Annals of Diabetes, Metabolic Disorders & Control

SCIENTIFIC LITERATURE

Special Issue Article "Diabetes Insipidus"

Research Article

Dipsogenic and Gestational Diabetes Insipidus

Loyo-Varela M, Ayala-Yanez R, Revilla-Pacheco F and Ayala AR*

Department of Neurosurgery, Gynecology & Obstetrics and Endocrinology, Mexico City

ARTICLE INFO

Received Date: May 09, 2022
Accepted Date: May 30, 2022
Published Date: May 31, 2019

KEYWORDS

Diabetes Insipidus (DI)
Arginin-Vasopressin (AVP)

Citation for this article: Loyo-Varela M, Ayala-Yanez R, Revilla-Pacheco F and Ayala AR. Dipsogenic and Gestational Diabetes Insipidus. Annals of Diabetes, Metabolic Disorders & Control. 2022; 3(1):125

Corresponding author:
Ayala AR,
Department of Neurosurgery, Gynecology & Obstetrics and Endocrinology, Mexico City,
Email: aquilesayala2@gmail.com

ABSTRACT

Study of central polydipsia and gestational Diabetes Insipidus (DI) provides a simple and comparative model for additional assessment of hypothalamic-pituitary control upon water metabolism where degrees of unbalance are usually less intense, short timed and varied as is the case of normal pregnancy or in association to hypertensive disease where dramatic changes in intravascular volume and vascular resistance occur within a margin of forty weeks. The inclusion of biologic markers (copeptin) in the study of these entities can contribute to a better understanding about the nature of more contrasting levels of Arginin-Vasopressin (AVP) deficiency different from cases of neurohypophyseal or nephrogenic DI.

INTRODUCTION

Water in the human body excels its properties to attract other polar molecules for cohesion, (energy) storage and high polarity that contributes for adherence to transport nutrients and cellular components of the immune system, carrying apart from oxygen and carbon dioxide, hormones for the endocrine system to function adequately [1,2]. Three main hormonal mechanisms have been so far characterized for water retention, namely: a) aldosterone, secreted by the adrenal granulosa with effect upon distal renal tubules retaining sodium and water; b) Atrial Natriuretic Peptide (ANP) released in the heart during atrial stretch, decreasing NaCl reabsorption in the distal nephron while inhibiting renin secretion and c) Vasopressin (AVP) or antidiuretic hormone released by the posterior pituitary with effect upon renal tubules (collector) and ascending limb of Hemle reabsorbing water mediated by elevation changes in serum osmolality. Quantitavely the AVP effect has a primary role for water preservation [3] Hydrosensors (osmoreceptors) located within the Supraoptic (SO) and Paraventricular (PV) hypothalamic nuclei release AVP every time that plasma osmolarity reaches concentrations above 300 mOsm /L. The exact cell or biochemical signal that triggers this mechanism still remains unknown, although it is suspected that a signal arises from the vasopressin-neurophysin-copeptin complex aside from other neuronal component [4]. It is highly effective since an increase of only 1% (2.8 mOsmols/L) releases AVP into circulation, being plasma hypertonicity or dehydration the most potent stimuli, a response that is genetically determined by an AVP gene located in chromosome 20p13 [5]. Despite precision of biomechanical forces involved, we thought of interest to review those elements that generate diabetes insipidus in the abscence of pituitary or renal lesion such as primary polydipsia (dipsogenic) and Gestational Diabetes Insipidus (GDI) to assess the possibility of other sensitive mechanisms for water control like beer potomania.

MECHANISM OF ACTION OF AVP

The main physiologic actions of AVP are mediated by V1a, V1b and V2 receptors located in blood vessels, pituitary corticotroph and renal duct epithelia respectively. Curiously V2 receptors also regulate the effect of AVP to stimulate factor VIII and Von Willebrand factor production whose impact upon water retention if any, remains to be clarified. When AVP is synthesised, about 2 hours, by the posterior pituitary to achieve normal plasma concentrations (< 4pg/mL, T1/2: 10-35 minutes), while contacting its receptors, water channel proteins (aquaporins) located in the cell membrane are activated modifying their molecular structure to passage water inside the cell. When the shut-off signal (normal osmolarity) for AVP resumes, aquaporins are internalized to reinstate its impervious state [6]. Thirst activators are AgRP (agouti-related protein) neuropeptides derived from MnPO (Median-Preoptic Nucleus) neurons located in the anterior hypothalamus whose activation counteracts water losses when decreases in intravascular volume or increases in osmolality arise.

DIPSOGENIC DIABETES INSIPIDUS [7,8]

It is due to a decreased or suppressed secretion of AVP commonly characterized by excessive fluid consumption. A distinction has been proposed depending on the apparition of polydipsia associated to exaggerated thirst (dipsogenic) or abnormal psychologic features. However some forms of dipsogenic DI, has been shown to be genetically dependent albeit such cases are scarce. An increased fluid intake slightly reduces plasma osmolarity/sodium thereby reducing AVP secretion. The decline in plasma AVP reduces urine osmolarity and increases urine volume thereby producing a compensatory increase in water excretion that prevents over-hydration. Thus, basal plasma osmolarity/sodium tends to be slightly lower than in patients with pituitary DI but is usually within the normal range. Fluid intake reverses these abnormalities resulting in normal rises in plasma osmolarity/sodium, plasma AVP and urine osmolarity. The levels of urine osmolarity achieved are submaximal and remain so even after administration of AVP or Desmopressin. Dynamic tests with water deprivation or using antidiuretic hormone seem to be of limited use specially in cases with partial DI. Distinction of these might be subtle and dependable on a succesful educational aproach, and copeptin may clarify differences observed.

GESTATIONAL DIABETES INSIPIDUS

This is a unusual condition of the third trimester of pregnancy which has been reported in association with preeclampsia or abnormalities derived from placental steroidogenesis. It is believed to be caused by excessive degradation of AVP procured by increasing amounts of a placental enzyme Vasopressinase [9] that vanishes after parturition but responds favorably to the administration of desmopressin, yet cases of hormone resistance have also been reported. Such variety of DI is of particular interest since it might occur in patients against a background of a coexisting subclinical deficiency of vasopressin secretion even when plasma levels of vasopressinase are normal [10]. Therefore, a search for underlying pituitary-hypothalamic or renal disease should be undertaken in cases of gestational diabetes, polyhydramnios, pregnancy associated hypertension before and after delivery while markers like copeptin (a surrogate of AVP) find their place in the assessment of corporal fluids.

COPEPTIN

Measurement of AVP is difficult due to its short half life and subject to preanalytical errors. In contrast Copeptin is probably a sensitive and stable surrogate marker for AVP release, since it is secreted in equimolar amounts to arginin vasopressin from the C-terminus glycosylated peptide and is also synthesized by the hypothalamic neurons of AVP. The size and half life permit an easier immunological testing. Although there is no known biological role its serum quantitation is apparently useful to diagnose DI and the syndrome of inappropriate antidiuresis, for monitoring septic shock, hyponatremia, metabolic syndrome, intracerebral hemorrage or cardiovascular diseases [11-13]. This potential efficacy would be advantageous to improve our understanding of body water control through the assessment of pathologies like dipsogenic and gestational DI.

FORESIGHT

So far dipsogenic or central polydipsia is characterized by supressed secretion of AVP provoked by the excessive ingestion of water whereas during gestation appears to occur by increased degradation or resistance of AVP. Both instances are apparently subject to degrees of clinical expression depending on hydrosensors or osmoreceptors (genetic or epigenetic) sensitivity, resembling nonetheless those of neurohypophyseal and nephrogenic origin. Hence differences

should not be phenotypically extreme except by symptomatology. The examples chosen for this short review might be good models to study AVP pathophysiology with plenty of areas to be considered such as development of biological markers, improved clinical characterization of diverse types of AVP resistance and newer ways of approach and treatment. In the case of gestational DI in a brief period (40 weeks) remarkable changes from increased intravascular volume with markedly 5decreased vascular resistance may swing inversely during late pregnancy with effect upon the posterior pituitary which is physiologically enlarged. The frequency of preeclampsia in our country is elevated (1/10) providing the opportunity for comparative studies on volume distribution, therefore quantitative promising tests like that of copeptin may enrich projects in this regard.

REFERENCES

1. Finney J. (2015). Water: a very short introduction. Oxford University Press. 1-13.
2. Lowell BB. (2019). New neuroscience of homeostasis and drives for food, water and salt. N Engl J Med. 380: 459-471.
3. Robertson GL, Christensen JH. (2012). Physiology of vasopressin, secretion and thirst. Trans Endocrinol Metab. 3: 27-56.
4. Honore PM, De Bets D, Barreto-Gutierrez L, Redant S, Gallerani A, et al. (2019). Sevoflurane and nephrogenic diabetes insipidus on the rise: copeptin to the rescue?. Critical Care. 23: 304.
5. Robertson GL. (2016). Diabetes insipidus: differential diagnosis and management. Best Pract Res Clin Endocrinol Metab. 30: 205-218.
6. Agre P, Kozono D. (2003). Aquaporin water channels: molecular mechanisms of human diseases. FEBS Lett. 555: 72-78.
7. Clara S, Bettina W, Mirjam CC. (2017). Primary polidipsia in the medical and psychiatric patient: characteristics, complications and therapy. Swiss Med Wkly. 147: 147-151.
8. Perkins RM, Yuan CM, Welch PG. Dipsogenic diabetes insipidus: report of a novel treatment strategy and literature review. Clin Exp Nephrol. 10: 63-67.
9. Durr JA, Hoggard JG, Hunt JM, Schrier RW. (1987). Diabetes insipidus in pregnancy associated with abnormally high circulating vasopressinase activity. N Engl J Med. 316: 1070-1074.
10. Ford SM, Lumpkin HL. (1986). Transient vasopressin-resistant diabetes insipidus of pregnancy. Obstet Gynecol. 68: 726-728.
11. Fenske W, Quinkler M, Lorenz D, Zopf K, Haagen U, et al. (2011). Copeptin in the differential diagnosis of the polidipsia-polyuria syndrome--revisiting the direct and indirect water deprivation tests. J Clin Endocrinol Metab. 96: 1506-1515.
12. Harrois A, Anstey JR. (2019). Diabetes insipidus and syndrome of inappropriate antidiuretic hormone in critically ill patients. Crit Care Clin. 35: 187-200.
13. Cavanagh C, Uy NS. (2019). Nephrogenic diabetes insipidus. Pediatr Clin North Am. 66: 227-234.