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Abstract Title

Pharmacogenetic Profiles of Children and Adolescents Prescribed with Alpha-2 Agonists: Insights from the PGx-SPaRK Study

Background

Alpha-2 agonists, guanfacine and clonidine, are increasingly prescribed to children and adolescents with mental disorders, often as monotherapy or in combination with stimulants. However, the impact of genetic variation on the treatment outcomes of alpha-2 agonists remains poorly understood.

Objective

We describe the demographics and pharmacogenetic profiles of children in the Pharmacogenomics-Supported Prescribing in Kids (PGx-SPaRK) study who were prescribed guanfacine and clonidine.

Methods

Data were collected from the PGx-SPaRK study, an implementation trial that provided pharmacogenetic testing to children and youth with mental disorders from Western Canada. Children aged 6–17 years with a history of guanfacine or clonidine use were included in the analysis. DNA was extracted from saliva samples, which were genotyped for candidate-gene variants relevant to the metabolism and transport of guanfacine (CYP3A4, CYP3A5, ABCB1) and clonidine (CYP2D6). Genotyping results were translated into metabolizer phenotypes. Descriptive statistics were used to summarize the demographics and metabolizer phenotype distribution.

Results

Among 1,515 participants, 13.8% were taking guanfacine and 7.6% clonidine at enrollment. The mean age for both groups was 11 years. For participants taking guanfacine, 68.4% were male, and 67.9% were of European ancestry. For participants taking clonidine, 74.8% were male, and 72.2% were of European descent. Among children taking guanfacine, P-gp (encoded by ABCB1) activity was intermediate in 46.8%, reduced in 29.4%, and normal in 23.9%. For CYP3A4, the majority were normal metabolizers (88%), with 11.5% being intermediate metabolizers and 0.5% being poor metabolizers. For CYP3A5, 82% were poor, 17% intermediate, and 1% normal metabolizers. For children taking clonidine, CYP2D6 results indicate that half of the cohort (50.4%) were normal metabolizers. 40.9% were intermediate, 6.1% poor, and 2.6% were ultrarapid metabolizers.

Conclusion

The observed metabolizer phenotype distributions indicate that genetic variation could influence treatment outcomes in children and adolescents treated with alpha-2 agonists.

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