Published in final edited form as:

J ECT. 2008 September ; 24(3): 179–182. doi:10.1097/YCT.0b013e318185fa6b.

Towards Individualized Post-ECT Care: Piloting the Symptom-Titrated Algorithm-Based Longitudinal ECT (STABLE) Intervention

Sarah H. Lisanby, MD¹, Shirlene Sampson, MD², Mustafa M. Husain, MD³, George Petrides, MD⁴, Rebecca G. Knapp, PhD⁵, Vaughn McCall, MD⁶, Robert C. Young, MD⁷, Joan Prudic, MD¹, and Charles H. Kellner, MD⁸

¹Columbia University / New York State Psychiatric Institute

²Mayo Clinic

³University of Texas Southwestern Medical School

⁴The Zucker Hillside Hospital/Northshore LIJ Health System

⁵Medical University of South Carolina

⁶Wake Forest University Medical Center

⁷Weill Cornell Institute for Geriatric Psychiatry

⁸UMDNJ-New Jersey Medical School

Abstract

Objectives—Effective strategies to prolong remission post ECT are urgently needed. Fixed schedules for continuation ECT cannot adapt to early signs of impending relapse. Symptom-Titrated, Algorithm-Based Longitudinal ECT (STABLE) is proposed as a novel patient-focused approach to individualize the ECT schedule. In STABLE, the ECT schedule adapts to symptom fluctuations to prevent over-treatment of those who do not need it, and to re-capture response in those who might have otherwise relapsed with a rigid dosing schedule. Here we back-test STABLE to optimize the algorithm for subsequent testing in a prospective trial.

Methods—Three variations of the STABLE algorithm, differing in cut-off points to trigger or withhold additional ECT, were back-tested in a dataset of 89 patients randomized to the C-ECT arm in the CORE study comparing C-ECT with combination pharmacotherapy.

Results—The selected algorithm identified 100% of patients who ultimately relapsed as requiring additional ECT at an average of 2.2 weeks prior to relapse, while exposing 20% of sustained remitters to additional ECT. Other variations either failed to capture impending relapse, or exposed an unacceptably large percentage of patients to potentially unnecessary ECT.

Conclusions—This patient-focused approach to relapse prevention is an attempt to provide the first operationalized guidance to the field regarding how to conduct continuation ECT. The effectiveness of this approach should be tested in a randomized controlled trial.

Keywords

ECT; relapse; major depression; maintenance ECT; continuation ECT

INTRODUCTION

Sustaining remission from depression is one of the greatest challenges in the treatment of mood disorders. While electroconvulsive therapy (ECT) and antidepressants are very effective acute treatments, failure to maintain remission is common to both, and effective strategies for improving long-term outcomes have lagged behind knowledge of acute treatment optimization.¹ With ECT, remission may be lost as early as the first few weeks after the acute course. This may represent a re-emerging index episode that was suppressed but incompletely treated by ECT.^{2, 3} Indeed, even a mild degree of residual symptoms at the end of the ECT course predicts early loss of remission,⁴ providing support for the concept that incomplete suppression of the index episode leads to an unsustainable remission. Patients who fail to achieve remission with medications appear to be at increased risk for losing their remission early after responding to ECT.^{3, 5} These observations argue for robust strategies to preempt relapse before it occurs, by flexibly responding to early signs of symptom re-emergence.

The most common practice after response to ECT is to place patients on antidepressants for continuation therapy.^{6, 7} Early controlled trials of continuation pharmacotherapy (C-PHARM) following ECT were encouraging.^{8, 9} However, with increasing numbers of medication resistant patients in ECT samples, the efficacy of C-PHARM has been questioned.¹⁰ Recent studies document high rates of relapse with C-PHARM, suggesting that after response to ECT, relapse may be particularly likely in medication resistant and/or psychotic patients.^{3, 11, 12} Combination pharmacotherapy was more effective in preventing relapse than monotherapy or placebo.³ However, despite aggressive combination pharmacotherapy, 39% of patients relapsed within 6 months. Relapse predictors were medication resistance, female sex, and residual symptoms. Most relapses were within 5 weeks of ECT. Treatment as usual following ECT administered in a controlled trial fared a bit worse, with 51% relapsing within 6 months post ECT.¹³ In a community sample, relapse rates were even worse (64.3% at 6 months).⁴

Consequently, many clinicians have turned to continuation ECT (C-ECT) to prolong remission. Observational studies consistently note the benefits of C-ECT, but those studies typically lack adequate controls, random assignment, independent behavioral assessments, measures of social functioning, careful assessment of adverse effects, and blinded ratings. Addressing this gap, the CORE group recently reported the results of the first and only controlled trial of the efficacy of C-ECT (10 ECTs over a 5 month period with a 1 week delay prior to the start of continuation treatment) versus combination pharmacotherapy. C-ECT was well tolerated and effective in prolonging remission in 46% of patients, however it fared no better than combination treatment with nortriptyline+Li.² While it is possible that a more intensive C-ECT schedule could have been more effective, an aggressive approach might also exacerbate cognitive side effects. Unfortunately, there is a dearth of information regarding optimal C-ECT schedules, and no operationalized guidance as to how to adjust ECT schedules to fluctuations in clinical status.^{14, 15}

The majority of studies have followed clinical practice, which is to reduce the number of treatments over time, and gradually increase the interval between treatments, using the recurrence of symptoms and the emergence of cognitive or adverse effects to guide frequency. Suzuki et al¹⁶ reported the successful use of a symptom driven tapering strategy of maintenance ECT in three elderly patients. Odeberg *et al.*, in a recently completed retrospective chart review study of 41 patients who had received continuation ECT plus medications, found suggestive

evidence that a flexible ECT schedule was helpful in prolonging remission.¹⁷ Beyond this, there is no evidence-based information on individualizing treatments. An uncontrolled review of the literature¹⁵ recommended that administering ECT earlier than scheduled could prevent illness relapse. However, practitioners lack evidence-based guidance as to optimized clinical management to prevent relapse.

Given the lack of evidence regarding optimal continuation ECT schedules, and given the recent suggestions that fixed schedules may be suboptimal, we developed a novel symptom-driven approach to guide clinical decision-making regarding the schedule for continuation ECT. Symptom-Titrated, Algorithm-Based, Longitudinal ECT (STABLE), a novel approach to sustain remission, operationalizes common clinical practice that has evolved to incorporate tapering ECT schedules rather than abrupt discontinuation after remission. The aim was to develop a strategy to reduce the risk of relapse in the critical first month post ECT, by allowing pharmacotherapy to reach steady state prior to ECT discontinuation and by providing a taper phase during the period of highest relapse risk. Furthermore, we hypothesized that a patient-focused and symptom-titrated flexible ECT schedule, rather than a rigid schedule, could provide the opportunity to detect and interrupt early signs of symptom re-emergence, as well as prevent over-treatment of patients who demonstrate stable remission.

Here we back-test the STABLE algorithm on data from the completed CORE study on relapse prevention,² contrasting 3 alternate versions in their ability to trigger additional ECT in patients who subsequently relapsed. These results informed the version of the STABLE algorithm that will subsequently be tested in a prospective, randomized controlled trial.

MATERIALS AND METHODS

Development of Symptom-Titrated, Algorithm-Based, Longitudinal ECT (STABLE)

We sought to enhance the efficacy of C-ECT by developing an algorithm designed to quickly suppress re-emerging depressive symptoms to sustain and stabilize remission. The aim of this algorithm is to operationalize whether an ECT treatment should be given to suppress symptoms, or withheld to minimize cognitive side effects. We required that the algorithm be simple enough for translation into clinical use.

We formulated, by consensus of the CORE investigators and informed by existing CORE data, a set of rules based on the HRSD₂₄ and MMSE (Table 1) to operationalize when a patient should get one or two additional ECTs in a given week for patients demonstrating unstable remission and signs of symptom re-emergence, and when no ECT should be given that week for those demonstrating stable remission or for those demonstrating cognitive side effects.

STABLE features an initial brief fixed, tapered schedule followed by a symptom driven, flexible component, in which treatment frequency is individualized based on symptom expression in each patient. The initial portion consists of 2 ECT in week 1, 1 ECT in week 2, and 1 ECT 10 days later (4 ECT in 24 days). Treatment frequency in the subsequent flexible component (weeks 5–24) is determined by application of the algorithm (Table 1). Based upon their weekly HRSD₂₄ and MMSE scores, patients may receive 0–2 ECT in that week. ECT is postponed for 2 days if MMSE <21. The algorithm is designed to be implemented through case management and intensive clinical contact to detect early signs of symptom re-emergence, and to detect potentially treatment-interfering side effects (cognition) that might lead to dropout.

Back-Testing of the STABLE Algorithm using CORE Data

To back-test STABLE, we compared the outcomes of three variants of the STABLE algorithm to the HRSD₂₄ dataset of the 89 patients randomized to the C-ECT arm in the prior CORE study.² Complete details and sample description can be found in Kellner et al.² We evaluated

3 variations of the STABLE rule set, both with higher and lower HRSD₂₄ cut points. In the first variation (Algorithm 1), we omitted the rule for which no ECT was given for an HRSD₂₄ ≤ 6. Algorithm 2 (presented in Table 1) withholds ECT for HRSD₂₄ ≤ 6, and uses the ≥ 3 HRSD₂₄ increase from baseline as a trigger for additional rescue treatments. Another variation (Algorithm 3) used a 5-point HRSD₂₄ increase from end of acute phase ECT to trigger an additional ECT treatment.

RESULTS

The 3 variants of the STABLE algorithm were applied to the longitudinal HRSD dataset of 89 patients from the CORE trial who were assigned to the C-ECT arm. The percentage of patients identified by each of the 3 algorithms as needing additional ECT was computed separately for those who subsequently sustained remission and for those who ultimately relapsed. As shown in Figure 1, STABLE Algorithm 1 would have resulted in 100% of patients who ultimately relapsed getting additional needed ECT, at an average of 2.2 weeks before observed relapse. However, it would also have resulted in 11/41 (27%) patients who ultimately sustained remission receiving additional, unnecessary ECT. STABLE Algorithm 2 would have resulted in 100% of patients who ultimately relapsed getting additional needed ECT, while 8/41 (20%) sustained remitters would have received additional ECT. STABLE Algorithm 3 would have failed to capture 4 patients who ultimately relapsed, while sparing only one additional sustained remitter from unnecessary treatment. We considered this reduction in the sensitivity of capturing relapsers in a timely fashion unacceptable. Therefore, we selected Algorithm 2 for further testing in a prospective randomized trial.

DISCUSSION

We developed and back-tested the STABLE algorithm to balance the need to intervene earlier in patients who are showing symptom re-emergence, while limiting the proportion of patients who receive additional ECT that might have not been necessary to maintain stable remission. Results from back-testing show that the STABLE Algorithm 2 would have called for additional ECT at least 2 weeks prior to relapse in 100% of patients who subsequently relapsed on the fixed C-ECT schedule. The algorithm would have exposed 8 out of 41 sustained remitters to additional ECT that may have been unnecessary, a conservative number when balanced against the very serious consequences of relapse.

When combination pharmacotherapy is insufficient to sustain remission post ECT, clinicians typically utilize C-ECT.¹⁸ However, we reported that a fixed schedule of C-ECT was only modestly effective and no more so than combination pharmacotherapy in sustaining remission over a six month period.² It is possible that the fixed schedule for the C-ECT limited its efficacy.

In contrast to a fixed schedule for C-ECT, the STABLE intervention is symptom-driven and personalized. The timing of treatments is clinically driven, to prevent over-treatment of those who do not need it and to permit re-capturing clinical response for those who might have otherwise relapsed with a rigid dosing schedule. Moving beyond the obvious step of combining C-ECT with pharmacotherapy, the STABLE intervention takes the innovative step of operationalizing a symptom-driven approach to C-ECT, balancing the need to stabilize remission, while maintaining tolerability.

Since this was a retrospective study, no definitive conclusions about the efficacy of STABLE can be drawn. However, if future randomized controlled trials support the efficacy of the STABLE approach, it may represent a useful patient-focused algorithm to assist clinical decision-making to sustain remission post-ECT.

Acknowledgement

NIMH R01MH055495

REFERENCES

1. Depression Guideline Panel. Clinical Practice Guideline, Number 5. Vol Vol AHCPR Publication No. 93-0551. Rockville, MD: US Department of Health and Human Services; 1999. Depression in Primary Care, Vol. 2 Treatment of Major Depression.
2. Kellner CH, Knapp RG, Petrides G, et al. Continuation electroconvulsive therapy vs pharmacotherapy for relapse prevention in major depression: a multisite study from the Consortium for Research in Electroconvulsive Therapy (CORE). Archives of general psychiatry 2006;63(12):1337–1344. [PubMed: 17146008][see comment]
3. Sackeim HA, Haskett RF, Mulsant BH, et al. Continuation pharmacotherapy in the prevention of relapse following electroconvulsive therapy: a randomized controlled trial. JAMA 2001;285(10):1299–1307. [PubMed: 11255384][see comment]
4. Prudic J, Olfson M, Marcus SC, et al. Effectiveness of electroconvulsive therapy in community settings. Biological psychiatry 2004;55(3):301–312. [PubMed: 14744473]
5. Prudic J, Haskett RF, Mulsant B, et al. Resistance to antidepressant medications and short-term clinical response to ECT. The American journal of psychiatry 1996;153(8):985–992. [PubMed: 8678194]
6. Abrams, R. Electroconvulsive Therapy. New York: Oxford University Press; 1992.
7. Task Force on Electroconvulsive Therapy. The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging. Washington, DC: American Psychiatric Association; 2001. American Psychiatric Association.
8. Imlah NW, Ryan E, Harrington JA. The influence of antidepressant drugs on the response to electroconvulsive therapy and on subsequent relapse rates. Neuropsychopharmacology 1965;4:438–442.
9. Kay DW, Fahy T, Garside RF. A seven-month double-blind trial of amitriptyline and diazepam in ECT-treated depressed patients. Br J Psychiatry 1970;117(541):667–671. [PubMed: 4923720]
10. Sackeim HA, Prudic J, Devanand DP, et al. The impact of medication resistance and continuation pharmacotherapy on relapse following response to electroconvulsive therapy in major depression. Journal of clinical psychopharmacology 1990;10(2):96–104. [PubMed: 2341598]
11. Sackeim HA, Prudic J, Devanand DP, et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. The New England journal of medicine 1993;328(12):839–846. [PubMed: 8441428]
12. Malcolm K, Dean J, Rowlands P, Peet M. Antidepressant drug treatment in relation to the use of ECT. J Psychopharmacol 1991;5:255–258.
13. Tew JD Jr, Mulsant BH, Haskett RF, et al. Relapse during continuation pharmacotherapy after acute response to ECT: a comparison of usual care versus protocolized treatment. Ann Clin Psychiatry 2007;19(1):1–4. [PubMed: 17453654]
14. Frederikse M, Petrides G, Kellner C. Continuation and maintenance electroconvulsive therapy for the treatment of depressive illness: a response to the National Institute for Clinical Excellence report. J ECT 2006;22(1):13–17. [PubMed: 16633200]
15. Andrade C, Kurinji S. Continuation and maintenance ECT: a review of recent research. J ECT 2002;18(3):149–158. [PubMed: 12394534]
16. Suzuki K, Awata S, Takano T, et al. Resolution of SPECT-determined anterior cerebral hypoperfusion correlated with maintenance ECT-derived improvement in residual symptoms in a case of late-life psychotic depression. Clinical nuclear medicine 2006;31(5):253–255. [PubMed: 16622329]
17. Odeberg HR-SB, Salander P, Martensson B. Individualized continuation ECT and medication as a bridge to relapse prevention following an index course of ECT in severe mood disorders: a naturalistic three-year cohort study. Journal of ECT. 2008In Press
18. Petrides G, Dhossche D, Fink M, et al. Continuation ECT: relapse prevention in affective disorders. Convulsive Therapy 1994;10(3):189–194. [PubMed: 7834255]

Fig. 1. Percent of patients identified as needing additional ECT to sustain remission with 3 variants of the STABLE algorithm. Using STABLE Algorithms #1 or 2, 100% of those who subsequently relapsed would have been identified as needing additional treatment.

Table 1.
STABLE Algorithm

Weeks 1–4: Fixed ECT schedule	
2 ECT in week 1, 1 ECT in week 2, and 1 ECT 10 days later (Total = 4 ECT in 24 days)	
Weeks 5–24: Symptom-Driven ECT Schedule	
# Additional ECTs	HRSD Conditions
0	HRSD $\leq$ 6 or HRSD increase from post acute phase ECT <3
1	HRSD increase from post acute phase ECT ≥ 3
2	HRSD increase from post acute phase ECT ≥ 8 or HRSD ≥ 16 *

* Maximum of 3 weeks with 2 ECT per week, then maximum of 1 ECT per week

Note: ECT is postponed for 2 days if MMSE <21