Long-Term Treatment of Restless Legs Syndrome
with Dopamine Agonists

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ABSTRACT

Background: Restless legs syndrome (RLS) may effect more than 10% of the population. Although several controlled trials robustly demonstrate short-term efficacy of dopamine agonists, little is known about their long-term efficacy, long-term adverse events, and the predictors and frequency of tolerance and symptom augmentation.

Methods: We queried all subjects seen in the Baylor College of Medicine Movement Disorder Clinic from 1996 to 2002 and specifically followed those initiated on any DA. Demographics, efficacy, adverse events, and augmentation were tracked over time. Results: After eliminating all RLS patients with factors that could effect DA dosing or the accuracy of data, 84 subjects were followed with at least six months of use of DA. In general, efficacy was maintained over time (mean 33 months) but at the expense of a significant late-onset of symptoms in a group of about 25% (p < 0.05). Significant augmentation occurred in 31% of subjects and was only predicted by a positive family history of RLS (p = 0.024).

Conclusion: DA are effective first line therapy for RLS and are generally well tolerated. Augmentation is not uncommon, but is generally much less severe than that historically reported with levodopa.

INTRODUCTION

Restless legs syndrome (RLS) as defined by the International Restless Legs Syndrome Study Group criteria may occur in more than 10% of predominantly Caucasians. Historically, numerous treatments have been employed with varying degrees of success, however evidence based medicine most consistently supports the use of levodopa and dopamine agonists (DA). These therapies are not without side effects and may be associated with long-term augmentation and tolerance. The identification of factors that predict problematic use of DA treatment for RLS have not been systematically evaluated.

METHODS

All patients seen with RLS at the Baylor College of Medicine Parkinson’s Disease and Movement Disorder Clinic between the January 1996 and January 2003 were initially included in a chart review. The onset coincides with when we began using DA for RLS. Patients with concurrent Parkinson’s disease (PD) or other diseases that may require dopaminergic therapy, patients previously started a DA, patients with RLS associated with uremia, and patients who did not meet strict criteria for RLS were immediately excluded. Patients followed for less than 6 months since the initiation of treatment were not included. In these data we address the long term use of DA for RLS. Some reports have raised concerns about both the development of tolerance and dopaminergic induced augmentation, a poorly defined scenario associated with a chronic shift of symptom onset and increased intensity. This is most notably with levodopa, which has the potential to induce augmentation and tolerance and is associated with a greater risk of severe augmentation and development of tolerance and dopaminergic induced augmentation.

RESULTS

We initially identified 262 patients with RLS. Seventeen patients did not meet strict criteria for RLS and were eliminated from further analysis. We excluded 89 for the concurrent diagnosis of a parkinsonism condition, and 14 for having a non-RLS, non-parkinsonism disorder. Patients were only included if the DA was previously started elsewhere on a DA and were thus eliminated from analysis. This left 106 subjects who were initially started on a DA on us. Sixteen of these lacked any data on any DA, Demographics, efficacy, adverse events, and augmentation were tracked over time. Results: After eliminating all RLS patients with factors that could effect DA dosing or the accuracy of data, 84 subjects were followed with at least six months of use of DA. In general, efficacy was maintained over time (mean 33 months) but at the expense of a significant late-onset of symptoms in a group of about 25% (p < 0.05). Significant augmentation occurred in 31% of subjects and was only predicted by a positive family history of RLS (p = 0.024).

Conclusion: DA are effective first line therapy for RLS and are generally well tolerated. Augmentation is not uncommon, but is generally much less severe than that historically reported with levodopa.

DISCUSSION

Our results demonstrate that DA effectively treat RLS for greater than six months. Efficacy is generally maintained with long-term use, specifically levodopa, whereas longer acting DA induce less augmentation. Patients with a positive family history of RLS were less likely to develop augmentation, whereas patients with a negative family history of RLS were more likely to develop augmentation.

REFERENCES