Favorable outcomes of pregnancy with use of sibutramine in a woman with polycystic ovary syndrome: a case report

Polikistik over sendromu olan bir kadında sibutramin kullanımı ile olumlu gebelik sonuçları: bir olgu sunumu

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ÖZET

Sibutramin şişmanlığın uzun vadeli tedavisi için kullanılan bir ilaçtır. Gebelikte sibutramine maruz kalma ile ilgili sınırlı sayıda yayınlanmış veri mevcuttur. Bu makalede, gebe olduğunun farkında olmadan 1-6. gebelik haftaları arasında 15 mg/gün sibutramine maruz kalan polikistik over sendromlu 29 yaşındaki Kafkas kökenli kadın olgu sunulmuştur. Gebeye 38. haftada sezaryen yapılmış ve 4150 gr ağırlığında sağlıklı erkek yeni doğan dünyaya gelmiştir. Bebek bir sene boyunca takip edilmiş ve bu süre içinde hiçbir konjenital anomali ya da gelişimsel bozukluğa rastlanmamıştır. Polikistik over sendromlu bir kadında,şişmanlık tedavisi için sibutraminin kullanımı sırasında başarılı spontan gebelik ve olumlu gebelik sonuçlarının sunumu, bu ilaca gebelikte maruziyetle ilgili sınırlı bilgiye katkıda bulunacaktır.

Anahtar kelimeler: sibutramin; polikistik over sendromu; gebelik; sezaryen; şişmanlık

ABSTRACT

Sibutramine is a drug used for long-term management of obesity. There is limited published data about sibutramine exposure during pregnancy. In this article, we present a 29-year-old, Caucasian woman with polycystic ovary syndrome who exposed to 15 mg/day of sibutramine during gestational weeks 1- 6 without knowing that she was pregnant. At 38th weeks, cesarean section was performed and a healthy male newborn weighted 4150 gram was born. We followed the infant for one year. No congenital abnormalities and developmental disorders were seen during this period. This report of the successful spontaneous pregnancy and favorable pregnancy outcomes following the use of sibutramine for obesity management in a woman with polycystic ovary syndrome may contribute to the limited knowledge about the exposure to this drug during pregnancy.

Key words: sibutramine; polycystic ovary syndrome; pregnancy; cesarean section; obesity

INTRODUCTION

The prevalance of obesity has started to increase markedly during the last decades and the importance of obesity has been recognised as a major public health problem affecting both the developed and the developing countries (1). At all ages women are commonly found to have a higher mean body mass index (BMI) and higher rates of obesity than men (2). Polycystic ovary syndrome (PCOS) is the most common form of female infertility and associated with a number of metabolic disturbances. Obesity is encountered in % 30- 70 of PCOS-affected women (3). The world health organization (WHO) accepts a body mass index (BMI) of 30 kg/m^2 or higher as obese. Antiobesity pharmacotherapy is accepted as appropriate for patients with a BMI of 30 kg/m^2 or higher without concomitant risk factors or a BMI of 27- 29. 9 kg/m^2 with

a major obesity–related comorbidity (eg. hypertension, diabetes) (4). There are only a few kinds of drugs available for the treatment of obesity. Sibutramine is a serotonin norepinephrine reuptake inhibitor that is approved for long-term management of obesity (5,6). To a smaller degree sibutramine also inhibits the reuptake of dopamine (5). It is reported that sibutramin in combination with lifestyle modifications result in significant weight reduction in obese patients with PCOS (7).

There is limited published data about sibutramine exposure during pregnancy. İn this report, we present a pregnant woman who used sibutramin in early pregnancy and her fetal outcomes.

CASE REPORT

Our case was a 29-year-old, Caucasian primigravida who had a cesarean delivery of a healthy male infant one year ago. She had some medical problems including polycystic ovary syndrome, hypothyroidism and metabolic syndrome. On physical examination, her calculated body mass index (BMI) was 32 kg/m^2. The patient reported taking 15 mg/day of sibutramine for losing weight during gestational weeks 1- 6, without knowing that she was pregnant. A chest x-ray was taken for check up in gestational week 5th. Her quad screen test in gestational week 17th showed increased risk of trisomy 18. Amniocentesis result was normal. Her serial obstetrical ultrasounds showed normal fetal growth. At 38th weeks, she delivered a male infant (4150 gr; 51 cm) by cesarean section. The infant had Apgar scores of 9 and 10, at 1 and 5 min, respectively. We followed the infant for one year. No congenital abnormalities and developmental disorders were seen during this period.

DISCUSSION

Orginally developed as an antidepressant, sibutramine is an orally administered agent for the treatment of obesity. Sibutramine is a serotonin norepinephrine reuptake inhibitor that induces weight loss by suppressing appetite, enhancing satiety and inducing thermogenesis (8, 9, 10). Sibutramine is usually started at a dose of 10 mg daily and the dose may be increased up to 15 mg daily after 4 weeks in nonresponders (11).

Pharmacotherapy during pregnancy, presents a special concern because of potential teratogenic effects of the drugs. Physiologic changes of pregnancy affect the pharmacokinetics of medications used by pregnant woman and some medications can reach the fetus and cause harm (12). Sibutramine belongs to pregnancy category C, hence its use is not recommended during pregnancy (13). From the studies in rats, there was no evidence of teratogenicity at sibutramine doses of 1, 3 or 10mg/kg/day. Whereas in rabbits maternal toxicity and increased cardiovascular anomalies were found at high doses (13).

There is little published evidence about human pregnancy outcomes following prenatal exposure to sibutramin (14, 15, 16, 17). Kadioglu et al. (14) reported normal fetal outcomes of two pregnant women exposed to sibutramine during the first trimester. Einarson et al.(15) observed 10 pregnant women who took sibutramine during the first trimester of pregnancy. Among these 10 women, 7 delivered normal healthy babies, 2 had spontaneous abortions and 1 had therapeutic abortion. A subsequent study described two pregnant women exposed to sibutramine during the second trimester of pregnancy. Among the two women, one delivered a normal healthy newborn, one had spontaneous abortion (16). Lastly, a study of 52 pregnant women exposed to sibutramine during the first trimester showed no increase in congenital anomalies or adverse pregnancy outcomes (17).

PCOS is a common clinical disorder characterized by ovulatory dysfunction, hyperandrogenaemia, rapid LH (GnRH) pulsatility, increased LH concentrations and LH: FSH ratios (18). It has been suggested that psychological stress and neurotransmitter levels may be linked to some of the hormonal derangements, including inappropriate gonadotropin secretion and elevated adrenal androgen levels in women with polycystic ovary syndrome (19). Increased prevalance of depression has been found in women with PCOS and an assosiation between depression and insulin resistance and BMI has been observed (20). It has been suggested that serotonin has an inhibitory effect on GnRH stimulated LH release (21) and dopamine has also been shown to supress serum LH levels (22). Based on this findings, in this case sibutramine may have increased the chance of spontaneous pregnancy by reducing stress and increasing the levels of serotonin and dopamine which supress LH release.

This report of the successful spontaneous pregnancy and favorable pregnancy outcomes following the use of sibutramine in a woman with polycystic ovary syndrome may contribute to the limited knowledge about the exposure to this drug during pregnancy.

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