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Negative Interaction between Lithium and Electroconvulsive Therapy – A Case-Control Study

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Background. Concurrent use of lithium and ECT is suspected to increase neurotoxicity.
Method. A retrospective case-control study over an eight-year period was conducted to investigate the adverse effects of a combined lithium/ECT treatment. Thirty-one subjects with combined lithium/ECT treatment were compared with a control group (ECT only) of 135 cases matched for age and sex.
Results. Most cases in both groups had no adverse effects. Three (10%) study group subjects and 15 (11%) controls experienced brief delirium. Three controls and none of the subjects developed a prolonged confusion. There were no significant differences in the profile of other adverse effects between the two groups.
Conclusion. Prescription of lithium together with ECT was not associated with higher frequency of adverse effects.

Lithium has been implicated in the causation of acute, reversible, delirious states after ECT, variously characterised by confusion, disorientation, mutism, and seizures. There are at least five published studies and nine reports with conflicting results.

Small *et al* (1980) conducted a retrospective controlled study on a group of 250 patients receiving ECT over a four year period, of which 25 were concurrently taking lithium. Their comparisons revealed that patients on lithium more often experienced memory loss and atypical neurological findings than the controls. Coppen *et al* (1981) conducted a double-blind prospective study in which 18 patients were prescribed lithium while receiving ECT, and did not observe any complication. Kukopulos *et al* (1988) evaluated the efficacy and side-effects of ECT combined with lithium in 256 patients, in comparison with 130 patients who received ECT alone. They reported no differences in efficacy or adverse effects between the two groups. Penney *et al* (1990) compared three groups of patients using a retrospective design, consisting of: 27 patients receiving concurrent ECT and lithium, 100 patients receiving ECT alone, and a third group of patients receiving lithium within 24 hours prior to ECT or within 48 hours post-ECT. There was no significant difference between these groups in the total incidence of complications. O'Brien & Berrios (1993) retrospectively studied a cohort of 66 subjects concurrently receiving ECT and psychotropic drugs. Among six subjects receiving lithium, they did not observe any complications.

We were unable to find suitable cases over a two year period to conduct a prospective study and therefore opted for a retrospective design. Our aim is to resolve the dilemma as to whether there are any deleterious effects when ECT and lithium are used together.

Method

Case notes of all patients receiving ECT at Hayes Grove Priory Private Hospital in Kent between December 1983 and 1991 were reviewed. ECT was given twice-weekly using Ectron machines. The number and laterality of ECT were decided by the treating psychiatrists.

The first author reviewed the case notes and recorded the demographic characteristics, diagnoses, psychotropic drugs given with the ECT, serum lithium level, number and laterality of ECT, nature and duration of adverse effects, treatment response, and the length of stay in hospital.

Subjects

Among 214 cases receiving ECT, only 31 received lithium concurrently and constituted the study group (lithium and ECT). From the remaining 183 cases, 135 cases were selected after matching for sex, and age within three years, and these formed

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the control group (ECT only). Data were analysed using the SPSS statistical package.

Results

There were 31 cases in the study group with an age range of 20–80 years (mean = 51, s.d. = 16.7); 11 men and 20 women. Among 135 controls with an age range of 21–81 years (mean = 49, s.d. = 13.5), 49 were men and 86 women.

There were more cases ($n = 118$, 87%) of unipolar depression and fewer of bipolar depression ($n = 3$, 2%) in the control than in the study group ($n = 19$, 61% and 7, 23% respectively). Both groups of patients received a similar number of ECTs (mean = 7, range 3–18 in the study group; mean = 7.4, range 1–18 in the control group). However patients in the control group received a higher proportion of unilateral ECT (12%) compared to only 7% of subjects in the study group. About 75% of patients in both groups received bilateral ECT.

Serum lithium levels ranged from 0.2 to 1.9 meq/l (mean = 0.69, s.d. = 0.35), and were below 1.2 meq/l in all cases except one.

Adverse effects

Table 1 shows the nature and proportion of adverse effects experienced by patients in both groups. Only seven cases (23%) in the study group and 33 (24%) in the control group developed any side-effects. The difference in the frequency of adverse effects between study and control groups was not significant.

Bilateral ECT was associated with a relatively higher proportion of adverse effects in both study and control groups than unilateral ECT.

Five (26%) out of 19 subjects and 12 (43%) out of 58 controls encountered adverse effects while receiving less than six ECTs, whereas two (17%) of 12 subjects and 21 (27%) of 77 controls who received more than six ECTs developed adverse effects.

Discussion

A comparison of data in the lithium and ECT group (subjects) and the ECT only group (controls) suggest no difference in the frequency of adverse effects in our study. There were no incidents of prolonged confusion on combined treatment, and only 10% of subjects and 11% controls experienced brief confusion (< 24 hours).

Our findings are similar to those reported by Coppen *et al* (1981) and Kukopulos *et al* (1988), but inconsistent with those observed by Small *et al* (1980) and Penney *et al* (1990). Further analyses of Small's data reveal that in their series of subjects 9% had mild confusion and 70% had moderate or severe confusion, whereas among controls, 30% (higher than study group) had mild confusion and only 26% experienced moderate or severe confusion and memory loss. Their findings, therefore, differed from ours only for prolonged confusion. Penney's group also found a trend toward a higher percentage of confusion and other complications in the patients receiving concurrent lithium and ECT. These findings do not invalidate the many published case reports on a neurotoxic interaction (e.g. Ahmed & Stein, 1987), but suggest that such reactions are rare, possibly idiosyncratic, as they were not detected in an appreciable number in this series.

Although El-Mallakh (1988) has warned against using lithium and ECT concurrently, there are patients for whom this combination may be necessary, for example this combination may prevent ECT-induced switch to mania in rapid

Table 1
Number (percentage) of patients showing adverse effects associated with different types of ECT

Adverse effects	Unilateral ECT		Bilateral ECT		Mixed ECT	
	Study	control	Study	control	Study	control
	n=2 (%)	*n*=16 (%)	*n*=24 (%)	*n*=101 (%)	*n*=5 (%)	*n*=18 (%)
None	2(100)	14(88)	18(75)	76(75)	4(80)	12(67)
Confusion (<24 hr)	0	0	2(8)	12(12)	1(20)	3(17)
Confusion (>24 hr)	0	1(6)	0	1(1)	0	1(6)
Others	0	1(6)	4(16)	12(12)	0	2(11)
χ^2 test (d.f.=2) Pearson value	0.28		2.95		0.96	
Significance (*P*)	0.87		0.81		0.92	

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cyclers and for patients who are unresponsive to other measures. Mukherjee (1993), in a comprehensive review, supports Rudorfer *et al* (1987) and Schou (1991), and concludes that "the hazards of this combination treatment may have been overestimated", and recommends its use as an alternative treatment strategy where conventional methods have failed.

Further research, using a prospective design, and sensitive measure of confusional state, is required to replicate these observations before drawing any firm conclusion.

Clinical implications

- The combination of ECT and lithium is safe in routine clinical practice.
- Adverse effects during a course of ECT and lithium are no greater than with ECT alone.
- The combination of ECT and lithium may be justified in selected cases.

Limitations

- Retrospective design of the study.
- Small number of cases in the study group.
- Lack of sensitive measures for seizure duration and confusional state.

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