

# 105 - Treatment refractory schizophrenia

## Treatment-refractory schizophrenia

108 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 Electroconvulsive therapy and psychosis Evidence from prospective RCTs and retrospective studies suggests that ECT augmentation of antipsychotic medication can have a beneficial effect on persistent positive symptoms in schizophrenia, including medication-resistant schizophrenia.<sup>1-7</sup> However, there is a relative lack of data on long-term effectiveness and efficacy, cognitive deficits and quality of life. A 2005 Cochrane systematic review<sup>8</sup> assessed RCTs that had compared ECT with placebo, sham ECT, non-pharmacological interventions and antipsychotic medication for patients with schizophrenia, schizoaffective disorder or chronic mental disorder. In studies where ECT was compared with placebo or sham ECT, more participants improved in the real ECT group and there was a suggestion that real ECT resulted in fewer relapses in the short term and a greater likelihood of being discharged from hospital. The review concluded that ECT combined with continuing antipsychotic medication is a valid treatment option for schizophrenia, particularly when rapid global improvement and reduction of symptoms are desired (for example, treating patients with a high risk of aggression or self-harm),<sup>9</sup> and where the illness has shown only a limited response to medication alone. A naturalistic, mirror-image study compared 2,074 people with schizophrenia on antipsychotic medication who had received ECT with a control group of patients prescribed continuing antipsychotic medication.<sup>10</sup> The rate of psychiatric hospitalisation over a 1-year post-treatment period decreased in those treated with ECT, but not in the control group. The effectiveness of ECT was more pronounced among those treated with clozapine or a medium to high antipsychotic dosage. Treatment-refractory schizophrenia The benefits and harms of adding ECT to standard care for people with TRS were examined in a 2019 Cochrane systematic review.<sup>6</sup> The investigators were able to reach the limited conclusion that the moderate-quality RCT evidence available suggested a positive effect for ECT on medium-term clinical response. It was noted that further evidence of better quality was required before a stronger conclusion could be made. Several studies have focused on ECT augmentation of antipsychotic medication for TRS.<sup>1-3,11,12</sup> For example, in a small sample of patients with TRS characterised by 'dominant negative symptoms', ECT augmentation of a variety of antipsychotic medications produced a significant decrease in symptom severity.<sup>13</sup> A 2016 meta-analysis of RCTs<sup>3</sup> in TRS that examined the efficacy of the combination of ECT and (non-clozapine) antipsychotic medication versus the same

antipsychotic medication as monotherapy found that the combination proved to be superior in terms of symptom improvement, study-defined response and remission rate. ECT augmentation of clozapine may be at least as effective as ECT augmentation of other antipsychotic medications, if not more so.<sup>4,12,14-16</sup> Response is probably unrelated to post-ECT changes in clozapine levels.<sup>17</sup> In a retrospective study<sup>1</sup> assessing the effectiveness and safety of the combination of clozapine and ECT in a sample of patients with TRS, almost two-thirds were responders (defined as a 30% or greater reduction in Positive and Negative Syndrome Scale [PANSS] total score).<sup>18</sup> Follow-up data on a sub- sample of these patients over a mean of 30 months revealed that the majority had

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