SLC6A3 polymorphism and response to methylphenidate in children with ADHD: A systematic review and meta-analysis.

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Abstract

Methylphenidate (MPH) is the most commonly used treatment for attention-deficit hyperactivity disorder (ADHD) in children. However, the response to MPH is not similar in all patients. This meta-analysis investigated the potential role of SLC6A3 polymorphisms in response to MPH in children with ADHD. Clinical trials or naturalistic studies were selected from electronic databases. A meta-analysis was conducted using a random-effects model. Cohen's d effect size and 95% confidence intervals (CIs) were determined. Sensitivity analysis and meta-regression were performed. Q-statistic and Egger's tests were conducted to evaluate heterogeneity and publication bias, respectively. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to assess the quality of evidence. Sixteen studies with follow-up periods of 1-28 weeks were eligible. The mean treatment acceptability of MPH was 97.2%. In contrast to clinical trials, the meta-analysis of naturalistic studies indicated that children without 10/10 repeat carriers had better response to MPH (Cohen's d: -0.09 and 0.44, respectively). The 9/9 repeat polymorphism had no effect on the response rate (Cohen's d: -0.43). In the meta-regression, a significant association was observed between baseline severity of ADHD, MPH dosage, and combined type of ADHD in some genetic models. Sensitivity analysis indicated the robustness of our findings. No publication bias was observed in our meta-analysis. The GRADE evaluations revealed very low levels of confidence for each outcome of response to MPH. The results of clinical trials and naturalistic studies regarding the effect size between different polymorphisms of SLC6A3 were contradictory. Therefore, further research is recommended.