP to the V2 receptor causes receptor internalization and degradation. However, details of regulation of vasopressin receptor expression, potential genetic aspects, and possible feed back mechanisms are still to be investigated *(Robben et al., 2004)*.