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Pramipexole-Treated Parkinson's Disease During Pregnancy

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Abstract: There are few reports about drug-related effects on PD pregnancy. We describe the case of a woman affected by PD treated with pramipexole monotherapy during pregnancy. The child, born by caesarean delivery, is healthy, whereas motor disability of the mother progressively increased to the point that levodopa therapy was necessary. © 2004 Movement Disorder Society

Key words: Parkinson's disease; pregnancy; pramipexole

There are few clinical reports concerning the pregnancy of parkinsonian women because of the rarity of this condition; consequently, we have little information about the safety of antiparkinsonian drugs during pregnancy. Most of the reported cases of PD in pregnancy were treated with levodopa,[1–5] some others with bromocriptine[2,3] and pergolide.[6] In these descriptions antiparkinsonian treatment with L-dopa or ergot dopamine-agonists has not been related to any teratogenic effect. To our knowledge, there is no report available on treatment of parkinsonian women with the non-ergot dopamine agonist pramipexole during their pregnancy. We describe the case of a woman with PD treated with high dose of pramipexole during pregnancy.

Case Report

A 42-year-old woman developed mild rest tremor and motor slowness in the right limbs at the age of 37. At the first neurological examination, she presented bradykinesia and rigidity of the right limbs and mild (infrequently present) rest tremor of the ipsilateral hand; the remaining neurological examination was normal. Hoehn and Yahr stage was I; the total Unified Parkinson's Disease Rating Scale (UPDRS) score was 14 (11 in section III); the Schwab and England scale was 80%. Family history was not significant for extrapyramidal diseases. Routine blood examination, ceruloplasmin, and CU^{++} levels were normal; cerebral magnetic resonance imaging scan was normal; 18-fluorodopa positron emission tomography showed mild decreased dopamine uptake in the left striatum. Treatment with pramipexole (4.5 mg per day) resulted in optimal control of motor symptoms.

At the age of 41, the patient became pregnant and refused to discontinue pramipexole because of concern of motor disability. Approximately 3 months before starting pregnancy, the total UPDRS score was 16 (12 in section III). During pregnancy, motor disability (mostly bradykinesia and rigidity) did progressively worsen, and by the sixth month, total UPDRS score was 36 (25 in section III). The patient underwent amniotic fluid examination with normal results (46 XX karyotype); the morphological fetal echography at the 22nd week of pregnancy showed no abnormalities.

She gave birth to a normal-term girl with an Apgar score of 9, by caesarean section because of motor impairment. General and neurological examination of the baby revealed no abnormalities and the routine neonatal blood tests were normal. At 6 months, the baby was healthy and showed normal development.

During the first month of the puerperal period, bradykinesia and rigidity improved, but 2 months later, these symptoms worsened again, reaching an UPDRS total score of 50 (34 in section III). In consideration of impairment with nursing tasks, we introduced small doses of L-dopa (150 mg/day) with complete motor control after 4 weeks. In agreement with the patient, we decided to avoid breastfeeding because medical information on this topic is lacking.

Discussion

The effect of pregnancy on PD course is controversial: some authors report unchanged symptoms,[2,3,5] but in the case described by Shulman and colleagues,[1] a marked increase of motor disability was noted, and Hagell and coworkers[2] in their review reported a significant worsening of motor disability during and after pregnancy in a PD patient.

In our case, worsening occurred in the second part of pregnancy and in the postpartum period and disease progression cannot be excluded. The mechanism underlying the increase of PD disability during pregnancy is poorly understood: some authors suggest both positive[7] and negative[8,9] dopaminergic effects of estrogens, others that changes of PD disability during pregnancy could be related to disease progression[2] or to pregnancy-induced pharmacokinetic variations of drug levels.[10–12] As recently suggested by Shulman and colleagues[1] and De Mari and coworkers,[6] it could be related to the low levels of estrogens.

Medical experience on the management of pregnancy in PD patients is limited. Whereas for L-dopa we find descriptions in the medical literature in favor of its substantial safety during human pregnancy in parkinsonian patients, [1–5,10] only anecdotal data are available for dopamine agonists,[2,3,6] and to date, no published data exist on ropinirole or cabergoline. To our

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knowledge, this is the first report on the safety of pramipexole during human pregnancy.

Studies about human teratogenicity of dopamine agonists generally describe their use in endocrine disorders such as hyperprolactinemia. In such disorders bromocriptine[13,14] and cabergoline[15] have not shown specific teratogenic effects in treated patients. Obviously, it must be born in mind that, for these disorders the dosages are usually lower than those used to treat Parkinson's disease motor symptoms.

In the premarketing studies on animals, bromocriptine,[16] pergolide,[17] and cabergoline[18] have not evidenced a significant teratogenicity. As far as pramipexole is concerned, we have not found any published study on this topic. Up to the present time, L-dopa and dopamine agonists have not demonstrated specific abortive or teratogenic effects on human pregnancy. In particular, we have no evidence that, among the dopamine agonists, one is more dangerous than others. More data concerning the safety of these drugs in the treatment of parkinsonian patients during pregnancy are needed. Considering the emerging role of genetic factors and the increasing number of young-onset presentations of the disease, more attention should be paid to the reproductive life of women affected by PD. Extended experience of these patients is needed to draw clinical guidelines and clarify interactions between the dopaminergic system and sexual hormones.

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