Management of Endocrinal Disturbances in Patients of Intensive Care Units

Essay
Submitted for Partial Fulfillment of Master Degree
In **Intensive Care**

By
Ahmed Abdullah Abdel-Fatah Matar
MB.B.Ch.
Faculty of Medicine - Zagazig University

Under Supervision of

Prof. Dr. Galal Adel EL Kady

Professor of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University

Assist. Prof. Dr. Heba Bahaa ElDin ElSerwi

Assistant Professor of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University

Dr. Diaa Eldin Shalaby Al Awady

Lecturer of Anesthesiology and Intensive Care
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2016

Introduction

Meticulous endocrinal regulation is required for various cellular and molecular functions of the human body. Serious disturbances in the endocrine functions may lead to disastrous impact on patient's health. Various endocrinal disturbances have been encountered in ICU patients either as primary cause of their admission or diagnosed during their critical illness course. Newer diagnostic and therapeutic modalities have greatly helped in understanding, diagnosing and treatment of these endocrinal disturbances or failures; however the morbidity and mortality is still high due to failure in its timely diagnosis especially in critically ill patients which can significantly affect the outcome and prognosis ***(Bajwa, 2011)***.

A plethora of endocrine emergencies represents a decompensation of a long-standing endocrine disorder and is precipitated in most cases by some stressful events. Conditions such as acute pituitary failure, addisonian crises, diabetic ketoacidosis, myxedema coma, and thyroid storm are some examples ***(Murad-Kejbou and Eggenberger, 2009; Hahner and Allolio, 2005)***. These conditions and others bear considerable morbidity and mortality rates even with prompt diagnosis and management which is not always the case ***(Pimentel and Hansen, 2005)***.

The acute and chronic phases of critical illness are associated with various endocrine disturbances. It poses a challenge to fragile hormonal axises. Sepsis, acute, and decompensated organ failures cause various hormonal imbalances that range from mild glycemic changes to severe hemorrhagic adrenalitis ***(Webster and Sternberg, 2004; Vermes and Beishuizen, 2001)***.

It remains a matter of argument whether or to what extent these changes are causative or resulting from the

metabolic disturbances present in the critically ill. The endocrine stress responses have both central and peripheral triggers. In addition, patients may have pre-existing central or peripheral endocrine diseases, either previously diagnosed or unknown. Hence, the puzzle is complex and endocrine function testing in a critically ill patient is a major challenge. Furthermore, the inability to delineate the endocrine changes as either adaptation or pathology renders the issue of treatment even more controversial ***(Van den Berghe et al., 1998)***.

Aim of the Study

The aim of the study is to identify diagnosis and management of endocrinal problems in intensive care unit.

Anatomy and physiology of endocrinal glands

(1) Pituitary gland

Anatomy:

The pituitary gland, or hypophysis, is an endocrine gland about the size of a pea and weighing 0.5 grams in humans. It is a protrusion off the bottom of the hypothalamus at the base of the brain. The hypophysis rests upon the hypophysial fossa of the sphenoid bone in the center of the middle cranial fossa and is surrounded by a small bony cavity (sella turcica) covered by a dural fold (diaphragma sellae).It is composed of three lobes: the anterior, intermediate, and posterior lobes ***(Castillo, 2005)***.

Anterior pituitary (Adenohypophysis):

It is composed of 3 regions:

(1) Pars distalis (distal part), represents the majority of the anterior pituitary and is where the bulk of pituitary hormone production occurs. The pars distalis contains two types of cells including chromophobe cells and chromophil cells. The chromophils can be further divided into acidophils and basophils ***(Childs, 1991)***.

(2) Pars tuberalis (tubular part), forms a part of the sheath extending up from the pars distalis which joins with the pituitary stalk (also known as the infundibular stalk or infundibulum), arising from the posterior lobe. (The pituitary stalk connects the hypothalamus to the posterior pituitary) ***(Morgan and Williams, 1996)***.

(3) Pars intermedia (intermediate part), sits between the pars distalis and the posterior pituitary, forming the boundary between the anterior and posterior pituitaries. It

is very small and indistinct in humans ***(Evans et al., 1994)***.

Posterior pituitary (Neurohypophysis):

(1) Pars nervosa:

Also called the neural lobe or posterior lobe, this region constitutes the majority of the posterior pituitary and is the storage site of oxytocin and vasopressin. Sometimes (incorrectly) considered synonymous with the posterior pituitary, the pars nervosa includes Herring bodies and pituicytes ***(Amar and Weiss, 2003)***.

(2) Infundibular stalk:

Also known as the infundibulum or pituitary stalk, the infundibular stalk bridges the hypothalamic and hypophyseal systems ***(Amar and Weiss, 2003)***.

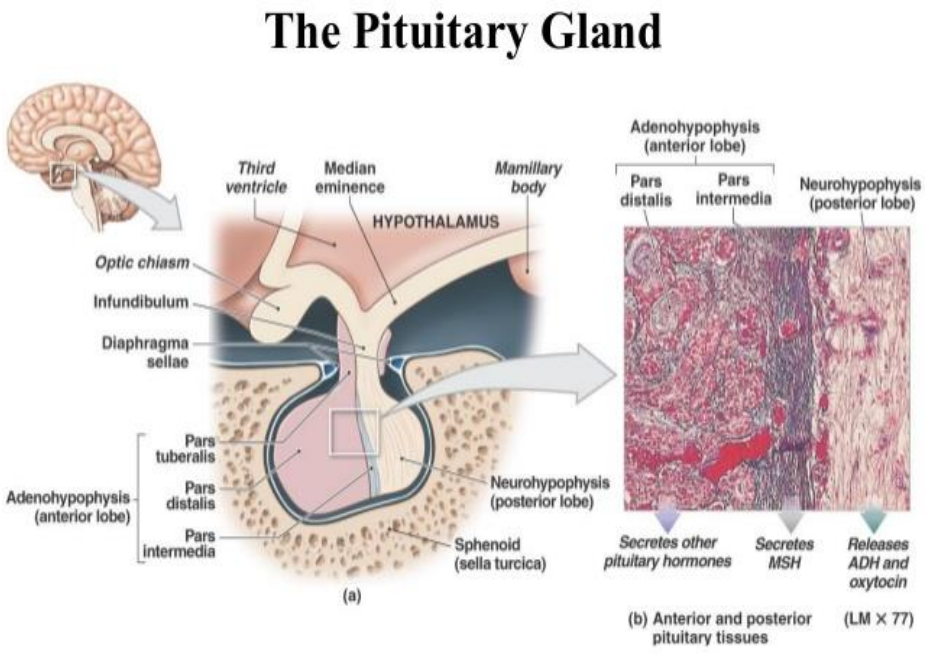

Figure 1: Anatomy of pituitary gland ***(http://www.slideshare.net/sonnareach 168/18-endocrine-system).***

Blood supply:

The adenohypophysis receives the majority of its blood supply from the paired superior hypophyseal arteries, which arise from the medial aspect of the internal carotid artery, within the ophthalmic segment ***(Krisht et al., 1994)***.

The neurohypophysis is supplied by the inferior hypophyseal arteries ***(Reisch et al., 1996)***.

The hypophyseal portal veins drain the primary capillary plexus formed by the superior hypophyseal arteries, which deliver blood to the pars distalis. The pars distalis in turn houses the secondary capillary plexus ***(Krisht et al., 1994)***.

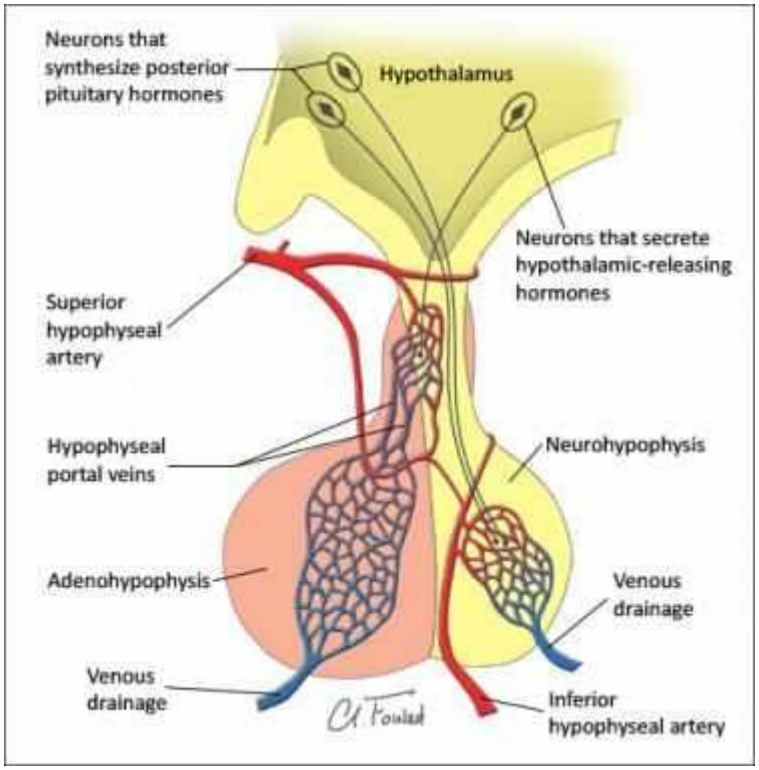

Figure 2: Blood supply of pituitary gland ***(Reisch et al., 1996)***.

Physiology:

The pituitary gland is called the master gland of the body because of its central role in governing homeostasis, maintaining the reproductive cycle, and directing the activity of other glands ***(Amar and Weiss, 2003)*.**

Posterior pituitary:

Communication between the hypothalamus and the posterior pituitary occurs through neurosecretory cells that span the short distance between the hypothalamus and the posterior pituitary ***(Rosso and Mienville, 2009)***.

Hormones produced by the cell bodies of the neurosecretory cells in hypothalamus are packaged in vesicles and transported through the axon and stored in the axon terminals that lie in the posterior pituitary. When the neurosecretory cells are stimulated, the action potential generated triggers the release of the stored hormones from the axon terminals to a capillary network within the posterior pituitary. Two hormones, oxytocin and ADH, are produced and released this way. Finally, the posterior pituitary does not produce its own hormones, but only stores and releases the hormones oxytocin and ADH ***(Amar and Weiss, 2003).***

ADH is released from paraventricular nucleus in the hypothalamus in response to osmoreceptors sensing of hyperosmolality and also baroregulated mechanisms. ADH acts on AVP2 receptors in the kidneys, to cause an increase in the water permeability of the renal collecting ducts; this occurs through the generation of a water channel (aquaporin-2) into the apical membrane of collecting ducts, resulting in urinary concentration and the reabsorption of water back into the circulation ***(Verbalis, 2003)***.

Oxytocin is secreted by paraventricular nucleus and a small quantity is secreted by supraoptic nucleus in hypothalamus. Oxytocin is secreted in both males and females. In female it acts on mammary glands causing milk to be let down into subareolar sinuses, from where it can be excreted via the nipple and uterus leading to uterine contractions during the second and third stages of labor. Oxytocin release during breastfeeding causes mild but often painful contractions during the first few weeks of lactation. In males it facilitates release of sperm into urethra by causing contraction of vas deferens ***(Lee et al., 2009)***.

Anterior pituitary:

Communication between the hypothalamus and the anterior pituitary occurs through hormones (releasing hormones and inhibiting hormones) produced by the hypothalamus and delivered to the anterior pituitary via a portal network of capillaries. The releasing and inhibiting hormones are produced by specialized neurons of the hypothalamus called neurosecretory cells. The hormones are released into a capillary network or primary plexus and transported through veins or hypophyseal portal veins, to a second capillary network or secondary plexus that supplies the anterior pituitary. The hormones then diffuse from the secondary plexus into the anterior pituitary, where they initiate the production of specific hormones by the anterior pituitary ***(Amar and Weiss, 2003)***.

Many of the hormones produced by the anterior pituitary are tropic hormones or tropins, which are hormones that stimulate other endocrine glands to secrete their hormones. The anterior pituitary lobe receives releasing hormones from the hypothalamus via a portal vein system known as the hypothalamic-hypophyseal portal system ***(Amar and Weiss, 2003).***

The anterior pituitary secretes TSH, ACTH, prolactin, FSH, LH, GH, endorphins and other hormones. It does this in response to a variety of chemical signals from the hypothalamus, which travels to the anterior lobe by way of a special capillary system from the hypothalamus, down the median eminence, to the anterior lobe. These include: TRH, CRH, dopamine, PIF, GnRH and GHRH ***(Dorton, 2000).***

These hormones from the hypothalamus cause release of the respective hormone from the pituitary. The control of release of hormones from the pituitary is via negative feedback from the target gland. For example homeostasis of thyroid hormones is achieved by the following mechanism; TRH from the hypothalamus stimulates the release of TSH from the anterior pituitary. The TSH, in turn, stimulates the release of thyroid hormones form the thyroid gland. The thyroid hormones then cause negative feedback, suppressing the release of TRH and TSH ***(Alkemade et al., 2006)***.

(2) Thyroid gland

Anatomy:

The thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings, *lobus dexter* (right lobe) and lobus sinister (left lobe), connected via the isthmus. Each lobe is about 5 cm long, 3 cm wide and 2 cm thick. The organ is situated on the anterior side of the neck, lying against and around the larynx and trachea, reaching posteriorly the esophagus and carotid sheath. It starts cranially at the oblique line on the thyroid cartilage (just below the laryngeal prominence or Adam's apple), and extends inferiorly to approximately the fifth or sixth tracheal ring ***(Dorland's, 2012)*.**

There is occasionally (28%-55% of population, mean 44.3%) a third lobe present called the pyramidal lobe of the thyroid gland. It is of conical shape and extends from the

upper part of the isthmus, up across the thyroid cartilage to the hyoid bone ***(Kim et al., 2013)***.

The thyroid gland is covered by a thin fibrous sheath, the capsula glandulae thyreoideae, composed of an internal and external layer. The external layer is anteriorly continuous with the pretracheal fascia and posteriorolaterally continuous with the carotid sheath ***(Braun et al., 2007).***

The gland is covered anteriorly with infrahyoid muscles and laterally with the sternoclei-domastoid muscle also known as sternomastoid muscle. On the posterior side, the gland is fixed to the cricoid and tracheal cartilage and cricopharyngeus muscle by a thickeningof the fascia to form the posterior suspensory ligament of thyroid gland also known as Berry's ligament ***(Yalçin and Ozan, 2006)***.

The thyroid isthmus is variable in presence and size, can change shape and size, and can encompass the pyramidal lobe. The thyroid is one of the larger endocrine glands, weighing 2-3 grams in neonates and 18-60 grams in adults, and is increased in pregnancy ***(Fehrenbach and Herring, 2012).***

Blood supply

The thyroid is supplied with arterial blood from the superior thyroid artery and the inferior thyroid artery and sometimes by the thyroid ima artery. The venous blood is drained via superior thyroid veins, draining in the internal jugular vein, and via inferior thyroid veins, draining via the plexus thyreoideus impar in the left brachiocephalic vein. Lymphatic drainage passes frequently the lateral deep cervical lymph nodes and the pre- and paratracheal lymph nodes. The gland is supplied by parasympathetic nerve input from the superior laryngeal nerve and the recurrent laryngeal nerve ***(Dorland's, 2012).***

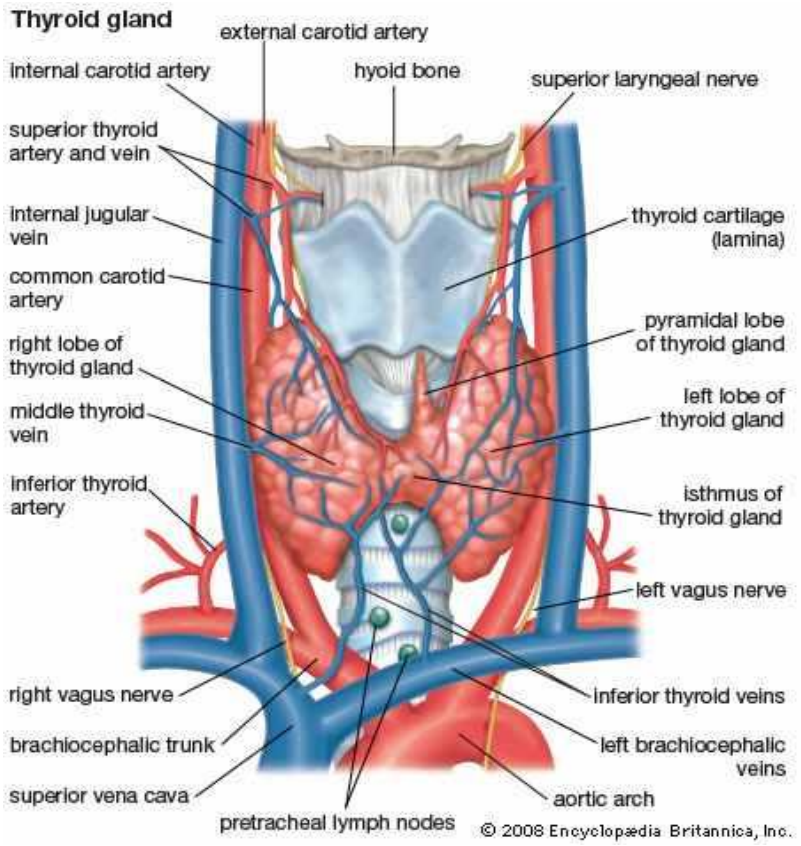

Figure 3: Anatomy, blood supply and nerve supply of thyroid gland ***(http://www.britannica.com/science/thyroid-gland)***.

Physiology:

The primary function of the thyroid is production of the hormones T_3, T_4 and calcitonin. Up to 80% of the T_4 is converted to T_3 by organs such as the liver, kidneyandspleen. T_3 is several times more powerful than T_4, which is largely a prohormone, perhaps four or even ten times more active ***(Boelaert and Franklyn, 2005)***.

T_3 and T_4 production:

T_4 is synthesized by the follicular cells from free tyrosine and on the tyrosine residues of the protein called Tg. Iodine is captured with the "iodine trap" by the hydrogen peroxide generated by TPO and linked to the 3'

and 5' sites of the benzene ring of the tyrosine residues on Tg, and on free tyrosine. Upon stimulation by TSH, the follicular cells reabsorb Tg and cleave the iodinated tyrosine from Tg in lysosomes, forming T_4 and T_3, and releasing them into the blood. Deiodinase enzymes convert T_4 to T_3. Thyroid hormone secreted from the gland is about 80-90% T_4 and about 10-20% T_3 ***(Bianco et al., 2002)***.

Cells of the developing brain are a major target for the thyroid hormones T_3 and T_4. Thyroid hormones play a particularly crucial role in brain maturation during fetal development ***(Kester et al., 2004)***.

T_3 and T_4 regulation:

The production of T3 and T4 is regulated by TSH, released by the anterior pituitary. The thyroid and thyrotropes form a negative feedback loop: TSH production is suppressed when the T_4 levels are high. The TSH production itself is modulated by TRH, which is produced by the hypothalamus and secreted at an increased rate in situations such as cold exposure (to stimulate-thermogenesis). TSH production is blunted by somatostatin, increased levels of glucocorticoids and sex hormones (estrogenand testosterone), and excessively high blood iodide concentration ***(Dohan et al., 2003)***.

An additional hormone produced by the thyroid shares in the regulation of blood calcium levels. Parafollicular cells produce calcitonin in response to hypercalcemia. Calcitonin stimulates movement of calcium into bone, in opposition to the effects of PTH. However, calcitonin seems far less essential than PTH, as calcium metabolism remains clinically normal after removal of the thyroid (thyroidectomy), but not the parathyroids ***(Arnold and Barton, 2015)***.

(3) Parathyroid glands

Anatomy:

The parathyroid glands are two pairs of glands usually positioned behind the left and right lobes of the thyroid. Parathyroid glands are small (20-40 mg) and have a bean like shape. The parathyroid glands have a distinct, encapsulated, smooth surface that differs from the thyroid gland, which is has a more lobular surface, and lymph nodes, which are more pitted in appearance **(*Lappas et al., 2012)***.

The color of the parathyroid glands is typically light brown to tan, which relates to their fat content, vascularity, and percentage of oxyphil cells within the glands **(*Lappas et al., 2012)***.

The superior parathyroid glands are most commonly located in the posterolateral aspect of the superior pole of the thyroid gland at the cricothyroidal cartilage junction. They are most commonly found 1 cm above the intersection of the inferior thyroid artery and the recurrent laryngeal nerve **(*Lappas et al., 2012)***.

The inferior parathyroid glands are more variable in location and are most commonly found near the lower thyroid pole of the thyroid **(*Lappas et al., 2012)***.

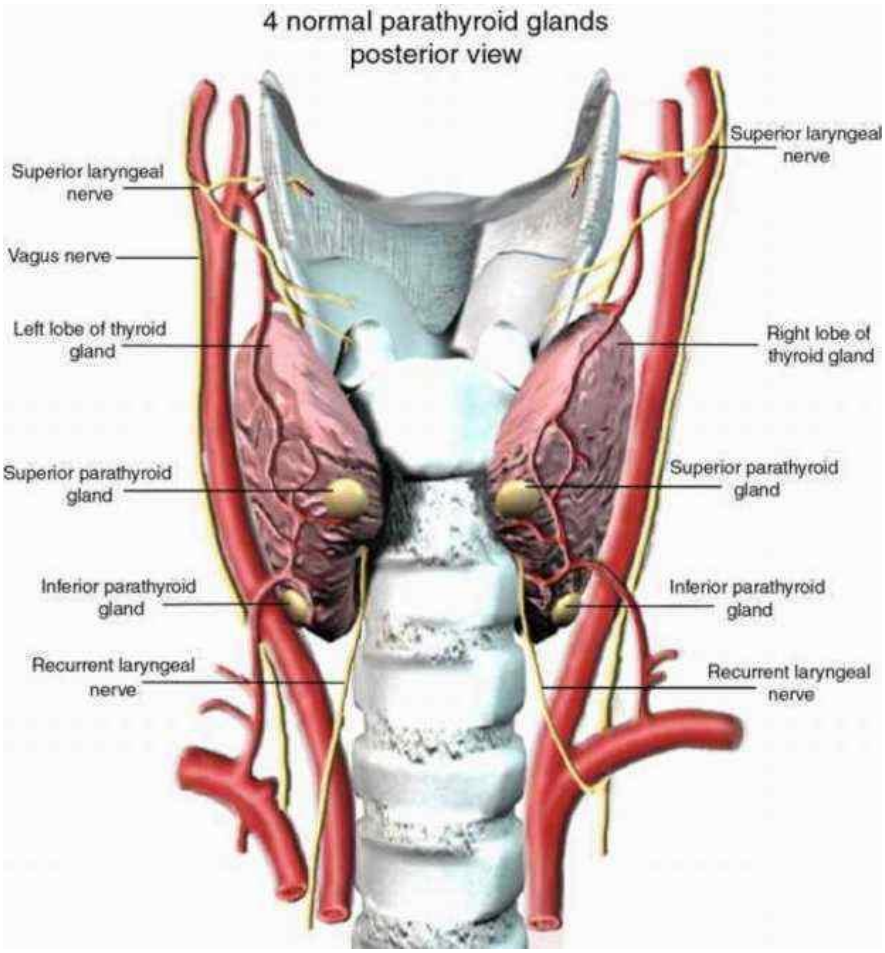

Figure 4: Parathyroid glands ***(http://www.aireurbano.com/thyroid-gland-and-parathyroid-gland).***

Blood supply:

The inferior parathyroid gland is supplied by the inferior thyroid artery from the thyrocervical trunk. In approximately 10% of patients, the inferior thyroid artery is absent, most commonly on the left side. In these cases, a branch from the superior thyroid artery supplies the inferior parathyroid gland ***(*Drake *et al., 2005)***.

The superior parathyroid gland is also usually supplied by the inferior thyroid artery or by an anastomotic branch