Repetitive transcranial magnetic stimulation versus electroconvulsive therapy in severe depression

The clinical effectiveness and cost of repetitive transcranial magnetic stimulation versus electroconvulsive therapy in severe depression: a multicentre pragmatic randomised controlled trial and economic analysis

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Executive summary

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Executive summary

Background

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive brain stimulation technique that can be used to target neuronal circuitry implicated in neuropsychiatric disorders, such as the dorsolateral prefrontal cortex (DLPFC) in depression. rTMS has been reported to be as effective as electroconvulsive therapy (ECT), which is currently the most powerful treatment available for severe depression.

Objective

The aim of this study was to investigate if rTMS was as effective as ECT in treating major depressive episodes and to perform a cost-effectiveness analysis.

Methods

Design

The study was a single-blind pragmatic multicentre randomised controlled trial (RCT) with 6 months of follow-up to test equivalence of rTMS with ECT.

Setting

The study took place in the South London and Maudsley NHS Trust and Pembury Hospital in the Invicta Mental Health Trust in Kent.

Participants

Right-handed adult patients referred for ECT for treatment of a major depressive episode (DSM-IV) were assessed. During the 2.5-year trial period, 260 patients were referred for ECT, of whom 46 entered the trial. The main reason for not entering the trial was not consenting to ECT while being formally treated under the UK Mental Health Act 1983.

Interventions

Patients were randomised to receive a 15-day course of rTMS of the left DLPFC (n = 24; 20 trains per day, 5 seconds of treatment at 10 Hz, 110% of motor threshold) or a course of ECT (n = 22; stimulus dosing method, 1.5 times the seizure threshold, course length decided by referring physician).

Main outcome measures

Patients were assessed before randomisation, at end of treatment and at the 6-month follow-up. Primary outcome measures were the 17-item Hamilton Rating Scale for Depression (HRSD) and proportion of remitters (defined as HRSD score $\leqslant$8) at the end-of-treatment time point. Secondary outcomes included self-ratings for mood on the Beck Depression Inventory-II (BDI-II) and visual analogue mood scales (VAMS), the Brief Psychiatric Rating Scale (BPRS), plus subjective and objective side-effects. Low scores on the BDI-II, VAMS and BPRS are positive in terms of health. The results were analysed on an intention-to-treat basis. Cost data were collected using the Client Service Receipt Inventory and the Short Form with 36 Items (SF-36) was used to obtain quality of life measures. Health economic outcomes were cost of treatments, costs incurred during the 6-month follow-up period and gains in quality-adjusted life-years (QALYs).

Data analysis

HRSD and other clinical outcome scores were compared between groups using an analysis of covariance (ANCOVA) model with baseline scores as covariates. Trial data that became available before recruitment began allowed revision of samples sizes such that 22 subjects per treatment group would be sufficient to have 80% power to demonstrate, using a one-sided equivalence test at the $\alpha = 0.5$ level, that the mean reduction in HDRS score using rTMS would be no more than 25% less than that achieved using ECT.

Results

One patient was lost to follow-up at end of treatment and another eight at 6 months. The end-of-treatment HRSD scores were lower for ECT [95% confidence interval (CI) 3.40 to 14.05, p = 0.002], with 13 (59%) achieving remission compared with four (17%) in the rTMS group (p = 0.005). However, HRSD scores did not differ

between groups at 6 months. BDI-II, VAMS and BPRS scores were lower for ECT at end of treatment and remained lower after 6 months. Improvement in subjective reports of side-effects following ECT correlated with antidepressant response. There was no difference between the two groups before or after treatment on global measures of cognition.

Although individual treatment session costs were lower for rTMS than ECT, the cost for a course of rTMS was not significantly different from that for a course of ECT as more rTMS sessions were given per course. Service costs were not different between the groups in the subsequent 6 months but informal care costs were significantly higher for the rTMS group ($p = 0.04$) and contributed substantially to the total cost for this group during the 6-month follow-up period. There was also no difference in gain in QALYs for ECT and rTMS patients. Analysis of cost-effectiveness acceptability curves demonstrated that rTMS has very low probability of being more cost-effective than ECT.

Limitations

Rater blinding was not maintained and is a potential source of bias. However, similar results were obtained on both observer- and self-rated measures. The optimal parameters for administering rTMS to achieve an antidepressant effect are not yet known.

Conclusions

ECT is a more effective and potentially cost-effective antidepressant treatment than 3 weeks of rTMS as administered in this study. Optimal treatment parameters for rTMS need to be established for treating depression. More research is required to refine further the administration of ECT in order to reduce associated cognitive side-effects while maintaining its effectiveness.

Recommendations for further research

There is a need for large-scale, adequately powered RCTs comparing different forms of ECT. The next generation of randomised trials of rTMS should also seek to compare treatment variables such as stimulus intensity, number of stimuli administered and duration of treatment, with a view to quantifying an effect size for antidepressant action.

Publication

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NIHR Health Technology Assessment Programme

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The research reported in this monograph was commissioned by the HTA Programme as project number 98/11/04. The contractual start date was in August 2001. The draft report began editorial review in September 2005 and was accepted for publication in February 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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