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A Case of Central Diabetes Insipidus: Evaluation in Pregnancy

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ABSTRACT

A 20 years old woman, admitted in our Centre at the 6th week of pregnancy, was affected by Central Diabetes Insipidus and since the age of 10 years old she assumed desmopressin at a dose of 30 mg/nostril/day. She was primigravida, with normal past medical history. Fasting blood levels were normal; specific gravity of the urine: 1006; no glucosuria or proteinuria was present. Urinary and plasma osmolality were 245 and 287 mOsm/l; water intake about 2700 mL/day; diuresis 2000 mL/day. On the basis of the value of urine output and osmolality the dose of desmopressin was increased at 40 mg/nostril/day. Patient was evaluated every month with fluid balance, urine volume, osmolality, and serum electrolytes. Daily dosage of desmopressin was 40 mg/nostril for all the duration of pregnancy according to a trend of an adequate fluid and electrolytes balance and in absence of symptoms. Mean blood Pressure was 100/60 mmHg; coagulation, liver, renal function were normal. Fetal monitoring with periodic ultrasound detected a normal intrauterine growth. Patient had an uncomplicated labor of a healthy male baby at the 39th week. Because of an insufficient dilatation of the cervical canal caesarian section was chosen. Despite a previous Central Diabetes Insipidus may worsen in a pregnant with impaired reserve of Antidiuretic Hormone because of the changes in osmoregulatory system and increased levels of vasopressinasis in middle and late pregnancy, our patient required a slightly higher dose of desmopressin in the first trimester. Contrary to expectations the need of desmopressin did not increase during the weeks.

Keywords*: *Diabetes Insipidus, Pregnancy, Desmopressin

1. Introduction

Diabetes Insipidus is a rare complication in pregnancy and its incidence in pregnant status is about 1 per 30,000 cases; three different subtypes of Diabetes Insipidus are described: central, nephrogenic and transient. The first one may predate the pregnancy or can be discovered during pregnancy and it's caused by an impaired pituitary release of vasopressin; the second one is related to the resistance of the kidney to circulating vasopressin. Transient Diabetes Insipidus typically occurs in the third trimester or at the end of pregnancy for an increase of levels and activity of enzyme vasopressinase and can be associated with preeclampsia, acute fatty liver and HELLP Syndrome (Hemolytic anemia; Elevated Liver enzymes and Low Platelet count)

We describe a case of a 20 years old woman, followed in our Centre for Diabetes Insipidus, during pregnancy.

2. Case Report

A 20 years old woman was affected by Central Diabetes Insipidus after a trauma of the skull during childhood, and since the age of 10 years old she was in therapy with desmopressin intranasally, at a dose of 30 mg for nostril/day. Past medical history was normal; familial history showed the presence of thyroid nodules, type 2 diabetes mellitus and hypertension. She had menarche at the age of 12 years, with regular menstrual cycles. At time of observation she was primigravida at the 6th week of pregnancy. She felt well, except for a slight breathlessness after moderate efforts. Her height was 153 cm; weight 47 Kg and target gene according to Tanner 159 cm. Blood pressure was 110/70 mmHg; heart rate 88; water intake about 2700 mL/day and diuresis 2000 mL/day.

Fasting blood levels were: hematocrit: 36%, platelets: 363,000, glucose: 90 mg/dL, serum sodium: 143 mmol/L, potassium: 4.02 mmol/L, and chloride: 105 mmol/L. Liver and renal function tests were normal; AST:17 IU/L, ALT: 19 IU/L, total bilirubin: 0.30 mg/dL, serum creatinine: 0.4 mg/dL, BUN: 20 mg/dL total protein: 6.9

g/dL, and Albumin 3.0 g/dL. The specific gravity of the urine was 1006 and no glucosuria or proteinuria was present. Urinary and plasma osmolality were 245 and 287 mOsm/L, respectively.

Pituitary function and thyroid function were normal (GH: 1.0 ng/mL; IGF1: 20 ng/mL; TSH: 2 IU/L; FT3: 2.8 pg/mL; FT4: 1.1 ng/dL;) and a MRI of the sellar region detected a partial empty sella.

She was assuming desmopressin at a dose of 30mg/ nostril every day.

On the basis of the value of urine output and osmolality the dose of desmopressin was increased at 40 mg/nostril/day.

During the course of pregnancy the patient was evaluated every month with fluid balance, urine volume and osmolality, serum electrolytes.

As summarized in **Table 1**, in the course of pregnancy was observed an adequate fluid and electrolytes balance, without evidence of changes in clinical situation during the weeks.

According to the trend showed in **Table 1**, and in absence of symptoms, daily dosage of desmopressin was 40 mg/nostril for the duration of pregnancy.

Patient referred no particular symptoms, except a mild back pain, and physical examination showed slight edema of the legs since the 16th week.

Mean Blood Pressure during the weeks was 100/60 mmHg; coagulation, liver and renal function were normal; mild anemia occurred in the third trimester.

Fetal monitoring with periodic ultrasound detected a normal intrauterine growth.

Patient had an uncomplicated labor at the 39th week. Because of an insufficient dilatation of the cervical canal was chosen cesarian section.

She gave birth to a healthy male baby, with a weight of 2900 g and Apgar index of 8.

3. Discussion

Pregnancy is hemodynamically characterized by a framework of low blood pressure, low peripheral resistance and high flow.

Systemic arterial vasodilatation in early pregnancy is accompanied by a compensatory rise in cardiac output and a decline in Blood Pressure. This relative arterial underfilling in early pregnancy is coupled to stimulation of the renin-angiotensin-aldosterone system and hypotonicity. Arterial underfilling induces the non-osmotic stimulation of arginine vasopressin and up-regulation of aquaporin 2 followed by trafficking of this water channel to the apical membrane of principal cells along the collecting ducts. Changes of osmoregulatory system in pregnancy are also caused by HCG, that plays a role in the reduction of the set point of the osmoregulatory system because induce the reduction at a lower concentration of threshold of vasopressin release and a decrease of threshold of thirst. Perception of thirst occurs at lower serum osmolality and serum sodium, with the effect of decreased plasma sodium concentration and osmolality.

In middle and late pregnancy, there is also a four-fold increase in vasopressinase, a cystine aminopeptidase produced by placental trophoblasts, which enhances the metabolic clearance of vasopressin, oxytocin and other small peptides. Levels of vasopressinase are related to the weight of the palcenta and achieve maximal concentrations at 24th week. Women with impaired reserve of antidiuretic hormone can develop symptoms as polyuria and polydipsia, and also intolerance for oral water intake, nausea, fatigue and weight loss. For these reasons during pregnancy a previous central diabetes insipidus may worsen or may be unmasked.

Nevertheless, Central Diabetes Insipidus does not reduce fertility.

Pregnants, in fact, can have delivery with appropriate clinical observation, monitoring fluid balance, body weight, renal function, and vital signs and fetal status. Initial biochemical evaluation should include a complete blood count, serum electrolytes, plasma and urine osmolality, serum creatinine, bilirubines, total proteins and liver enzymes. It's necessary to have periodic measurements of urine volume of 24 hours, serum osmolality and urine osmolality. Urine volume more than 2.5l, serum osmolality > 295 mOsm/Kg and urine osmolality < 300 mOsm/Kg are indicative of overt and uncontrolled Diabetes Insipidus. An important finding to be taken into account is the sodiemia: in pregnancy sodium values greater than or equal to 140 mEq/L should be considered as hypernatremia.

Is often required an adjustment in the dose of desmopressin during the weeks. As described in literature, patients with a history and partial diabetes insipidus, treated with low doses of desmopressin, can require an increase in dosage since the start of pregnancy. Polyuria and Polydipsia in central DI can be recurrent and can occur from the early weeks of gestation, before the increase of serum vasopressinase. In some pregnancies

Table 1. Mean values of diuresis, urine specific gravity, electrolytes, serum osmolality for trimester.

	1 trimester	2 trimester	3 trimester
diuresis	2500	2600	2600
urine specific gravity	1009	1012	1010
potassium	3, 8	3, 9	4, 1
sodium	138	136	136
serum osmolality	287	289	284

there aren't changes compared to previous situation and it's not necessary to adapt dosage of desmopressin. Our patient, in fact, required a slightly higher dose of desmopressin in the first trimester. Contrary to expectation, the need of desmopressin did not increase during the weeks, allowing an easy management in the administration of the drugs.

The primary aim of the therapy is the control of nicturia, using the lowest dosage possible of desmopressin, followed by a daytime dose for the control of daytime diuresis. It's also important to maintain water intake at 1000 mL for day.

Safety in administration of desmopressin in pregnancy is nowadays testing because of lack of controlled studies regarding pregnant women treated. Available studies agree on the safety of the drugs for maternal and fetal outcome and show an incidence of fetal malformations, Down syndrome, intrauterin growth retardation, low birth weight or neonatal death comparable to uncomplicated pregnancies. Preeclampsia has been documented in few cases and there aren't described severe cases of hypertension of the pregnant. This finding confirms the lack of effect of vasoconstriction of desmopressin. As observed in our case, ossitocino-like effects of this drug, which can lead to preterm delivery, are not reported.

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