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Exposure to Rosiglitazone and Fluoxetine in the First Trimester of Pregnancy

Rosiglitazone is a thiazolidinedione oral hypoglycemic drug that seems to be a promising alternative not only as an oral hypoglycemic agent but also for women with polycystic ovary syndrome. However, information regarding exposure to rosiglitazone in pregnancy is limited to two previous case reports. In the first case, a 35-year-old woman was exposed until the 8th week of pregnancy to 4 mg/day rosiglitazone and to glicazide, acarbose, atorvastatin, spironolactone, hydrochlorothiazide, carbamazepine, thiridazine, amitryptiline, chlordiazepoxide, and pipenzolate bromide (1). The second case was a woman exposed to 4 mg/day rosiglitazone between gestational weeks 13 and 17 (2). The two cases delivered normal babies at gestational weeks 36 and 37, respectively.

We are reporting the case of a 29-year-old Korean primiparous woman with a 6-month history of type 2 diabetes. She had been taking 400 mg metformin and 2.5 mg glibenclamide every 12 h. Because of the difficulties in controlling her hyperglycemic levels, 500 mg metformin every 12 h was added to her combined treatment. Five months later, her physician decided to switch her treatment to 4 mg rosiglitazone maleate every 12 h. In addition, she received 20 mg fluoxetine hydrochloride every 12 h for a body weight reduction plan. She had control of her diabetes and took both medications until the 5th week of gestation, when she had symptoms of pregnancy.

She was seen at The Korean Motherisk Program at 8 weeks of pregnancy, where she reported negative exposure to other medications, alcohol, illicit drugs, cigarette smoking, or radiation. She was not taking folic acid. Her BMI was 31.2 kg/m^2 (weight 85 kg and height 165 cm). Her fasting plasma glucose and HbA_{1c} levels were 138 mg/dl and 6.8% (normal range 4.5–6.0), respectively. A single embryo of 20 mm crown-lump length and normal heart rate was identified by ultrasound. Her treatment with rosiglitazone was switched to insulin, and fluoxetine administration was discontinued.

She was followed up periodically by clinical, laboratory, and ultrasound examinations. There were no ultrasonographic evidences of fetal malformations at the different follow-up examinations. The course of her pregnancy was considered to be normal. Previous to delivery, her total weight gain was 15 kg and her BMI was estimated to be 36.7 kg/m^2. At 40 weeks of gestational age, she vaginally delivered a 3.7-kg male baby. A detailed neonatal examination did not detect any clinical evidence of external, cardiac, pulmonary, or gastrointestinal congenital malformations. His cephalic circumference was 34.5 cm (within normal range), and his neurological development was found to be normal by a detailed physical and neurological examination. The baby was periodically followed up by a pediatrician. At the age of 18 months, the child was weighing 13.5 kg, was a healthy baby, and had a neurological development similar to that expected for his age-group.

Preclinical studies on rosiglitazone (GlaxoSmithKline, Mississauga, ON, Canada) found no increase in congenital malformations in rats and rabbits treated with 19 and 73 times the human dose, respectively. The two previous case reports, in addition to the present one, suggest that this drug is also not teratogenic in humans. On the other hand, fluoxetine is a serotonin reuptake inhibitor antidepressant drug with sufficient reproductive and developmental studies in humans to prove a lack of an increased risk of teratogenicity.

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Recent Trend Toward Decrease in the Incidence of Childhood Type 2 Diabetes in Tokyo

We previously reported that the annual incidences of children with type 2 diabetes as detected by urine glucose screening at school in Tokyo during 1981–1995 were significantly higher than the incidence in 1974–1980 (1). We evaluated recent changes in the annual incidence of childhood type 2 diabetes in Tokyo. The results were analyzed using Fisher's exact probability test.

From 1974 to 2004, a total of 9,242,259 school students were tested for glucosuria to detect diabetes. A total of 236 children were diagnosed as having type 2 diabetes through this screening program. Overall, 83.9% of children with diabetes were obese. The overall incidence was 2.55 per 100,000 per year. Junior high school children had a significantly higher incidence than primary