Anemia treatment with darbepoetin alpha in pregnant female with chronic renal failure: report of two cases

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Abstract

Pregnancy is a rare finding in females with CRF. It is well known that in these cases pregnancy worsens the renal function and accelerates the beginning of dialysis therapy. Pregnancies in uremic females are complicated by a worsening of anemia as well as hypertension, fluid imbalance, electrolyte difficulties, malnutrition, polyhydramnios and preterm labor or sudden intrauterine death. The use of erythropoiesis stimulating agents (ESA) allows a better hematocrit control. Data concerning anemia treatment in pregnants with CRF and data regarding the use of ESA in these patients is scarce. We report two cases of anemia treatment with darbepoetin alpha in pregnant women with CRF in predialysis period and during the hemodialysis therapy. Both patients during the darbepoetin treatment did not require any blood transfusions and at 32nd and 37th weeks of pregnancy delivered healthy infants. The high darbepoetin doses did not cause any side effects, were well tolerated and safe for both gravida and fetus. The effective anemia treatment in pregnants with CRF improves the prognosis for a successful pregnancy.

Key words: pregnancy, anemia, chronic renal failure, darbepoetin alpha, hemodialysis.

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Introduction

Pregnancies in uremic females are complicated by a worsening of anemia as well as hypertension, fluid imbalance, electrolyte difficulties, malnutrition, polyhydramnios and preterm labor or sudden intrauterine death. The principal problem is chronic anemia. Anemia in pregnant women results from iron defficiency and from hypervolaemia. The iron requirement during pregnancy as well as its absorption from the digestive tract increases systematically, especially in the 3rd trimester [1]. Anemia treatment in a pregnant is based mostly on iron supplementation. In a pregnant with renal failure, the factors that intesify the anemia are inadequate erythropoiesis, folic acid deficiency, hyperparathyroidism and concomitant inflammation. In a pregnant without CRF, the EPO concentration is normal, and it increases systematically during the pregnancy [2]. It has been observed that in dialyzed patients and those treated with EPO, pregnancy causes a considerable increase in the EPO requirement [3]. Data concerning anemia treatment in pregnant women with renal failure and data regarding the use of erythropoiesis stimulating agents (ESA) in these pts is scarce. We report two cases of anemia treatment with darbepoetin alpha in pregnant women with chronic renal failure (CRF). In the first case, treatment with darbepoetin was started during the predialytic period; in the second case – at the beginning of HD treatment.

Case Reports

Patient 1. A 33-year-old female was admitted to the renal clinic in the 16th week of her pregnancy due to symptoms of weakness, dizziness and arterial hypertension. Laboratory data showed haemoglobin 7.73 g/dl, RBC 2.53 T/l, WBC 5.9 G/l with a normal differential count and platelets 222000/mm^3. Serum creatinine was 2.85 mg/dl, blood urea 91.4 mg/dl, total protein 6.05 g/dl and the uric acid – 7.8 mg/dl. The iron levels were low during the pregnancy (40-48 μg/dl); TIBC was 280-300 μg/dl;

TSAT – 14-16%. Antinuclear antibodies (ANAs) and antineutrophilic cytoplasmic antibodies (p/cANCA) were negative. Haematuria (5-8 RBCs) and proteinuria were observed. Urine protein excretion was 2.5-3.0 g/24 h. Her blood pressure was 150/90 mmHg. An ultrasonography of the maternal kidney showed a decrease in kidney dimension to 8 cm. The etiology of CRF was unknown. The patient had regular treatment with methyldopa 400 mg/day and iron per os. An injection of darbepoetin alpha 10 μg once a week subcutaneously was initiated in the 22nd week of the pregnancy and continued throughout her pregnancy. After 5 weeks of treatment, the Hb concentration was 8.86 g/dl and serum creatinine elevated to 3.3 mg/dl. The blood pressure remained on the level of 140/80 mmHg. After another 5 weeks of darbepoetin treatment in unchanged dose, the Hb concentration was 7.7 g/dl and the anemia was well tolerated. The patient did not require any blood transfusion. Ultrasound examinations of the fetus in the 16th, 20th, 27th and 35th weeks of gestation revealed normal intrauterine development. At the 37th week of gestation the patent delivered a 2010-gm healthy infant by spontaneous labour with an Apgar score of 10. The post-partum serum creatinine increased to 5.8 and 6.2 mg/dl, blood urea to 160 mg/dl. As the pregnancy progressed, her requirement for antihypertensives increased. Post partum, her blood pressure was 180/110, and amlodipine 10 mg/day and perindopril 4 mg/day were added. Metabolic acidosis and hypervolaemia were found, and peritoneal dialysis (CAPD) was started. During the two-month period a slow increase in Hb concentration up to 12 g/dl was observed.

Patient 2: A 31-year-old female undergoing haemodialysis (HD), with a 15-year history of IDDM complicated by hypertension and diabetic nephropathy. The pre-pregnancy serum creatinine levels ranged from 2.0 to 3.0 mg/dl. She began HD therapy in the 20th week of gestation when the serum creatinine was 3.15 mg/dl and BUN was 56.0 mg/dl. From the first HD session, a darbepoetin alpha was administrated intravenously once a week. The initial dose was 0.48 μg/kg b.m./week (40 μg), and it increased during the pregnancy to 1.15 μg/kg b.m./week (100 μg). The serum albumin levels decreased, and the patient required several albumin transfusions during the dialysis sessions. The patient received iron, vitamin C, D, folic acid, calcium and zinc during the pregnancy. She was dialyzed with a biocompatible polysulphone high-flux membrane (1.3 m^2) using a bicarbonate bath. The HD dose was increased from 12 to 21 hrs, and the frequency increased from 4 to 6 times per week. Her blood pressure was not stable, and she required changes in her antihypertensive regimen. The Hb level increased from 9.44 to 11.4 g/dl. The patient did not require any blood transfusions during the dialysis treatment. At the 32nd week of gestation the patient delivered a 1730-gm female infant by cesarean section. The Apgar score was 9 and 10 at the 1st and 5th minutes, respectively. The postoperative course was benign, and both mother and baby are currently doing well. The patient continues the dialysis treatment and she is being prepared for kidney and pancreas transplantation.

Discussion

Anemia treatment in pregnant women with renal failure is a matter of interest to researchers. Positive results of anemia treatment with rHuEPO during pregnancy were described in a number of publications [4,5]. Treatment with EPO in pregnants after renal transplantation was equally successful [6,7]. The aim of EPO treatment is to obtain a Hb value on the level of healthy pregnant women (11 to 12 g/dl) [8]. In a number of publications, a relevant increase of gravida's blood cell count and an absence of fetus complications, including malformations that could be possibly related to the treatment, were pointed out [9]. Erythropoietin does not penetrate from the mother's blood into the fetal circulation, which guarantees safety for the fetus. EPO treatment in a pregnant with CRF is a much better alternative than blood transfusion. 26% of pregnants require blood transfusions, irrespective of rHuEPO treatment [10]. In the cases described, there was no need for blood transfusion during the darbepoetin alpha treatment, even in a patient in which the expected Hb value increase during the predialytic period was not obtained. In this case the increase in Hb value was obtained after the labour. Hyporesponsiveness to EPO in pregnants results from hypervolaemia and an apparent decrease in Hb value. Also, in concomitant CRF, the EPO synthesis decreases, which gives reason for its supplementation in pregnant women. Hyporesponsiveness to treatment increases during pregnancy. Diabetic pregnants treated with hemodialysis required a gradual increase of darbepoetin doses, up to 100 μg/week. ESA treatment in pregnants require iron supplementation from the beginning of the pregnancy, preferably intravenously [4]. Darbepoetin alpha stimulates erytropoiesis the same way as rHuEPO. Due to the 3 times longer half-time period and the greater biological activity, compared to rHuEPO, the darbepoetin maintains a constant Hb concentration despite the doses being administrated in longer intervals. This drug may be administrated intravenously as well as subcutaneously, which proves its value and usefulness during the predialytic period as well as during HD-therapy. The use of darbepoetin alpha in anemia treatment in patients with CRF is effective and well tolerated [11]. The described cases prove that the drug is well tolerated and safe for both gravida and fetus. To date, no red cell aplasia (PRCA) has been described during the darbepoetin treatment [11].

Conclusions

Darbepoetin alfa appears to be a safe and effective drug correcting anemia in pregnant females with chronic renal failure. These cases indicate hyporesponsiveness to darbepoetin alpha in uremic females, and the need for using much larger doses than in dialysis patients. The high drug doses did not cause any side effects in either mother or her infant. It demonstrates that anemia treatment with darbepoetin improves the prognosis for a successful pregnancy.

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