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Diabetes insipidus: Differential diagnosis and management

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Diabetes insipidus (DI) is a syndrome characterized by the excretion of abnormally large volumes of dilute urine. It can be caused by any of 4 fundamentally different defects that must be distinguished for safe and effective management. They are: (1) pituitary DI, due to inadequate production and secretion of antidiuretic hormone, arginine-vasopressin (AVP); (2) gestational DI due to degradation of AVP by an enzyme made in placenta; (3) primary polydipsia, due to suppression of AVP secretion by excessive fluid intake; and (4) nephrogenic DI due to renal insensitivity to the antidiuretic effect of AVP. This review describes several methods of differential diagnosis, indicates the advantages and disadvantages of each and presents a new approach that is simpler and less costly but just as reliable as the best of the older methods. The various treatments for the different types of DI and recent findings on the genetic basis of the familial forms of DI are also discussed with emphasis on their contributions to improved diagnosis and management.

Introduction

Diabetes insipidus (DI) is a syndrome characterized by chronic excretion of abnormally large volumes of dilute urine [1,2]. The polyuria is associated with a commensurate increase in fluid intake that is often but not always due to increased thirst. Other signs and symptoms include urinary frequency, incontinence, nocturia and enuresis. It is distinguished from the polyuria and polydipsia of

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uncontrolled diabetes mellitus or other forms of solute diuresis by the absence of glucosuria and a relatively normal rate of total urinary solute excretion.

This review will describe the clinical criteria for the diagnosis of DI, the four fundamentally different types of defect that can cause it, the methods for differentiating between them and the safest and most effective way to manage each.

Diagnosis

The symptoms of DI (Table 1) are similar to those in several other disorders caused by fundamentally different abnormalities. Therefore, the diagnosis should be based on the measurement of 24 h volume, osmolarity and glucose collected while the patient is eating and drinking normally and is not taking any medication that can interfere with or cause a water diuresis. In an adult or child over 2 years of age, a volume of more than 40 mL/kg body weight, an osmolarity of less than 300 mosms/L and a negative test for glucose is diagnostic of DI. In infants or children below the age of 2 years, the upper limit of normal for urine volume is slightly higher (Table 1) due to the greater water content of their diet.

Other methods of diagnosis may be required in certain patients or clinical settings. In infants or children who are not toilet trained, daily urine output can be estimated by weighing diapers before and immediately after each change. Alternatively, spontaneous fluid intake can be measured. It is normally about 10–30 mL/kg/day higher than urine output owing to the need to replace insensible as well as urinary losses (Table 1). Diagnosing DI is also problematic if the patient is unconscious or otherwise unable to drink or requires intravenous fluids for other reasons. In that setting, it is often advisable to defer diagnostic tests until the patient is able to eat and drink normally.

Pathophysiology

There are four different types of DI each of which is due to a fundamentally different defect and must be managed differently (Table 2).

The most common type of DI is due to a deficiency of AVP production and secretion caused by an acquired or genetic defect in the neurohypophysis [1]. It is variously referred to as pituitary, neurohypophyseal, hypothalamic, neurogenic, central or cranial DI. It occurs when the amount of AVP secreted at normal basal levels of osmotic stimulation is too low to concentrate the urine. The polyuria that results produces a slight decrease in body water and a commensurate rise in plasma osmolarity/sodium that stimulates thirst and a compensatory increase in water intake (polydipsia) which prevents further decline in body water. As a result, plasma osmolarity/sodium are maintained a level that is only 1–2% above normal and usually within the normal range [3]. However, if water intake is restricted, there is a further decline in body water and a rise in plasma osmolarity/sodium that intensifies the

Table 1
Criteria for diagnosis of DI. All values from 24 h collection. Fluid intake is always higher than urine output due to the need to replace insensible water loss. The difference shown here apply to afebrile subjects at rest in a temperature controlled environment. They may be much larger when physical activity or temperature are increased.

Age years	Symptoms	24 h Urine osmolarity mOsm/L	24 h Urine volume mL/kg	24 h Fluid intake mL/kg	Urine glucose
<2	Heavy wet diapers Urinary frequency Irritability Increased thirst Hypernatremia	<300	>60	>100	Negative
>2	Polyuria, Nocturia Incontinence Enuresis Polydipsia, +/− Thirst	<300	>40	>70	Negative