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Electroconvulsive Therapy for Treatment-Resistant Schizophrenia

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Background

Electroconvulsive therapy (ECT) involves the induction of a seizure by the administration of an electrical stimulus via electrodes usually placed bilaterally on the scalp and was introduced as a treatment for schizophrenia in 1938. However, ECT is a controversial treatment with concerns about long-term side effects such a memory loss. Therefore, it is important to determine its clinical efficacy and safety for people with schizophrenia who are not responding to their treatment.

Objectives

Our primary objective was to assess the effects (benefits and harms) of ECT for people with treatment-resistant schizophrenia. Our secondary objectives were to determine whether ECT produces a differential response in those treated with unilateral compared with bilateral ECT, long (more than 12 sessions) compared with a short course ECT, continuation compared with maintenance ECT, well-defined treatment-resistant schizophrenia compared to less well-defined treatment-resistant schizophrenia (who would be expected to have a greater affective component to their illness).

Search Methods

We searched the Cochrane Schizophrenia Group's Study-Based Register of Trials including clinical trial registries on September 9, 2015 and August 4, 2017. There were no limitations on language, date, document type, or publication status for the inclusion of records in the register. We also inspected references of all the included records to identify further relevant studies.

Selection Criteria

Randomized controlled trials investigating the effects of ECT in people with treatment-resistant schizophrenia.

Data Collection and Analysis

Two review authors independently extracted data. For binary outcomes, we calculated the risk ratio (RR) and its 95% confidence intervals (CIs), on an intention-to-treat basis. For continuous data, we estimated the mean difference (MD) between the groups and its 95% CIs. We employed the fixed-effect model for all analyses. We assessed risk of bias for the included studies and created "summary of findings" tables using the GRADE framework (table 1).

Main Results

We included 15 studies involving 1285 participants (1264 completers with an age range of 18–46 years) with treatment-resistant schizophrenia. We rated most studies (14/15, 93.3%) as at high risk of bias due to issues related to the blinding of participants and personnel. Our main outcomes of interest were: (1) clinically important response to treatment; (2) clinically important change in cognitive functioning; (3) leaving the study early; (4) clinically important change in general mental state; (5) clinically important change in general functioning; (6) number hospitalized; and (7) death. No trial reported data on death.

The included trials reported useable data for four comparisons: ECT plus standard care compared with sham-ECT added to standard care; ECT plus standard care compared with antipsychotic added to standard care; ECT plus standard care compared with standard care; and ECT alone compared with antipsychotic alone.

Table 1. Summary of Findings: ECT Plus Standard Care Vs Standard Care for Treatment-Resistant Schizophrenia

Patient or population: people with treatment-resistant schizophrenia
Settings: hospital
Intervention: ECT plus standard care
Comparison: standard care

Outcomes	Anticipated Absolute Effects[a] (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Quality of the Evidence (GRADE)	Comments
	Risk With Placebo (No Treatment)	Risk With ECT (Add-on)				
Response to treatment (medium term) Clinically important response to treatment as defined by each study Follow-up: 8–12 weeks	308 per 1000	635 per 1000 (539 to 746)	RR 2.06 (1.75 to 2.42)	819 (9 studies)	⊕⊕⊕⊖ moderate[b]	
Cognitive functioning (short term)—memory deterioration Follow-up: 3–4 weeks	0 per 1000	13 per 1000 (1 to 219)	RR 27 (1.67 to 437.68)	72 (1 study)	⊕⊖⊖⊖ very low[b,c,d]	Data for predefined outcome "clinically important change" not reported
Satisfaction and acceptability of treatment (medium term)—leaving the study early Follow-up: 8–12 weeks	23 per 1000	27 per 1000 (9 to 82)	RR 1.18 (0.38 to 3.63)	354 (3 studies)	⊕⊖⊖⊖ very low[a,d]	
Mental state (medium term)—total scores (BPRS, high = poor) Follow-up: 8–12 weeks	The mean mental state—average scores (BPRS, high = poor, medium term) was **33.4**	**MD 11.18 lower** (12.61–9.76 lower)	—	345 (2 studies)	⊕⊕⊖⊖ **Low**[b,c]	Data for predefined outcome "clinically important change" not reported
General functioning (medium term)—average scores (GAF, high = good) Follow-up: 12 weeks–6 months	The mean mental state—average scores (GAF, high = good, medium term) was **47.3**.	**MD 10.66 higher** (6.98–14.34 higher)	—	97 (2 studies)	⊕⊖⊖⊖ **very low**[b,c,e,f]	Data for predefined outcome "clinically important change" not reported
Service use—hospitalization	See comment	See comment	See comment	See comment	See comment	No studies reported this outcome, so there is no evidence to support or refute benefits of the intervention.
Adverse event/effect(s)—death	See comment	See comment	See comment	See comment	See comment	No studies reported this outcome, so there is no evidence to support or refute benefits of the intervention

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Note: BPRS, Brief Psychiatric Rating Scale; CI, confidence interval; ECT, electroconvulsive therapy; GAF, Global Assessment of Functioning; MD, mean difference; RR, risk ratio. GRADE Working Group grades of evidence. *High quality:* we are very confident that the true effect lies close to that of the estimate of the effect. *Moderate quality:* we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different. *Low quality:* our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect. *Very low quality:* we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]*The risk in the intervention group* (and its 95% confidence interval) is based on the assumed risk in the comparison group and the *relative effect* of the intervention (and its 95% CI).

[b]Downgraded by one level due to risk of bias: high risk of bias with blinding of participants and personnel.

[c]Downgraded by one level due to indirectness: scores from scale were employed as a surrogate index of the intended outcome.

[d]Downgraded by two levels due to imprecision: low event rate.

[e]Downgraded by one level due to heterogeneity.

[f]Downgraded by one level due to imprecision: small sample size.

For the comparison ECT plus standard care vs sham-ECT plus standard care, only average endpoint BPRS (Brief Psychiatric Rating Scale) scores from one study were available for mental state; no clear difference between groups was observed (short term; MD = 3.60, 95% CI = −3.69 to 10.89; participants = 25; studies = 1; *very low-quality evidence*). One study reported data for service use, measured as number readmitted; there was a clear difference favoring the ECT group (short-term; RR = 0.29, 95% CI = 0.10 to 0.85; participants = 25; studies = 1; *low-quality evidence*).

When ECT plus standard care was compared with antipsychotics (clozapine) plus standard care, data from one study showed no clear difference for clinically important response to treatment (medium term; RR = 1.23, 95% CI = 0.95 to 1.58; participants = 162; studies = 1; *low-quality evidence*). Clinically important change in mental state data was not available, but average endpoint BPRS scores were reported. A positive effect for the ECT group was found (short-term BPRS; MD = −5.20, 95% CI = −7.93 to −2.47; participants = 162; studies = 1; *very low-quality evidence*).

When ECT plus standard care was compared with standard care, more participants in the ECT group had a clinically important response (medium term; RR = 2.06, 95% CI = 1.75 to 2.42; participants = 819; studies = 9; *moderate-quality evidence*). Data on clinically important change in cognitive functioning were not available, but data for memory deterioration were reported. Results showed that adding ECT to standard care may increase the risk of memory deterioration (short term; RR = 27.00, 95% CI = 1.67 to 437.68; participants = 72; studies = 1; *very low-quality evidence*). There were no clear differences between groups in satisfaction and acceptability of treatment, measured as leaving the study early (medium term; RR = 1.18, 95% CI = 0.38 to 3.63; participants = 354; studies = 3; *very low-quality evidence*). Only average endpoint scale scores were available for mental state (BPRS) and general functioning (Global Assessment of Functioning). There were clear differences in scores, favoring ECT group for mental state (medium term; MD = −11.18, 95% CI = −12.61 to −9.76; participants = 345; studies = 2; *low-quality evidence*) and general functioning (medium term; MD = 10.66, 95% CI = 6.98 to 14.34; participants = 97; studies = 2; *very low-quality evidence*).

For the comparison ECT alone vs antipsychotics (flupenthixol) alone, only average endpoint scale scores were available for mental state and general functioning. Mental state scores were similar between groups (medium-term BPRS; MD = −0.93, 95% CI = −6.95 to 5.09; participants = 30; studies = 1; *very low-quality evidence*); general functioning scores were also similar between groups (medium-term Global Assessment of Functioning; MD = −0.66, 95% CI = −3.60 to 2.28; participants = 30; studies = 1; *very low-quality evidence*).

Authors' Conclusions

Moderate-quality evidence indicates that relative to standard care, ECT has a positive effect on medium-term clinical response for people with treatment-resistant schizophrenia. However, there is no clear and convincing advantage or disadvantage for adding ECT to standard care for other outcomes. The available evidence was too weak to indicate whether adding ECT to standard care is superior or inferior to adding sham-ECT or other antipsychotics to standard care. There was insufficient evidence to support or refute the use of ECT alone. Substantial good-quality evidence is needed before firm conclusions can be made. Full details are published in the Cochrane Review.[1]

Reference

1. Sinclair DJM, Zhao S, Qi F, Nyakyoma K, Kwong JSW, Adams CE. Electroconvulsive therapy for treatment-resistant schizophrenia. *Cochrane Database of Syst Rev.* 2019;(3):CD011847.