Piribedil and Pathological Gambling in six Parkinsonian patients

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ABSTRACT

Impulse control disorders (ICD) in Parkinson’s disease (PD) have attracted increasing interest. They are characterized by the inability to control the impulse to perform an act that can be detrimental to them or to others. Although dopamine agonists (DA), as a group, have been associated with impulse control disorders (ICD), piribedil has rarely been reported to cause them. Method: Case reports of six parkinsonian patients on piribedil presenting pathological gambling (PG). Results: All of the patients presented ICD associated with piribedil use. Two of them received this medication as first treatment and four of them who had developed ICDs secondary to other DA that reappeared with piribedil. Conclusion: Despite piribedil is commercially available in only a few countries, it should be considered in the differential diagnosis of PG in patients with PD.

Keywords: impulse control disorders, dopamine agonists, piribedil, pathological gambling.

CASE 1

A 67-year-old man suffering from an acineto-rigid form of PD for eight years and a long history of depression. He was initially put on low doses of pramipexole, which were eventually increased to 4.5 mg/day. After 2 years of treatment he developed PG. Pramipexole was discontinued and carbidopa/levodopa (C/L) 500 mg/day was initiated in
association with paroxetine 20 mg/day and psychotherapy. As the response was poor, quetiapine 25 mg/day was added with complete control of the PG. Due to progressive worsening of the rigidity and walking difficulties, piribedil 150 mg/day was added. He presented considerable motor improvement, however he developed severe PG after 23 months of treatment, and piribedil had to be withdrawn. After discontinuation PG disappeared and C/L had to be increased up to 1,250 mg/day to control his motor symptoms.

**CASE 2**

A 48-year-old woman suffering from PD for 5 years was first put on pramipexol 3 mg/day. She developed compulsive shopping and eating disorders with a weight increase of 15 Kg. pramipexole was discontinued and ropinirole started at 6 mg/day associated with paroxetine at 20 mg/day and psychotherapy. As there was no improvement of the ICD, ropinirole had to be stopped. He was put on piribedil 200 mg/day and quetiapine 50 mg/day. However, despite initial improvement after 3 months of treatment she developed PG and hypersexuality. Piribedil was completely stopped and C/L at 250 m/day started while quetiapine was kept at the same dose. The patient improved her ICDs.

**CASE 3**

A 49-year-old man with PD initially treated with piribedil at 150 mg/day developed PG after 24 months of exposure causing him severe social and familial problems. Piribedil was switched to ropinirole 8 mg/day and psychotherapy was initiated. As his PG did not improve, the DA was stopped and C/L was prescribed at a dose of 1,000 mg/day to control his motor symptoms. The patient experienced little improvement in PG, and refused to receive antidepressants, psychotherapy, or any other medication for his compulsions.

**CASE 4**

A 65-year-old man suffering from PD for 9 years was initially treated with piribedil at 150 mg/day for 30 months when he developed PG. Piribedil was discontinued and Stalevo 50 mg/tid was added. Stalevo was later changed for C/L at 500 mg/day resulting in good control of his motor symptoms, without PG.

**CASE 5**

A 67-year-old man suffering from PD for 10 years was initially treated with pramipexole 1.75 mg/day. Five years later, due to progressive worsening, pramipexole was increased to 4.5 mg/day, and Stalevo 50 mg four times/day was added. A year later, he developed irritability, compulsive eating and PG and pramipexole had to be progressively withdrawn. Paroxetine at 20 mg/day and quetiapine at 25 m/day were introduced with the resolution of his PG. As his motor function worsened, piribedil up to 200 mg/day was added with Stalevo 100 mg/tid, stallevo 50 mg/qid, levodopa/benzerazide (L/B) in the fast release formulation 100/25 mg/tid and paroxetine 20 mg/day. The patient stopped quetiapine by himself. Two years later, he developed compulsive eating and PG, piribedil was then stopped with complete resolution of the ICDs. Stalevo, L/B and paroxetine were increased due to worsening of motor symptoms and depression.

**CASE 6**

A 50-year-old woman suffering from tremor predominant PD for 11 years had been treated with pramipexole in low doses with progressive increases reaching 4 mg/day and L/B, up to 600 mg/day with good control of her parkinsonian symptoms, except for her right hand resting tremor. Three years after the diagnosis was made and while on pramipexole,
she developed compulsive eating and shopping disorders. Pramipexole was discontinued and she was put on piribedil at 200 mg/day, however she developed PG, along with hypersexuality, binge eating and compulsive shopping. At the time piribedil was reduced to 100 mg/day and amantadine 300 mg/day was added with no control of the ICDs. A left thalamotomy was performed for the severe right hand resting tremor. As she continued presenting ICDs, piribedil was stopped, and she was put on L/B 500 mg/day, and L/B in the fast release formulation 100/25 mg qid, with a marked improvement in the ICDs.

DISCUSSION

Four of our cases first developed ICD while on other DA, which promptly disappeared after stopping the DA but reappeared when piribedil was added. The other two cases, first manifested ICD (pathological pamelbing) with piribedil as a first therapy.

Patients with PD who develop ICD, particularly PG, are usually male, have younger PD age of onset, a personal or family history of alcohol abuse, or a previous history of ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD. They are generally receiving DA as PD treatment although any anti-Parkinsonian treatment is liable to trigger ICD.


