Propofol versus methohexital for electroconvulsive therapy: a meta-analysis

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Authors' objectives
To search systematically for published, randomised controlled trials (RCTs) comparing propofol with methohexital for anaesthesia during electroconvulsive therapy (ECT). In addition, to critically appraise the data, to combine the data from independent trials, and to quantify any difference in efficacy and harm between these two hypnotics.

Searching
MEDLINE, Excerpta Medica and the Cochrane Library were searched for publications in any language, using the following free text terms alone and in combination: 'propofol', 'methohexital', 'epilepsy', 'electroconvulsive shock' and electroconvulsive therapy'. The reference lists of retrieved reports and review articles were also checked.

Study selection

Study designs of evaluations included in the review
The authors' inclusion criteria specified RCTs. Eleven of the fifteen included trials were of a crossover design. Review articles and abstracts from scientific meetings were not considered.

Specific interventions included in the review
The authors' inclusion criteria specified studies in which propofol was compared with methohexital for use in ECT. In the included studies, the mean dose and mean duration of anaesthesia (where reported) for propofol ranged from 0.75 to 2.4 mg/kg and from 6.6 to 19 minutes, respectively. The corresponding values for methohexital were 0.75 to 1.4 mg/kg and 8.1 to 19 minutes, respectively.

Participants included in the review
The authors did not specify any inclusion criteria relating to the characteristics of the participants. Studies performed in animals were excluded.

Thirteen of the 15 included studies reported the gender of the participants; 63% of the total population were women and 37% were men. Eleven studies mentioned the underlying disease of patients: all 11 studies included depressive patients, whereas 4 also included psychotic patients. Concomitant antidepressive treatment and/or neuroleptica were reported in 6 and 4 trials, respectively.

Outcomes assessed in the review
The authors did not specify any inclusion or exclusion criteria relating to the outcomes. However, it was stated that the end points of primary interest were the duration of motor seizure, the duration of anaesthesia, improvement of the underlying disease at the end of the ECT sessions, and adverse drug reactions.

The duration of motor seizure was defined as the time from electroshock application to the end of the manifest clonic phase; ECT-related motor seizures were observed using the isolated limb method. The duration of electroencephalographic seizure activity was defined as the time from stimulus to postictal electroencephalogram (EEG) suppression. The duration of anaesthesia was defined as the time from drug administration to the eye opening.

How were decisions on the relevance of primary studies made?
The retrieved reports were screened for relevance by one author.

Assessment of study quality
The methodological validity of the included studies was assessed using the 3-item, 5-point Oxford score as described by Jadad et al. (see Other Publications of Related Interest no.1). All authors independently scored all the included trials for
methodological validity, and any disagreements were resolved by consensus.

**Data extraction**
The data were extracted from the included studies by one author, with the other two authors assessing the adequacy of the data extraction process. Data were extracted on the patients’ characteristics, the propofol and methohexital regimens, any concomitant drugs, and the end points of interest.

**Methods of synthesis**

How were the studies combined?

Narrative and quantitative syntheses were undertaken. The weighted mean differences were calculated for continuous data (duration of seizures and duration of anaesthesia), along with 95% confidence intervals (CIs). The dose effects (association between the dose and the duration of seizure or anaesthesia) for both hypnotics were tested using a variance-weighted regression analysis of the natural logarithm of time for each study (see Other Publications of Related Interest no.2). The data synthesis was performed using a fixed-effect model (see Other Publications of Related Interest no.3) when the data were homogeneous (P greater than 0.1), and a random-effects model (see Other Publications of Related Interest no.4) when the data were not.

How were differences between studies investigated?
The authors do not state a method for assessing any differences between the studies.

**Results of the review**

Fifteen RCTs with a total of 706 participants, which compared propofol (349 participants) with methohexital (357 participants), were included.

The mean duration of seizures with propofol was significantly shorter than that with methohexital: the weighted mean difference (fixed-effect model) was 8.4 seconds (95% CI: 6.6, 10.0) for motor seizure, and 14.3 seconds (95% CI: 10.8, 17.8) for EEG seizure activity. For both hypnotics, the variance-weighted regression analysis of the natural logarithm of duration of seizure against dose did not indicate a clear correlation (r²) for either motor seizure (propofol, r²=0.25, P=0.08; methohexital, r²=0.11, P=0.27) or EEG seizure activity (propofol, r²=0.00001, P=0.99; methohexital, r²=0.21, P=0.25).

There was no significant difference in the duration of anaesthesia between propofol and methohexital: the weighted mean difference was 0.25 minutes (95% CI: 0.35, 0.85). For both hypnotics, the variance-weighted regression analysis of the natural logarithm of duration of anaesthesia against dose did not indicate any correlation (propofol, r²=0.00004, P=0.99; methohexital, r²=0.03, P=0.63). Three trials reported on improvement of the underlying disease at the end of an ECT series. One of these reported that a significantly greater number of participants showed improvement with propofol (86%), compared with those receiving methohexital (59%). Fourteen trials reported qualitatively on respiratory adverse events, e.g. hypoventilation; this was shown to occur with both hypnotics. Five trials reported adverse cardiovascular events. Qualitatively, there was on average a smaller increase in blood-pressure with propofol than with methohexital. One report described pain on injection with propofol.

**Authors’ conclusions**

Propofol and methohexital are appropriate anaesthetics for patients undergoing ECT. There was little evidence of an association between dose and seizure duration with either hypnotic. Although propofol was associated with an improved outcome in two small reports, it is unknown whether that relation was causal. The duration of motor and EEG seizure activity is likely to be a surrogate end point for the efficacy of ECT; these end points should not be used in future assessments.

**CRD commentary**
The review question was clearly defined, and the inclusion and exclusion criteria were specific in terms of the study
design and interventions. However, the population of interest was not defined, and although the outcomes of interest were defined, these were not used as inclusion or exclusion criteria.

The search strategy presented was adequate for the retrieval of published literature. However, the authors made no attempt to identify any unpublished data and did not assess potential publication bias.

The authors reported the use of a published, validated scoring system to assess the methodological quality of the included studies. However, it was unclear whether the results of this assessment were used to either exclude studies of low quality, or to give differential weight to those studies included in the analysis.

The treatment regimens and outcome measures used in the included studies were reported in detail, in tabular form. Details of the characteristics of the participants were sparse, although it was apparent that there was a variety of disease states and some concomitant treatments. This, together with the small sample size and generally poor quality of the included studies (median Oxford validity score = 2), casts doubt upon the generalisability of the review's findings to patients undergoing ECT.

In general, the included primary studies were appropriately combined and the results were clearly reported. However, there was an apparent error in the reported weighted mean difference and CI for the duration of anaesthesia. In addition, although the authors reported that a fixed-effect model was used where the data were homogeneous and a random-effects model where they were not, no method for assessing between-study heterogeneity was reported. The shortcomings of the included studies were highlighted. Overall, the authors' conclusions follow from the results as reported, and are suitably cautious given the nature of the available evidence.

**Implications of the review for practice and research**

**Practice:** The authors did not make any specific recommendations for practice based upon the current findings.

**Research:** The authors state that the research agenda must include trials investigating the impact of anaesthetic drugs on psychiatric outcome after ECT. There is a lack of data on the long-term outcome.

Data on drug-related adverse affects are needed for rational decision-making. Additional research is required to identify valid markers for psychiatric outcome during and after ECT.

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**Other publications of related interest**


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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.