Hallucinations and other psychotic symptoms in response to methylphenidate in children and adolescents with attention-deficit/hyperactivity disorder: a Cochrane systematic review with meta-analysis and trial sequential analysis

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ABSTRACT

Background:
There is little evidence in the literature on the association between methylphenidate treatment and psychotic symptoms in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Objective:
We examine the occurrence of psychotic symptoms during methylphenidate treatment of children and adolescents with ADHD. The data arise from our two Cochrane systematic reviews on methylphenidate, reported elsewhere.

Methods:
Electronic databases were searched up to January 2016 (for observational studies) and March 2017 (for randomized trials). We summarized data as risk ratios and pooled prevalences. Trial Sequential Analysis was used to control for random errors. We assessed the risk of bias and the quality of evidence according to Cochrane guidelines.

Results:
Ten randomized trials (1103 participants), 17 non-randomized studies (76,237 participants) and 12 patient reports or series (18 patients) were identified. In the randomized trials, there was no significant difference in the risk of developing psychotic symptoms [10 of 654 (pooled prevalence, 2.5%) methylphenidate versus 1 of 508 (pooled prevalence, 1.7%) placebo patients; risk ratio, 2.07; 95% confidence interval, 0.58 to 7.35]. Nine of 10 trials had a high risk of bias, and according to the Trial Sequential Analysis, the required information size was not achieved, that is, the meta-analysis was considerably underpowered. There were 873 instances of psychotic symptoms in the non-randomized studies among 55,603 participants (pooled prevalence, 1.2%; 95% confidence interval, 0.7 to 2.4). In the comparative cohort study, methylphenidate significantly increased the risk for any psychotic disorder by 36% (risk ratio, 1.36; 95% confidence interval, 1.17 to 1.57). The overall risk of bias was rated as critical for this study.

Conclusions:
Because of sparse data and low quality of evidence, we cannot confirm or refute whether methylphenidate increases the risk of psychotic symptoms in children and adolescents with ADHD. This possible adverse event may affect 1.1% to 2.5%, and physicians, patients and caregivers should be aware of this to ensure proper treatment in case of occurrence during methylphenidate treatment.