Combined use of electroconvulsive therapy and antipsychotics in schizophrenia: the Indian evidence. A review and a meta-analysis

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CRD summary
The review examined whether the combination of electroconvulsive therapy (ECT) and antipsychotic drugs was more efficacious than antipsychotic drugs alone in the acute phase treatment of schizophrenia. The authors concluded that ECT-antipsychotic combinations might be better than antipsychotic drugs alone in the first few weeks of treatment. The authors' conclusions were suitably cautious and are likely to be reliable.

Authors' objectives
To examine whether the combination of electroconvulsive therapy (ECT) and antipsychotic drugs was more efficacious than antipsychotic drugs alone in the acute phase treatment of schizophrenia.

Searching
EMBASE, PubMed and IndMED (Bibliographic database of Indian biomedical journals) databases were searched; search terms were reported. The authors also conducted a manual search of Indian psychiatric journals and Index Medicus. Additional studies were sought through checking all relevant reference lists.

Study selection
Inclusion criteria for participants were not specified, although it was clear that Indian studies of participants with schizophrenia were eligible for inclusion. Patients with a range of durations of illness and a variety of diagnostic classifications were used in the included studies.

Open trials and randomised controlled trials (RCTs) with data on efficacy of the ECT-antipsychotic combination were considered for the review. The antipsychotics used were either chlorpromazine, haloperidol or trifluoperazine, in a range of doses. Five of the included studies used sham ECT as part of the comparator group treatment. Numerous outcome measures were used in the included studies, the most common being the Brief Psychiatric Rating Scale (BPRS), which was used in six studies.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Studies were assessed for methodology in order to be considered for inclusion in the meta-analysis section of the paper. Six criteria had to be met. Studies had to: be a randomised, double-blinded and controlled study; have a minimum duration of three weeks; include only patients with schizophrenia diagnosed according to standardised operational criteria; compare the combination of ECT and antipsychotics with antipsychotics alone; use structured assessments for comparison (one had to be BPRS); have used antipsychotics in adequate doses (300 to 1,200 mg/day of chlorpromazine equivalents). Two authors independently assessed methodology.

Data extraction
It appeared that for the studies included in the meta-analysis the mean Brief Psychiatric Rating Scale scores and standard deviations for the intervention and comparator groups were extracted, along with the mean treatment difference with 95% confidence intervals (CI). Brief descriptive summaries of efficacy outcomes were extracted for all studies. The authors stated neither how the data were extracted for the review nor how many reviewers performed the extraction.

Methods of synthesis
A meta-analysis examining pooled mean differences (MD) was performed using a random-effects model, with studies weighted by inverse variance. Use of a funnel plot for assessing publication bias was inappropriate due to the small
number of studies. A standard $\chi^2$ analysis was used to examine heterogeneity among studies. A narrative synthesis was carried out for all included studies.

**Results of the review**
Eleven studies ($n=651$) were included in the review. Eight trials were RCTs ($n=343$) and three were open trials ($n=308$).

Four studies ($n=113$) were of sufficient methodological quality to be included in the meta-analysis. Treatment with the ECT-antipsychotic combination resulted in a statistically significant decrease in Brief Psychiatric Rating Scale score in the first four to five weeks of treatment (mean difference was 4.89, 95% CI:0.50 to 9.38, $p<0.05$).

Heterogeneity was observed to be statistically significant among studies ($\chi^2=8.48$, $p<0.05$). This became non-significant when one study that had not reported baseline Brief Psychiatric Rating Scale scores was removed from the analysis.

Results of the narrative synthesis suggested that the ECT-antipsychotic combination was more effective than antipsychotic drugs alone for just the first three to six weeks of treatment.

**Authors' conclusions**
ECT-antipsychotic combinations might be better than antipsychotic drugs alone in the first few weeks of treatment of schizophrenia.

**CRD commentary**
The review addressed a clear question and the inclusion criteria were appropriate, although not always explicit. Search dates and language restrictions were not reported and no attempt appeared to have been made to identify unpublished studies, so it was possible that some relevant studies could have been missed. In addition, methods used for selecting studies and extracting data were not reported, so it was difficult to comment on the risk of bias and errors being introduced during the review process. Sufficient details were provided of the included studies, although details of results for studies that did not form part of the meta-analysis were basic. Appropriate methods were used to pool the results and to investigate statistical heterogeneity. The meta-analysis combined studies using a variety of drugs, doses and durations of prior illness, which raised questions about the legitimacy of pooling data from clinically diverse trials. Despite restricting the meta-analysis to double-blind RCTs, the authors did not assess many areas of study quality (for example, use of a power calculation, the method of randomisation and reporting of losses to follow up) that would have been useful in interpreting results considering all the studies in the meta-analysis recruited fewer than 40 participants. The authors acknowledged some of the limitations of the review; in light of these, their conclusions were suitably cautious and are likely to be reliable.

**Implications of the review for practice and research**
**Practice:** The authors stated that ECT in conjunction with drugs could be used to reduce the period of hospital stay for some patients.

**Research:** The authors stated that there was a need for further trials to determine the usefulness of the ECT-antipsychotic combination in the treatment of schizophrenia, particularly in relation to long-term efficacy, stage of illness and use of second-generation antipsychotics.

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