Bupropion and Iron for Restless Leg Syndrome: Do They Have Efficacy Similar to Ropinirole?

Sir,

I read with interest the study on efficacy and tolerability of ropinirole, bupropion, and iron for the treatment of restless leg syndrome (RLS) reported by Vishwakarma *et al*.[1] in October-December issue of 2016. The authors have rightly pointed out that the dopamine agonist, ropinirole is considered as the standard treatment of idiopathic RLS (beside pramipexole and rotigotine), at a dose ranging from 1.5 to 4.6 mg in the systematic review and meta-analysis by Aurora *et al*.[2] Similar conclusions were reached in the meta-analysis by Scholz *et al*.[3] There is only one randomized, placebo-controlled trial[4] that found bupropion to be efficacious than placebo in RLS at 3 weeks but not at 6 weeks. Although iron therapy has been evaluated in six randomized-controlled trials, the meta-analysis by Trotti *et al*.[5] found that the evidence is not sufficient to conclude that it is beneficial in RLS. In the current study, the authors have compared fixed-dose bupropion and combination of iron with folic acid, with ropinirole, which is the standard treatment available and acts as an active control. However, the authors have not specified whether this is a superiority or a noninferiority trial; the latter can be conducted with smaller sample sizes.[6]

The authors have recruited 103 patients but presented the data for 90 patients. It is not clear whether the 13 dropouts received treatment and did not complete 6-week follow-up and at which stage they were lost. A CONSORT diagram depicting the flow of participants in the study is desirable, which improves the understanding of the results.[7] Furthermore, in addition to

completer analysis, an intention-to-treat analysis including all randomized patients would reduce the bias in reporting results.[8] Furthermore, from the description, it is not clear about the process of randomization and the allocation concealment.[9]

For the primary outcome, i.e., International Restless Legs Scale (IRLS) score, there were significant effect of time, which suggests improvement in all the three groups, and significant group × time interaction, suggesting differences in efficacy between the treatment groups. *Post hoc* comparison suggested ropinirole be more effective than bupropion and iron and folate combination as shown in Figure 1 of Vishwakarma *et al*.[1] However, in the absence of control group, it was assumed that both bupropion and iron and folate combination were effective treatment in RLS. In reality, both treatment groups were neither superior nor equivalent to ropinirole, which is considered as standard treatment. In such situations, it is better to report the effect sizes of the differences with 95% confidence intervals and discuss the practical significance of the finding, i.e., reduction in IRLS scores. Furthermore, it was interesting to observe that ropinirole was effective at a dose of 0.5 mg/day, which is much lower than the recommended dose of 1.5–4.6 mg/day.[2]

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Conflicts of interest

There are no conflicts of interest.

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