Modafinil for Attention-deficit/hyperactivity disorder (ADHD): an Updated Systematic Review And Meta-Analysis

Rosane Lowenthal¹, Ivan Taia¹, Marcelo B Generoso¹, Amanda Soares³, Quirino Cordeiro¹, Mailu Enokibara da Silva¹, Pedro Shiozawa¹

¹ Santa Casa School of Medical Sciences, Evidence-based Psychiatry Unit, São Paulo, Brazil

Background

Attention-deficit/hyperactivity disorder (ADHD) is a common psychiatric disorder with a prevalence varying between 5% to 10% in children within the first decade. Clinical presentation is characterized by inattention, hyperactivity and impulsivity, besides school impairment and social life commitment. up to 30% of ADHD patients fail to respond to first line treatment options. Modafinil is a central actuating agent that in high doses seems to change GABA and glutamate balance leading to hypothalamus activation, prescribed originally as a wake-promoting agent. It can be used to ADHD ameliorating symptoms through the same mechanisms by which reduces sleepiness, in addition to greater tolerance to side effects (1).

Methods

We performed a systematic review based on Cochrane group and PRISMA statement guidelines, searching for randomized controlled trials on modafinil for ADHD in MEDLINE and EMBASE databases following the recommendations of Cochrane group (2). To the best of our knowledge, this analysis has not been run hitherto.

For the main outcome (ADHD symptoms score), we initially calculated the standardized mean difference and the pooled standard deviation of each comparison. The Hedges’ g was used as the measure of effect size. The pooled effect size was weighted by the inverse variance method and measured using the random-effects model. The rationale for using random models was based on the fact that it can rarely be assumed that all studies involved in a meta-analysis share the exact same effect size. Therefore, a more robust and conservative analysis can be preferably achieved by using random models instead of fixed ones. Heterogeneity was evaluated with the I² (>35% for heterogeneity) and the χ² test (p<0.10 for heterogeneity). Publication bias was evaluated using the funnel plot, which displays confidence interval boundaries to assist in visualizing whether the studies are within the funnel, thus providing an estimate of publication bias.

Results

A total of six controlled trials were eligible for the statistical analysis (n=834; mean age=9.5±0.59). All but one trial used placebo as comparator group. One trial used methylphenidate as active comparator group. Modafinil dosage varied between 175-300mg daily. Every study used The Parent and Teacher ADHD Rating Scale-IV for assessing clinical symptoms.

Regarding main outcome we found modafinil to be superior to comparator groups for ameliorating ADHD symptoms. Interestingly we observed a difference regarding symptoms assessment between parents and teachers dimensions (teachers: Hedges’g=1.06 95%CI 0.45 – 1.68; parents: Hedges’g=0.46 95%CI 0 – 0.86)

Conclusion

We found that modafinil is superior to comparator groups in the treatment of ADHD. However, given the relatively small number of trials available up-to-date further trials assessing longer follow-ups and larger samples are fundamental for clarify the precise impact of modafinil in the treatment of ADHD in daily clinical practice.