Guanfacine extended release for children and adolescents with attention-deficit/hyperactivity disorder: efficacy following prior methylphenidate treatment.

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Abstract

Guanfacine extended release (GXR) and atomoxetine (ATX) are nonstimulant treatments for attention-deficit/hyperactivity disorder (ADHD). As nonstimulant treatments are often used after stimulants in ADHD, GXR was assessed relative to prior stimulant treatment in a randomized controlled trial (RCT), in which ATX was included as a reference arm, and in the open-label phase of a randomized-withdrawal study (RWS). Participants were 6-17 years old with ADHD Rating Scale version IV (ADHD-RS-IV) scores ≥32 and Clinical Global Impressions - Severity scores ≥4. RCT participants received dose-optimized GXR (1-7 mg/day), ATX (10-100 mg/day), or placebo for 10-13 weeks. RWS participants received dose-optimized GXR (1-7 mg/day) for 13 weeks. Participants' last stimulant medication prior to enrolment, and reasons for stopping this medication, were collected at baseline. Change from baseline ADHD-RS-IV score and the proportion of responders were assessed by prior stimulant exposure. Of 163 RCT and 296 RWS participants who had previously received stimulant treatment, 142 and 224, respectively, had received methylphenidate (MPH); due to the low number of participants and the heterogeneity of non-MPH treatments, we only report data for prior MPH treatment. The most frequent reasons for stopping MPH were lack of effectiveness or side effects. Placebo-adjusted ADHD-RS-IV changes from baseline were significant in participants receiving GXR (prior MPH, -9.8, P<0.001, effect size [ES] 0.85; stimulant-naïve, -7.6, P<0.001, ES 0.65). In ATX-treated participants, significant placebo-adjusted differences were seen in stimulant-naïve (-5.0, P=0.022, ES 0.43) but not prior MPH-treated (-1.8, P>0.05, ES 0.15) participants. More participants met responder criteria with GXR versus placebo, regardless of prior treatment. GXR response was unaffected by prior stimulant treatment; ATX produced improvement only in stimulant-naïve participants relative to placebo. These findings may be relevant to clinical decision-making regarding sequencing of ADHD treatments.