

**Significant treatment effect of rotigotine in patients with periodic limb movements
in sleep (PLMS): a meta-analysis**

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Abstract:

Introduction

Periodic limb movement in sleep (PLMS) has been believed as abnormality of autonomic system in decades. However, recently, some evidences suggested dopaminergic dysregulation also played roles in PLMS. Some dopaminergic medication had been preliminarily introduced in patients with PLMS. However, the results were controversial. The aim of current meta-analysis was to summarized the current evidence of treatment effect of rotigotine, one of the dopaminergic medication, in patients with PLMS.

Method and Materials

Upon the target of interventional studies, the current meta-analysis followed the guideline of *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) statement, which is designed for meta-analysis of interventional studies. From the electronic platform of PubMed, ScienceDirect, and ClinicalTrials.gov, the two authors made electronic search with inclusion criteria of (1) published articles investigating treatment effect of rotigotine on PLMS, either in forms of Pre-Post comparison design or in forms of placebo-controlled trials, and (2) articles that were clinical trials in humans and hand search from the reference lists of review articles relevant to this topic. We chose the primary outcome measure as the changes of PLM index, which was defined as the rate of PLM happened at sleep (PLM/hour), which was recorded by polysomnography and secondary outcomes as the changes of sleep parameter, including PLM with arousal index.

Result

Total five articles were recruited into the current meta-analysis. Among them, 3 provided changes of PLM index before and after rotigotine treatment and yielded 55 patients with PLMS (mean age=40.7, mean female proportion=45.5%); three articles were eligible for the meta-analysis of placebo-control of rotigotine treatment effect (rotigotine participants = 107, mean age=59.0, mean female proportion=63.2%; placebo participants= 70, mean age=56.1, mean female proportion=61.4%).

The main results of the meta-analysis showed significantly decreased PLM index after rotigotine treatment in patients with PLMS (difference in means = -5.755, 95% CI = -7.430 to -4.079, $P < 0.001$) in pre-post treatment comparison. Similarly, the treatment effect of rotigotine in PLM index is also significantly better than that of placebo (difference in means = -32.105, 95% CI = -42.539 to -21.671, $P < 0.001$). For secondary outcome, the treatment effect of rotigotine in PLM with arousal index is significantly better than that of placebo (difference in means = -7.160, 95% CI = -9.310 to -5.010, $P < 0.001$).

Conclusion

The current study provided evidences that rotigotine both improve patient's PLM index in pre-post treatment comparison and had better treatment effect than that of placebo. This also provide hint about the dopaminergic mechanism in the pathophysiology of PLMS.