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Case Report Open Access

Preeclampsia as a Rare Cause of Hyponatremia

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Abstract

Background: Severe hyponatremia is a very rare, mortal complication of preeclampsia and has been described in fourteen cases.

Case presentation: A previously well, 29-year-old woman, gravida 2, para 1, was admitted at 34 weeks' gestation with premature contractions. Her blood pressure was 150/90 mm Hg in both arms and she had mild proteinuria. On the third day of hospitalisation, sodium level was 120 mEq/L. On the same day, patient started to have headache. Cesarean delivery was performed because of prior cesarean section. On the first postoperative day, serum sodium level fell to 115 mEq/L. Patient had a generalised seizure After 24 hours of oral fluid restriction and 50 ml/hour isotonic sodium chloride administration, serum sodium increased to 127 mmol/L and by 48 hours, it returned to normal.

Conclusion: The prediction, prevention and management of hyponatremia in preeclamptic patients require attention since this condition may predispose to convulsions, maternal mortality and fetal damage.

Keywords: Hyponatremia; Severe; Preeclampsia; Seizure; Pregnancy

Background

Preeclampsia is a multisystem disorder that complicates 3-8% of pregnancies and accounting 18% of maternal deaths [1,2]. Classically, it is defined as hypertension and proteinuria with onset following the 20th week of pregnancy and associated with symptoms and signs such as edema, visual disturbances, headache and epigastric pain. In preeclamptic cases, no changes in serum sodium, potassium and calcium were found when compared with uncomplicated pregnancies. Total serum magnesium level was found to be significantly lower [3,4]. As a rare complication of preeclampsia, hyponatremia has been described in fourteen cases. The prediction, prevention and management of hyponatremia in these cases requires attention since this condition may predispose to convulsions, maternal mortality and fetal damage.

Our case is a preeclamptic patient, presented with severe hyponatremia and convulsion. In this report, we discussed preeclampsia as a rare cause of severe hyponatremia that should be an indication for delivery. Also, the risk factors of preeclamptic hyponatremia were investigated, using a multifactorial approach for a further preventive strategy. Preeclampsia in twin pregnancies may be an independent risk factor for severe hyponatremia.

Case Presentation

A 29-year-old woman, gravida 2, para 1, was admitted at 34 weeks' gestation with premature contractions. She had no significant medical or family history and the pregnancy to date had been uneventful with maximum blood pressures of 120/80 mm Hg. Her blood pressure was 150/90 mm Hg in both arms and she had mild proteinuria (2+ on urine dipstick). Neither headache nor visual changes was present in our patient. The haematological and biochemical parameters relevant to preeclampsia was unremarkable (Table 1). On digital examination, 2 cm cervical dilation and 30% cervical effacement was detected. Amniotic fluid index was 50 mm. The growth of fetus was <10th percentile for gestational age with normal umbilical artery and middle cerebral artery Doppler. On the third day of hospitalisation, sodium level was 120 mEq/L, the urinary sodium was <10 mEq/L, the urine osmolality was 425 mosmol/kg and the serum osmolality was 256 mosmol/kg, reflecting hypervolemic hyponatremia. Restricted volume of isotonic sodium chloride solution, and magnesium sulfate administration was started. On the same day, patient started to have headache. A diagnosis of severe preeclampsia was made and cesarean delivery was performed because of prior cesarean section. Female infant, weight 1690 gr was delivered with Apgar scores 7-9 and normal cord blood gase values. On the first postoperative day, serum sodium level fell to 115 mEq/L (Table 1), patient had a generalised seizure despite continuing magnesium sulphate prophylaxis. İmmediately after the acute convulsive period, airway potency was established, oxygen administration via a face mask at 8-10 L/min was maintained and 10 mg diazepam was given by intramuscular injection and the patient regained consciousness. After 24 hours of oral fluid restriction and 50 ml/hour isotonic sodium chloride administration, serum sodium increased to 127 mmol/L and by 48 hours, it returned to normal. On discharge (6 days later), her sodium level was 138 mEq/L with normal blood pressure and normal renal function and without proteinuria.

Baby had mild hyponatremia with serum sodium level of 127 mEq/L. Other biochemical parameters were unremarkable.

Blood pressure, mmHg	150/90	140/90	150/100	140/90	140/90	120/80	120/70
Edema	Mild	Marked	Marked	Marked	Mild	Mild	Mild
Na, mmol/L (130-150)	134	129	120	115	127	132	134
K, mmol/L (3-5)	4.6	3.9	4	4	3.9	4.1	4
Urea, mg/dL (10-50)	27.1	27.6	28.4	29	28.8	29.1	27.3
Creatinine, mg/dL (0.6-1.1)	1.04	0.8	0.8	1.06	0.9	0.9	0.9
ASTa, U/L (0-31)	23	28	55	63	36	29	27
ALTb , U/L (0-31)	6	27	33	58	30	18	15
Albumine, g/dL (3.5-5.2)	2.7	2.6	2.4	2.4	2.8	2.8	3.2
Urate, mg/dL (2.3-6.1)	7.04	6.4	6.9	7.1	6.2	5.5	5.6
Serum osmolality (mOsm/kg)	284	274	256	246	270	280	284
Urinary osmolality (mOsm/kg)	810	670	425	418	634	680	815

[a]: Aspartate Aminotransferase; [b]: Alanine Aminotransferase; C/S: cesarean section

Table 1: Laboratory results, edema status and blood pressure during admission.

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Hyponatremia resolved spontaneously within 48 hours in the neonatal intensive care unit.

Discussion

The plasma osmolality in normal pregnancy falls to a new set point of about 270 mosmol/kg, with a fall in the serum sodium concentration of about 5 meq/L [5]. The release of human chorionic gonadotropin during pregnancy may be responsible for mild hyponatremia [5]. Oxytocin is natriuretic, partly by stimulating atrial natriuretic peptide secretion [6]. Additionally, within the brain, oxytocin is proposed to suppress salt appetite [7]. A peptide hormone, relaxin, also increases fluid intake and vasopressin secretion in pregnancy and hence of the hyponatremic hypervolemia of pregnancy [8]. The physiological responses to changes in osmolality above or below the new set point are intact.

Hyponatraemia may be asymptomatic if it is mild to moderate (>125 mmol/L) and chronic (>48 hours) [9]. Severe hyponatraemia is defined as sodium <125 mmol/L [10]. Although mild hyponatremia in pregnants may be ignored, it is very important to remember that when serum sodium drops below 120 mmol/L within 24 hours, death can occur up to 50% of individuals.

The initial approach to the hyponatremic patient is to measure the serum osmolality to determine whether the hyponatremia represents a true hypo-osmolar state [11]. In 14 published cases, serum osmolality was found to be low with a mean level of 254.5 mosmol/kg (range: 236-266 mosmol/kg) (Figure 1). In a case, presented by Goodlin, serum osmolality level was missing [18].

More than one classification system have been used for the etiology of hyponatremia with a low serum osmolality. Hyponatremia in preeclampsia cases are discussed by using one of them, stratifies patients according to volume status (hypovolemia, normovolemia or hypervolemia). Hyponatremia with hypovolemia can occur due to gastrointestinal losses (eg, vomiting or diarrhea) or renal losses (eg, mineralocorticoid deficiency, sodium- losing renal disorders and diuretic excess). In all of the cases discussed here, hyponatremia was exist with normovolemia or hypervolemia. So, our discussion will focus on causes of hyponatremia with normovolemia or hypervolemia

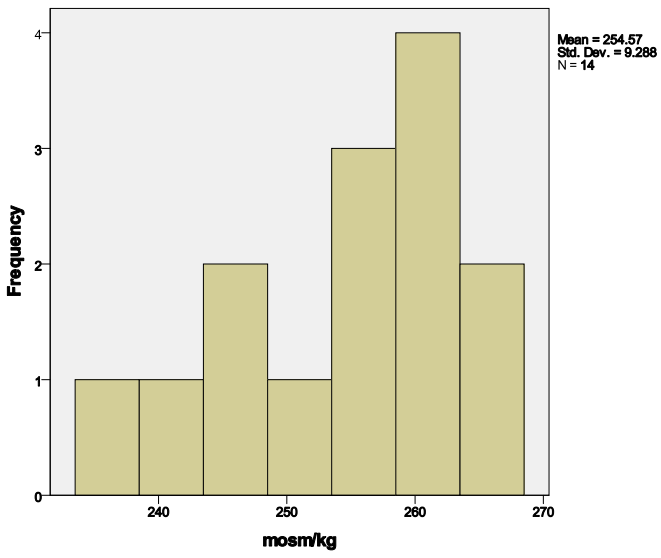

Figure 1: Serum osmolality levels of all patients with preeclamptic hyponatremia (except Goodlin et al.).

Normovolemia	Hypervolemia
SIADH: -Sutton et al. [12] - Hayslett et al. [13] -Ravid et al. [14] -Ray et al. [15] -Wilson and Shutt [16] -Sandhu et al. [17]	Heart failure
Primary polydipsia	Nephrotic syndrome
Low dietary solute intake	Liver cirrhosis
Glucucocorticoid deficiency	Inappropriate administration of intravenous fluids
Hypothyroidism	Preeclampsia: -Goodlin and Mostello [18] -Hayslett et al. (case 1 and 3)* [13] -Magriples et al. (case 1* and 2) [19] -Burrell and de Swiet [20] -Linton and Gale [21] -Jhaveri et al. [22] -Our case, 2013

*: presence of preeclampsia-induced nephrotic syndrome

Table 2. Causes of hyponatremia with normo- or hypervolemia.

(Table 2). Normovolemia is most often associated with the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) but can also be seen with primary polydipsia, low dietary solute intake, glucucocorticoid deficiency and hypothyroidism [23]. Hyponatremia in the presence of edema indicates increased total body sodium and water. This increase in total body water is greater than the total body sodium level, resulting in edema. The main causes of hypervolemic hyponatremia are heart failure, nephrotic syndrome, liver cirrhosis and inappropriate administration of intravenous fluids [2]. In our patient, renal and non-renal causes were excluded with no medical history of cardiac, thyroid, liver or adrenal disease and having new-onset of proteinuria in the 34th week of pregnancy with hypertension. There was no evidence of diarrhoea and vomiting or administration of any drugs that can cause hyponatremia. The urine/plasma osmolality ratio was >2, so SIADH was excluded. Preeclampsia was thought to be the main cause of hyponatremia. In the four previous cases , the postulated mechanism was inappropriate secretion of antidiuretic hormone (Table 3). There are two theories for the mechanism of SIADH in the setting of preeclampsia:

1. Preeclampsia causes a decrease in effective circulating volume, resulting a non-osmotic release of ADH.
2. A defective placenta in patients with preeclampsia can not produce sufficient vasopressinase, an enzyme that rapidly inactivates ADH [23].

Six in 15 cases, preeclampsia-induced nephrotic syndrome was thought to be the cause of hyponatremia (Table 3). It is suggested that preeclampsia is one of the most common cause of nephrotic syndrome that occurs de novo during pregnancy [24]. However, the distinction between renal disease and preeclampsia may be difficult. In patients without underlying renal disease, the clear documentation of new-onset proteinuria after 20 weeks of gestation, when accompanied by new-onset hypertension, strongly suggest preeclampsia. Still, this distinction can only be made in retrospect for most of cases, as clinical signs of preeclampsia generally resolve within 12 weeks after delivery, while proteinuria due to underlying renal disease does not [25]. In 4 of 6 cases, proteinuria was resolved within 4 weeks. Magriples and Wilson did not reported this info in their cases [16,19].

In all other cases, preeclampsia was found to be an only cause of hyponatremia without SIADH or nephrotic syndrome.

Severe hyponatremia should be kept in mind as a serious complication of preeclampsia, even in its mild stage, while 8 of

Authors, year	Age	Parity	Gestational age at delivery (weeks)	Severity of preeclampsia	The cause of hyponatremia	Indication for delivery
Goodlin and Mostello [18]	28	1	28	Severe	PE	HELLP syndrome
Sutton et al. [12]	41	3	37	Mild	PE (SIADH)	Term
Hayslett et al., -1 [13]	35	0	33	Severe	PE, NS	Fetal distress
-2	41	0	37	Mild	PE, NS	Term+ Oligohydramnios
-3	35	0	35	Mild	PE, NS	Hyponatremia+ worsening blood pressure
Magriples et al., -1 [19]	30	1	33	Mild	PE, NS	Hyponatremia
-2	30	0	30	Mild	PE	Hyponatremia
Burrell and de Swiet [20]	31	0	33	Severe	PE	Hyponatremia+ worsening preeclampsia+ fetal growth restriction
Ravid et al. [14]	33	0	38	Mild	PE (SIADH)	Term
Ray et al. [15]	38	0	37	Mild	PE	Term+ non-reassuring cardiotocography
Wilson and Shutt [16]	32	0	34	Severe	PE (SIADH), NS	Worsening preeclampsia
Linton and Gale [21]	33	0	37	Mild	PE	Term
Jhaveri et al. [22]	35	0	34	Severe	PE	Hyponatremia
Sandhu et al. [17]	30	0	32	Severe	PE (SIADH), NS	Hyponatremia
Our case, 2013	29	1	34	Severe	PE	Hyponatremia

Table 3: Preeclamptic hyponatremia cases.

Blood pressure of 160 mm Hg systolic or higher, or 110 mm Hg diastolic or higher on two occasions at least 6 hours apart while the patient is on bed rest
Proteinuria of 5 g or higher in a 24-hour urine specimen, or 3+ or greater in two random urine samples collected at least 4 hours apart
Oliguria of less than 500 ml in 24 hours
Cerebral or visual disturbances
Pulmonary edema or cyanosis
Epigastric or right upper-quadrant pain
Impaired liver function
Fetal growth restriction
Thrombocytopenia

Table 4: Diagnostic criteria for severe preeclampsia defined by ACOG, 2002.

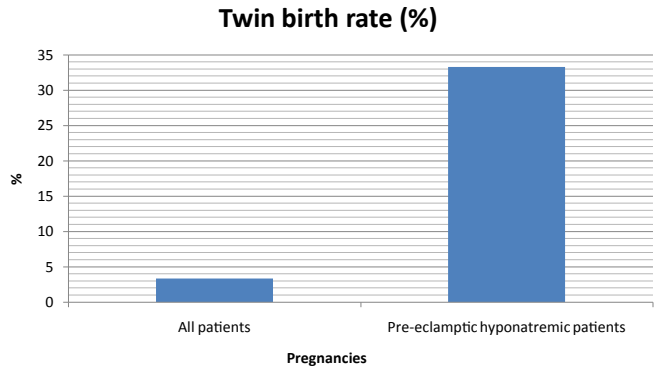

Figure 2: Twin birth rate among all patients and preeclamptic hyponatremic patients.

15 patients had mild preeclampsia (Table 3). Hyponatremia can be regarded as a criteria for severe preeclampsia. In this manner, hyponatraemia may be an indication for delivery to avoid potentially life-threatening clinical events, that can occur suddenly. Our patient had generalised seizure on the first postoperative day with a blood pressure level of 140/90 mmHg and serum sodium level of 115 mmol/L, suggesting hyponatremia predispose to seizure.

Preeclampsia is an important cause of maternal and fetal morbidity and mortality worldwide, characterized by hypertension and excess protein excretion in the urine. The only effective treatment for preeclampsia is delivery of the fetus and placenta. However, observation is an option to reduce the morbidity and mortality of preterm birth for mild preeclampsia. Preeclampsia is considered severe if one or more of the criteria defined by American Congress of Obstetricians and Gynecologists (ACOG) is present (Table 4) [2]. It is generally recommended that patients with severe preeclampsia deliver once they reach 32-34 0/7 weeks of gestation. Expectant management of severe preeclampsia at 24-34 weeks, should be undertaken only in tertiary care centers. The presence of one of the signs indicates the need for immediate delivery: uncontrolled severe hypertension, eclampsia, acute pulmonary edema, abruptio placentae, subcapsular hepatic hematoma, or thrombocytopenia <50,000/mm$^{3.}$ In the presence of any of the following criteria, delivery after corticosteroid therapy is recommended: persistent epigastric pain, signs of imminent eclampsia (headaches or persistent visual disorders), de novo creatinine >120 µmol/L, oliguria below 20 mL/hour, progressive HELLP syndrome, prolonged or severe variable decelerations with short-term variability less than 3 milliseconds [26].

As discussed above, in preeclamptic patients, the criteria for deliver were based on two factors, 'gestational age at diagnosis and severity of preeclampsia'. 10 of 15 cases were delivered before 37 weeks of gestation. All of preeclamptic hyponatremia cases were presented in Table 3 with their gestational age at delivery and indication for delivery.

It is notable that twin pregnancies comprised more than 30 percent of preeclamptic, hyponatremic patients (5/15) while the reported twin birth rate in the USA in 2009 was 33.2 per 1000 total births (Figure 2) [27]. Parity was not associated with hyponatremia in preeclamptic patients while 11 of 15 (73.3%) patients were nulliparous. A similar rate of nulliparity in preeclamptic patients was found in the literature (71.2%) [28].

Review of the present and previous cases has shown that preeclampsia can cause severe hyponatraemia alone. The risk is higher among twin pregnancies, in particular. Hyponatremia may

be though out as a diagnostic criteria for severe preeclampsia. These patients should be managed as severe preeclampsia to prevent severe complications.

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