

The study's pilot design has several limitations. The sample size was small and excluded detained patients. A substantial number of drop-outs occurred, but these were not excessive in light of the sample's morbidity. The sealed envelope technique is a simple, though not entirely reliable method of randomisation, but it produced broadly comparable groups. It is uncertain whether improved knowledge scores were specifically due to the structured consent process as enthusiasm and time spent were not adequately controlled for, however pre-ECT, 87% of the control group patients were satisfied with the information received. Multiple raters were used but the questionnaire demonstrated good inter-rater reliability on a stringent measure.

We feel that a further study is justified and allowing for drop-outs, it is estimated that approximately 50 patients in each group would be required to give the study 80% power to detect a two-point difference in knowledge scores post-ECT between structured and routine consent procedures at a 5% level.

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# Onset of clinical improvement of depressive illness following electroconvulsive therapy

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**Aims and method** To examine the onset and course of clinically observable improvement in patients receiving electroconvulsive therapy (ECT). A prospective design

was used in which 19 consecutive patients receiving ECT were followed up from commencement to termination of ECT. The Clinical Global Improvement

Scale was administered at every ECT session to monitor their improvement.

**Results** Eleven of the 19 subjects improved minimally and another subject improved substantially after the first two ECT treatments.

**Clinical implications** ECT produces clinically observable improvement in depression within a few days of starting treatment, perhaps earlier than is generally acknowledged.

Knowing the onset of antidepressant effect of electroconvulsive therapy (ECT) would be of potential clinical importance in advising patients and relatives and in designing a treatment package for patients. There is a dearth of literature on the subject of the time taken for ECT to begin to exert antidepressant effect. The important methodological issues for evaluating the onset of antidepressant effect of antidepressant drugs have been highlighted by Hackett (1998). In his review of the subject, he pointed out that few, if any, studies have specifically set out as their primary aim that of evaluating the onset of action. Nevertheless, antidepressant drugs are known to have a latent period of about two weeks during which little or no clinical improvement is expected, although this has recently been questioned. ECT is believed to have a rapid onset of antidepressant activity although there has been limited investigation in this area (Nobler *et al.*, 1997). Dinan & Barry (1989), compared lithium augmentation with supplementary treatment with ECT in people who did not respond to adequate treatment with tricyclic antidepressant. They found that improvement (measured by a drop in Hamilton Depression Rating Score (Hamilton, 1960)) became apparent after four ECT treatments but the lithium augmentation group had earlier onset of improvement. This report was based on a small sample of 30 subjects with only 15 subjects in the ECT group.

Extensive Medline and Psychlit searches generated only two other papers relating to this subject. Segman *et al.* (1995) randomised 47 subjects to three times a week ECT therapy and twice a week treatment plus one sham session. They observed the onset and time course of the antidepressant effects. 'Rapid' improvement was observed in the three times a week group. Substantial improvement (defined as 30% reduction in Hamilton Depression Rating Score) occurred after 3.2 (95% CI 1.3–5.1) ECT sessions. Although the time of onset of the antidepressant activity of ECT was not the primary focus of their study, they observed that among responders in both groups 29.5% of the overall improvement was gained during the first ECT and 60% during the first four ECTs. These results point to the fact that patients receiving ECT may begin to improve

earlier than is generally acknowledged. Rodger *et al.* (1994) reviewed the files of 124 patients who had taken part in an ECT research programme at the Royal Edinburgh Hospital since 1985. Of the 124 subjects in their series, only 11 subjects met the inclusion criteria to provide the data that were then re-analysed. They found that the first three sessions of ECT contribute significantly to the total improvement attributable to ECT.

## Methods

The study, a pilot project, was designed as a real time longitudinal study. All consecutive patients prescribed ECT at the City General Hospital, Stoke-on-Trent during the study period were included. The ECT suite is approved by the Royal College of Psychiatrists and the ECT machine is a modern machine, Thymatron-DG, which has facilities for electroencephalogram monitoring and automatic recording of the seizure duration. The machine has been found to be 99–100% reliable in producing seizures (di Michele *et al.*, 1992).

The ECT nurses at the City General Hospital are qualified mental health nurses with many years of experience. They attend every ECT session and see every patient at each treatment session. We practised using the Clinical Global Impression Scale (CGI; Guy, 1976) and agreed on what constituted each level of improvement before starting the study. At least two of us had to agree on the assessment of the severity of depression of each patient and the improvement gained during treatment.

The subjects were included regardless of the age or severity of depression, presence of psychotic features or somatic syndrome. For patients undergoing a second course of ECT during a single episode of hospitalisation, only the data from the first course of ECT are included in this report. The outcome variable of interest is any clinically observable change in depressive state as measured by the CGI. Observable change is defined as 'minimal improvement' if the assessment of improvement is recorded as 'improved' on the CGI and 'substantial' if 'much improved' is recorded on the CGI. The study was approved by the local research ethics committee.

There was no requirement that other antidepressants be stopped before entering the study. Over the pilot period of this study, 19 patients satisfied the inclusion criteria and are reported here.

## Procedure

Every patient prescribed ECT by the responsible medical officer was seen by our research team shortly before the ECT was started to record the

baseline severity of illness. The machine setting equivalent to the age of the patient as recommended by the manufacturers was used in all cases reported here. This obviates the need for complicated dosing strategy and calculation of threshold stimulus. This machine uses normative data to automatically determine the threshold stimulus and it employs a brief square wave stimulus rather than sine wave stimulus.

In all cases, we used bilateral electrodes held in place by the treating doctor and the ECT nurse presses the treatment button to deliver the current after testing for impedance. The protocol procedure is that should there be no seizure, the dose of the current would be increased by 20% and a second and final treatment given. However, there was no need to give a second treatment to any of the subjects reported here because all of them had central seizure exceeding 20 seconds.

The subjects were then followed up for the duration of the course of ECT and during each ECT session the clinical improvement was recorded just before another treatment was given.

## Results

Data were collected fully for 19 subjects for this report. Five were males and 13 were females, a ratio of 1:2.6. All subjects were in-patients except one female subject who was treated as an out-patient.

The global severity of illness on the CGI Scale at the start of ECT showed that one subject was mildly ill, eight were moderately ill and 10 were markedly or severely ill. The global clinical improvement on the CGI Scale showed that seven patients gained minimal improvement after the first ECT, and a further five patients, gained minimal improvement after two ECTs. Three patients improved substantially after the third treatment. Thus 12 of our 19 patients recorded some improvement after two ECTs although most of them improved only minimally.

Of the 10 patients who were markedly or severely ill at the outset, three showed minimal improvement after the first ECT compared with four of the nine subjects who were moderately or mildly ill.

## Discussion

To the best of our knowledge, this is the first prospective study of the onset and time course of antidepressant activity of ECT. We found that some patients receiving ECT began to show minimal improvement after the first ECT session (seven of our 19 subjects). After two ECTs 12 of our 19 subjects improved minimally or substantially. These findings accord with available empirical data on ECT. Like Rodger *et al* (1994) we found that the first few ECT sessions probably contribute

substantially to the improvement accumulated during the whole course of ECT. However, our report is the first prospectively collected data to show that patients begin to respond to ECT as early as the second ECT treatment.

We also found that the proportion of the less severely ill patients who responded to ECT was similar to that of the more severely ill. It is generally accepted that ECT is indicated for the greater degrees of depressive disorders manifesting with delusions and psychomotor retardation, which presumably do better with ECT. This originated from the experiences in the early 1940s when the main indication for shock therapy was depression with 'endogenous features', delusions and psychomotor retardation. More recently however, Sobin *et al* (1996) produced evidence to show that the lesser degrees of depression without delusions or psychomotor retardation, responded almost equally well to ECT. Our findings, from a prospective study, agree with their conclusion that was based on reanalysis of a combined data from their two previous studies, that ECT is a viable treatment option for patients with a major depressive disorder regardless of the presence or absence of delusions or retardation.

Being a pilot study, the sample size is small and therefore the precision of our estimates is low. This limitation will be avoided in the main study, which is designed with sequential analysis and will be continued until enough subjects have been recruited. On the basis of our current estimate of 36.68% improving minimally after the first ECT and with a precision of 10%, that is, a standard error of 0.05, the calculated sample size for such a study is about 92 subjects.

The effect of concurrent antidepressant medication is a serious confounding factor. It is difficult to eliminate this confounder unless a very large sample size can be recruited such that the subjects can then be stratified into various concurrent antidepressant subgroups for further analysis. Alternatively, matching different antidepressants and those without antidepressants can be used to eliminate this confounder.

Having acknowledged the confounder potential of concurrent antidepressant medication, it can be argued that this project has been conducted in the real world of clinical situation. Anecdotal clinical experience suggests that it is unusual for patients to be started on ECT without concurrent antidepressant medication. The Royal College of Psychiatrists recommends that it is best to continue established antidepressants through the course of ECT. Furthermore, there is no evidence for a synergistic effect between ECT and (tricyclic) antidepressants (Curran & Freeman, 1995). Thus, our study can be regarded as the study of effectiveness of ECT in clinical settings

rather than the more hypothetical study of efficacy under experimental conditions.

The real time prospective nature of our design with assessment twice a week to minimise bias. Second, we used the same raters throughout the study to assess our subjects thereby eliminating inter-rater bias. All the assessments were carried out just before each ECT was administered thus ensuring that all the antidepressant activity produced by any number of ECT was correctly attributed. Finally we used a simple scale for this pilot study, the CGI scale, an instrument that has face validity and that is widely used in clinical research. It has been demonstrated that CGI scale has the same responsiveness as other depression rating scales during the initial improvement phase of antidepressant therapy (Lauge *et al.* 1998).

### Conclusions

Our pilot study of the onset of antidepressant activity of ECT produced crude estimate of the time onset of clinical improvement after ECT treatment. There are a few limitations but useful inferences can be drawn from this study.

- (a) The issue of the time course of improvement following ECT treatment needs further investigation, preferably using a prospective design. A more extensive study is planned with a larger sample size but using, in addition, the Hamilton Rating Scale and the Montgomery and Asberg Depression Rating Scale, to monitor improvement.
- (b) ECT probably begins to exert antidepressant effect earlier than is generally appreciated, perhaps even from the first treatment.
- (c) About 63% of our patients recorded some improvement after two ECTs.

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