

Abstracts

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Alternative Psychopharmacology Regimens in Clozapine-Resistant Schizophrenia Patients: A Scoping Review of PubMed

Adil Elahi, MD^{1,2}, Ayyub Imtiaz, MD¹, Asmeret Berhane, MD^{1,3}, Enque Endeshaw, MD¹, Ava Hashemi, MS³ and Muhammad Zaidi, MD¹

¹Saint Elizabeths Hospital – Department of Behavioral Health, Washington, DC; ²Aga Khan University, Karachi, Pakistan; ³Addis Ababa University School of Medicine, Addis Ababa, Ethiopia and ⁴Ross University School of Medicine, Bridgetown, Barbados

Introduction. Clozapine is the standard of care for treatment-resistant schizophrenia. However, up to a third of patients will have a partial or no response to treatment despite an adequate trial of clozapine. There are no accepted guidelines for alternative pharmacological regimens in the treatment of clozapine-resistant schizophrenia (CRS) and electroconvulsive therapy is not always a feasible option. This paper is a scoping review of PubMed literature, reviewing various pharmacological regimens attempted for treating CRS.

Methods. A systematic search using the [Title/Abstract] filter was conducted on PubMed to identify articles related to clozapine-resistant schizophrenia (or similar terms). Three researchers reviewed a total of 130 abstracts. The inclusion criteria were limited to observational articles that assessed psychopharmacological modifications with objective measurement tools. After screening 27 full-text articles, only 18 were included in the final analysis.

Results. In this scoping review, the most commonly tested medication was amisulpride, which was explored both as an adjunct and a replacement for clozapine in patients with CRS. The randomized controlled trials and retrospective studies on amisulpride demonstrated significant improvements in symptoms on objective assessments such as the Positive and Negative Symptom Scale (PANSS), The Brief Psychiatric Rating Scale (BPRS), and Scales for the Assessment of Negative Symptoms (SANS). Other assessment tools used by researchers included the SAPS, CGI, RBANS, GAF, and UKU scales, among others.

As adjuncts to clozapine, several medications exhibited significant improvements on the PANSS negative subscale score, such as Amisulpride, Brexpiprazole, Memantine, Ropinirole, and Sodium Nitroprusside. Papers also reported positive outcomes after switching from clozapine to cariprazine or clotiapine, as measured by the SANS and PANSS, respectively. Quetiapine, Loxapine and Fluvoxamine augmentation also showed a significant improvement on the BPRS.

In contrast, one study indicated no significant improvement in outcomes when augmenting clozapine with olanzapine compared to placebo, using the Global Assessment of Functioning (GAF) and Clinical Global Impression Scale (CGIS).

Conclusion. Managing CRS can be challenging, particularly due to the absence of set guidelines on the pharmacological treatment of CRS. Most clinicians choose to add adjunctive medications to clozapine, while others opt to switch to a different medication altogether. Both approaches are viable options with varying results. The findings in this study underscore the potential benefits of various pharmacological regimens in the treatment of CRS. However, it is crucial to consider each patient's individual needs when making treatment decisions. It is prudent to do further objective analyses on the treatment of CRS.

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Factors Associated with Length of Stay in Psychiatric Inpatients with Bipolar Disorder

Alejandra Martinez Garza, MD¹, Sofia Luna-Garza, MD¹, Rodrigo Huereca-Lucio², Hector A. Vaquera-Alfaro³ and Erasmo Saucedo, MD²

¹Department of Psychiatry, Hospital Universitario “Dr. José Eleuterio González”, Monterrey, México; ²Centro de Neurociencias Avanzadas, UANL, Monterrey, México and ³Facultad de Medicina, UANL, Monterrey, México

Bipolar disorder (BD) is a lifelong mental disorder with a variable course, comprising one of the primary psychiatric illnesses warranting hospitalization due to its recurrent and chronic nature. Despite the existence of extensive evidence regarding factors influencing psychiatric hospitalization

duration, limited scientific evidence establishes the duration of psychiatric hospitalization in patients with BD. The objective of this study is to assess the clinical characteristics and factors influencing the duration of hospital stay in patients with BD.

This is a retrospective observational and descriptive study. The protocol was approved by the ethics and research committee of the Hospital Universitario "Dr. José Eleuterio Gonzalez" in Monterrey, Nuevo León, México under the name "Factores predictores del tiempo de hospitalización psiquiátrica en pacientes con trastorno bipolar". Retrospective investigation was carried out of patients admitted between July 2015 and May 2022. Clinical and socio-demographic characteristics of 276 patients diagnosed with BD type 1 and type 2 were collected. Descriptive analyses were conducted for all variables using frequencies and percentages for categorical variables. Typical dispersion measures were applied to quantitative variables. Mann-Whitney U test was used to compare means between groups for dichotomous variables, and the Kruskal-Wallis test for variables with more than two categories. Spearman's correlation coefficient was used for quantitative variables. Statistically significant values were considered at $p < 0.05$.

Factors associated with longer hospital stay included younger age ($p < 0.001$), being separated or divorced ($p = 0.002$), unemployment ($x=27.94$ vs. $x=23.77$; $p=0.12$), absence of medical comorbidity ($x=27.21$ vs. $x=20.73$; $p=0.11$), previous hospitalization history ($x=28.50$ vs. $x=23.26$; $p=0.005$), history of substance abuse ($x=28.55$ vs. 24.68 ; $p=0.26$), use of pharmacological restraint ($p=0.28$), and non-use of mood stabilizers during hospitalization ($x=27.54$ vs. $x=24.11$; $p=0.27$).

Overall, this study highlights the significance of comprehensive and personalized treatment approaches for patients with bipolar disorder. By addressing specific risk factors and optimizing therapeutic strategies, healthcare professionals can potentially reduce the length of hospital stays, leading to improved patient well-being and resource utilization within psychiatric care facilities. However, further research and intervention studies are warranted to validate and implement these findings in clinical practice.

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Sex Differences in Attention Improvements Across Two Clinical Trials of AKL-T01, A Novel Digital Therapeutic for Inattentive Symptoms in Children and Adolescents with ADHD

Antonia Savarese, PhD¹, Amanda M. Maple, PhD¹, Caitlin A. Stamatis, PhD¹, Catherine Mercaldi, MPH¹, Stephen Hinshaw, PhD² and Scott H. Kollins, PhD¹

¹Akili Interactive, Boston, MA and ²University of California, Berkeley, Berkeley, CA

Objectives. Attention-deficit/hyperactivity disorder (ADHD) remains underdiagnosed and undertreated in girls. One important contributor is the predominance of inattentive symptoms in girls

relative to boys. Though less "visible," inattentive symptoms represent a key driver of impairment, often persisting into adulthood. EndeavorRx (AKL-T01) is a game-based, FDA-authorized digital therapeutic directly targeting inattention. This analysis sought to examine potential sex differences in the efficacy of AKL-T01.

Methods. We conducted a secondary analysis of clinical outcomes by sex in 326 children and adolescents from two trials of AKL-T01 ($n1 = 180$ children; 30.6% female, M age = 9.71; $n2 = 146$ adolescents; 41.1% female, M age = 14.34). All participants had high inattention per a baseline score ≤ -1.8 on the Test of Variables of Attention (TOVA), a computerized, FDA-cleared continuous performance task objectively measuring attention. Participants used AKL-T01 for 25 minutes/day over 4 weeks. Primary outcomes included change in attention on the TOVA Attention Comparison Score (ACS) and sub-metrics, and change in symptoms on clinician-rated ADHD Rating Scale (ADHD-RS). To evaluate study hypotheses, we conducted a series of t-tests of TOVA and ADHD-RS change scores by sex.

Results. Across the pooled sample, girls using AKL-T01 demonstrated significantly greater improvements in attention on the TOVA ACS ($M\Delta = 2.44$) compared to boys ($M\Delta = 1.32$; $t[211.77] = 2.62$, $d = .31$, $p = .009$), as well as TOVA reaction time standard score (girls' $M\Delta = 13.22$; boys' $M\Delta = 3.54$; $t[229.12] = 3.93$, $d = .46$, $p < .001$). We did not observe sex differences in the 2 other TOVA sub-metrics, nor in ADHD-RS ($ps > .05$). There were sex differences in compliance ($t[207.99] = 2.17$, $d = .26$, $p = .031$), with girls completing more sessions on average ($M = 90.22$) compared to boys ($M = 80.19$).

Conclusions. Results suggest that AKL-T01 may be associated with particularly strong improvements to attentional functioning in girls relative to boys. That there were no significant sex differences in ADHD symptom change over the course of treatment in either sex underscores the specificity of these effects to inattention processes rather than broad ADHD symptoms. Limitations include categorization based on binary sex, which may not capture nuances of gender identity.

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A Single-Arm Pivotal Trial to Assess the Efficacy of AKL-T01, a Novel Digital Intervention for Attention, in Adults Diagnosed with Attention Deficit Hyperactivity Disorder

Amanda M. Maple, PhD, Antonia Savarese, PhD, Caitlin A. Stamatis, PhD, Catherine Mercaldi, MPH and Scott H. Kollins, PhD

Akili Interactive, Boston, MA

Objectives. Rates of attention deficit hyperactivity disorder (ADHD) have increased among adults, and barriers to treatment (e.g., medication shortages; inaccessibility of behavioral treatments) underscore need for novel, scalable interventions. There is a