

MEETING REPORT-

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Defining Functional Benefits of ADHD Therapy

Montreal - Evidence presented here on the functional impact of therapies for attention deficit hyperactivity disorder (ADHD) emphasizes that there is more to successful treatment than symptom reduction. Therapeutic combinations may assist optimization of treatment. Clarification of expected benefits on quality of life for the child and family may also have an impact on adherence.

Dr. Margaret Weiss and colleagues from the University of British Columbia exhibited data on the efficacy and tolerability of extended-release guanfacine [GXR]* in 333 children aged 6 to 12 years. The new data supplement findings from an earlier trial demonstrating that among children with ADHD-RS total score \geq 28 and a Clinical Global Impressions-Severity of Illness (CGI) score of \geq 4 at baseline, GXR monotherapy administered once daily in the morning or evening for 8 weeks had significant clinical advantages over placebo. The primary efficacy measure, ADHD-RS-IV score, decreased by a mean of 9.6 points with active treatment.

The secondary efficacy measure of the study was the Weiss Functional Impairment Rating Scale, parents' report (WFIRS-P), a 50-item instrument which measures the parents' perception of ADHD-related functioning globally and in separate domains for family, learning and school, life skills, child's self-concept, social activities and risk activities. The use of the WFIRS in research is

important because "there is a great need to determine whether the child improves when the symptoms get

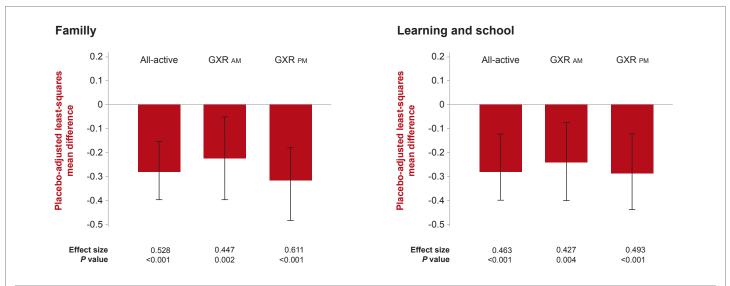
better. This is the beginning of a new research paradigm in which we hope to identify what aspects of functioning are responsive to different types of interventions," commented Dr. Weiss.

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Patients receiving GXR displayed significantly greater improvement from baseline to final assessment in mean WFIRS-P global score. The two questionnaire items leading to the greatest improvement in global score were "[ADHD] makes it difficult to keep up with school work" and "provokes others to hit or scream at him/her", the researchers reported.

Significant improvements were observed in family, learning and school (both academic performance and behaviour) (Figure 1), social activities and risky activities.

FIGURE 11 Differences in mean WFIRS-P domain scores from baseline to final on-treatment assessment. a.b.



^a Data represent placebo-adjusted least-squares mean changes from baseline; error bars indicate 95% Cls. Statistical analyses were based on type III sum of squares from an ANCOVA model for the change from baseline, including treatment group as a fixed effect and baseline value as a covariate. A negative difference in least-squares mean (GXR – placebo) indicates a positive effect of the active treatment over placebo.

^a Pinal on-treatment assessment defined as Visit 10 or last observation carried forward; full analysis set.

Adapted from Weiss M.D. et al. As presented during CACAP 2012, poster 30

There was no significant improvement versus placebo for the life skills and child's self-concept domains.

Add-On Therapy Provides Further Symptom Reduction

Adding GXR to a psychostimulant is a safe and effective approach for children with ADHD who experience a partial response but inadequate symptom relief with stimulant therapy alone, noted Dr. Ann Childress, Center for Psychiatry and Behavioral Medicine, Las Vegas, Nevada. She estimated that about a quarter to a third of children receiving psychostimulants would fit this description.

Dr. Childress and colleagues presented evidence from an 8-week placebo-controlled study of 455 children and adolescents aged 6 to 17 with a baseline ADHD-RS-IV total score \geq 24 and a CGI-Severity score \geq 3. All had been on a stable dose of psychostimulant for at least a month. The patients were randomly assigned to receive GXR early in the morning or at bedtime along with placebo at the alternate dosing time, or placebo at both times of day. The GXR dose was titrated to a maximum of 4 g/day, with the objective to achieve at least a 30% reduction in ADHD-RS-IV score. Compared with placebo (i.e. stimulant only) recipients, the active-treatment groups experienced significantly greater improvement from baseline in ADHD-RS-IV. The change was similar for both hyperactivity/ impulsivity and inattentiveness subscales.

The most common adverse events in the GXR + psychostimulant group were headache (21.2%) and somnolence (13.6%). The rate of somnolence in this study was lower than that generally observed with GXR monotherapy, likely due to the effect of the stimulant therapy, Dr. Childress commented. There were no unique adverse experiences associated with the GXR adjunctive therapy compared with the effects reported historically for either treatment alone.

Benefits and Adherence

Definition and communication of the functional benefits of ADHD therapy can potentially help parents and children accept and persist with medication, suggested researchers from McGill University. "Psychostimulants do reduce symptoms and improve outcomes and yet adherence to these medications is very low," commented Julien Hébert, a medical student and the lead author of the group's poster presentation. The

investigators administered several questionnaires to investigate knowledge and attitudes about ADHD among 27 children with a positive response to a stimulant and/or their parents. Adherence to medication was evaluated in a parent interview.

Communication of the functional benefits of ADHD therapy can potentially help parents and children accept and persist with medication.

Adherence was correlated to parental knowledge about ADHD, as well as parents' acceptance and perception of benefit from medication, Hébert indicated. Lowadherence tended to be the result of the child's perception of being stigmatized for taking medication.

When initiating ADHD therapy, "it's important to make the parents understand the psychosocial benefits of medication— [that the child is] going to be able to get along better with their family, they are likely to make more friends. That seems to be what predicts higher adherence," said Hébert.

It is also important to let the child express how he or she feels with the medication, remarked Dr. Natalie Grizenko, McGill University and Douglas Hospital Research Institute, Montreal. "When the parent hears the child say 'this seems to be helping me' [they are more likely to] give the medication regularly, and you see the benefits in the response rate."

Conclusion

Given as monotherapy or as an adjunct to a stimulant, GXR leads to symptom reduction and improvement in functioning – both of which appear to be required for optimal therapy. Communication of expected positive changes in the child's functioning can help promote adherence.

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^{*} Extended-release guanfacine (GXR) is currently approved by the U.S. Food and Drug Administration and is off-label in Canada.