Long-Term Efficacy of Combination Therapy of Transcranial Magnetic Stimulation with Ketamine for Patients with Treatment-Resistant Depression

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Abstract

Background. Repetitive transcranial magnetic stimulation (rTMS) is a safe, effective and non-invasive treatment for many psychiatric illnesses, including treatment-resistant depression (TRD). Ketamine, an NMDA receptor antagonist, is also an effective antidepressant. This retrospective review examined the clinical benefits of combining these two established treatments for patients suffering from TRD in a novel approach coined combination TMS with ketamine (CTK).

Methods. A group of 28 adult patients with a primary diagnosis of unipolar (n=18) or bipolar (n=10) depression received three CTK treatments a week at a private neuropsychiatric practice. Patients were given a concurrent treatment of rTMS (1Hz; 40 minutes; 130% of motor threshold) with bio-marker-determined IV ketamine infusions (0.2–4.7 mg/kg; 30 minutes). The TMS coil was positioned on the mid-prefrontal area. Frequency of treatment was dependent on patient responsiveness (10–30 sessions), which was measured as symptom reduction on the Clinical Global Impression (CGI) scale. CGI data was evaluated pre-treatment, post-treatment and at two-year follow-up.

Results. Mean reduction in CGI severity for the patient group following CTK was 4.46 ± 0.54 at a 99% confidence interval and was deemed statistically significant using a paired t-test ($a=0.01$, $t=22.81$, $p < 0.0001$). This significant reduction in CGI severity was sustained for at least 2 years following treatment completion.

Conclusions. Despite years of unsuccessful treatments, all 28 patients in this trial obtained substantial and enduring reductions in their depressive symptoms following CTK therapy. Further research into method optimization and randomized controlled trials are warranted.

Aripiprazole Lauroxil 2-Month Formulation With 1-Day Initiation for Acute Schizophrenia: ALPINE Exploratory Efficacy and Patient-Reported Outcomes

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Abstract

Objective. The randomized, controlled, phase 3b ALPINE study evaluated efficacy and safety of a 2-month formulation of aripiprazole lauroxil (AL) initiated with a 1-day regimen during hospitalization for an acute exacerbation of schizophrenia; paliperidone palmitate (PP) was included as an active control. The primary efficacy outcome, within-group change from baseline in PANSS total score at 4 weeks, was previously reported. Here we report additional exploratory PANSS subscale endpoints and patient-reported outcomes (PROs).

Methods. Adults aged 18–65 years were enrolled as inpatients and randomized to AL 1064 mg q8wk or PP 156 mg q4wk and discharged after 2 weeks of study treatment if clinically stable. Patients were followed as outpatients through week 25. Exploratory efficacy endpoints were PANSS subscale (Positive, Negative, and General) and Clinical Global Impression-Severity (CGI-S) scores. The Burden Assessment Scale was administered to patients' nonprofessional caregivers (family member or friend). Exploratory PROs (Quality of Life Enjoyment and Satisfaction Questionnaire Short Form [Q-LES-Q-SF] and Medication Satisfaction Questionnaire) were assessed during the outpatient period. Within-group changes in PANSS subscales and CGI-S scores from baseline through week 25 were analyzed for AL and PP using mixed models with repeated measures. PROs were summarized based on observed data.

Results. In total, 200 patients were randomized (AL, n=99; PP, n=101); 99 (AL, n=56; PP, n=43) completed the 25-week study. PANSS Positive, Negative, and General subscale scores improved with AL treatment as measured by change from baseline to week

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