

Darbepoetin alfa for treatment of anaemia in a case of chronic renal failure during pregnancy - case report

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Summary

Oral haematinics are frequently, if not ubiquitously, used to supplement dietary iron in pregnancy. A 21 years-old patient attended the antenatal clinic because she suffered from nephritic syndrome due to focal segmental glomerulosclerosis. Despite treatment with oral haematinics, her haemoglobin level continued to fall. After a blood transfusion, her renal function deteriorated. She was started on darbepoetin alfa, a long-acting erythropoietin, for treat the anaemia caused by renal failure.

Key words: Darbepoetin alfa; Pregnancy; Chronic renal failure.

Introduction

During pregnancy, haemoglobin concentration falls, which is known as 'physiological anaemia of pregnancy'. Oral haematinics are frequently, if not ubiquitously, used to supplement dietary iron in pregnancy. Occasionally additional measures, like parenteral iron supplementations, are required. We present a case where darbepoetin alfa, a long-acting erythropoietin, has been utilised with good effect for treating severe anaemia as a result of chronic renal failure.

Case Report

A 21-years-old woman was booked in our department. She had a previous history of spontaneous miscarriage at 14 weeks' gestation. She suffered from nephrotic syndrome; her renal biopsy proved the presence of focal segmental glomerulosclerosis and she had had previous surgery for spina-bifida.

Her admission parameters, at six weeks gestation, revealed haemoglobin (Hb) of 9.9 g/dl and serum creatinine of 265 $\mu\text{mol/l}$. At 11 weeks gestation her urinary protein was 6.37 g/24 hours; Hb was 8.9 g/dl and serum creatinine had deteriorated to 289 $\mu\text{mol/l}$. As she had a history of recurrent urinary tract infection, 250 mg daily of amoxicillin was commenced prophylactically. Iron supplementation was started at 11 weeks, which was increased to thrice daily by 15 weeks' gestation. At 15 weeks' gestation, her serum creatinine was 281 $\mu\text{mol/l}$ and Hb had fallen to 8.2 g/dl. The Hgb continued to fall to 7.1 g/dl and the patient was transfused three units of blood at 19 weeks of gestation. The serum creatinine value started rising and peaked at 389 $\mu\text{mol/l}$ at 26 weeks gestation, before starting to decrease slowly. At 24 weeks' gestation, the patient's urinary protein was relatively unchanged at 6.39 g/24 hours.

Meanwhile, her Hb started to go down again. Rather than doing another blood transfusion to maintain the Hb level, we considered the use of darbepoetin after having discussed it with the renal physicians. The patient was started on a weekly dose of darbepoetin from 26 weeks gestation, and continued with

oral iron supplements, along with folic acid and vitamin B₁₂. Her Hb became static at 7.1 g/dl at 28 weeks gestation, and then started to rise. Serum creatinine remained stable at around 265 $\mu\text{mol/l}$. Serum ferritin, transferrin, B₁₂, folate, iron and total iron binding capacity (TIBC) were all normal throughout the pregnancy.

The patient was monitored with serial growth scans which were normal, until 34 weeks, when she developed polyhydramnios. She was induced at 36 weeks gestation as her serum creatinine rose to 568 $\mu\text{mol/l}$. Prior to labour, the Hb level was 8.9 g/dl. She delivered vaginally without any complications. Despite the impaired renal function, the patient remained normotensive throughout her pregnancy

Discussion

Erythropoietin plays a major role in helping blood undergo changes required to meet the increased demand during pregnancy. The red cell mass increases steadily, between the end of first trimester and term. The stimulus for increased red cell production is mainly due to rise in erythropoietin levels that occur from early pregnancy [1]. The cause of anaemia in patients with chronic renal failure is ascribed to the relative lack of erythropoietin [2]. The anaemia in these individuals becomes more acute during pregnancy, as the kidneys are unable to meet the increased demand of pregnancy [3].

Erythropoietin is a glycoprotein hormone secreted by the cells of the peritubular capillary endothelium of the kidneys. Minute amounts are also synthesized in the hepatocytes of healthy adults [4]. It is responsible for regulation of erythrocytosis, by binding to a specific erythropoietin receptor (EpoR) on the surface of red cell precursors in the bone marrow, stimulating them to develop into mature erythrocytes [4]. In anaemia, its level does not rise above normal until Hgb levels fall below 11 g/dl. However, in patients with renal insufficiency, erythropoietin levels remain inappropriately low despite anaemia [4].

Recombinant erythropoietin was launched in 1989, and has been used for treating anaemia resulting from chronic kidney disease ever since [2]. It is injected subcutaneously

or intravenously several times a week. Hypertension may occur in 20-35% of patients, mainly mediated by endothelin [2, 5]. Erythropoietin has a rare and serious side-effect, pure red cell aplasia [2, 4]. A longer acting form of erythropoietin, darbepoetin, also known as novel erythropoiesis-stimulating protein (NESP), is also available.

Since its introduction, erythropoietin has been used to treat anaemia in pregnancy, even without renal problems [3, 4, 6]. Its use seems to be safe for the foetus; it does not cross the placental barrier, and therefore lacks any direct foetal effect [7]. The main disadvantages are multiple weekly dosing and development of hypertension, with superimposed preeclampsia. Therefore, anaemia needs to be corrected gradually, with an individually tailored target haematocrit [7].

Darbepoetin alfa is a unique compound that can be administered in an extended dosing interval, usually weekly, because of its longer half-life [8]. Though data is limited, it is considered to be quite safe to both the mother and the foetus [8]. The rise in haemoglobin is more gradual, and the risk of subsequent development of hypertension is quite low. It should therefore be considered more convenient and preferable to conventional human erythropoietin.

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