IJACT, Volume 2, Issue 4, 2024 ISSN: 2995-5378
http://medicaljournals.eu/index.php/IJACT

INTERNATIONAL JOURNAL OF ALTERNATIVE AND CONTEMPORARY THERAPY

Non-Diabetes Mellitus: A Modern Perspective on Etiopathogenesis, Diagnosis and Treatment

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Abstract: Non-sugar diabetes is a severe disease with an underlying defect in the synthesis, secretion or action of argininevasopresin, resulting in loss of the kidneys' ability to reabsorb water and concentrate urine and manifested by marked thirst and excretion of large amounts of dilute urine. Thirst and the excretion of large amounts of dilute urine. Its prevalence in the population is 0.004-0.01% with a peak with a peak incidence in the 20s and 30s. There are several types of non-sugar diabetes, the characteristics, pathogenesis, clinical picture and differential diagnosis of which are covered in this article. The paper also presents modern approaches to the treatment of different types of non-sugar diabetes. Different types of non-sugar diabetes and the variants of the most effective drug therapy schemes depending on the etiology of the disease and concomitant diagnostics are given depending on the etiology of the disease and associated complications.

Keywords: diabetes insipidus, vasopressin, desmopressin, polyuria, polydipsia, osmolality, osmolarity.

Non-sugar diabetes, also known as diabetes insipidus, is a serious condition caused by a defect in the synthesis, secretion, or action of the hormone arginine vasopressin (AVP). This leads to the kidneys losing their ability to reabsorb water and concentrate urine, resulting in excessive thirst and the production of large amounts of diluted urine. AVP, which is produced in the hypothalamus, plays a crucial role in regulating water and electrolyte balance in the body. It is synthesized by neurons in the hypothalamus and transported to the neurohypophysis, where it is stored and released into the bloodstream. Once in the bloodstream, AVP binds to vasopressin type 2 receptors in the renal collecting tubules, leading to the activation of proteins that increase the permeability of cells to water, allowing for its reabsorption into the bloodstream and decreasing urine production.

The text describes the pathogenesis and clinical symptomatology of different types of ND (nephrogenic diabetes insipidus) except for primary polydipsia. ND is characterized by a deficiency of AVP (antidiuretic hormone), either absolute or relative, leading to decreased renal water reabsorption and the excretion of large amounts of dilute urine. This results in dehydration, plasma hyperosmolality, activation of osmoreceptors in the hypothalamus, and increased thirst. The main symptoms of ND include excessive thirst (polydipsia) with fluid intake ranging from 3 to 20 litres, frequent and excessive urination (polyuria) including nocturnal urination (nicturia), and general dehydration such as dry skin and mucous membranes, reduced salivation and sweating. Inadequate fluid replacement can lead to severe dehydration with symptoms including weakness, headaches, nausea, vomiting, fever, convulsions, tachycardia, blood clotting abnormalities, and collaptoid states or psychomotor agitation. Primary polydipsia is a condition characterized by excessive fluid intake and constant water overload. This leads to various gastrointestinal manifestations such as gastric distension, decreased secretory function of the gastrointestinal tract, and constipation. Unlike other conditions, primary polydipsia does not involve a deficit of secretion or action of anti-diuretic hormone (ADH). The causes of primary polydipsia are usually related to a decreased threshold of thirst centre sensitivity, where patients feel

thirsty even when they have normal or reduced thirst. Excessive fluid intake is often observed in patients with psychiatric disorders. Despite the excessive fluid intake, patients with primary polydipsia have normal or reduced electrolyte concentration/osmolality and do not exhibit symptoms of dehydration. The excess water in these patients leads to dilution of the blood, resulting in a decrease in electrolyte levels and osmolality. This physiological response blocks the synthesis and secretion of ADH, causing increased urine production to eliminate the excess water from the body.

Differential diagnosis. In clinical practice, it is important to differentiate between central diabetes insipidus (CDI), nephrogenic diabetes insipidus (NDI), and primary polydipsia (PP). This is crucial for prescribing appropriate treatment and avoiding potential side effects. A diagnostic algorithm developed in FGU ENC suggests four main stages for differential diagnosis. The first stage involves confirming hypotonic polyuria in patients with polyuria-polydipsia syndrome. The second stage aims to exclude the most common causes of NDI, such as diabetes, hypercalcaemia, hypertension, and chronic renal failure. The third stage involves conducting a water deprivation test and a desmopressin test to rule out PP and NDI, respectively. The fourth stage focuses on actively searching for the causes of the condition, such as performing an MRI examination of the brain if CDI is confirmed. This diagnostic approach helps guide treatment decisions and further investigation into the underlying causes of the disease. Measuring the osmotic concentration of blood and urine is crucial for making a differential diagnosis of ND (nephrogenic diabetes insipidus). This measurement is important because it affects the secretion of AVP (antidiuretic hormone) and indirectly indicates the hormone's action on V2-receptors in the kidneys. The normal osmolality of blood is between 280-300 mOsm/kg, while the concentration of nocturnal or maximally concentrated urine can range from 600-1200 mOsm/kg. However, using the determination of urine relative density is less specific for diagnosing ND and has limitations, such as its inability to be measured in blood and its dependence on the presence of various components like blood cells, epithelium, and bacteria, leading to diagnostic errors. Studies have shown that using relative urine density for the diagnosis of ND can result in overdiagnosis and unnecessary prescription of desmopressin in over 15% of patients. Osmotic concentration can be measured using an osmometer or calculated using a formula based on biochemical analysis.

The **treatment** of central ND (neurohypophyseal diabetes insipidus) can be traced back to 1912 when the first use of posterior pituitary extract was documented. In 1954, biochemist Vincent du Vigneaud synthesized AVP (arginine vasopressin) and received the Nobel Prize for his achievements. However, both synthetic and endogenous AVP preparations had limitations such as low efficacy, short duration of action, and frequent side effects during intranasal administration. Tannate AVP (Pitressin) was considered the most effective at the time but had drawbacks like painful intravenous injections, abscess development, and overdose episodes. A turning point came in 1974 with the introduction of desmopressin, a synthetic analogue of natural AVP that had stronger and longer-lasting antidiuretic effects and lacked vasoconstrictor activity. Desmopressin has been used in substitution therapy for over 30 years, primarily in the form of intranasal drops (Adiuretin). Currently, in Russia, desmopressin is available in two forms: Minirin tablets (Ferring, Sweden) and Presaynex nasal dosed spray (Mipharm, Italy). A study on the use of desmopressin therapy for central diabetes insipidus (CDI) showed that the daily doses of the drug range from 0.1 to 1.6 mg orally and from 10 to 40 mcg intranasally. The variability in dosage is due to individual response and differences in absorption. Patients with postoperative and traumatic CDI require lower doses (0.1-0.2 mg/day) while those with idiopathic CDI may need higher doses (1.2-2.4 mg/day). Intranasal administration has a faster onset of action (15-30 minutes) compared to oral administration (1 hour). Taking the drug with food reduces its effectiveness, but it can be taken under the tongue if necessary. Crushing the tablet does not affect its efficacy. In cases where intranasal administration is not possible, nebulisation into the oral cavity can help alleviate polyuria symptoms associated with CDI. When changing from one form of desmopressin to another, a dose conversion can be used. The clinical efficacy of a 0.2 mg tablet of desmopressin is equivalent to 10 μg of intranasal desmopressin. The tablet form is more convenient for small dose requirements, as it comes in different dosages (0.1 and 0.2 mg) and can be easily divided if necessary. On the other hand, the intranasal form is essential for patients with a high need for the drug. The goal

of desmopressin treatment is to find the minimum effective dose to control excessive thirst and polyuria, rather than increasing urine density. It is important to instruct patients on their drinking regime, recommending they only drink when thirsty to avoid excessive fluid intake. Successful treatment of central ND depends on the sensitivity of the thirst centre, as changes in its function can lead to complications like water intoxication. In these cases, patients may need to skip doses or regulate their fluid intake.

The text describes the condition of adipsia, which is characterized by hypo- and hypernatremia, and the polyuria-polydipsia syndrome. This syndrome refers to excessive water intake and frequent urination. The diagnostic process involves several steps, including urine analysis, blood tests, and a desmopressin test. Central nephrogenic adipsia, which is caused by brain lesions or trauma, is often treated with desmopressin. Monitoring fluid intake and osmolality and sodium concentration in the blood is crucial for patients with impaired sensation of thirst. After neurosurgical interventions or craniocerebral trauma, specific attention should be given to the treatment of central adipsia, as it can have a transient or three-phase course. Permanent therapy with desmopressin is recommended after 3-4 weeks to avoid complications such as water intoxication. Patients should be educated about the symptoms of water intoxication and its prevention and treatment.

The primary treatment for renal nephrogenic diabetes insipidus (ND) involves the use of thiazide diuretics and non-steroidal anti-inflammatory drugs (NSAIDs). However, this treatment is not curative and only helps to reduce urine volume and thirst in most patients. It is not as effective as desmopressin therapy for central ND, and diuresis is rarely reduced by more than 50%. Moreover, there are concerns about the safety of these drugs, as they can have serious side effects in prolonged use. In acquired nephrogenic ND, treatment focuses on addressing the underlying conditions such as hyperparathyroidism and hypokalaemia. For mild forms of ND, therapy may consist of ensuring sufficient fluid intake to satisfy thirst without drug therapy. In cases of psychogenic polydipsia, some patients may experience relief of thirst with the use of carbamazepine, although its effectiveness may vary. Desmopressin can also be used intermittently to reduce urine volume and thirst in certain patients with primary polydipsia, but caution should be exercised to avoid water intoxication. Psychotherapy and psychotropic drugs may not always be effective in treating ND.

Conclusion. The article provides an update on non-sugar diabetes, covering its epidemiology, classification, pathogenesis, clinical symptoms, and differential diagnosis. It emphasizes the importance of selecting the appropriate form and dose of medication to maintain a comfortable quality of life for patients. However, the article highlights that some patients who are not well-educated about the disease may stop their treatment, leading to decompensation and potentially life-threatening situations. In rare cases, patients may temporarily compensate for the disease by making lifestyle changes, such as increasing fluid intake to offset excessive urination. However, any new illness or condition can disrupt this delicate balance. The article suggests that timely and adequate patient education, along with regular follow-up by a specialist, can help prevent such situations.

List of references used:

1. Абрарова Д. Л., Негматова Г.Ш., Тогаева Г.С. «Клинико функциональный течения у больных сахарным диабетом 2 типа с автономной нейропатией». // The American Journal of Academic research. // Volume 2. (5). 409-415. 2022
2. Нарбаев А.Н. Тогаева Г.С. «The Use of daily continuous glucose monitoring in clinical practice». //The American Journal of medical sciences and pharmaceutical research. // Volume 2. Issue 9. 2020.Стр 82-85
3. Орипов Ф.С., Тогаева Г.С. «Распространенность диабетической стопы пациентов с сахарным диабетом 2 типа в Самаркандской области» //Биомедицина ва амалиёт журнали. Жилд 7. сон 5. 143-147. Тошкент 2022г.
4. Орипов Ф.С., Тогаева Г.С. «Структурные особенности клеток островков Лангерганса у потомства с аллоксоновым диабетом». //Тиббиётда янги кун. №2. 2020г. Бухоро. 218-220.

5. Тогаева Г.С. «Ўз-узини назорат қилиш мактабида ўқиган қандли диабет 2 тип билан касалланган беморларнинг клиник ва биохимиявий курсаткичлари». //Биомедицина ва амалиёт журнали 2 махсус сон. 2020 й Тошкент. 132-135-бет.
6. Тогаева Гулнора Сиддиковна., Орипов Фирдавс Суратович., Давранова Азиза Даврановна.: "Structural features of cells of the islets of Langerhans in offspring with alloxonic diabetes" (Review article). //Annals of the Romanian Society for Cell Biology 2021; P.158-162
7. Тогаева Г.С., Орипов Ф.С. «Наследственность сахарного диабета первого типа у детей как медико-социальная проблема». //Тиббиётда янги кун. 6 (44) 22. Бухоро. 261-265.
8. Тогаева Г.С., Clinical And Biochemical Parameters Of Patients With Type 2 Diabetes Who Were Trained At The School Of Self- Control. //JOURNAL OF BIOMEDICINE AND PRACTICE SPECIAL ISSUE-2. P-131-136, 2020
9. Хамраев Х.Т., Тогаева Г.С., «Клинико-Биохимические показатели больных сахарным диабетом 2 типа, прошедших обучение в школе самоконтроля». //Проблемы биологии и медицины. №1.72 Самарканд. 2013.75-77.
10. Азимбегова С.Н., Давранова А.Д. “Болаларда 1-тур қандли диабетни даволашини ўзгартириш ва диабетик ретинопатиясини олдини олиш хусусиятлари”. Журнал гепато-гастроэнтерологических исследований. 2022/7/31.
11. Каримова Н.А. Тогаева Г.С., Давранова А.Д. Даминов А.Т., “Cardiovascular complications in patients who have had covid on the background of diabetes mellitus 2.” Central Asian Journal of Medical and Natural Science, 2(3), (2021). 37-41.
12. Негматова Г.Ш., Тогаева Г.С., Давранова А.Д., Азимбегова С.Н. “Assessment of the effectiveness of cardioprotectiva drugs in treatment of childeren with diabetic cardiomyopathy”/ The American juornal of medical sciences and pharmaceutical research//4.01. 79-83.
13. Тогаева Г.С., Давранова А.Д. “PREDICTION OF POSTOPERATIVE WOUND HEALING IN PATIENTS WITH DIABETIC FOOT SYNDROME” World Bulletin of Public Health// 2023/2/18. 194-196.
14. Давранова А.Д. “QALQONSIMON BEZ PATOLOGIYASI BO'LGAN O'SMIR QIZLARDA HAYZ DAVRINING BUZILISHINI O’ZIGA XOSLIGI”/ Eurasian Journal of Medical and Natural Sciences// 2022/8/30. 113-115.