Effects of general anesthetic agents in adults receiving electroconvulsive therapy: a systematic review

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CRD summary
The authors concluded that all of the available induction agents included in this review would be suitable for electroconvulsive therapy (ECT) as seizure duration was greater than 17 seconds; if the clinician wanted to prolong seizure duration, methohexital or a short-acting opioid should be considered. The review had some limitations that restricted the reliability of the authors’ conclusions.

Authors' objectives
To determine the differential effects of general anaesthetic induction agents on electroconvulsive therapy (ECT) induced motor and electroencephalogram seizure duration.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and PsycINFO were searched to December 2006 for articles in any language. Reference lists of retrieved trials were searched and specialist textbooks on ECT were handsearched. DARE was searched for published systematic reviews.

Study selection
Randomised controlled trials (RCTs) that compared induction agents with each other for ECT in adult patients (aged >18 years) diagnosed with major depression, schizophrenia, schizoaffective disorder or bipolar disorder were eligible for inclusion. Trials in individuals with concomitant Alzheimer's-type dementia, vascular dementia and Parkinson's disease were eligible for inclusion. Trials that compared an induction agent with no induction agent were excluded. Trials had to report the seizure duration and had to be of cross-over or parallel design.

The included trials studied the induction agents: propofol, methohexital, midazolam, thiopental, sevoflurane, etomidate, propanidid, methohexital-remifentanil, propofol-alfentanil, propofol-remifentanil thiopental-remifentanil, thiamylal and propofol-alfentanil. Mean age of the included patients, where reported, ranged from 27 to 74 years. Both unilateral and bilateral ECT were included. The number of ECT treatments ranged from 14 to 448.

Both authors independently reviewed all full-text articles for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Both authors independently assessed the method of randomisation, masking of study participants, concealment of allocation and completeness of trial data; disagreements were resolved by consensus.

Data extraction
Data were extracted on the primary outcome of seizure duration, both electroencephalogram (EEG) and clonic seizure activity in an isolated limb. Data were used to calculate weighted mean differences (WMD). Emergence time, recovery time, cardiac morbidity and adverse effects were extracted and used to calculate WMD or risk differences (RD) depending on data type. Missing data were requested from authors.

The authors did not state how many reviewers performed data extraction, but stated that disagreements were resolved by consensus (which indicated that both authors were involved in the process).

Methods of synthesis
Pooled WMDs and risk differences, together with 95% confidence intervals (CI), were calculated using a random-effects meta-analysis. Statistical heterogeneity was assessed using the $I^2$ statistic. Sensitivity analysis was conducted for study quality and other sources of clinical heterogeneity.
Results of the review

Forty-one RCTs were included in the review (n=1,134 patients): 31 cross-over design and 10 parallel design trials. Sample sizes of included trials ranged from seven to 58 patients. Trial quality was variable: 22 trials masked investigators and subjects; 10 trials reported the method of randomisation and only four trials adequately concealed allocation; and 20 trials adequately reported data.

**Motor seizure duration:** Mean seizure duration was significantly longer in the methohexital group compared with the propofol group (WMD 9.06 seconds, 95% CI 5.72 to 12.40; 11 trials). There was evidence of statistical heterogeneity ($I^2=79\%$). Mean seizure duration was not statistically different from methohexital compared with methohexital-remifentanil (three trials). When propofol was compared with etomidate, mean seizure duration was significantly longer in the etomidate group (WMD 9.50 seconds, 95% CI 2.41 to 16.60; three trials). There was evidence of statistical heterogeneity ($I^2=66\%$) for this comparison. When propofol was compared with propofol-alfentanil, mean seizure duration was significantly longer in the propofol-alfentanil group (WMD 12.57 seconds, 95% CI 8.63 to 16.51; three trials). There was evidence of statistical heterogeneity ($I^2=34\%$) for this comparison.

**EEG seizure duration:** Mean EEG seizure duration was significantly longer in the methohexital group compared with the propofol group (WMD 14.82 seconds, 95% CI 9.97 to 19.67; seven trials). There was evidence of statistical heterogeneity ($I^2=79\%$) for this comparison.

**Emergence Time:** Mean emergence time was not significantly different in the methohexital group compared with the propofol group (eight trials). There was evidence of statistical heterogeneity ($I^2=79.6\%$). When thiopental was compared with propofol, mean emergence time was significantly shorter in the propofol group (WMD 1.75 minutes, 95% CI 1.18 to 2.32; three trials). There was no evidence of statistical heterogeneity ($I^2=0\%$) for this comparison.

**Recovery Time:** Mean recovery time was not significantly different in the methohexital group compared with the propofol group (five trials). There was evidence of statistical heterogeneity ($I^2=64\%$). When propofol was compared with propofol-alfentanil, mean recovery time was not significantly different in the propofol group (three trials). There was evidence of statistical heterogeneity ($I^2=86\%$) for this comparison.

Further results were reported in the paper.

Authors’ conclusions

All of the available induction agents included in this review would be suitable for ECT as the seizure duration was greater than 17 seconds with all of the induction agents.

CRD commentary

Inclusion criteria for the review were well defined. Several relevant sources were searched without language restrictions. It appeared that unpublished data were not sought and so relevant unpublished studies may have been missed; publication bias was not assessed. Both authors appeared to be involved with study selection, data extraction and quality assessment, which should have minimised error and bias. A basic quality assessment was undertaken that was not based on a validated tool, but which indicated variable quality of the included trials. A random-effects meta-analysis was undertaken and statistical heterogeneity was explored, which was appropriate. The authors’ conclusions that any of the induction agents were suitable for ECT seemed reasonable assuming 17 seconds duration of seizure was clinically effective. However, the recommendation that when clinicians needed to prolong seizure duration, methohexital or a short-acting opioid should be added was based on the pooled results of a few variable quality small studies with notable clinical and statistical heterogeneity. Given these data limitations, the authors’ conclusions have to be viewed with some degree of caution and clinical judgment.

Implications of the review for practice and research

Practice: The authors stated that when a clinician needed to prolong seizure length, methohexital or the addition of a short-acting opioid to methohexital or propofol should be considered.
Research: The authors stated that future research should focus on improving methodological quality in an attempt to reduce the clinical heterogeneity of trial data.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.