Pediatr Pol 2024; 99 (2): 1-6
DOI: https://doi.org/10.5114/polp.2024.139872
Submitted: 19.09.2023, Accepted: 04.01.2024, Published: 24.05.2024

PEDIATRIA Polska
Polish Journal of PAEDIATRICS

CASE REPORT

Feeding difficulties in infancy as an early symptom of different forms of diabetes insipidus – a series of cases

Katarzyna Anna Banasiak[1], Małgorzata Barbara Stańczyk[2,3], Elżbieta Szczepanik[2,3], Katarzyna Monika Krawiranda[1], Anita Janus[1], Kacper Piotr Kościelny[1], Marcin Tkaczyk[2,3]

[1]Student's Paediatric Scientific Association at the Department of Paediatrics, Immunology and Nephrology, Polish Mother's Memorial Hospital Research Institute, Łódź, Poland
[2]Department of Pediatrics, Immunology and Nephrology, Polish Mother's Memorial Hospital Research Institute, Łódź, Poland
[3]Department of Pediatrics, Nephrology and Immunology, Medical University of Łódź, Łódź, Poland

ABSTRACT

Feeding disorders of infancy are common in paediatric practice. Among rare causes of this disturbance is diabetes insipidus (DI), which is a clinical syndrome characterized by polyuria, polydypsia and dehydration with hypernatraemia. Central diabetes insipidus (CDI, vasopressin deficiency) is more common in children than nephrogenic diabetes insipidus (NDI, an inability to respond adequately to vasopressin). Regardless of the type of DI, the main goal of treatment is to decrease thirst and urine output and achieve proper ion and fluid balance.

We present three cases of infants with feeding difficulties. The first two cases concerned patients with semilobar holoprosencephaly (HPE). Their stories show the importance of knowing the most common abnormalities associated with HPE, such as CDI. The third child had similar problems with feeding which resembled a defect of the central nervous system, but was finally diagnosed as NDI. The diagnostic and therapeutic approach is demonstrated in the paper with special regards to safe management of hypernatraemic dehydration.

KEY WORDS:

diabetes insipidus, holoprosencephaly, hypernatraemia, infant, feeding and eating disorders.

INTRODUCTION

Feeding disorders of infancy are common in paediatric practice. Among rare causes of this disturbance is diabetes insipidus (DI), which is a clinical syndrome characterized by polyuria, polydypsia, and dehydration with hypernatraemia. Diabetes insipidus results from a deficiency of antidiuretic hormone (ADH) – central DI (CDI) – or resistance to ADH – nephrogenic DI (NDI). Diabetes insipidus is rare, with an estimated prevalence of 1 : 25 000 [1]. Less than 10% of cases are hereditary. Central DI accounts for over 90% of cases of DI and because of different causes it can present at any age [2]. Diabetes insipidus in infants can have different symptoms compared to adults and is challenging to treat due to the need to adjust drug doses and the need to consume liquid calories. Here we present three cases of infants with feeding difficulties which were the main symptom of DI in all of them. Two patients with holoprosencephaly (HPE) were diagnosed with CDI and one with NDI. We aimed to show how important it is to know the symptoms and complications of the disease. We present our therapeutic and diagnostic approach with special regards to symptoms and signs of both central and NDI in early infancy including the management of water and ion imbalance.

ADDRESS FOR CORRESPONDENCE:

Katarzyna Anna Banasiak, Student's Paediatric Scientific Association at the Department of Paediatrics, Immunology and Nephrology, Polish Mother's Memorial Hospital Research Institute, Łódź, Poland, e-mail: katarzyna.banasiak@stud.umed.lodz.pl

CASE REPORTS

CASE 1

A 2-month-old girl was admitted to the paediatric department with increasing feeding difficulties and ineffective sucking activity. One day before admission she had an episode of apnoea with cyanosis. The child was born at 37 weeks gestational age (GA), gravida III (GIII), para II (PII) by caesarean section (CS) (placenta praevia) with body weight 2650 g, Apgar score 9/10. Prenatally she was diagnosed with HPE – the diagnosis was confirmed after birth in magnetic resonance imaging (MRI); additionally, complete agenesis of the corpus callosum was described. The mother had hypothyroidism during pregnancy. For the first 6 weeks of life the girl was hospitalized in the neonatal ward. There were no data on ionic disturbances during the stay. She gained weight properly, although difficulties in feeding were observed after she was discharged from the hospital.

On admission the patient was in good condition. Her body length was 54 cm (7 pc), weight 3.9 kg (< 3 pc), head circumference 31 cm (< 1 pc – microcephaly). She presented with facial dysmorphic features, slightly sunken, small anterior fontanelle, chaotic eye movements, increased peripheral and decreased axial muscle tone. She was normotensive with a normal heart rate. Laboratory tests revealed mild anaemia, hypernatraemia of 170 mmol/l, as well as hyperchloraemia, hyperphosphataemia, hypermagnesaemia and increased lactate concentration. Serum creatinine was slightly elevated (0.60 mg/dl, normal range: 0.2–0.4) with epidermal growth factor receptor (eGFR) in lower reference limits (eGFR estimated with Schwarz equation: 37.2 [ml/min/1.73 m^2], reference range: (35–85); lactate dehydrogenase and uric acid were also slightly above normal (446 U/l, reference range: 180–435 U/l and 6.5 mg/dl; reference range: 1.4–5.8, respectively). Specific gravity of urine was low, 1.002, as was osmolality in the urine, 96 mOsm/kgH_2O. Serum osmolality was above the normal range – 348 mOsmkgH_2O (Table 1).

Due to the inability to feed the girl – increased anxiety, tensing up, ineffective sucking – a nasogastric tube was placed. A 5% glucose infusion at a rate of 10 ml/h was stared. Fluid balance was monitored. In the following days, glucose infusion was continued and normalization of serum ions was observed. Rehydration aligned with clear polyuria and increased appetite. She passed 625 ml of urine in 24 hours, which exceeded 2 litres *per* m^2 of body surface area (BSA). The overall clinical picture led to a diagnosis of CDI and desmopressin (dDAVP) acetate (2 × 7.5 μg [3.8 μg/kg/day], then 1 × 7.5 μg – 1.9 μg/kg/day) was commenced with the expected clinical result – gaining weight, stable ion balance with natraemia in the 135–146 mmol/l range and decrease of polyuria. Therefore, the continuous infusion of glucose was first reduced and eventually discontinued. The patient presented with transient overload of the circulatory system (oedema, increase in cardiac enzymes), probably because of excessive intravenous fluid intake (after starting treatment with dDAVP). Due to anaemia (which was significant after proper hydration, worsened by frequent blood collecting) the treatment with iron supplementation, haematopoietic vitamins and erythropoietin was started.

Because of CDI, additional tests evaluating the endocrine system were performed, showing normal thyroid function but abnormal prolactin and cortisol levels, probably resulting from central nervous system (CNS) structural defects and sleep pattern abnormalities.

In the meantime, the result of array comparative genomic hybridization genetic tests was obtained – no abnormalities were found in the scope covered by the test technique – the genetic cause of the HPE was ruled out. Urine gas chromatography/mass spectroscopy and the plasma aminogram were obtained after the discharge of the patient; the results were negative.

On day 21, after stabilization of the child's condition, serum sodium concentration and fluid balance, the girl was discharged home under the care of an inpatient hospice. She was on partial oral feeding with supplementation through a gastric tube. On the day of discharge, the body weight was 4.5 kg (3–10 pc).

TABLE 1. Cases 1, 2, 3 – relevant laboratory results on admission

Parameters	Case 1	Case 2	Case 3	Reference ranges
Na+ [mmol/l]	170	149	151	133–145
Cl– [mmol/l]	127	112	111	98–112
PO43– [mmol/l]	2.84	–	1.92	0.9–1.6
Mg2+ [mmol/l]	1.24	–	–	0.7–1.1
Lactates [mg/dl]	106.6	22	–	6.3–18.9
Urine specific gravity	1.002	1.006	1.002	1.005–1.035
Urine osmolality [mOsm/kgH_2O]	96	88	94	800–1000
Serum osmolality [mOsm/kgH_2O]	348	305	316	270–285

CASE 2

A 6-month-old girl was admitted to the hospital due to vomiting and signs of a mild respiratory infection. A child from natural delivery was born at 39 GA (GI, PI) with body weight of 3800 g, Apgar 9/10. The patient already had the diagnosis of complex CNS defect in the form of HPE with agenesis of the corpus callosum – it was suspected prenatally and confirmed after the childbirth. The girl also presented with coarctation of the aorta. The patient was breastfed, with no history of previous hospitalizations, infections or chronic treatments.

Physical examination revealed body weight of 6.8 kg (10–25%), length 67 cm (25–50%); body mass index (BMI) 15.1 kg/m^2 (5–15%), head circumference 37 cm (< 3% – microcephaly); flattened occiput, a small haemangioma in the area of the sternal zygomatic notch; slightly increased general muscle tone and reddened urethral orifice. In laboratory tests the main disturbance was hypernatraemia (149 mmol/l) with hyperchloraemia (118 mmol/l). The patient was treated with intravenous infusion of 5% glucose solution and a gradual improvement in natraemia was observed, but it was not possible to finally determine the child's good hydration and normal sodium concentration – after a few days of normonatraemia, the sodium concentration went up to 152 mmol/l. During hospitalization, the patient presented with polyuria (> 2 l of urine/m^2 BSA) and high need for feeding. Therefore the diagnostics was extended with the evaluation of serum and urine osmolality – serum osmolality was high and urine osmolality was low (305 mOsm/kgH_2O, 50–80 mOsm/kgH_2O, respectively). Those results led to a suspicion of CDI. To confirm the diagnosis, a test with dDAVP was performed. The result was positive, and dDAVP at a dose of 15 µg (2.2 µg/kg) was started as recommended for CDI. In the following days, the child was normonatraemic with stable diuresis and a good appetite. The child was discharged home after 6 days with diagnosis of CDI in the course of semilobar HPE in good general condition with a recommendation of dDAVP continuation.

CASE 3

A 2-month-old boy was transferred to the paediatric department from a district hospital because of suspicion of diabetes insipidus. His symptoms comprised significantly impaired appetite and lack of weight gain.

The boy was full term, born from the 1st pregnancy by CS (threatening fetal asphyxia) with a body weight of 4540 g. He was not naturally fed and cow's milk formulas were modified several times due to regurgitation and vomiting. The patient ate small portions, rarely woke up at night to feed, but he drank a lot of water and willingly. He passed constipated stools every 3–4 days. Despite the small supply of liquids, the patient was passing a lot of urine (up to 10 full diapers per day).

On admission, the patient was in good general condition, with signs of dehydration. Laboratory tests revealed high plasma osmolality (316 mOsm/kgH_2O), low urine osmolarity (94 mOsm/kgH_2O) and hypernatraemia up to 151 mmol/l – these parameters improved after intensive fluid therapy. The monitoring of balance of fluid intake and excretion revealed polyuria. On the basis of reproducibly high serum osmolality, low urine osmolality and hypernatraemia, the indications for the dDAVP test were established. The patient was given 15 µg of dDAVP first followed by 30 µg of the drug, with no significant change in the laboratory test results or reduction in diuresis. Then hydrochlorothiazide was administered at a dose of 1.5 mg/kg/day – also no significant change was noted.

Due to feeding disorders, temporary nasogastric tube feeding was implemented. During hospital stay the boy presented with abnormal movement patterns, temporarily associated with vomiting. Due to the diagnosis of muscle tone disorders, physical therapy was started. After neurological and neurologopaedic assessment, Sandifer's syndrome was suspected. This led to the implementation of a therapeutic trial with omeprazole. After the beginning of this therapy, the patient was much more willingly and effectively fed orally and required less and less feeding with a nasogastric tube. He was systematically gaining weight. Four days after the modification of the diet, the natraemia was normal, and the serum osmolality decreased < 300 mOsm/kgH_2O, but stayed elevated. Due to the overall picture, especially the uncertain response to therapeutic attempts to diagnose DI, a consultation with a clinical geneticist was held. Genetic tests were performed to confirm or exclude DI and genetic disorders characteristic of eating disorders.

After 20 days of hospitalization, the patient was discharged home in an optimal general condition. He was fed orally, with the possibility of feeding by tube, treated with proton-pump inhibitors (PPI) due to suspected gastroesophageal reflux disease and hydrochlorothiazide due to suspected nephrogenic diabetes insipidus. The genetic test, performed ambulatorily, confirmed the diagnosis of NDI – an X-linked defect of the arginine vasopressin receptor was found.

Initially, the omeprazole therapy was successful. After a few weeks, the treatment was modified – ranitidine and trimebutine were introduced – after which regression in oral food intake and increased vomiting were observed. Due to this fact, omeprazole was restored.

At the age of 7 months, the patient was hospitalized again because of lack of weight gain. Because the patient did not vomit and consumed milk orally willingly (800 ml/day), the nasogastric (NG) tube was pulled out 3 weeks earlier. In addition, the parents gradually discontinued omeprazole without aggravating the symptoms.

The boy did not accept solid food due to reluctance and retching. The child was permanently treated with hydrochlorothiazide at a dose of 3 mg ter in die (1.5 mg/kg/day), cyproheptadine for aversion to food, macrogols for constipation, and probiotic. On admission, the physical examination revealed a body weight of 6.1 kg (< 3%), length of 72 cm (25–50%), BMI: 11.77 kg/m^2 (< 5 pc), BP: 83/49 mm Hg. The child was in good general condition, with no signs of dehydration. The boy was cachectic, his head was larger than the rest of the body, and the skin was pale without pathological lesions. He gained 430 g in 3 months. Laboratory tests revealed a decreased iron saturation index, slightly elevated liver enzymes, increased serum osmolality, and decreased urine osmolality, without ionic disturbances, slight hyperammonaemia, of 96.6 µg/dl (reference 27–90 µg/dl), elevated CK levels of 204 U/l (reference < 171 U/l), and hyperglycaemia of 143 mg/dl. Given other than only NDI associated symptoms the patient had whole genome sequencing that revealed a mutation in the *CEL* gene associated with MODY VIII type diabetes with autosomal dominant inheritance – which could explain the hyperglycaemia. The boy also turned out to be a carrier of a variant in the *FECH* gene associated with erythropoietic protoporphyria 1 and a variant in the *TMEM67* gene associated with Joubert syndrome. However, these findings seemed to be clinically irrelevant as the patient did not present any symptoms of these entities.

The boy was discharged home in good condition after laboratory and genetic tests and gastroenterological consultation in which a higher caloric supply was ordered. Due to elevated levels of ammonia and CK he was referred to a metabolic disorders outpatients clinic where he is being observed without new diagnoses. Due to elevated glycaemia and a genetic predisposition to the development of MODY VIII type diabetes, regular blood glucose measurements and body weight measurements were recommended, as well as follow-up at a diabetes clinic for children.

DISCUSSION

We have described three cases of infants with feeding difficulties. In all of them the main disturbance was dehydration with hypernatraemia. All of them were eventually diagnosed with diabetes insipidus.

Although polydipsia and polyuria, the main clinical symptoms of DI, seem easy to notice, neonates and children with neurological defects, who cannot communicate their thirst, are at risk of developing fever, constipation and severe dehydration. Older children often present with weight loss as they prefer liquids to solid intake [3]. The severity of dehydration depends on the age of the child and the time in which it developed. Typical for DI is hypernatraemic dehydration. Hypernatraemia is diagnosed when the serum blood sodium concentration is above 145 mmol/l. It occurs most often in severely dehydrated patients. The symptoms of severe dehydration include lethargy, somnolence, weight loss of over 10%, significantly impaired skin elasticity, very little or lack of thirst, very dry mucous membranes, collapsed and drying eyeballs, lack of tears, very extended (over 5 s) capillary refill time, significantly accelerated heart rate, decreased blood pressure, and oliguria. Feeding difficulties, highlighted in our article, represent one of the symptoms of hypernatraemia. Additional symptoms of hypernatraemia are increased muscle tension and disturbances in consciousness. Convulsions and coma may occur in severe cases. Moreover, a common manifestation of this condition is high fever.

The diagnosis of DI is based on the urine concentration test (no or reduced ability to concentrate urine during limited fluid intake) and response to ADH administration. The urine concentration test is contraindicated in children under 1 year old [4]. Desmopressin (an analogue of ADH) is also used to differentiate between CDI and NDI. Because of potential causes of CDI it is crucial to perform MRI of the forebrain to exclude organic causes of CDI [5].

The treatment of DI depends on the aetiology. In CDI the treatment with dDAVP is implemented in order to replace natural vasopressin. In NDI the treatment is targeted to reverse the effects of lack of response for ADH in the kidney tubules.

The first two presented children had HPE – a rare condition resulting from incomplete cleavage of the prosencephalon, occurring in about 1/8,000–1/16,000 live births and 1/250 conceptuses [6]. Diagnosis of alobar HPE is possible within 10–14 weeks of gestation (abnormal morphology of the face in ultrasound examination) [7]. Abnormalities associated with this defect are both structural (craniofacial anomalies, median or bilateral cleft lip/palate, microcephaly) and functional (pituitary dysfunction, developmental delay, seizures, sleep pattern disorders, feeding difficulties) [7]. Other factors which damage the CNS causing CDI are tumours, infiltrative, autoimmune and infectious disease, trauma, septic shock (infarction), and neurosurgical intervention. Diabetes insipidus may be the first symptom of Langerhans cell histiocytosis in the paediatric population [3]. Another rare cause of CDI is a genetic defect of vasopressin synthesis. In some of these clinical situations the lack of more than one pituitary hormones is observed [5].

Central DI is the most common endocrinopathy in patients with HPE [8]. It leads to hypernatraemia and dehydration. The other potential cause of hypernatraemia in HPE is neurogenic hypernatraemia. It is important to differentiate between these two conditions, as they are treated in different ways. In neurogenic hypernatraemia the patient presents with adypsia, without polyuria and signs of dehydration [9]. The treatment consists of proper hydration, because this condition results from the lack of thirst [9].

The main concern during rehydration of patients with DI is maintaining proper sodium balance.

It should be remembered that the more slowly the hypernatraemia develops, the more slowly the excess sodium should be balanced. Too fast changes of sodium concentration result in severe brain injury. Serum sodium should be reduced by up to 12 mmol/l *per* day at a rate of 0.5 mmol/h (chronic hyperthermia – if the onset of hypernatraemia is unknown one should assume it is chronic) to 1 mmol/h (acute hyperthermia lasting for less than 48 h). Unless the patient is not in hypovolaemic shock the best way is to start therapy with sodium-free fluids – 5% glucose solution or 0.33% sodium chloride up to daily fluid needs of the body in order to reach the ion balance. Deficit of water can be calculated from the formula: $0.6 \times \text{body weight} \times ({}_{\text{current}}\text{Na} - {}_{\text{target}}\text{Na})/{}_{\text{taget}}\text{Na}$ + ongoing loss. It is highly important to monitor sodium, potassium, and calcium concentrations, glucose, and serum osmolality, and perform blood gas analysis. A careful fluid balance (3–12 hours), vital signs, and kidney function should be monitored [10].

Both polyuria and dehydration are characteristic for CDI, where polydipsia also occurs. Polyuria is defined as urine output > 150 ml/kg/24 h at birth, > 100–110 ml/kg/24 h by the age of 2 years, and > 50 ml/kg/24 h in children > 2 years old [1]. If polyuria occurs, the CDI diagnosis is very likely. As the CDI mechanism relies on lack of vasopressin secretion, dDAVP – an analogue of vasopressin – is an appropriate treatment for the disease. Vasopressin dosing varies depending on the route of administration and patient needs – the recommended dose off dDAVP is 100–1200 μg/d in three divided doses orally; 2–40 μg once or twice a day intranasally; and 0.1–1 μg parenterally [11]. Ooi *et al*. treated orally with 9.5 μg/kg/d (4.2–17.0) in 2–3 divided doses [12]. Subsequent doses depend on the patient's response. In most patients, the maintenance dose is 60–120 μg of dDAVP sublingually 3 times a day [13].

Treatment with dDAVP is usually safe. The medication may cause headache, abdominal pain, nausea, vomiting, lethargy, weight gain, dizziness, confusion, bad mood, memory disorders, seizures, balance disorders, falls and, in severe cases, convulsions and coma. The most serious side effect of dDAVP is hyponatraemia, so it is crucial to monitor sodium concentration at the beginning of dDAVP therapy and later on during inter-current illness when normal fluid intake is compromised. Hyponatraemia may be a cause of brain injury in the mechanism of *brain oedema* as water shifts into the brain cells by osmosis from the dilute plasma [1]. Diabetes insipidus patients are at risk of developing adverse effects of treatment with dDAVP in the case of acute illness with fluid and electrolyte disturbances. In such a case they should be promptly and carefully assessed, as sometimes temporary cessation of dDAVP is needed.

Precautions to avoid hyponatraemia, including restrictions on fluid intake and more frequent monitoring of serum sodium levels, should be observed in cases of concomitant use of drugs that cause inappropriate release of antidiuretic hormone (SIADH) or use of non-steroidal anti-inflammatory drugs (following the summary of the product characteristics).

Awareness of the frequent co-occurrence of CDI in patients with HPE led to quick identification of the cause of hypernatraemia in both described patients and proper treatment was implemented.

The third child's diagnosis and treatment proved to be more challenging than the former ones. He did not have a CNS defect but he suffered from concomitant gastroesophageal reflux, which made the diagnosis of DI difficult, as the reflux at the beginning was considered as the main reason for dehydration. Results of tests with dDAVP and hydrochlorothiazide were not clear, nor was the response to the treatment. Finally the diagnosis of NDI was established only based on results of genetic examination. Feeding difficulties were present even after implementation of treatment of NDI as the patient had other disorders which affected food intake. The complexity of this case needed multispecialistic cooperation; nevertheless only partial improvement was achieved.

In NDI (prevalence 1–9: 1 000 000 [14]) the renal response to ADH is impaired. Acquired causes of NDI are more common than genetic ones. Nephrogenic diabetes insipidus may be caused by hypercalcaemia, hypokalaemia, release of ureteral obstruction and drugs (lithium, methicillin, rifampin, foscarnet, demeclocycline, amphotericin B, cyclophosphamide). Most genetic causes of NDI are related to a mutation in the V2 receptor gene which is inherited in an X recessive manner [3].

Treatment of NDI is challenging and, as shown by the description of patient 3, requires the cooperation of a multidisciplinary team, which however does not always bring success. Treatment aims to provide good symptom control and prevention of complications. Treatment is based on a low-solute diet, diuretics, and sometimes prostaglandin inhibitors. The most important requirement is to prevent dehydration and hypernatraemia. The reduction of sodium consumption is necessary and it should not exceed the recommended consumption of sodium in the diet of a healthy child up to 6 months, which is about 120 mg, and which is completely covered by the consumption of breast or infant formula**.** Sodium intake decreased < 1 mEq/kg/24 h is even recommended [15]. In the NDI therapy hydrochlorothiazide can be implemented in a dose of 1–3 mg/kg/day in 2–3 divided doses [16]. Its action is based on increased sodium and water reabsorption in the proximal tubule, reducing urine output. Because of frequent occurrence of hypokalaemia during thiazide treatment, amiloride 0.3–0.6 mg/kg/day may be added to the therapy [5]. In the large cohort study by D'Alessandri-Silva *et al*. it was confirmed that thiazides and potassium sparing agents were the most commonly used for NDI (74 and 67% respectively), as well as it being the most com-

mon combined therapy [17]. Also prostaglandin synthesis inhibitors, such as non-steroidal anti- and coxibs, are used in treatment of NDI, especially if the patient is not responsive to thiazides and amiloride [1, 5, 18]. Ibuprofen is given at 20–25 mg/kg/day in 2–3 divided doses and indomethacin at 0.75–2 mg/kg in 3 doses; however, gastric bleeding and abdominal pain can be expected if use is prolonged. In the presented case 3 the response to typical therapy was hampered by other concomitant conditions and optimal treatment for this patient still remains a challenge.

By presenting the cases the authors wanted to highlight that feeding difficulties may be an initial symptom reported by parents or primary physicians of both central and nephrogenic DI. Polydipsia and polyuria may not be noticed at first, especially in the youngest infants. Difficulty in assessing the amount of urine excreted due to diapering and lack of self-supply ability makes it hard to establish a quick diagnosis. It is important to be cautious especially in children with mentioned signs of hypernatraemia and in children with weight deficits.

These three reported cases confirmed that awareness of symptoms of DI and hypernatraemia enables optimal treatment to be quickly instituted, resulting in resolution of symptoms and improvement of the children's condition and allowing them to return home.

CONCLUSIONS

Feeding difficulties are common in infancy. Among all typical paediatric problems DI as a cause is considered rarely. In patients with CNS abnormality CDI should always be considered in the first line. In the absence of CNS involvement suspicion of NDI should be put forward in patients with failure to thrive accompanied with polyuria and polydipsia and not responding to dDAVP. Careful treatment of hypernatraemia should be carried out to prevent irreversible brain injury. It is crucial to educate caregivers of children with DI about health situations when chronic treatment can put patients at risk of a threat to health or life.

In cases of an unclear picture, genetic assessment can be crucial to establish the proper diagnosis.

DISCLOSURES

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

REFERENCES

1. Hui C, Khan M, Khan Suheb MZ, et al. Diabetes Insipidus. StatPearls Publishing 2023
2. Dabrowski E, Kadakia R, Zimmerman D. Diabetes insipidus in infants and children. Best Pract Res Clin Endocrinol Metab 2016; 30: 317-328.
3. Jain V, Ravindranath A. Diabetes insipidus in children. J Pediatr Endocrinol Metab 2016; 29: 39-45.
4. Paediatric Improvement Collaboration. Clinical Practice Guidelines: diabetes insipidus. In: The Royal Children Hospital Melbourne. Available from: https://www.rch.org.au/clinicalguide/guideline_index/diabetes_insipidus (accessed: 05.2022).
5. Smyczyńska J, Lewiński A, Hilczer M. Disorders of water-electrolyte balance during endocrine diseases in children part i-disorders of vasopressin secretion and action 1, 2. Pediatr Endocrinol 2010; 9: 49-62.
6. Ramakrishnan S, Gupta V. Holoprosencephaly. In: StatPearls. Treasure Island (FL): StatPearls Publishing 2023 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560861/ (accessed: 18.06.2022).
7. Tekendo-Ngongang C, Muenke M, Kruszka P. Holoprosencephaly overview. In: Adam MP, Mirzaa GM, Pagon RA, et al. (eds.). GeneReviews®. Seattle (WA): University of Washington, Seattle 1993–2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1530/ (accessed: 05.03.2020).
8. Hahn JS, Hahn SM, Kammann H, et al. Endocrine disorders associated with holoprosencephaly. J Pediatr Endocrinol Metab 2005; 18: 935-941.
9. Ziora K, Lenarczyk A, Oświęcimska J, et al. Hipernatremia neurogenna u dzieci z holoprosencefalią – opis dwóch przypadków. Pediatr Pol 2007; 82: 731-734.
10. Buda P, Książyk J. Leczenie zaburzeń gospodarki sodowej u dzieci. Stand Med, Pediatr 2011; 8: 926-937.
11. Muglia L, Majzoub J. Disorders of the posterior pituitary. In: Sperling M (ed.). Pediatric endocrinology. 3rd ed. Saunders, Philadelphia 2008, 356-373.
12. Ooi HL, Maguire AM, Ambler GR. Desmopressin administration in children with central diabetes insipidus: a retrospective review. J Pediatr Endocrinol Metab 2013; 26: 1047-1052.
13. De Waele K, Cools M, de Guchtenaere A, et al. Desmopressin lyophilisate for the treatment of central diabetes insipidus: first experience in very young infants. Int J Endocrinol Metab 2014; 12: 16120.
14. Bockenhauer D. Nephrogenic diabetes insipidus. In: Orphanet. Available from: https://www.orpha.net (accessed: 04.2020).
15. Sreedharan R, Avner ED. Nephrogenic diabetes insipidus. In: Kliegman RM, Stanton BF, St Geme JW, Schor NF (eds.). Nelson Textbook of Pediatrics 2016. 20th ed. Elsevier, 2532-2533.
16. Priya G, Kalra S, Dasgupta A, at al. Diabetes insipidus: a pragmatic approach to management. Cureus 2021; 13: e12498.
17. D'Alessandri-Silva C, Carpenter M, Ayoob R, et al. Diagnosis, treatment, and outcomes in children with congenital nephrogenic diabetes insipidus: a pediatric nephrology research consortium study. Front Pediatr 2020; 7: 550.
18. Duicu C, Pitea AM, Săsăran OM, et al. Nephrogenic diabetes insipidus in children (review). Exp Ther Med 2021; 22: 746.