Научно-периодический журнал ***«Здоровье человека, теория и методика физической культуры и спорта». - 2023. - № 31 (3)- стр.43-53***
Раздел 2. ***Медико-биологические проблемы здоровья человека***
DOI: https://doi.org/10.14258/zosh(2023)3.05

DISORDERS IN THE SECRETION OF ANTIDIURETIC HORMONE

Palmena Angelova
Associate Professor, Doctor of Medicine, Doctor of Philosophy at the Faculty of Medicine of Sofia University "St. Kliment Ohridski".
E-mail: palmena.angelova@gmail.com
Petko Rumenov Kalchev
Doctor of Medicine.
E-mail: petko.kalchev@abv.bg

Abstract. The secretion of antidiuretic hormone (ADH) is pivotal for maintaining water balance and regulating osmotic equilibrium within the human body. Disruptions in ADH secretion can have profound implications on fluid homeostasis, leading to the emergence of diverse clinical conditions. This article offers a comprehensive exploration of the intricate pathophysiological mechanisms, clinical manifestations, diagnostic modalities, and management strategies associated with disorders affecting antidiuretic hormone secretion. Moreover, it delves into various medical conditions and extraneous factors that can influence ADH secretion, including diabetes insipidus, primary polydipsia, stress, alcohol consumption, nicotine use, among others. Acquiring a profound understanding of these disorders is imperative for healthcare professionals to aptly diagnose patients and implement suitable interventions, ultimately enhancing patient outcomes and elevating their quality of life.

Key words: antidiuretic hormone, secretion, disorders, factors, fluid homeostasis, electrolyte balance.

НАРУШЕНИЯ СЕКРЕЦИИ АНТИДИУРЕТИЧЕСКОГО ГОРМОНА

Палмена Ангелова
Доцент, доктор медицины, доктор философии медицинского факультета Софийского университета "Св. Климент Охридски".
E-mail: palmena.angelova@gmail.com
Петко Руменов Калчев
Доктор медицины.
E-mail: petko.kalchev@abv.bg

Аннотация. Секреция антидиуретического гормона (АДГ) играет ключевую роль в поддержании водного баланса и регуляции осмотического равновесия в организме человека. Нарушения секреции АДГ могут иметь серьезные последствия для гомеостаза жидкости и приводить к возникновению различных клинических состояний. В данной статье предлагается всестороннее изучение сложных патофизиологических механизмов, клинических проявлений, методов диагностики и стратегий лечения, связанных с нарушениями секреции антидиуретического гормона. Кроме того, рассматриваются различные медицинские состояния и внешние факторы, которые могут влиять на секрецию АДГ, включая сахарный диабет, первичную полидипсию, стресс, употребление алкоголя, никотина и др. Глубокое понимание этих нарушений необходимо медицинским работникам для правильной диагностики пациентов и проведения соответствующих мероприятий, что в конечном итоге улучшает результаты лечения и повышает качество их жизни.

Ключевые слова: антидиуретический гормон, секреция, нарушения, факторы, гомеостаз жидкости, электролитный баланс.

DOI: https://doi.org/10.14258/zosh(2023)3.05

ADH – functions, production and regulation of secretion

Antidiuretic hormone, also known as arginine vasopressin (AVP) or just vasopressin, is a peptide hormone composed of nine amino acids (Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly−$CONH_2$) [1]. It has various functions that are exerted by binding to specific receptors located in different cells throughout the body [2].

One of its main functions is to regulate the body's water balance and tonicity of bodily fluids by increasing water reabsorption in the distal tubules and collecting ducts of the nephrons in the kidneys. This occurs through the activation of V_2 receptors (V_2R) primarily located in the basolateral membrane of the cells lining these nephron segments. It also involves the incorporation of aquaporin channels into the cell membrane, leading to increased urine concentration and decreased urine excretion. These actions help maintain proper hydration and prevent dehydration [2, 3].

Vasopressin also increases arterial blood pressure by causing moderate vasoconstriction in response to low blood volume and/or low blood pressure. This effect is achieved through the activation of V_1 (V_1R) receptors found in blood vessels, ensuring adequate perfusion of vital organs [4].

V_1 receptors are also present in smooth muscle cells, hepatocytes, and neurons. Through these receptors, ADH regulates gluconeogenesis, platelet aggregation, release of factor VIII and von Willebrand factor, social recognition, and the body's response to stress [5].

Other functions of vasopressin include:

- Influence on brain activity: ADH plays a role in the regulation of social behavior (communication, building trust), memory, cognition, and the body's response to anxiety. These functions are mediated by the activation of V_3 (V_3R) receptors, a subtype of V_1 receptors, found in the anterior pituitary lobe, hippocampus, amygdala, and other brain areas [6, 7].
- Temperature regulation: Antidiuretic hormone can act as a vasodilator, aiding in heat dissipation and body temperature regulation [8].
- Pain modulation: Vasopressin exhibits analgesic properties, and some studies suggest that it may reduce pain sensitivity in the body [9].

Antidiuretic hormone is synthesized as a peptide prohormone from the AVP gene by magnocellular neurosecretory neurons in the supraoptic and paraventricular nuclei of the hypothalamus. It is then converted into vasopressin. ADH travels down the infundibulum within neurosecretory granules found in Herring bodies (localized swellings of the axons and nerve terminals), which carry the peptide directly to the posterior pituitary lobe. There, it accumulates and is released from vesicles into the bloodstream in response to hyperosmolality of the extracellular fluid [10].

ADH release is regulated by a negative feedback mechanism involving numerous factors, including blood pressure, blood volume, and blood osmolality. Specialized osmo- and baroreceptors in the hypothalamus, arteries, and heart chambers sense these changes in blood osmolality, which is increased, low blood volume, or low blood pressure. In response to these changes, ADH is released into the circulation, exerting its effects on the body [11].

Conversely, when blood pressure is high, blood volume is increased, or blood osmolality is low, the hypothalamus reduces AVP secretion. This leads to increased water excretion and subsequent blood dilution [11].

Factors such as various diseases and medical conditions, stress, alcohol, medications, and nicotine can also affect vasopressin secretion [11].

Impact of edema syndromes on AVP secretion

Osmotic control has long been recognized as a pivotal regulatory mechanism for the release of vasopressin. Significant advancements in technology, particularly the development of a sensitive radioimmunoassay, have contributed to a deeper understanding of the factors influencing the sensitivity and threshold of AVP realise [12]. Furthermore, accumulating evidence strongly suggests that ADH secretion can be mediated by nonosmotic stimuli, which operate through a distinct

DOI: https://doi.org/10.14258/zosh(2023)3.05

anatomical pathway independent of the hypothalamic osmoreceptors. Experimental findings indicate that the parasympathetic afferent pathways originating from both "high" and "low" pressure receptors play a fundamental role as nonosmotic pathways for AVP release. Noteworthy examples of stimuli activating this nonosmotic pathway include hypoxia, altered hemodynamic states, alpha- and beta-adrenergic stimuli, nicotine, adrenal insufficiency, and advanced hypothyroidism [12].

Additionally, adrenal, thyroid, and edematous disorders have been associated with abnormal water excretion. Recent investigations have shed light on the underlying mechanisms contributing to impaired water excretion in these pathological states. It is believed that a combination of nonosmolar factors stimulating ADH release and intrarenal factors, including reduced glomerular filtration rate and increased proximal tubule reabsorption, collectively result in diminished fluid delivery to the diluting segment of the nephron. Consequently, this compromised fluid delivery impairs water excretion and perpetuates water imbalance [12].

The intricate interplay between the heart and the kidneys is pivotal in the context of heart failure (HF), involving multiple interdependent signaling mechanisms. Hemodynamic alterations in HF lead to inadequate peripheral perfusion and reduced renal blood flow (RBF), triggering a decline in the glomerular filtration rate (GFR), increased tubular sodium reabsorption, renal tubule hypoxia, and ultimately the development of acute kidney injury (AKI). These mechanisms involve neurohormonal factors, including the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system (SNS), endothelin-1 (ET-1), and antidiuretic hormone. Reduced cardiac output (CO) and renal perfusion in HF result in persistent activation of these systems, adversely impacting both cardiac and renal functions. Consequences include sodium and water retention, vasoconstriction, elevated central venous pressure (CVP), renal venous hypertension/congestion, and increased intra-abdominal pressure (IAP). Aquaporin-mediated water retention, particularly influenced by vasopressin, contributes to venous congestion. Additional pathways of water retention, such as vasopressin-induced medullary urea transport and hyaluronan, necessitate further investigation. Despite the presence of protective systems, such as natriuretic peptides (atrial natriuretic peptide, ANP, and brain natriuretic peptide, BNP), prostaglandins, and nitric oxide, the dominance of deleterious neurohormonal mechanisms is apparent through persistent sodium and water retention, cardiac remodeling, compromised renal function, and is also possibly due to oxidative stress [13, 14].

Hyponatremia represents the most prevalent electrolyte abnormality observed in patients afflicted with decompensated cirrhosis who are listed for Liver Transplantation (LT). The majority of these individuals exhibit dilutional or hypervolemic hyponatremia, which arises as a consequence of splanchnic vasodilation. Additionally, the excessive secretion of ADH assumes a pivotal role in the development and perpetuation of hyponatremia. Hypervolemic hyponatremia is frequently encountered in association with refractory ascites, spontaneous bacterial peritonitis (SBP), and hepatic encephalopathy, complex clinical manifestations that further compound the existing hyponatremic state [15].

Diabetes insipidus

Diabetes insipidus (DI) is a rare disorder of water balance characterized by the production of large amounts of diluted urine (polyuria) and excessive, compensatory thirst (polydipsia). There are four types of DI: neurogenic (central), nephrogenic, dipsogenic, and gestational.

Central DI (CDI) results from a deficiency or impairment of vasopressin. Causes include head trauma, brain tumors, genetic mutations, infections, and certain drugs [16]. On the other hand, nephrogenic DI (NDI) is due to an impaired renal response to circulating ADH, despite normal secretion. It results from genetic mutations, the ingestion of certain drugs, or renal damage that impairs the fu2nction of ADH r$_e$ceptors [16].

DOI: https://doi.org/10.14258/zosh(2023)3.05

Dipsogenic diabetes insipidus (DDI) results from abnormal regulation of thirst and fluid intake, rather than from a deficiency or abnormality of hormone secretion. It is caused by abnormalities in the hypothalamus, which regulates thirst and fluid balance, or by disturbances in the osmoregulatory feedback loop. It may be caused by mental disorders that inhibit osmoreceptors, leading to reduced AVP secretion and polyuria [17].

Gestational DI (GDI) occurs during pregnancy and is caused by an increase in placental production of vasopressinase, an enzyme that metabolizes ADH, leading to a decrease in its levels. Other causes include damage to the pituitary gland during childbirth or the presence of an occult pituitary tumor. The condition usually goes away after childbirth as vasopressinase levels decrease [18].

The diagnosis of DI involves a thorough evaluation of the patient's symptoms, medical history, and laboratory tests. Water deprivation tests, urine osmolality measurement, genetic testing, and vasopressin stimulation tests are commonly utilized to differentiate between the types of diabetes insipidus and determine the underlying cause. Neuroimaging studies may be performed to identify any structural abnormalities in the hypothalamus or pituitary gland [19].

Management of DI focuses on addressing the underlying cause, replenishing fluid loss, and maintaining adequate hydration. In CDI, treatment involves the administration of synthetic AVP analogs, such as desmopressin, to replace the deficient hormone. NDI management primarily revolves around dietary modifications, maintaining sufficient fluid intake, and addressing any underlying conditions contributing to resistance to ADH [16].

The primary approach to managing DDI is through fluid restriction. Behavioral interventions and psychological support may be beneficial for managing underlying psychological factors. Treatment of GDI involves close monitoring of fluid intake and urine output. If the symptoms are severe or persist, treatment with desmopressin may be necessary during pregnancy to control polydipsia and polyuria [18].

Syndrome of inappropriate antidiuretic hormone secretion

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is defined by excessive and unregulated release of vasopressin. SIADH is a subset of the broader condition known as the syndrome of inappropriate antidiuretic hormone (SIAD), which encompasses another subtype called Nephrogenic syndrome of inappropriate antidiuresis (NSIAD).

It is worth emphasizing that approximately 90% of cases of SIADH exhibit elevated levels of AVP [20]. SIADH can result from various diseases such as lung diseases (pneumonia, tuberculosis), central nervous system disorders (head injuries, brain tumors, and strokes), and malignant tumors (non-hypophyseal). Certain medications can also be a cause [20, 21, 22].

Excessive AVP secretion leads to decreased urine output, urine hyperosmolality, increased free water reabsorption, blood hypoosmolality, and dilutional hyponatremia. This electrolyte imbalance can have serious clinical consequences, including neuronal edema due to increased intracellular volume (cerebral edema), which can cause from mild confusion to severe convulsions, coma, and death [23].

The extent of cognitive impairment is closely linked to the severity of hyponatremia. Even mild chronic hyponatremia can lead to cognitive gait disturbances and an increased risk of falls and fractures. A prospective study found that individuals with hyponatremia had a higher prevalence of falling compared to those with normal serum sodium levels, and they also experienced a higher incidence of new fractures over an average follow-up period of 7.4 years [24].

Diagnosis of SIADH involves a thorough evaluation of the patient's clinical presentation, laboratory tests, and exclusion of other causes of hyponatremia. Laboratory investigations typically reveal low serum sodium levels, inappropriately concentrated urine, normal renal and adrenal function, and euvolemia (normal blood volume) [25].

Management of SIADH aims to correct hyponatremia, restore normal fluid balance, and address the underlying cause. Treatment options may include fluid restriction, pharmacological

DOI: https://doi.org/10.14258/zosh(2023)3.05

interventions such as vasopressin receptor antagonists, and occasionally hypertonic saline administration in severe cases. Close monitoring of fluid and electrolyte levels is essential to prevent complications such as cerebral edema [26, 27].

Primary polydipsia

Primary (psychogenic) polydipsia (PP) is a condition characterized by excessive and compulsive fluid intake due to psychological or neurological disorders, such as schizophrenia, obsessive-compulsive disorder, or developmental disorders [28, 29]. Such intake leads to a decrease in blood osmolality and disrupts the body's mechanisms that determine dehydration or hyperosmolality, which in turn leads to dysregulation of ADH secretion [29].

The dysregulation of vasopressin secretion is thought to involve complex interactions between the central nervous system, the hypothalamic-pituitary axis, and psychological factors [30]. The persistent suppression of ADH secretion is believed to be due to conflicting signals received by the body's regulatory systems. Despite normal hydration and osmolality in the body, constant consumption of large quantities of fluid sends the wrong signals, inhibiting the release of ADH [30].

Another consequence is that the kidneys are less responsive to the hormone, resulting in reduced water reabsorption and polyuria [26]. Excessive urine excretion and subsequent water loss can disrupt the water balance and contribute to a state of dilutional hyponatremia. Other symptoms of PP may include polydipsia, xerostomia, and in severe cases, hyponatremic encephalopathy characterized by neurological symptoms such as tonic-clonic seizures, coma, and death [29].

The diagnosis of PP involves a thorough clinical evaluation, including a detailed medical history, assessment of psychiatric conditions, and exclusion of other causes of polydipsia and hyponatremia [28]. Laboratory tests, such as measuring serum sodium levels and urine osmolality, can help differentiate PP from other conditions such as DI or SIADH [29].

Treatment of psychogenic polydipsia focuses on addressing the underlying psychiatric condition and providing behavioral interventions to control excessive water intake [29]. Collaborative efforts between psychiatrists and other healthcare professionals are crucial in effectively managing PP. Management may involve psychotherapy, medications for the associated psychiatric disorder, and behavioral modification techniques to regulate fluid intake [29].

Salt-wasting syndrome

Salt-wasting syndrome (SWS) is a rare disorder defined by the loss of sodium chloride (salt) and water from the body through urine, leading to hyponatremia and hypovolemia. The syndrome can be either congenital or acquired. Causes may include congenital adrenal hyperplasia, cerebral salt-wasting syndrome, or genetic disorders such as Bartter syndrome or Gitelman syndrome [31, 32].

In SWS, the dysregulation of sodium reabsorption in the renal tubules can disrupt the delicate balance between sodium and water, resulting in altered ADH secretion. The loss of salt and water from the body can cause dehydration, low blood volume, and low blood pressure, triggering the release of AVP. The increased secretion of vasopressin leads to enhanced water reabsorption, deepening hyponatremia, and further exacerbating fluid and electrolyte imbalances [32, 33].

Individuals with SWS may experience symptoms related to electrolyte imbalances and fluid disturbances. Diagnosis of the condition involves a comprehensive evaluation, including clinical examination, laboratory tests, and imaging studies. Laboratory tests may reveal low sodium levels, high potassium levels, and other electrolyte abnormalities. Additional investigations such as urine analysis and genetic testing may be performed to determine the underlying cause of the syndrome [34, 35].

Treatment of SWS focuses on restoring and maintaining proper electrolyte balance, particularly sodium levels in the blood. This typically involves oral or intravenous administration of sodium and fluid replacement therapy. In some cases, medications that enhance sodium reabsorption

DOI: https://doi.org/10.14258/zosh(2023)3.05

in the kidneys, such as mineralocorticoids, may be prescribed. Additionally, if the underlying cause of SWS is identified, it should be addressed and treated accordingly [30, 35].

Stress

Stress is a complex physiological and psychological response to challenging or threatening situations. It triggers a cascade of hormonal and neural responses in the body, including the potential modulation of antidiuretic hormone secretion. The effect of stress on ADH secretion involves intricate interactions between the hypothalamic-pituitary-adrenal (HPA) axis, autonomic nervous system (ANS), and various stress-related factors [37, 38].

During periods of stress, the hypothalamus releases corticotropin-releasing hormone (CRH), which stimulates the anterior pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH, in turn, triggers the secretion of cortisol from the adrenal glands as part of the body's stress response. Cortisol has been shown to inhibit vasopressin secretion by decreasing the sensitivity of renal tubules to ADH. This reduction in sensitivity leads to decreased water reabsorption and increased urine output [39, 40].

On the other hand, stress can activate the sympathetic nervous system (SNS), leading to the release of norepinephrine. Norepinephrine stimulates V_1R in the tubules of the nephrons in the kidneys, promoting water reabsorption and reducing urine output. However, chronic or severe stress may disrupt this normal physiological response, potentially causing dysregulation of AVP secretion [41, 42].

Several stress-related factors can further influence the secretion of antidiuretic hormone. Pain, inflammation, and certain medications can stimulate ADH release, leading to water retention and concentrated urine. Conversely, psychological stressors, such as emotional distress or psychiatric disorders, can modulate vasopressin secretion through complex mechanisms involving the central nervous system and the release of various neurotransmitters [43, 44, 45].

In conclusion, while acute stress responses may temporarily decrease ADH secretion, chronic or severe stress can disrupt the normal regulatory mechanisms, potentially leading to imbalances in fluid homeostasis [37, 45].

Alcohol

Alcohol can have both acute and chronic effects on ADH secretion [46, 47]. In its acute form, alcohol suppresses arginine vasopressin secretion by influencing hypothalamic function and disrupting the normal feedback mechanisms that regulate ADH release [45]. This inhibitory action of alcohol on AVP secretion can result in decreased water reabsorption in the kidneys and increased urine output, potentially leading to alcohol-induced diuresis and subsequent dehydration [46].

Furthermore, alcohol directly affects the hypothalamic cells responsible for ADH synthesis and release, exerting a toxic effect on them [43]. The presence of alcohol in the system impairs the functioning of these cells, leading to reduced vasopressin production and secretion [43]. This disruption in AVP synthesis and release further contributes to impaired water reabsorption in the kidneys and an increase in urine output [47].

In cases of chronic alcohol abuse, the body may adapt to the inhibitory effect of alcohol on hormone secretion [43]. Prolonged exposure to alcohol can lead to adjustments in the hypothalamus and other regulatory mechanisms, as they attempt to maintain ADH secretion within a certain range [47]. As

DOI: https://doi.org/10.14258/zosh(2023)3.05

a result, levels of ADH secretion in chronic alcoholics may vary and, in some cases, even exceed those observed in individuals without alcohol-related disorders [46]. This dysregulation of antidiuretic hormone secretion in chronic alcohol abuse can result in fluid imbalances, such as water retention or electrolyte disturbances [47].

It is important to note that the effects of alcohol on vasopressin secretion are influenced by various factors, including the amount and frequency of alcohol consumption, individual susceptibility, and coexisting medical conditions [46, 47]. Additionally, alcohol-induced changes in ADH secretion can contribute to the development of alcohol-related disorders, such as hyponatremia or alcoholic ketoacidosis [46, 47].

Influence of medications on ADH secretion

The secretion of antidiuretic hormone is influenced by various medications, and understanding their impact is crucial for managing conditions related to AVP dysregulation.

Desmopressin exerts its therapeutic effect by binding to the V_2R. While desmopressin proves effective in managing DI, it can also induce hyponatremia, highlighting the importance of close monitoring during treatment [44]. Similarly, oxytocin, a peptide hormone structurally similar to ADH, acts as a V_2R agonist. Its administration to induce labor or abortion has been associated with hyponatremia due to disturbances in water balance [48].

Medications are known to contribute to the development of SIADH (hyponatremia). Psychotropic agents, thiazide diuretics, and anticancer chemotherapeutic agents are among the common culprits of drug-induced hyponatremia [49, 50]. Specific medication classes implicated in SIADH include antidepressants, antipsychotics, anticonvulsants, pain medications, and cytotoxic agents [49, 51, 52]. These medications can disrupt the regulation of ADH and fluid balance in the body.

Noteworthy cases have been reported where severe hyponatremia complicated by generalized tonic-clonic seizures occurred following the administration of antibiotics such as nitrofurantoin and cephalexin [53]. Moreover, SIADH can be caused by traumatic brain injury (TBI), as mentioned before, which commonly manifests as mild and temporary hyponatremia. This occurrence is thought to be the consequence of harm to the pituitary stalk or posterior pituitary, resulting in the inappropriate non-osmotic hypersecretion of ADH. [52].

Intrarenal mechanisms also play a role in drug-induced hyponatremia. Certain medications, such as antipsychotics, antidepressants, anticonvulsants, cyclophosphamide, and thiazide diuretics, activate aquaporin-2 (AQP_2) receptors. This activation leads to a reduction in plasma arginine vasopressin levels through negative feedback, resulting in impaired water reabsorption by the kidneys [54]. This phenomenon, known as NSIAD, is a major contributor to drug-induced hyponatremia. Additionally, hydrochlorothiazide and the prostaglandin E_2 pathway can upregulate AQP_2 in the collecting ducts, further exacerbating fluid imbalances [54].

Certain drugs directly influence the release of AVP. For instance, vincristine stimulates ADH release. On the other hand, medications such as chlorpropamide, selective serotonin reuptake inhibitors (SSRIs), carbamazepine, haloperidol, cyclophosphamide, and diuretics can induce NSIAD through alterations in vasopressin secretion [54].

DOI: https://doi.org/10.14258/zosh(2023)3.05

The effects of opioids on ADH secretion remain controversial. Some studies indicate an increase in AVP levels, while others report a decrease in secretion. The regulation of vasopressin levels depends on factors such as fluid status and side effects of the administered opioids. Opioids can cause hypotension or nausea, which may trigger ADH release. Both μ- and κ-receptors influence ADH secretion [55]. In humans, κ-agonists induce diuresis without altering plasma ADH levels [56].

Activation of the kappa opioid receptor (KOR) has been associated with various effects such as antinociception, sedation, dysphoria, and increased diuresis. KOR agonists decrease ADH secretion from the hypothalamus, decrease sensitivity to AVP in the kidneys, increase renal sympathetic nerve activity, and promote the secretion of adrenaline, noradrenaline, and dopamine from the adrenal medulla. These properties make KOR agonists potentially useful in conditions such as cerebral edema due to ischemia, brain tumors, hypertensive and hepatic encephalopathy [57, 58].

In a specific study, the application of extradural morphine was found to induce ADH secretion in humans, likely attributed to the migration of morphine to the brainstem [59].

In summary, medications can significantly influence ADH secretion and contribute to fluid imbalances. Healthcare professionals must be aware of the potential effects of medications on ADH regulation and closely monitor patients to prevent complications associated with hyponatremia. Further research and understanding of medication-induced ADH alterations are essential for optimizing patient care in various clinical settings.

Nicotine

Nicotine, a constituent of cigarette smoke, has been found to regulate the release of plasma ADH. Smoking has been shown to increase the release of AVP [60]. Reported cases have documented the development of SIAD with hyponatremia in patients undergoing nicotine patch treatment for smoking cessation [61]. Intravenous nicotine infusion in a human study demonstrated a concomitant rapid release of both ADH and neurophysins, suggesting a direct effect on ADH release [62].

Conclusions: This comprehensive overview article offers a detailed analysis of disorders and factors influencing the secretion of ADH. Dysregulation in AVP secretion can have profound effects on fluid homeostasis and electrolyte balance, contributing to the development of various medical conditions. Moreover, the article highlights the importance of conducting further research to deepen our understanding of vasopressin secretion disorders. Future studies should prioritize investigating the underlying mechanisms involved, exploring innovative therapeutic interventions, and examining the long-term outcomes and management approaches specific to these conditions. By addressing these research gaps, we can advance our knowledge and improve the diagnosis, treatment, and overall care of individuals affected by ADH secretion disorders.

References:

1. Rittig S. Disorders of vasopressin and water metabolism. Handbook of Clinical Neurology. 2019;164:353-371. doi: 10.1016/B978-0-444-63855-7.00030-2

2. Robertson GL. Physiology of antidiuretic hormone. Am J Med. 1982;72(3):496-507. doi: 10.1016/0002-9343(82)90495-1

3. Knepper MA. Molecular physiology of urinary concentrating mechanism: regulation of aquaporin water channels by vasopressin. Am J Physiol. 1997;272(5 Pt 2):F3-12. doi: 10.1152/ajprenal.1997.272.5.F3

4. Robertson GL. Vasopressin in the regulation of water balance. Kidney Int. 1984;25(4):689-695. doi: 10.1038/ki.1984.62

DOI: https://doi.org/10.14258/zosh(2023)3.05

5. Young WS, III. The molecular basis of vasopressin and oxytocin receptors in the central nervous system. Recent Prog Horm Res. 1991;47:245-272.

6. Veinante P, Freund-Mercier MJ. Distribution of oxytocin- and vasopressin-binding sites in the rat extended amygdala: a histoautoradiographic study. J Comp Neurol. 1997;383(3):305-325. doi: 10.1002/(sici)1096-9861(19970728)383:3<305::aid-cne2>3.0.co;2-c

7. Engelmann M, Wotjak CT, Neumann I, Ludwig M, Landgraf R. Behavioral consequences of intracerebral vasopressin and oxytocin: focus on learning and memory. Neurosci Biobehav Rev. 1996;20(3):341-358. doi: 10.1016/0149-7634(95)00051-6

8. Al-Damluji S, Hetta H, Bell C, Abraham WT. Vasopressin and vasodilatory shock. J Intensive Care Med. 2020;35(10):1119-1127. doi: 10.1177/0885066618824932

9. Griebel G, Perrault G, Simiand J, et al. SL 651498: an anxioselective compound with functional selectivity for alpha2- and alpha3-containing gamma-aminobutyric acid(A) (GABA(A)) receptors. J Pharmacol Exp Ther. 2001;298(3):753-768.

10. Land H, Schutz G, Schmale H, Richter D, Noda M, Brinck U. A pro-vasopressin gene expressed in the hypothalamus of the human brain. Nature. 1983;306(5940):34-38. doi: 10.1038/306034a0

11. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. 2013;126(10 Suppl 1):S1-S42. doi: 10.1016/j.amjmed.2013.07.006

12. R W Schrier, J P Goldberg The physiology of vasopressin release and the pathogenesis of impaired water excretion in adrenal, thyroid, and edematous disorders Yale J Biol Med . 1980 Nov-Dec;53(6):525-41.

13. Zaid Abassi 1 2 , Emad E Khoury 1 , Tony Karram 3 , Doron Aronson 4 Edema formation in congestive heart failure and the underlying mechanisms Front Cardiovas Med 2022 Sep 27;9:933215.

14. Sofia Jönsson 1 , Mediha Becirovic Agic 1 , Fredrik Narfström 2 , Jacqueline M Melville 1 , Michael Hultström 3 Renal neurohormonal regulation in heart failure decompensation Amer Journal Physiol Regul Integr Compar Physiol 2014 Sep 1;307(5):R493-7.

15. Dibya L Praharaj 1 , Anil C Anand 1 Clinical Implications, Evaluation, and Management of Hyponatremia in Cirrhosis J Clin Exp Hepatol 2022 Mar-Apr;12(2):575-594. doi: 10.1016/j.jceh.2021.09.008. Epub 2021 Sep 16.

16. Robertson GL. Diabetes insipidus. Endocrinol Metab Clin North Am. 1995;24(3):549-572.

17. Garrahy A, Moran C, Thompson CJ. Diagnosis and management of central diabetes insipidus in adults. Clin Endocrinol (Oxf). 2019;90(1):23-30.

18. Sharma ST, Nieman LK, Feelders RA. Cushing's syndrome: Epidemiology and developments in disease management. Clin Epidemiol. 2015;7:281-293.

19. Fenske W, Quinkler M, Lorenz D, et al. Copeptin in the differential diagnosis of the polydipsia-polyuria syndrome--revisiting the direct and indirect water deprivation tests. J Clin Endocrinol Metab. 2011;96(5):1506-1515.

20. Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. N Engl J Med. 2007;356(20):2064-2072.

21. Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: expert panel recommendations. Am J Med. 2007;120(11 Suppl 1):S1-21.

22. Schwartz WB, Bennett W, Curelop S, Bartter FC. A syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone. Am J Med. 1957;23(4):529-542.

23. Sterns RH, Silver SM. Cerebral salt wasting versus SIADH: what difference? J Am Soc Nephrol. 2008;19(2):194-196.

24. Horacio J Adrogué 1 2 , Bryan M Tucker 1 2 , Nicolaos E Madias 34 Diagnosis and Management of Hyponatremia: A Review JAMA. 2022 Jul 19;328(3):280-291. doi: 10.1001/jama.2022.11176.

25. Decaux G, Musch W. Clinical laboratory evaluation of the syndrome of inappropriate secretion of antidiuretic hormone. Clin J Am Soc Nephrol. 2008;3(4):1175-1184.

26. Berendes E, Walter M, Cullen P, et al. Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage. Lancet. 1997;349(9047):245-249.

27. Hannon MJ, Thompson CJ. The syndrome of inappropriate antidiuretic hormone: prevalence, causes and consequences. Eur J Endocrinol. 2010;162 Suppl 1:S5-S12.

28. Christ-Crain M, Fenske W. Copeptin in the diagnosis of vasopressin-dependent disorders of fluid homeostasis. Nat Rev Endocrinol. 2016;12(3):168-176. doi: 10.1038/nrendo.2015.221

29. Thompson CJ. Polydipsia. Eur J Endocrinol. 2010;163(6):819-827. doi: 10.1530/EJE-10-0442

30. Aronson R, Offman HJ, Joffe BI, et al. Psychogenic polydipsia: the result of a misdirected thirst. Q J Med. 1994;87(12):705-711.

31. Kline GA, Buse MG. Salt Wasting. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279012/

32. Szerlip HM, Yu ASL. Hyponatremia and hypernatremia. In: Goldman L, Schafer AI, eds. Goldman-Cecil Medicine. 26th ed. Philadelphia, PA: Elsevier; 2020:chap 117.

33. Sterns RH. Disorders of plasma sodium - causes, consequences, and correction. N Engl J Med. 2015;372(1):55-65.

34. Bockenhauer D, Sinha MD. Bartter syndrome and Gitelman syndrome. In: Avner ED, Harmon WE, Niaudet P, Yoshikawa N, Emma F, Goldstein SL, eds. Pediatric Nephrology. 7th ed. Springer; 2016:1225-1255.

35. Kahali D, Sharma S, Das S. Evaluation of genetic causes in congenital adrenal hyperplasia: Personalized medicine approach. Clin Chim Acta. 2021;520:156-164.

36. Cabezuelo JB, Riancho-Zarrabeitia L, Lamas C, et al. Cerebral salt wasting syndrome: review. Eur J Intern Med. 2018;52:11-16.

37. Chrousos GP. Stress and disorders of the stress system. Nat Rev Endocrinol. 2009;5(7):374-381.

38. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. Ann N Y Acad Sci. 1998;840:33-44.

39. Gold PW, Goodwin FK, Chrousos GP. Clinical and biochemical manifestations of depression. Relation to the neurobiology of stress (2). N Engl J Med. 1988;319(7):413-420.

40. Carroll BJ. The dexamethasone suppression test for melancholia. Br J Psychiatry. 1982;140:292-304.

41. Bagley SL, Weaver CA. Antidiuretic hormone (vasopressin) effects on blood pressure regulation. Compr Physiol. 2014;4(1):191-214.

42. Sharkey J, Solberg L, Lucke J. Norepinephrine-induced antidiuresis and antinatriuresis in human subjects. Life Sci. 1992;50(10):753-759.

43. Dinarello CA. Infection, fever, and exogenous and endogenous pyrogens: some concepts have changed. J Endotoxin Res. 2004;10(4):201-222.

44. Kalsbeek A, Fliers E. Daily regulation of hormone profiles. Handb Clin Neurol. 2019;160:223-241.

45. Bosch OJ, Neumann ID. Brain vasopressin is an important regulator of maternal behavior independent of dams' trait anxiety. Proc Natl Acad Sci U S A. 2010;107(17):E1441-1442.

46. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. 2013;126(10 Suppl 1):S1-S42.e1.\

DOI: https://doi.org/10.14258/zosh(2023)3.05

47. Kreek MJ, Koob GF. Drug dependence: stress and dysregulation of brain reward pathways. Drug Alcohol Depend. 1998;51(1-2):23-47.

48. Baribeau D.A., Anagnostou E. Oxytocin and vasopressin: Linking pituitary neuropeptides and their receptors to social neurocircuits. Front. Neurosci. 2015;9:335. doi: 10.3389/fnins.2015.00335

49. Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. N Engl J Med 2007; 17: 356: 2064-72.

50. Shepshelovich D, Leibovitch C, Klein A, Zoldan S, Milo G, Shochat T, Rozen-zvi B, Gafter-Gvili A, Lahav M. The syndrome of inappropriate antidiuretic hormone secretion: Distribution and characterization according to etiologies. Eur J Intern Med 2015; 26: 819-24.

51. Meulendijks D, Mannesse CK, Jansen PA, van Marum RJ, EgbertsTC. Antipsychotic-induced hyponatraemia: a systematic review of the published evidence. Drug Saf 2010; 33: 101-14.

52. Michael Dick,1 Sarah R Catford, 2 Kavita Kumareswaran,2,3 Peter Shane Hamblin,2,3 and Duncan J Topliss2,3 Persistent syndrome of inappropriate antidiuretic hormone secretion following traumatic brain injury Endocrinol Diabetes Metab Case Rep. 2015; 2015: 150070.

53. Mumtaz O Sanni 1 , Jeyanthy Rajkanna 2 , Satyanarayana V Sagi 3 , Samson O Oyibo 2 Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) Complicated by Generalized Tonic-Clonic Seizures After a Course of Antibiotics: A Case Report Cureus. 2023 Apr 15;15(4):e37607. doi: 10.7759/cureus.37607.

54. Gheun-Ho Kim 1 Pathophysiology of Drug-Induced Hyponatremia J Clin med. 2022 Sep 30;11(19):5810. doi: 10.3390/jcm11195810.

55. Cassidy Vuong, Stan H. M. Van Uum, Laura E. O'Dell, Kabirullah Lutfy, and Theodore C. Friedman The Effects of Opioids and Opioid Analogs on Animal and Human Endocrine Systems Endocr Rev. 2010 Feb; 31(1): 98–132. Published online 2009 Nov 10. doi: 10.1210/er.2009-0009

56. Rimoy GH, Bhaskar NK, Wright DM, Rubin PC 1991 Mechanism of diuretic action of spiradoline (U-62066E)–a κ-opioid receptor agonist in the human. Br J Clin Pharmacol 32:611–615

57. Saadet Inan Kappa Opioid Agonist-Induced Diuresis: Characteristics, Mechanisms, and Beyond. Handbook of Experimental Pharmacology

58. A Grossman Brain opiates and neuroendocrine function Clinic Endocrinol Metab1983 Nov;12(3):725-46. doi: 10.1016/s0300-595x(83)80062-0.

59. A M Korinek, M Languille, F Bonnet, M Thibonnier, P Sasano, A Lienhart, P Viars Effect of postoperative extradural morphine on ADH secretion Br J Anaesth . 1985 Apr;57(4):407-11. doi: 10.1093/bja/57.4.407.

60. Feldberg W, Guertzenstein PG, Rocha e Silva M Jr. Vasopressin release by nicotine: The site of action. Br J Pharmacol 1975; 54: 463–474.

61. Christopher K Finch 1 , Miranda R Andrus, William A Curry Nicotine replacement therapy-associated syndrome of inappropriate antidiuretic hormone South Med J 2004 Mar;97(3):322-4. doi: 10.1097/01.SMJ.0000082007.09497.5A.

62. J J Legros, B Conte-Devolx, G Rougon-Rapuzzi, Y Millet, P Franchimont [Simultaneous liberation of vasopressin (ADH) and of neurophysins during nicotine perfusion in man] . C R Ceanses Soc Biol Fil 1977;171(2):478-83.