PBLD – Table #17

Water! Water! Everywhere!
Diagnosis and Management of Nephrogenic Diabetes Insipidus

Goals:

1. Understand diabetes insipidus and the role of arginine vasopressin production and its role at the kidney
2. Understand how to differentiate nephrogenic diabetes insipidus from central diabetes insipidus and primary polydipsia
3. Understand the etiology of nephrogenic diabetes insipidus
4. Understand the available diagnostic tools and their usefulness in characterizing the picture of nephrogenic diabetes insipidus in the perioperative environement
5. Understand the management plan and/or treatment options for children diagnosed with nephrogenic diabetes insipidus in the perioperative setting

Case:

A 42-kg 13-year-old female presents with a three-month history of increasing abdominal girth. MRI revealed a cystic retroperitoneal mass. The patient underwent laparoscopic excision of the cyst and drainage of over 7 L of peritoneal fluid. Intraoperative urine output was 0.5 cc/kg/hr. Postoperatively, urine output was 1,050 ml in the first hour and blood pressure (BP) decreased to 68/45. BP responded to fluid resuscitation, however urine output remained elevated. Serum and urine electrolytes and osmolalities were obtained. We will provide a general understanding of diabetes insipidus and then discuss the possible etiologies of acquired nephrogenic diabetes insipidus and its management in the perioperative setting.

Questions:

1. What is Diabetes Insipidus? What is the role of arginine vasopressin?
2. What are the three main subgroups?
3. What is the difference between Central and Nephrogenic Diabetes Insipidus?
4. What causes Central vs. Nephrogenic Diabetes Insipidus?
5. What diagnostic tools can be used to determine the cause of polyuria as nephrogenic diabetes insipidus vs. central, etc.?
6. What treatment options are available for acquired and familial forms of nephrogenic diabetes insipidus?

Discussion:

- ***What is Diabetes Insipidus?***

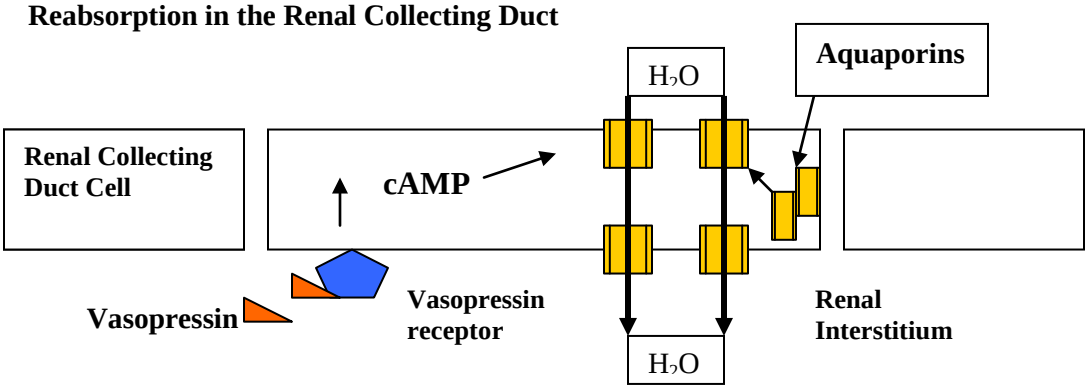
Diabetes Insipidus refers to the inability to conserve free water. It is characterized by the excessive production of dilute urine, namely polyuria, in volumes of $2L/m^2/24hr$, or about 150mL/kg at birth, 110 ml/kg at 2 years, and 40ml/kg/24hr in the older child and adult (Cheetham, 2002). Collectively, diabetes insipidus requires careful regulation of the amount of water ingested and the quantity and concentration of urine produced in order to maintain fluid volume and osmolality in the normal range.

- ***What is the role of Arginine Vasopressin or AVP in Diabetes Insipidus?***

Arginine vasopressin (AVP) or desmopressin is produced in the hypothalamus, transported

through the neural component of the pituitary stalk and stored in nerve terminals in the posterior pituitary. Small changes, even 1 percent, in blood solute concentration (plasma osmolality) regulate vasopressin release from the pituitary. An increase in plasma osmolality, which usually indicates a loss of extracellular water, stimulates vasopressin release into the systemic circulation, whereas a decrease in plasma osmolality inhibits vasopressin secretion. Vasopressin then acts on its major target organ, the kidney, where it increases free water absorption, and hence increases urine osmolality. The hormone binds to the vasopressin V_2 receptor (the antidiuretic receptor) on the basal aspect of the renal-collecting tubular cell. A subsequent chain of events involves stimulation of adenylyl cyclase via stimulatory G-proteins which controls the arrangement and insertion of cAMP-mediated incorporation of 'water-channel' proteins (aquaporin-2) into the cell membrane. These channels allow water to pass from the lumen of the nephron into the cells of the collecting duct along an osmotic gradient, thereby concentrating the urine. Aquaporins-3 and –4 are mostly responsible for the passage of water from within the cell into the renal interstitium, and finally the circulation. Other factors that can regulate vasopressin secretion as well as plasma osmolality changes include blood pressure alterations (usually a 10% change is required), nausea, hypoglycemia, some medications, such as morphine, ethanol, and nicotine. In understanding this mechanism, it is then possible to comprehend that lack of production or impairment of delivery of arginine vasopressin to the kidney as well as a damaged kidney response to the hormone can have deleterious effects on water balance.

Figure 1. Arginine Vasopressin and the Aquaporin Interaction leading to Water Reabsorption in the Renal Collecting Duct



- ***What are the three main subgroups of Diabetes Insipidus?***

In addition, when considering diabetes insipidus in the differential diagnosis of polyuria, it is crucial to understand and distinguish the different types to better formulate a diagnostic plan and then treatment strategy. Diabetes Insipidus, a polyuric water imbalance, can be divided into three main groups, which describe the three main factors that determine water balance: thirst, vasopressin, and kidney function. Primary polydipsia or dipsogenic diabetes insipidus is characterized by ingestion of large amounts of fluid. The second group is cranial or central diabetes insipidus in which there is an abnormally low production of vasopressin. Thirdly, nephrogenic diabetes insipidus results from either an intrinsic renal defect or an acquired disorder secondary to metabolic disease and/or medications causing the kidney to have an impaired response to vasopressin. Each of these subgroups of diabetes insipidus has specific etiologies, diagnostic criteria via history, exam, and clinical evaluation, and treatment options, which will be discussed in order to emphasize and distinguish the features for the diagnosis and management of nephrogenic diabetes insipidus.

- ***What causes the different forms of Diabetes Insipidus?***
  i. ***What is Primary Polydipsia?***

Each of the subgroups of diabetes insipidus can be linked to certain etiological factors. Primary Polydipsia will be briefly mentioned here because it is part of the differential diagnosis in characterizing a specific form of diabetes insipidus to then focus treatment. Excessive fluid intake seen with primary polydipsia can suppress vasopressin release, induce polyuria, and lead to low-normal levels of plasma sodium and osmolality. It is often caused by compulsive or habitual excessive fluid intake, but in children, a psychiatric illness or rare hypothalamic defects leading to increased thirst are uncommon. Once ruled out by history either from the child and/or family, lab evaluation, and fluid restriction, the other two main categories of diabetes insipidus can then be distinguished and characterized to formulate a diagnosis and management plan. In relation to this case, the patient did not have this history and so other forms of diabetes insipidus could be entertained in the differential diagnosis.

ii. ***What causes Central or Cranial Diabetes Insipidus?***

The specific etiologies of Central and Nephrogenic diabetes insipidus help to differentiate each disorder. There is either a deficiency of or lack of normal kidney response to arginine vasopressin (AVP or ADH). This hormone is normally transported from the hypothalamus through the neural component of the pituitary stalk and stored in nerve terminals in the posterior pituitary. **Central or Cranial Diabetes Insipidus** is mainly characterized by a deficiency of antidiuretic hormone (ADH) or vasopressin. This leads to polyuria and a dilute urine relative to plasma osmolality with wide range in severity from mild forms to patients with profound polyuria up to 400ml/kg/24hr. The causes of central diabetes insipidus can be divided into inherited or familial forms that may or may not be linked to various cerebral malformations and those have an acquired etiology. The familial forms are rare, accounting for only 5% of all cases, some of which exhibit substitutions or deletions of the gene on chromosome 20, which encodes for a large vasopressin precursor molecule. The clinical expression of the familiar autosomal dominant disorder does not occur as an infant, but more commonly at the age of 5 to 10 years. There is also a rare syndrome called DIMOAD, which does not often present in infancy but more so in early childhood. It is characterized by cranial diabetes insipidus (DI), diabetes mellitus (DM), optic atrophy (OA), and deafness (D), as well as hydronephrosis and atonia of the bladder. The acquired forms of cranial diabetes insipidus can include trauma (head injury, after a neurosurgical procedure), hypoxic or ischemic brain injury, idiopathic, tumors (craniopharyngioma, optic glioma, or germinoma), granulomas (such as in tuberculosis, sarcoidosis, langerhans cell histiocytosis), and infectious causes (congenital cytomlomegalovirus and toxoplasmosis, encephalitis or meningitis).

iii. ***What causes Nephrogenic Diabetes Insipidus?***

Nephrogenic Diabetes Insipidus is defined as a lack of appropriate renal response to vasopressin or antidiuretic hormone. The disorder can be categorized into familial, an intrinsic renal defect, and acquired forms.

The Inherited Form: The renal tubules of patients with the familial forms of nephrogenic diabetes insipidus are partially or totally resistant to vasopressin (ADH). X-linked recessive (vasopressin V2 receptor gene defect) and autosomal recessive (aquaporin-2 gene defect) inheritance patterns have been found in certain familial forms of nephrogenic diabetes insipidus. Molecular studies of families with nephrogenic diabetes insipidus uncovered various genetic mutations or deletions of the gene encoding the vasopressin V2 or antidiuretic receptor located on Xq28. This receptor is a 7-domain transmembrane protein. Mutations have been located in the transmembrane domain and the internal and external segments of the receptor. About 10% of patients with familial nephrogenic diabetes insipidus have a genetic abnormality of the water channel protein, aquaporin-2, with either autosomal recessive or dominant inheritance patterns.

The Acquired Form: Acquired nephrogenic diabetes insipidus can be categorized based on etiology, such as metabolic causes (hypercalcemia, hypokalemia), which can impair the action of vasopressin on the distal nephron and chronic renal failure. Type I diabetes mellitus can also lead to an osmotic diuresis and reduce the osmotic gradient across the renal tubule necessary for the action of vasopressin. Pharmacological agents, such as lithium and amphotericin B can impair the action of antidiuretic hormone at the renal tubule as well.

Table 1. Causes of Nephrogenic Diabetes Insipidus

Congenital	*X-linked* *Autosomal recessive*
Acquired	*Metabolic (hypokalemia, hypercalcemia)* *Nephrocalcinosis* *Osmotic (diabetes mellitus)* *Polycystic Kidney Disease* *Sickle Cell Disease* *Drugs (Demeocycline, lithium, amphotericin B, foscarnet, rifampin)* *Urinary Tract Obstruction* *Chronic Renal Failure*

- ***What Diagnostic Tools are helpful to differentiate Nephorgenic from Cranial DI?***

i. History and Physical Exam:

Comprehension of the two main categories of diabetes insipidus and the various etiologies of each disorder supports the formulation of a diagnostic plan. The assessment begins with a thorough history, a detailed family history, recent head trauma, focused surgical history, and chronic renal illness or condition, the age of onset of the symptoms, whether they have polyuria and the time frame; for instance, children with cranial and nephrogenic diabetes insipidus will often have polyuria both day and night. Children with diabetes insipidus may also have a lack of preference for fluid source, thereby drinking from the tap, toilet or bath water, information gathered from the family. A finding of more pronounced growth retardation occurs more commonly in cranial rather than nephrogenic diabetes insipidus and can be a distinguishing historical find. Clinical examination then evaluates the child's nutritional status, and focus on the skeleton, central nervous system, and abdomen is important. In addition, polyuria leading to dehydration and hypernatremia may lead to behavioral or development problems in children with nephrogenic diabetes insipidus. Serious sequelae, such as intracerebral calcifications, seizures, psychosomatic retardation, hydronephrosis (a non-obstructive dilatation of urinary tract due to in this case excessive urine production), and hydroureters, can be seen with untreated nephrogenic diabetes insipidus.

ii. Laboratory Investigation:

Clinical laboratory investigation and imaging provides the next crucial step toward a definitive diagnosis.

1.) Document a 24-hour urine sample and confirm polyuria. One should note that polyuria in excess of 5L/m2/day in a thriving child suggests primary polydipsia because a typical daily osmolar load (500 mosm/kg) can be excreted, even with very dilute urine (100mosm/kg). This polydipsia could lead to hyponatremia because of the sodium loss with the polyuria.

2.) A set of baseline laboratory evaluations should be taken as nephrogenic or central diabetes insipidus is characterized by hypernatremia with an increased plasma osmolality in a polyuric patient with a lower than normal urine osmolality, whereas a patient with primary polydipsia would reveal a low serum sodium and plasma osmolality. Blood samples should be taken to evaluate plasma sodium, potassium, bicarbonate, chloride, urea, creatinine, phosphate, calcium including a random glucose, plasma osmolality, liver function tests, full blood count and serology for any congenital infections. Also, in addition to a 24-hour urine sample, a urinalysis and microscopy and random urine osmolality should be taken. Detection of diabetes mellitus leading to osmotic diuresis, hypercalcemia, hypokalemia and chronic renal failure may be accomplished with this preliminary laboratory analysis. Further in depth investigation can then be undertaken with the Water Deprivation Test and the renal Response to Desmopressin Test.

3.) The Water Deprivation Test

The Water Deprivation Test helps to establish the ability of the central nervous system to make antidiuretic hormone and the kidney to respond to arginine vasopressin. This test must be utitlized with caution in very young children and prove unsuitable in infants. The commonly used protocol is based on the original test by Dash et al in 1963. There should be free access to fluid prior to starting the fluid deprivation test and the patient must be closely supervised to avoid surreptitious intake and vital signs monitored throughout the study.

- The study should begin in the early morning to better supervise the child
- The laboratory made aware of the need for immediate report and feedback of collected samples both to ensure efficacy and appropriateness of termination.
- The patient should be weighed prior to the start, fluids should be restricted for about 8-hours, and then patient then weighed at 2-hour intervals during this dehydration phase ensuring that blood and urine are collected and assessed for osmolality and volume measurements as soon as possible.
- The test must be discontinued if weight loss exceeds 5% of the starting weight or if thirst becomes intolerable to the patient.
- Measurement of plasma vasopressin during the dehydration phase of the deprivation test may help to confirm a diagnosis of nephrogenic diabetes insipidus.

The results of the water deprivation test would reveal a low urine osmolality, less than 300 mosm/kg in both nephrogenic and central diabetes insipidus and greater than 750mosm/kg in primary polydipsia. However, many pediatricians are faced with equivocal results, such as a normal serum osmolality and a urine osmolality <600mosm/kg after an 8-hr fast in a child who has neither cranial nor nephrogenic diabetes insipidus. This could happen in polyuria of any cause because the renal interstitial solute is washed out, leading to a reduction in the osmotic gradient across the distal renal tubular cell, which is essential for the action of vasopressin. Irrespective of the underlying cause of the polyuria, this may result in a degree of renal resistance to vasopressin. Another useful piece of information from this test in formulating a diagnosis is that the maintenance of a normal serum sodium and osmolality during an 8-hr fast, with little weight loss, supports that underlying abnormality of arginine vasopressin is unlikely. In addition, if the child will not micturate and/ or the sample is unobtainable but the weight is stable, then major abnormalities of vasopresssin production or action at the renal tubule are also unlikely.

Applying results to the patient in question:
Discuss expected findings for Plasma and Urine Osmolality.

In this patient, creatinine clearance had risen to 92 ml/min, **urea** 9.3 mmol/l, **sodium**142 mmol/l, **potassium** 4.2 mmol/l, **creatinine** 149 mmol/l and **calcium** 2.5 mmol/l. The rest of her routine

biochemistry parameters were normal. **Plasma osmolality was 297** mmol/kg (normal range 275-295**), urine osmolality 191 mmol/kg**.

In this case, the patient exhibits a slightly high plasma osmolality with a low urine osmolality. The sodium is high-normal with an increased creatinine clearance, but otherwise normal calcium and potassium levels. This supports a potential DI picture, unlikely due to hypercalcemia or renal failure based on these preliminary labs.

What other labs or tests would be important in the postoperative workup? TSH/ Cortisol? Other radiological exams?

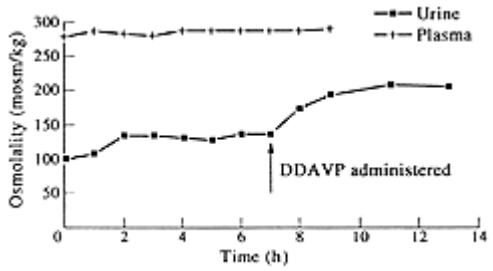
Thyroxine 106 nmol/l and **thyroid-stimulating hormone (TSH)** 3.92 mU/l indicated a euthyroid state. **Serum cortisol** at 9 a.m. was 564 nmol/l and **parathyroid hormone (PTH)** was 3.3 pmol/l (both within normal ranges).

These tests are also important to evaluate anterior pituitary function. Hypothyroidism, for instance can influence sodium balance. In addition, Diabetes Insipidus can be masked by an underlying adrenal insufficiency. Therefore, a cortisol level would be prudent to determine if glucocorticoid therapy is required prior to instituting diagnostic tests of diabetes insipidus.

A standard water deprivation test was carried out which suggested the diagnosis of nephrogenic diabetes insipidus.

The patient had subjective improvement after intranasal deamino-D-arginine vasopressin (DDAVP). Discuss this intervention.

Figure 2. The Change in urine and plasma osmolality upon DDAVP administration.



3.) Desmopressin Administration:

Desmopressin administration also proves valuable, especially when considering the results of the water deprivation test. It may be dangerous to administer desmopressin at the end of the deprivation test so it should not be done as a matter of routine. If the prior investigations confirm the general diagnosis of diabetes insipidus, then assessing renal responsiveness could be done at a later time to provide recovery time and avoid the need for sample collection out of hours. Eventual administration of desmopressin to evaluate renal responsiveness requires monitoring fluid balance and ensuring that input does not exceed output plus insensible loss. Although the test may not definitively differentiate between partial cranial diabetes insipidus and primary polydipsia, it should between cranial and nephrogenic diabetes insipidus. Desmopressin administration should increase urine osmolality to greater than 750mosm/kg in a patient with cranial diabetes insipidus who classically produces less antidiuretic hormone but maintains a normal renal responsiveness to the hormone; however, in nephrogenic diabetes

insipidus, the administration of desmopressin does not alter the urine osmolality because the kidney is relatively resistant to it's effects.

4.) Combining Results: Deprivation Test + Desmopressin Administraiton

However, if it is still unclear whether a child may have partial cranial diabetes insipidus or primary polydipsia because of an unclear history, combining results a couple tests may prove fruitful. A water deprivation test yielding a urine osmolality between 300 and 750 mosm/kg, and a desmopressin administration test showing a urine osmolality of less than 750mosm/kg, wherein there is possible responsiveness to desmopressin but not a confirmatory result, then some physicians may administer a "trial" of desmopressin. After a period of 3 to 4 days during which weight, plasma sodium, urine volume, and osmolality are monitored, the patient is given a small dose of oral, intranasal, subcutaneous, or intramuscular desmopressin daily for about 7 to 10 days. Measurements are continued during the desmopressin trial and for a few days after stopping the drug.

- ✓ Patients with cranial diabetes insipidus will exhibit a reduction in thirst and a progressive reduction in urine output, but plasma sodium remains in the normal range.
- ✓ Those with primary polydipsia will remain thirsty and are at risk of hyponatremia if their fluid intake is not halted.
- ✓ Nephrogenic diabetes insipidus, as previously discussed, is characterized by a lack of renal response to desmopressin, with persistence of thirst and polyuria.

Table 2: Interpretation of fluid deprivation and desmopressin (DDAVP) tests in patients with polyuria

Urine Osmolality (mOsm/kg)		**Diagnosis**
Post Fluid Deprivation	**Post Desmopressin**	
<300	**> 750**	**Cranial DI**
<300	**<300**	**Nephrogenic DI**
>750	**>750**	**Primary Polydipsia**
300-750	**<750**	**Possible: Partial Cranial DI, Partial Nephrogenic DI, or Primary Polydipsia**

6.) What about Hypertonic Saline as a Diagnostic Tool?

Although not commonly used as a diagnostic tool, in presence of an inconclusive water deprivation test, some physicians have conducted a hypertonic saline infusion study to assess whether the hypothalamus and/or pituitary gland can produce arginine vasopressin in the presence of a rising serum osmolality. Hypertonic saline 5% (850mmol/L) is infused over 2 hours at a rate of 0.05 to 0.1ml/kg/min or until plasma osmolality of 200mosm/kg is achieved, and arginine vasopressin is measured sequentially. A normogram describing the relationship between plasma osmolality and arginine vasopressin can be used to determine if a child has cranial diabetes insipidus in which there will be a subnormal response vasopressin; whereas patients with primary polydipsia or nephrogenic diabetes insipidus would have vasopressin levels in the normal reference range. This study has limited use than the other diagnostic tools because of practical difficulties in administering an irritant hypertonic saline solution to children, the limited availability of a reliable arginine vasopressin assay, and relatively large sample volume needed for its measurement.

7.) Are Imaging Studies Useful?

Application to this case: The brain C.T. scan showed no evidence of intracerebral metastatic disease, or ventricular enlargement.

Cranial diabetes insipidus can further be substantiated with diagnostic imaging studies, such as MRI scans of the pituitary/ hypothalamus for associated mass, tumors, intracerebral calcifications, as well lab studies for tumor markers. However, there are instances when cerebral imaging does provide conclusive evidence in support of the clinical picture.

Nephrogenic Diabetes Insipidus: Expectations of an Abdominal Ultrasound?

Since Nephrogenic Diabetes Insipidus (NDI) occurs when there is insensitivity of the renal collecting tubules to the physiological effects of antidiuretic hormone (ADH), abnormalities of the renal anatomy may be suspected and then correlated with the clinical picture. Abdominal ultrasound, for instance, can evaluate for any adrenal masses or hyperplasia as well as mephrocalcinosis, hydronephrosis, polycystic kidney disease or a urinary tract obstruction. These findings can help support or refute a diagnosis of nephrogenic diabetes insipidus.

Application to this case: Abdominal Ultrasound demonstrated mild hydronephrosis on the the right plus slight dilatation of the left calyceal system. Ultrasound revealed moderate bilateral hydronephrosis secondary to pelvic extension, measuring 12 cm x 13 cm x 12cm.
Despite this, renal function was adequate, with urea 7.7 mmol/l, creatinine 125 mmol/l, and a creatinine clearance 56ml/min.

- **Once there is clinical and laboratory evidence for Nephrogenic Diabetes Insipidus, what are the current treatment options?**

Each subgroup maintains different treatment regimens. Since a diagnosis has been established in this scenario, treatment may be tailored to address the underlying cause of the nephrogenic diabetes insipidus, namely metabolically (hypercalcemia or hypokalemia) or pharmacologicallly (lithium or amphotericin B) induced cases. Usually withdrawal of the agent or correction of the metabolic disorder (such as proper control of diabetes mellitus to prevent a worsening osmotic diuresis) can reverse the renal resistance to vasopressin but this may take weeks to months. However, in the familial forms of nephrogenic diabetes insipidus, the profound polyuria may be difficult to manage.

Pharmacology:

1.) **Thiazide diuretics** may be useful since they act by enhancing sodium excretion at the expense of water and reduce the glomerular filtration rate. Some studies have shown that salt restriction combined with the administration of a thiazide diuretic (such as hydrocholorothiazide 3mg/kg/day) can reduce urine output by 40% in infants.

2.) **Indomethacin, a prostaglandin synthetase inhibitor**, given in doses of 1.5 to 3.0 mg/kg may also produce a similar reduction in polyuria, but side effects, such as gastrointestinal irritation must be considered, and so it may be used with a prostaglandin analog like misoprostol to reduce this side effect risk.

3.) **A combination of indomethacin/ hydrochlorothiazide** has been described as being even more effective than indomethacin alone in diminishing urine production by 50 to 70 percent. However, hypokalemia must still be expected including the side effects on indomethacin itself.

4.) **Amiloride/ hydrochlorothiazide:** Studies have showed that the combination of hydrochlorothiazide/ amiloride is as effective as the previous combination, and that potassium intake is not necessary and patients do not need to suffer the effects of indomethacin. Kirschlechner et al described four children with nephrogenic diabetes insipidus taking 3mg/kg/day of hydrochlorothiazide/ 0.3mg/kg/day of amiloride over a period of one to five years. None of the children had signs of dehydration or electrolyte imbalance. Most of the subjects showed normal body growth and were without evidence of intracerebral calcifications or seizures; however they still required large fluid intakes and had high urine volumes. These amounts were similar to those taking indomethacin/ hydrochlorothiazide and to the quantities reported by other studies. Despite the large fluid turnover, which was less intense than for untreated patients, normal energy intake with adequate growth and weight gain were attainable for the children.

Side Effects: Caution with these medications must be advised as there have been a couple case reports of patients with nephrogenic diabetes insipidus, who developed paradoxical water intoxication due to liberal water intake while being started on thiazides and/or indomethacin combination therapy. Therefore, it is essential that these patients are monitored in terms of their fluid intake and volumes.

Fluid Management:

Fluid replacement is also important in the management of patients with postoperative diabetes insipidus. If the patient is awake and has an intact thirst mechanism, the patient's own thirst is the best guide to their water replacement needs. Increases in plasma osmolality of 2-3% trigger the sensation of thirst, which prevents significant hyperosmolality. If the patient is unable to respond to thirst, fluid balance can be maintained by intravenous fluids.

- ✓ **The free water deficit can be estimated by a mathematical formula:**
  0.6 × ([serum sodium concentration ÷ 140] - 1).

This formula is, at best, an estimate of the patient's fluid requirements; their serum electrolytes should, therefore, be measured frequently (e.g. every 6-8 h) to ensure that fluid replacement is sufficient. Although the development of hyperosmolality is due to water loss in most cases, a careful analysis of tonicity balance reveals that infused sodium can contribute to a hyperosmolar state in the immediate postoperative period. Consequently, all sodium-containing intravenous fluids should be avoided, unless there is clear evidence of hypovolemia as was in this case. Once stabilized, hypotonic vs D5W must be used for replacement based on the above formula. However, in patient post cranial surgery with a diagnosis of central diabetes insipidus, use of hypotonic solutions may be ill advised and therefore careful selection of fluid choice and rate should be a team approach in conjunction with neurosurgery and endocrinology services.

Corticosteroids

Any patient with postoperative diabetes insipidus should be presumed to have anterior pituitary insufficiency as well, and should receive **corticosteroid replacement therapy**. In the immediate postoperative setting, hydrocortisone (50-100 mg intravenously every 8 h) is generally used, which is then rapidly tapered to a maintenance dose (15-25 mg daily) until anterior pituitary function can be definitively evaluated.

Consultations:

Finally, consultations to consider based on AAP recommendations:

- ✓ If structural renal diseases leading to polyuria then refer to a pediatric nephrologist.
- ✓ Children with vasopressin deficiency are best referred to an endocrinologist or neurologist so that the cause of the diabetes insipidus can be determined.

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