Dopa Therapy May Up Impulse Disorders in PD

ARTICLES BY PATRICE WENDLING
Chicago Bureau

CHICAGO — Evidence continues to mount that dopaminergic therapy increases the odds of impulse control disorders in patients with Parkinson's disease.

Dopamine agonist (DA)-treated patients had two- to threefold elevated odds of having a current impulse control disorder (ICD), compared with non–DA-treated patients (17% vs. 7%, odds ratio 2.72, *P* less than .001) in an international, cross-sectional study of 3,090 patients with idiopathic Parkinson's disease.

This pattern was observed across all four impulse control disorders assessed: pathological gambling (3.5% vs. 1.6%, OR 2.15), compulsive sexual behavior (4.4% vs. 1.7%, OR 2.59), compulsive buying (7.2% vs. 2.9%, OR 2.53), and binge-eating disorder (5.6% vs. 1.7%, OR 3.34), Dr. Daniel Weintraub and associates reported in a late-breaking poster at the 12th International Congress of Parkinson's Disease and Movement Disorders.

Previous case reports and cross-sectional studies have suggested an association between DA treatment and ICDs in Parkinson's.

However, they have typically assessed convenience samples of patients, have had relatively small sample sizes, and have not concurrently assessed for all commonly reported ICDs in Parkinson's, according to Dr. Weintraub, a psychiatrist at the University of Pennsylvania, Philadelphia.

Patients in the current study were prospectively recruited from 46 movement disorder centers in the United States and Canada, and assessed using a modified Massachusetts Gambling Screen, a modified Minnesota Impulsive Disorders Interview for compulsive sexual behavior and buying, and DSM-IV Text-Revised proposed research criteria for binge eating.

Their mean age was 64 years, 420 patients (14%) had at least one current ICD, and 36% of patients with an ICD had more than one.

ICD frequencies were similar in patients treated with pramipexole (228 of 1,286, 18%) ropinirole (101/651, 16%) and pergolide (11/50, 22%), suggesting that DA treatment as a class may be a risk factor for ICD development in Parkinson's, the authors concluded.

An ICD was present in 18% of patients taking both a DA and levodopa, 14% of patients taking a dopamine agonist without levodopa, and 7% of patients taking levodopa without a DA.

Dr. Weintraub said that physicians should notify patients that ICDs are a potential adverse event associated with dopamine-agonist and levodopa treatment, and should conduct routine questioning in the context of clinical care.

Dr. Weintraub acknowledged that ICDs have been reported as a complication of deep brain stimulation, but said most patients with an ICD prior to surgery do better after surgery, probably because of decreased medication.

In a logistic regression analysis, independent risk factors for ICD development included: age of 65 years or younger (OR 2.39), dopamine agonist treatment (OR 2.76) and higher DA dosage (greater than 150 mg, OR 2.15), levodopa treatment (OR 1.53) and higher levodopa dosage (greater than 450 mg, OR 1.45), not being married (OR 1.47), and self-reported family history of gambling problems (OR 2.21).

The study was funded by Boehringer Ingelheim. Dr. Weintraub has received consulting fees, honoraria, or grant support from Boehringer Ingelheim, BrainCells, EMD Serono, Novartis, Ovation, and Wyeth. ■

Impulse Control Disorders Often Go Undiagnosed

Impulse control disorders in Parkinson's disease are often undiagnosed as patients tend to deny or minimize their existence, according to Dr. Howard D. Weiss, a neurologist with Sinai Hospital in Baltimore.

Among 165 patients with idiopathic Parkinson's followed in community-based neurology practices, 23 (14%) were diagnosed with a current or past impulse control disorder (ICD). Nine patients had multiple ICD diagnoses.

However, only 10 cases were identified before participation in the study, according to Dr. Weiss, who reported the findings in a poster at the 12th International Congress of Parkinson's Disease and Movement Disorders.

In 12 cases, the family member was the crucial source of information necessary to make the diagnosis. "We often lack the time or [fail to] ask the right questions," Dr. Weiss said in an interview.

In one case, a daughter reported that her father was spending large amounts of money at the race track. When specifically asked if he went to the track, said he had no reason to go because he didn't gamble.

Another patient said she was a churchgoer and didn't believe in gambling. However, when asked if she bought lottery tickets, she admitted to spending $200 a week on tickets and said they were like a magnet she couldn't resist.

Patients with a current or past ICD were significantly younger than were those without an ICD (mean 60 vs. 67 years), had an earlier age of Parkinson's onset (50 vs. 60 years) and diagnosis (51 vs. 61 years), had longer disease duration (10.3 vs. 7 years), had worse Unified Parkinson's Disease Rating Scale motor scores (23.4 vs. 17.5), and used higher doses of dopaminergic medications (917 vs. 589 total daily L-dopa equivalents).

Patients treated with dopamine agonists had an increased odds of developing an ICD (odds ratio 7.1). The odds increased further with a combination of a dopamine agonist and L-dopa (OR 9.9). Levodopa alone was not significantly associated with an ICD.

Brain Stimulation Effective in Long Term for DYT1 Dystonia

CHICAGO — The efficacy of deep brain stimulation can be maintained for up to 10 years in DYT1 dystonia, according to data from a prospective study in 26 consecutive patients.

DYT1 dystonia is a form of primary dystonia that typically presents in early childhood, starting in the foot or hand, and is caused by a specific mutation in the DYT1 gene.

Significant decreases in Burke-Fahn-Marsden dystonia rating scale motor and disability scores were observed 1 year after DBS surgery. No significant difference was found when the 1-year scores were compared with the scores at 3, 5, and 6 years for the whole population, Dr. Laura Cif reported in a poster at the 12th International Congress of Parkinson's Disease and Movement Disorders.

Efficacy of DBS therapy was maintained in the two patients who were followed as long as 10 years.

"The homogeneity of the population we studied minimized any variations in the interindividual response, which could be due to genetic background or surgical procedure," she wrote.

Long-term disease progression is even more important in DYTI dystonia than in other disorders treated with DBS because patients are much younger at the time of surgery and therefore require significantly longer-term follow-up, according to Dr. Cif of the University of Montpellier (France). The age at onset ranged from 6 to 20 years in the study. Moreover, DYT1 dystonia can develop into a life-threatening condition.

Eighteen patients were implanted with a single pair of electrodes in the internal globus pallidus (GPi) and eight patients had a second pair of GPi electrodes implanted because of incomplete initial response or subsequent worsening. In spite of there being no significant difference one year after surgery, a significant difference was observed at 5 years between patients with a single lead vs. those with double leads in motor (8.95 vs. 31.5, $P = .01$) and disability (3.61 vs. 7.85, $P = .021$) scores. After implantation of additional pairs of leads, only four of eight patients showed improvement.

During the follow-up, no patient died, Dr. Cif said in an interview. ■

Data Suggest Restless Legs Syndrome May Be Neurodevelopmental Disorder

CHICAGO — A group of German researchers have identified a fourth genetic risk variant for restless legs syndrome.

The PTPRD gene located on chromosome 9 joins a list of common risk variants found to be associated with the disorder. Carriers of one risk allele have a 50% increased risk of developing restless legs syndrome (RLS), Dr. Juliane Winkelmann said at the 12th International Congress of Parkinson's Disease and Movement Disorders.

Moreover, two of the four genes where the variants are located are clearly involved in early embryogenesis, suggesting that RLS may be a developmental disorder.

"It's possible that minor alterations of spinal neuron circuits in early embryonic stages—together with genetic and nongenetic risk factors such as aging or uremia—finally manifest the symptoms of restless legs syndrome," she said.

RLS is a familial disorder in 40%-60% of patients and has a high concordance in twins. Previous linkage studies in families revealed several loci but failed to identify disorder-causing sequence variants.

In a previous genome-wide association study, Dr. Winkelmann of the Technical University of Munich and associates identified an association between RLS and variants in the MEIS1, BTBD9, and MAP2K5/LBXCOR1 genes (Nat. Genet. 2007;39:938-9).

The team expanded their sample size to 2,600 patients with RLS and 5,000 controls and focused on the the RLS3 region on chromosome 9.

Fine mapping identified the PTPRD gene, which is involved in axonal guidance during early embryonic development.

The association reached a genome-wide significance, with an odds ratio of more than 1.5, Dr. Winkelmann said at the international congress.

"The main thing we have to do now is to investigate if these genetic variants play a role in RLS in embryonic stages or if they have a completely different function in the adult nervous system," she said.

During a discussion of the study, it was asked whether the variants are distributed less frequently is some populations, as epidemiologic studies have shown that RLS is present in about 10% of the population in Canada, the United States, and Europe but is less frequent in Asia.

The MEIS1 variant is less common in Asians, but this is not true of the other variants, Dr. Winkelmann responded. ■