Adverse Effects of Ropinorole-treated Restless Leg Syndrome (RLS) During Smoking Cessation

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Performed at Madison Veterans Hospital
There was no financial support. This is not an off-label or investigational drug use report.

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Case report

Adverse Effects of Ropinirole-treated Restless Leg Syndrome (RLS) During Smoking Cessation: A Case Report

ABSTRACT

The impact of nicotine on drug metabolism should be carefully considered, including its impact on ropinirole. The author presents a case in which a patient with RLS effectively treated with ropinirole (Requip) experienced profound side effects from ropinirole when she stopped smoking.

INTRODUCTION

A provider is always excited when a patient tells them they quit smoking, knowing this is one of the best ways to lower health risks. However, consideration regarding the impact of nicotine on drug metabolism should be considered, including its impact on ropinirole.

Restless leg syndrome affects 5-10% of the general population\(^1\). In the United States 21% of the population smokes, a number that is lower than many other countries. In more recent years greater attention and resources have been devoted to encouraging smoking cessation. Given the high percentages of these two conditions, attention to the impact of smoking cessation on the levels of medications treating RLS needs to be considered.

REPORT OF CASE

A fifty-four (54) year-old woman with RLS had responded well to dopaminergic therapy with ropinirole. She was stable on this medication for two years at a dose of 1 mg per day, and had reported good efficacy of medication without complaints of side effects. IRLS (International Restless Leg Severity Scale) scores went from 27 pre treatment to 7 post treatment.

The woman quit smoking and relayed the following symptoms. About 4 days after quitting smoking, she noted prolific sweating at nights to the point her shirt was drenched and needed to be changed most nights. She also described much more disturbed sleep with increased awakenings for several nights in a row.

She then decreased her ropinirole by half of her previous dose, taking 0.5 mg at night instead of 1.0 mg. She felt full relief of her RLS symptoms, and no sweating at night or increased awakenings by the second night at this dose. No other medications were adjusted in the months prior to the ropinirole dose changes. The patient was not on nicotine replacement therapy during her smoking cessation. As she was amazed such could be due to the ropinirole, she did try going back to the 1 mg dose for 2 nights. She again had return of much night sweating and more awakenings. Returning to the half dose of 0.5 mg at night resulted in cessation of the night sweating, no more awakenings, and good control of her RLS symptoms.

DISCUSSION

Smoking induces cytochrome P450 isozyme CYP1A2. Since ropinirole is a CYP1A2 substrate, the plasma concentrations of ropinirole may be decreased in smokers
compared to nonsmokers taking similar doses. In a study of patients with restless leg syndrome, smokers compared to nonsmokers had a lower area under the concentration curve (AUC) and lower maximal concentration of ropinirole of about 1/3 when adjusted for dose\(^2\).

If a person smokes, they may require higher doses of ropinirole to reach clinical response. Conversely, as in this case, if a person is on a stable dose of ropinirole and stops smoking, they may require a dose reduction of ropinirole. By stopping a CYP1A2 inducer (smoking nicotine), the metabolism of ropinirole slows with smoking cessation. This decrease in dose would allow the patient to reach the same blood concentration as they had at the higher dose when they were smoking.

Nicotine replacement therapy (patch, gum, inhaler) is commonly used for a few weeks after a person stops smoking. This nicotine would be expected to induce CYP1A2 in the same way as nicotine from smoking. Therefore, the increase in ropinirole blood concentrations and corresponding symptom would occur only after all forms of nicotine are discontinued.

The adverse reaction described in this case occurred while on ropinirole. There are other dopaminergic agents commonly used to treat RLS, including pramipexole and carbidopa/levodopa. These would not be expected to elevate in blood concentrations with smoking cessation as they are not metabolized by the CYP1A2 route.

Sweating and hyperhidrosis have been reported in clinical trials and in overdose of ropinirole\(^2,3\).

This case highlights the importance of thorough review of medications when any drug, including nicotine is going to be started or stopped. Patients with RLS who are on ropinirole therapy should be warned, and assessed for symptoms that may require dose adjustments when they start or stop the use of nicotine.

REFERENCES