

Hyponatraemia during pregnancy

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Abstract

Hyponatraemia during pregnancy is a problem not commonly recognised by physicians. However, it can have serious clinical consequences. Knowledge of the physiology of electrolyte disorders is necessary to distinguish between the various causes of hyponatraemia. Being able to identify the symptoms and signs of hyponatraemia is of vital importance in order to initiate the correct therapy. In this paper we present three patients with hyponatraemia during pregnancy. The various (patho)physiological mechanisms involved in hyponatraemia found in these cases are discussed. Possible iatrogenic mechanisms are outlined. The symptoms and signs of hyponatraemia are mentioned. Finally, different therapies tailored to the various causes are discussed. In conclusion, hyponatraemia during pregnancy is a complex and potentially hazardous disorder that requires optimal and swift cooperation between internist and gynaecologist.

INTRODUCTION

Hyponatraemia is a common disorder in the elderly population. Hyponatraemia in pregnancy is less well known, but can have major consequences for both the mother and child. It is important to anticipate a hyponatraemia, recognise its symptoms, and commence prompt treatment. Understanding the physiology and pathophysiology of salt and water homeostasis are therefore essential. In this article we describe three cases of pregnant women who presented with peripartum hyponatraemia.

CASE REPORTS

Patient 1, a 28-year-old primigravida in labour, was referred to our hospital by the midwife at 42 weeks gestation, due to a prolonged first stage of labour. So far her pregnancy had been uncomplicated. Her blood pressure was 124/70 mmHg. She had no signs of oedema. Labour was augmented with oxytocin. However, because of persistent stagnation at a cervical dilatation of 6 cm a caesarean section was planned. All of a sudden the patient started having seizures, without having had any prior signs or symptoms of eclampsia. The patient was stabilised and treated with intravenous magnesium sulphate. An emergency caesarean section was performed., which was uncomplicated. A live healthy baby boy was extracted. During the operation the patient was found to have a severe hyponatraemia with a plasma sodium concentration of 122 mmol/l. This was a possible cause of the convulsions. A CT-scan of the brain excluded intracerebral pathology. Immediately after the operation, the

patient was treated with a fluid restriction, after which the serum-sodium level normalised. Retrospectively it was found that patient had been dinking more than 4 litres of water within a short period during the first stage of labour. Postoperatively she developed a pneumonia, most likely secondary to aspiration during her convulsions. She was treated with antibiotics, after which she improved. On discharge her plasma sodium concentration was 139 mmol/l.

Patient 2, a 40-year-old primigravida was admitted at 37 weeks amenorrhoea, because of severe headache, nausea and hypertension. Her blood pressure was 155/95 mmHg. She had signs of hyperreflexia without clonus. The laboratory results revealed a proteinuria of 4.0 gram per 24 hrs, and a hyponatraemia of 128 mmol/l. All other laboratory results were normal. She was treated with methyldopa and magnesium sulphate. Because a SIADH was suspected, she was given a fluid restriction, without any further diagnostic testing. One day after admission the plasma sodium concentration decreased to 125 mmol/l and the patient complained of progressive headache. Because of the severity of the headache, the rapid decrease in plasma-sodium and the necessity to induce labour, she was treated with hypertonic NaCl 5.85%. The plasma-sodium concentration increased to 128 mmol/l in a few hours. The headaches subsided. Labour was induced using prostaglandins. The hypertonic NaCl administration was ceased after a plasma sodium concentration of 133 mmol/l was reached. Intravenous administration of oxytocin was commenced. She

then vaginally delivered a healthy son. Without further treatment the plasma sodium concentration increased in a few days to 137 mmol/l.

Patient 3, a 38-year-old primigravida, was referred to us at 37 weeks amenorrhoea, because of diastolic hypertension (120/90 mmHg) and a proteinuria of 1.9 gram per 24 hours. She complained of nausea and vomiting. She had slight peripheral oedema. Her laboratory results were consistent with an imminent HELLP-syndrome (Haemolysis, Elevated Liver enzymes, Low platelets). The plasma sodium concentration was 134 mmol/l. Because of an increase in blood pressure (185/110 mmHg) and hyperreflexia, intravenous ketanserin and magnesium sulphate was administered. The day after admission, labour was induced with prostaglandins. Her plasma sodium concentration was 131 mmol/l. It decreased to 129 mmol/l after administering oxytocin. This value was accepted. The labour progressed well, and several hours after having started the oxytocin, the patient delivered a healthy son. Because of a poorly contracted uterus the intravenous oxytocin was continued. The plasma sodium concentration then decreased to 123 mmol/l. She had no complaints. After cessation of the oxytocin, the plasma sodium concentration had increased to 133 mmol/l in one day. On discharge it was 137 mmol/l.

PHYSIOLOGIC CHANGES IN SALT AND WATER HOMEOSTASIS IN PREGNANCY

During pregnancy, physiologic changes occur in volume- and osmoregulation that effect plasma osmolality and sodium concentration. In a normal pregnancy, the average plasma-osmolality is decreased by 5-10 mmol, and the sodium concentration is decreased by 5 mmol/l. ¹This drop in plasma osmolality is caused by a 'reset osmostat' phenomenon: the osmotic threshold above which ADH-release and a thirst stimulus occur is decreased to a lower steady state value. The mechanism that causes the reset-osmostat phenomenon is unknown, but from experimental work, it is clear that presence of the foeto-placental unit is required; a simulated pregnancy in the absence of this foeto-placental unit does not cause the reset-osmostat phenomenon. ²

Pregnancy is also characterized by an accumulation of significant amounts of sodium (approximately 900 mmol) and fluid (8-10 litres). Sodium and fluid retention is needed to accommodate the expanding maternal extracellular compartment and the fluid demands of the growing foetus. The accumulation of sodium occurs despite an increase in

GFR (increased with 50% by the end of the first trimester) that causes an increase in filtered sodium of 20000 to 30000 mmol / day. ³ Consequently, this additional 10000 mmol of sodium reaches the tubules and must be absorbed to prevent sodium loss. Activation of the renin angiotensin system -that leads to an increased concentration of aldosterone- plays an important role in sodium retention despite the increased GFR. Nevertheless, pregnant women adapt less readily to low-salt than to high-salt diets.

Another important observation that influences sodium- and fluid balance is a physiological decrease in blood pressure that occurs as early as in the first 6 weeks of pregnancy, and is caused by vasodilatation, resulting in a diminished effective circulating volume, or relative underfilling. These changes trigger non-osmotic AVP release and stimulate both the sympathetic nervous system and renin angiotensin system to ensure adequate organ perfusion. Some authors have suggested that these non-osmotic factors contribute to lowering of plasma osmolality and sodium concentration. ⁴

Furthermore, there are several hormones that are potentially natriuretic during pregnancy, such as progesterone and nitric oxide. Estrogen and deoxycorticosterone are potentially antinatriuretic. ^{5,6,7} The exact contribution of the several above mentioned mechanisms on changes in salt homeostasis during pregnancy, remain unclear.

PATHOPHYSIOLOGICAL MECHANISMS THAT MAY LEAD TO HYPONATRAEMIA DURING PREGNANCY

SIADH during pregnancy. SIADH (Syndrome of inappropriate secretion of antidiuretic hormone) is characterized by ADH release without an appropriate hypovolemic or hyperosmolar trigger. This results in water retention and expansion of plasma volume that, by activating volumereceptors, stimulates natriuresis by the kidney. Thus, SIADH causes hyponatraemia by both water retention and sodium loss. Usually, a steady state is reached rapidly. Aggravated hyponatraemia will only occur when there is either increased ADH-release or increased water intake. SIADH is mostly seen related to neurological disorders, medication (especially psychiatric medication) and pulmonary disease. ⁸ However, most of these causes are not very likely to be found during pregnancy.

More importantly, pain, nausea and fear (frequently encountered during pregnancy) can cause increased ADH-production. ⁸

In Patient 1, who was diagnosed with pneumonia postoperatively, a pre-existing respiratory tract infection with concurrent SIADH was considered as a cause of her hyponatraemia and seizures. However, her history and physical examination had not been suggestive of a respiratory tract infection. Excessive water-intake and ADH-secretion due to pain might have been important causative factors, in her case.

Polydipsia. Polydipsia signifies an excessive intake of water. When water intake exceeds the excretion capacity of the kidney, a dilutional hyponatraemia will ensue.

Hyponatraemia caused by excessive water intake during sport activities has been described previously.⁹ Excessive water intake during pregnancy can be due to stress or encouragement by others to drink water during labour. Furthermore, drugs such as promethazine, used frequently for sedation durante partum, can cause a dry mouth leading to increased water intake. Under physiologic circumstances, primary polydipsia does not cause hyponatraemia, because the kidney is capable of excreting the excess amount of fluid. However, in case of an intake of more than 10 litres of water per day, the diluting capacity of the kidney will be exceeded, and hyponatraemia will ensue. When polydipsia and disturbed water excretion (ADH release) co-exist, a hyponatraemia will follow after less water intake.⁸ Some cases of hyponatraemia during pregnancy due to primary polydipsia have been described previously¹⁰. Laboratory findings that are characteristic of polydipsia are: low plasma sodium osmolality, in combination with maximally diluted urine (table 1). Patient 1, was found to have had excessive water-intake, and which could indeed explain the hyponatraemia. Because her urine sodium and urine osmolality were relatively high, other factors may have contributed, such as increased ADH-secretion and oxytocin, as explained in the next paragraph.

Figure 1

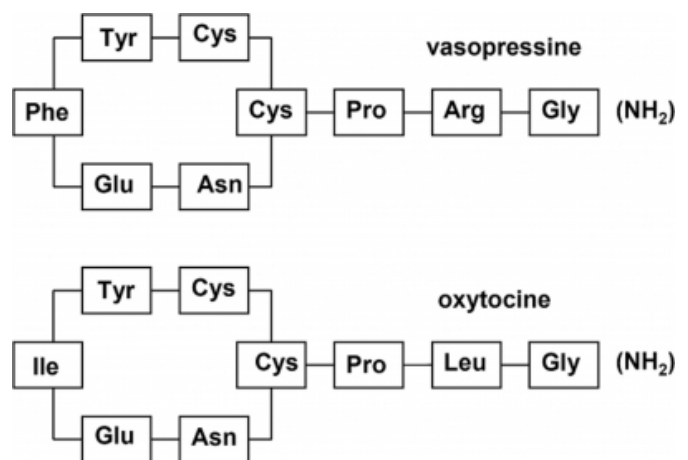
Table 1. Plasma- and urine sodium concentrations and osmol values during a normal pregnancy, patient 1, 2, 3 and under various pathophysiological conditions.

	Normal pregnancy	Patient 1	Patient 2	Patient 3 (SI)ADH	Oxytocin	Preeclampsia	Polydipsia
P-Na (mmol/l)	>130	122	125	123	<135	<135	<135
P-Osm (mOsm/kg)	> 270	257	259	268	<270	<270	<270
U-Na (mmol/l)	Variable	37	105	7	>40	> 40	10 – 50
U-Osm (mOsm/kg)	Variable	126	483	419	>300	> 300	<100

Oxytocin. Oxytocin is produced by the posterior pituitary gland. It causes uterine contraction. Its molecular structure resembles ADH (see fig. 1), and similar to ADH has an effect on water reabsorption in the kidney. Synthetic oxytocin, that can be administered to stimulate uterine contractions during labour, has similar characteristics. Due to its effects on water reabsorption in the kidney, oxytocin can play a role in the development of hyponatraemia. Importantly, oxytocin is administered intravenously, dissolved in iv-fluids, which is likely to worsen hyponatraemia.¹¹ The type and amount of iv-fluid is important. Women who are treated with oxytocin dissolved in NaCl 0,9 % or Ringers Lactate, develop hyponatraemia less frequently than those who receive oxytocin in Glucose 5 %.^{12,13,14} The hyponatraemia in Patient 3 seems to be explained by use of oxytocin. Additionally, her low urine sodium concentration may have been due to RAAS-activation, due to a decrease in effective circulating volume.

Figure 2

Figure 1. Amino-acid structure of Vasopressin and Oxytocin. The structural resemblance is clear.



Preeclampsia. Preeclampsia is characterized by

hypertension, edema and proteiuria during pregnancy. Although water and electrolytes are abundant, they are mainly localized in the interstitium, and there is actually a decreased effective circulating volume. The body responds as it would during physiologic blood pressure decrease, with stimulation of baroreceptors, hence release of ADH, causing water reabsorption in the distal tubulus. This sequence results in hyponatraemia. The hyponatraemia in Patient 2 could thus be explained. In the literature, nine cases of hyponatraemia during preeclampsia have been described.¹⁵

Sodium depletion. Hyponatraemia caused by sodium depletion can be the result of salt loosing such as is the case in diarrhoea, vomiting, excessive sweating, or renal salt loosing, for example due to diuretics or salt-wasting nephropathy. If the fluid demand is met by water intake only, hyponatraemia will result. Absolute lack of salt in pregnancy has rarely been described in the literature.

SYMPTOMS

Symptoms of hyponatraemia are mostly caused by water shifts due to an altered plasma osmolality. Symptoms may vary from headache, nausea, dizziness, general discomfort, drowsiness, coma and seizures. Hyponatraemia can be fatal.⁹ During delivery, it can be difficult to relate these symptoms to hyponatraemia, especially in patients with preeclampsia. Thus, in Patient 2 it was unclear whether her symptoms were caused by hyponatraemia or preeclampsia. Importantly, osmotic exchanges take place in the placenta, and thus the child may display hyponatraemia as well, both in utero as post-partum¹⁵.

TREATMENT

Hyponatraemia caused by SIADH or oxytocin is treated by fluid restriction and / or cessation of oxytocin infusion. If necessary, infusion of hypertonic saline can be administered, in combination with a loop-diuretic.⁸ In case of polydipsia, a fluid restriction should suffice. Treatment of hyponatraemia due to preeclampsia needs to be tailored to the individual case, in which both risks and benefits of fluid restriction and iv-fluid therapy need to be considered. Absolute lack of salt is treated with sodium supplementation and treatment of the underlying cause. Detailed description of the speed of correction and frequency of laboratory measurements can be found elsewhere and are beyond the scope of this text.

CONCLUSION

Hyponatraemia during pregnancy is a complex problem in which many factors may play a role. As hyponatraemia is

partly physiological, it may be difficult to distinguish pathological hyponatraemia from the physiological state. Measurement of plasma sodium concentration, plasma osmolality, urine sodium concentration and urine osmolality are necessary to distinguish between various pathophysiological causes. Treatment depends on the underlying cause. When iv-fluid therapy is necessary, a NaCl 0.9% solution is preferred. In case of serious hyponatraemia, hypertonic NaCl-solution may be administered. Hyponatraemia during pregnancy is complex and potentially hazardous; it requires excellent cooperation between internist and gynaecologist.

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