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EVIDENCE BASED GUIDELINES AND THE CONTEXT OF CARE: THE CASE OF E.C.T FOR PEOPLE WITH SCHIZOPHRENIA

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Practice guidelines that are based on best evidence are useful for clinicians and consumers. The guidelines published from time to time by the National Institute of Clinical Excellence (NICE) in the UK have a reach far beyond their intended sphere of influence in the UK. Un- fortunately, the NICE guidelines on Electroconvulsive Therapy (ECT) do not recommend that ECT be used for people with schizophrenia (except catatonia, which may be also result from other disorders).1 This guidance was based on the results of two systematic reviews2, 3, one of which has subsequently been updated4. This guidance contrasts with the recommendations of professional bod- ies that cite schizophrenia as an indication for ECT5,6 and the results of surveys of practice that demonstrates that schizophrenia continues to be a common indication for the use of ECT in India7.

The NICE guidelines are based on the results of systematic reviews and meta-analysis of randomized con- trolled trials (RCTs) and as such are superior to the rec- ommendations published by the American Psychiatric Association5, and the Royal College of Psychiatrists6, that based recommendations only from a search of Medline and did not attempt a quantitative synthesis. The results of the survey of practice7 suggests that the NICE guide- lines have not rung a death knell for the use of ECT for people with schizophrenia, either because people in India (and possibly Pakistan) have not heard of the NICE guidelines or are less influenced by them then their own clinical experience or other recommen- dations.

The reasons for this disconnection between guide- lines and practice may lie in the belief in the former that more evidence may be needed before ECT is recom- mended for those with schizophrenia or the conviction in the latter instance that the context of care in the coun- tries producing these guidelines differs from those where ECT continues to be commonly used for those with

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schizophrenia. It is my contention that both reasons are involved.

The Cochrane systematic review on ECT in schizo- phrenia4 concluded that, “The evidence in this review sug- gests that ECT, combined with treatment with antipsy- chotic drugs, may be considered an option for people with schizophrenia, particularly when rapid global im- provement and reduction of symptoms is desired. This is also the case for those with schizophrenia who show limited response to medication alone. Even though this initial beneficial effect may not last beyond the short term, there is no clear evidence to refute its use for people with schizophrenia. The research base for the use of ECT in people with schizophrenia continues to expand, but even after more than five decades of clinical use, there remain many unanswered questions regarding its role in the management of people with schizophrenia”. The NICE guidelines were based on earlier versions of this review3 that had included fewer studies and that had not clearly endorsed the use of ECT in schizophrenia; these guidelines are to be updated soon and it is hoped that the revised NICE guidelines will reflect the recommen- dations of the updated review. Science is cumulative and evidence based guidelines ought to reflect this.

Contextualizing research evidence is at the heart of evidence informed clinical practice and the NICE guidelines rejected evidence from trials where people with schizophrenia who had not responded to antipsychotc medication were given ECT before a trial of clozapine; in the UK people schizophrenia who do not respond to antipsychotics are likely to be tried on clozapine before ECT is considered (if at all). In our clini- cal context the reverse is likely to be true, underscoring the need to develop treatment algorithms that are ap- propriate to clinical situations where ECT may be pre- ferred in people for whom clozapine is not a viable op- tion or who had limited options to begin with.

However, the fact remains that in spite of contin- ued clinical use in the Indian subcontinent, more research evidence from RCTs is required if the continued use of ECT is to rest on the secure research base that exists for its use in depressive disorders8. The latest update of the Cochrane review on ECT for those with schizophrenia3 included 50 reports of 26 trials conducted in eight coun- tries on four continents (Africa, Asia, Europe and North America), with the majority of the trials originating in two Asian countries, India and Thailand; these trials random-

ized 798 participants to ECT. Trials in this review spanned five decades, and it is not surprising that there was con- siderable variation in research design, trial quality, qual- ity of reporting, and methods of administering ECT.

When ECT, with or without antipsychotic drugs, was compared with placebo or sham ECT, meta-analysis of data from 10 RCTs involving 392 people showed that more people improved in the real ECT group (pooled weighted relative risk 0.76; 95% confidence intervals

0.59 to 0.98). This indicates that 6 people would need to be given ECT to demonstrate improvement in one per- son over sham ECT (NNT 6; 95% CI 4 to 12). This advan- tage of ECT appears largely to lie in a more rapid im- provement in symptoms, but there is insufficient evidence to indicate that this advantage over sham ECT, with or without concurrent antipsychotics, persists beyond the initial six to eight weeks. However, this is similar to the effect of ECT in the treatment of depressive disorders, where ECT is recommended for short term improvement in acute symptoms,1,2,5 and prevention of relapses re- quires continued medication that may not always pre- vent relapses, especially in those with prior medication resistance.9

When ECT was directly compared with antipsy- chotic drug treatments, meta-analysis of data from 3 RCTs involving 175 participants favored the medication group (RR 2.18; 95% CI 1.31 to 3.63). Limited evidence from one RCT of 40 participants suggested that ECT com- bined with antipsychotic drugs results in greater improve- ment in mental state than with antipsychotic drugs alone. The review noted the dearth of good evidence on the role of ECT in combination with antipsychotics (conven- tional and atypical) when antipsychotics alone have failed.

There is also surprisingly little evidence regarding the use of long (> 12 treatments) versus short courses (<12) of ECT, in spite of assertions that schizophrenia is a condition that requires longer courses of treatment that does depression. The review contained data from one small but well conducted RCT that suggested that when continuation ECT was added to antipsychotic drugs, the combination was superior to the use of antipsychotics alone or continuation ECT alone; this certainly needs replication considering the difficulties in preventing re- lapses in some people with schizophrenia prescribed ECT. Other intriguing findings in the review in need of replication include faster recovery when stimulus inten- sities 4 times over the threshold required to elicit an ad- equate seizure are used compared to threshold or twice threshold stimuli.

It may surprise clinicians to note that there is only one RCT on the use of ECT in people with catatonia.10 This small RCT reported that people with catatonic schizo- phrenia who do not show rapid improvement following an initial trial of a benzodiazepine, improve faster with a course of ECT than with the newer antipsychotic risperidone. The review noted the irony that the frequently

quoted assertion that catatonia is an important indica- tion for ECT in people with schizophrenia1,5,6 is currently supported by data of the highest level of evidence from a single trial of only 14 participants, eight of whom were given ECT and four of whom were required to continue with ECT beyond the period of the trial.10

The place of ECT in treatment resistant schizophre- nia is unclear. The review included trials where people referred for ECT had, to various extents, failed to respond to treatment with conventional antipsychotics. However, since people in the trials were not stratified before ran- domization based on prior response to antipsychotics, this review was unable to report clear data for this popu- lation. However, data in the review from the only trial that directly studied the effects of ECT versus sham ECT in people with stringently defined treatment resistant schizo- phrenia on concurrent antipsychotics, did not support the use of ECT. Lower levels of evidence from phase I of a continuation ECT trial from Thailand11 for people with treatment resistant schizophrenia referred for ECT re- ported that 58/101 patients treated with ECT met pre- stated criteria for remission after seven to 25 treatments. While these results approximate or better those obtained in trials of clozapine in treatment resistant schizophre- nia12, the lack of a control group and randomization lim- its their strength. The Cochrane review is due to be up- dated in 2007 and hopefully will include the results of the ongoing trial of ECT in people with schizophrenia who have exhausted all other established treatment op- tions other than ECT.13 This important trial will, however, still not provide an answer to whether ECT, when added to conventional or newer antipsychotic drugs, would benefit those who show an insufficient response to se- quential trials of available drugs, but for whom clozapine may not be a viable option. Unfortunately, this is the case with the majority of people with treatment resistance in developing countries.

The introduction of ECT in clinical practice began with its use in schizophrenia and if ECT is to outlive its obituary for this indication in the NICE and other guide- lines, more appropriate and robust research is called for to support its use. Since ECT seems to be used for people with schizophrenia largely in developing coun- tries, where more expensive options like clozapine are a limited option, it is necessary that such research should originate from within these settings. This is an area where high-quality collaborative research from the subcontinent could inform practice in the rest of the world.

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