Management of Treatment-Resistant Schizophrenia With Clozapine Augmentation

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ABSTRACT: A 44-year-old woman with a history of chronic schizoaffective disorder, epilepsy, social phobia, anxiety, and panic attacks presented with concern for “feeling anxious.” After a history, physical examination, and laboratory tests, the woman received a diagnosis of treatment-resistant schizophrenia. While clozapine is the standard therapy for schizophrenia, certain patients such as the woman in this case do not respond well to clozapine monotherapy, requiring clozapine to be augmented with other antipsychotics or antidepressants. This case outlines the unique challenges of managing patients with treatment-resistant schizophrenia, especially when they present with comorbid conditions such as epilepsy that can limit treatment options. A multi-pronged approach, including pharmacologic therapy as well as cognitive behavioral therapy, should also be considered.

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Gender Differences in Prodromal Symptoms of Dementia

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ABSTRACT: Study Objectives: This study proposed to test the postulate that the anxiety and insomnia symptom cluster (A/I) is a predictor of dementia.

METHODS: A retrospective data analysis was conducted on the Aging, Demographics, and Memory Study (ADAMS) dataset in order to determine whether A/I symptoms or treatment were associated with subsequent dementia or cognitive impairment (DOCI). The study used logistic regression analysis and comparison of incidence rates on a sample of 249 participants.

RESULTS: There was a significant relationship between A/I symptoms and subsequent DOCI in the male gender that was not found in the total sample or in females. No association with subsequent DOCI was found for benzodiazepine usage or non-benzodiazepine A/I medication usage.

CONCLUSIONS: The gender differences identified suggest prodromal dementia phenotypes that are differentially expressed in males and females. By triangulating the approaches from multiple disciplines—such as neuroimaging and genetics—with prodromalsymptoms, it is possible that reliable early prediction may be accomplished.

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Dasotraline in Children With Attention Deficit Hyperactivity Disorder: Results of a Randomized, Double-Blind, Placebo-Controlled Study

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ABSTRACT: Objectives: Once-daily dosing with dasotraline, a novel dopamine and norepinephrine reuptake inhibitor, achieves stable plasma concentrations over 24 hours with once-daily dosing. This study evaluated dasotraline in children aged 6–12 years (NCT02428088).
METHODS: Patients were randomized 1:1:1 to 6 weeks of once-daily, fixed-dose dasotraline 2 or 4 mg/day, or placebo. The primary efficacy endpoint was change from baseline (CBF) at Week 6 in ADHD Rating Scale Version IV – Home Version (ADHD RS-IV HV) total score, using a mixed model for repeated measures (MMRM) in the intent-to-treat (ITT) population. Secondary endpoints included Clinical Global Impression–Severity (CGI-S) score and safety endpoints.

RESULTS: The mean age of 342 randomized patients was 9.1 [SD: 1.9] years; 66.7% were male. Overall, 79% of patients completed the study. In the ITT population (N = 336), ADHD RS-IV HV total score improved significantly with dasotraline 4 mg/day vs placebo (least squares [LS] mean [SE] CFB at Week 6: −17.53 [± 1.31] vs −11.36 [± 1.29], respectively, p < 0.001; effect size [ES]: 0.48). Inattentiveness and hyperactivity/impulsivity subscale scores significantly improved with 4 mg/day vs placebo at Week 6 (p = 0.001, p = 0.003, respectively). Improvement in CGI-S score was statistically significant with dasotraline 4 mg/day vs placebo (LS mean [SE] CFB at Week 6: −1.39 [± 0.12] vs −1.04 [± 0.12], respectively, p = 0.040; ES: 0.29). No significant improvement was observed on the ADHD RS-IV HV total score and the CGI-S score for dasotraline 2 mg/day vs placebo. The most frequent treatment-emergent AEs (≥25% and higher than placebo) were (2 mg/day; 4 mg/day; placebo): insomnia (15.3%; 21.7%; 4.3%, all terms combined), decreased appetite (12.6%; 21.7%; 5.2%), weight loss (5.4%; 8.7%; 0%), irritability (3.6%; 7.0%; 6.0%), nasopharyngitis (0.9%; 5.2%; 0.9%), and nausea (0%; 5.2%; 2.6%).

CONCLUSIONS: Compared with placebo, dasotraline 4 mg/day significantly improved ADHD symptoms in children, as assessed by ADHD RS-IV HV total score and inattentiveness and hyperactivity/impulsivity subscale scores. Dasotraline was generally well tolerated; most common AEs were insomnia, decreased appetite, weight loss and irritability.

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