Who Gets ECT Without Failing Medication First?

To the Editor: I read with interest the article "Response of Depression to Electroconvulsive Therapy: A Meta-Analysis of Clinical Predictors" by Haq et al.[1] The article describes a rigorous meta-analysis of potential clinical and demographic predictors of electroconvulsive therapy (ECT) response using research published after 1980 (*DSM-III* era). The article is thorough and well written, and the authors describe a clear logic behind their methodology and statistical analysis. Two main findings came from the study: shorter duration of index episode and absence of a history of medication failure during the current episode predicted better ECT response. Several other clinical predictors were analyzed and found to either have no consistent predictive value or have suspect value based on study heterogeneity or bias.

I am concerned that the definition of medication failure used in the analysis, history of having failed at least 1 medication trial during the index episode, limits the value and generalizability of one of the study's 2 main findings. ECT is rarely prescribed as an initial treatment for an episode of depression. There are a few circumstances, such as catatonia, severe suicide risk, patient preference, and prior excellent response to ECT, that may result in a patient's receiving ECT as the initial treatment in an episode of major depression, but these are unusual circumstances. Indeed, medication failure in today's clinical environment is essentially a prerequisite to initiation of ECT, despite this therapy's excellent track record of response.[2] If the group defined as lacking a history of medication failure included only individuals such as I have described above, it clearly limits the study's clinical relevance. It would limit the finding of better ECT response in patients who do not have a history of medication failure to those individuals who either were the most severely ill or had a history of excellent response, which in either case would limit the relevance of this finding. I believe the authors need to clarify the definition of subjects who had failed versus not failed medication, or discuss further how their findings contribute to the literature despite this significant limitation.

References

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Drs Haq and Mickey Reply

To the Editor: We thank Dr DeQuardo for his interest and for his thoughtful questions about our study. Most of the studies (9 of 11) in our meta-analysis defined medication failure as lack of response despite at least 1 *adequate* antidepressant medication trial in the current episode, operationalized as an Antidepressant Treatment History Form (ATHF) score ≥ 3. A score ≥ 3 indicates that the patient has received the medication at a minimally adequate daily dose (eg, nortriptyline ≥ 76 mg/d) for ≥ 4 weeks; for psychotic depression, coadministration of antipsychotic medication (chlorpromazine ≥ 400 mg/d or equivalent) for ≥ 3 weeks is also required.[1]

Dr DeQuardo expresses concern that this criterion may not be clinically relevant because "medication failure in today's clinical environment is essentially a prerequisite to initiation of ECT." We disagree. Achieving an ATHF score ≥ 3 is not always easy in practice, given the requirements of adequate dosage, adequate duration, good adherence, and verification through medical records. Consequently, treating a patient with an ATHF score < 3 is not equivalent to using electroconvulsive therapy (ECT) as an initial treatment for an episode of depression. Furthermore, there are many clinical scenarios in which ECT is appropriate in the absence of a failed adequate medication trial. Besides catatonia, high suicide risk, patient preference, and prior ECT response, we would add severe functional impairment, psychosis, and medication intolerance as valid reasons. Indeed, lack of medication failure was not rare in the studies we reviewed: 402 out of 1,036 patients (39%) did not meet the criterion of an ATHF score ≥ 3 (9 studies).

On the other hand, we appreciate the perspective that the dichotomous "ATHF ≥ 3" criterion may not be relevant to many patients. We suspect that ECT response is actually predicted by the *degree* of medication resistance; that is, the fewer the failed trials, the greater the likelihood of ECT response. Although the available data are not compatible with meta-analysis, we found some evidence for this notion in the reviewed studies. Two studies that examined degree of medication resistance found a significant association with ECT response in the expected direction,[2,3] 2 studies found nonsignificant associations in the expected direction,[4,5] and 1 study found no significant association and no obvious trend.[6]

Thus, we are confident that lack of an adequate medication trial in the current episode predicts a greater likelihood of ECT response. Greater degree of medication resistance may also predict a lesser likelihood of ECT response, but future work will be needed to rigorously test this idea.

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