

Antidepressants during ECT

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INTRODUCTION

In this new section of the journal, I present a series of evidence-based case conferences. The clinical question that we seek to solve in each of this series is real, in the sense that it emanated from a real patient, a real clinical case that one of my residents was treating and that we discussed in our evidence-based case conferences. In presenting the case, however, I completely anonymise the scenario but hope it remains as real as it was.

The procedure of evidence-based practices that I depict in this series may be completely familiar to some of our readers or may be quite new to others. How and why of this process may also be known or unknown, depending on your familiarity with *EBM*. In order to learn this process, please consult any one of the textbooks of *EBM* such as *JAMA Users' Guides to the Medical Literature*. A series of short videos in which I explain and introduce how to practice evidence-based mental health (<http://ocw.kyoto-u.ac.jp/17-graduate-school-of-medicine/2013/department-01/001>) may be helpful too.

The presentation in this series may appear too brief and rushed to some of you but this is how *EBM* can be practiced by busy clinicians, once you are familiar with the process. We hope the new series of articles will be an enjoyable and inspiring reading, helping you improve your own clinical practices.

CLINICAL CASE

Patient: 48-year-old man

Present illness: The patient developed his first major depressive episode due to increasing pressures at work in year X. He started the treatment at a general practitioner with paroxetine up to 40 mg/day, and was on sickness leave for 3 months after which he tried to return to work but failed. He was then on sickness leave for 12 more months. Because of this unfavourable and prolonged course, he was advised by the industrial consultant physician to see a psychiatrist, who tried sertraline up to 150 mg/day, amitriptyline up to 150 mg/day and several augmentation attempts without noticeable success. The psychiatrist then referred him to our department for electroconvulsive therapy (ECT).

Present status: On presentation to our outpatient clinic in year X+2, he, accompanied by his wife, was well dressed but appeared thin, fatigue and moved slowly. He reported loss of energy and poor sleep at night. He scored 25 on 17-item Hamilton Rating Scale for Depression. He had no other psychiatric or medical history. He was currently on nortriptyline 75 mg/day and mirtazapine 30 mg/day. In preparation for ECT, we wanted to know whether antidepressants should be discontinued or whether it is more effective to administer ECT with antidepressants.

FORMULATE YOUR CLINICAL QUESTION

Patients: With major depression receiving ECT

Intervention: With antidepressants

Comparison: Without antidepressants

Outcomes: Response in depression, side effects including delirium

LITERATURE SEARCH

First, we searched the most important secondary sources of evidence (The Cochrane Library, Evidence-Based Mental Health and EvidenceUpdates websites) with the keyword 'electroconvulsive therapy'. Each hit several articles, but none of them seemed relevant. Then we searched PubMed: the first step was to identify MeSH terms for ECT, antidepressants and major depression (terms representing patients and intervention of the clinical question), then their combinations were entered on the clinical queries page, setting category to therapy and scope to narrow. This quick search retrieved 41 systematic reviews and 45 clinical trials. None of the listed systematic reviews concerned our clinical question but the fifth in the clinical trials

list appeared highly relevant: *Sackeim et al. Effect of concomitant pharmacotherapy on electroconvulsive therapy outcomes: short-term efficacy and adverse effects. Arch Gen Psychiatry 2009; 66:729-37.*

CRITICAL APPRAISAL OF THE LITERATURE

ARE THE RESULTS AT RISK OF BIAS?

(Did intervention and control groups start with the same prognosis?)

Were patients randomised?

YES. In the abstract it says: 'Design: Prospective, randomised, triple-masked, placebocontrolled study.'

Was randomisation concealed?

YES. In the Methods section: "The treating psychiatrist prescribed NT [nortriptyline] and VEN [venlafaxine] for each patient. The site pharmacist had access to the randomisation code and substituted PL [placebo] for NT and/or VEN as needed." So when enrolling a patient, the clinician had no way of telling which treatment the patient would be assigned to.

(Were patients in the study groups similar with respect to known prognostic factors?)

Was prognostic balance maintained as the study progressed?

YES. Table 2 indicates that there was no important difference in the clinical parameters of ECT or pharmacotherapy between drug and placebo arms. The triple-blind procedure would seriously decrease the possibilities of imbalance in the co-interventions.

To what extent was the study blinded?

YES, blinded to the participant, therapists and outcome assessors. Furthermore, this study is exceptional in checking the integrity of the blind: 'The chi-squared analyses indicated that there was no association between the best guesses of either patients or clinical raters and actual treatment conditions.'

(Were the groups prognostically balanced at the study's completion?)

Was follow-up complete?

YES. The ITT analyses included all the randomised patients.

Were patients analysed in the groups to which they were randomised?

YES.

WHAT ARE THE RESULTS?

(How large was the treatment effect? How precise was the estimate of the treatment effect?)

Remission rates were 66/135 on placebo, and 114/184 on either nortriptyline or venlafaxine. Using the NNT calculator (<http://ebmh.med.kyoto-u.ac.jp/toolbox.html>), the NNT was 8 (95% CI: 5 to 48).

HOW CAN I APPLY THE RESULTS TO PATIENT CARE?

Were the study patients similar to my patient?

The mean age of the study patients was 49; 64% were women; 89% were unipolar; the mean duration of the current episode was 9 months; the mean Hamilton score was 31.1. There is no reason to assume that the results based on these study patients would not apply to this patient.

Were all patient-important outcomes considered?

Serious adverse events, overall adverse effects and cognitive adverse effects were measured. For serious and overall adverse effects, there was no discernible difference among treatments (only two cases of delirium were noted in the whole sample). With regard to cognitive adverse effects, nortriptyline was less harmful than placebo or venlafaxine. Although less harmful than ECT+placebo, substantive impairment (effect size >1.5) was still noted in autobiographical memory when ECT+nortriptyline was given.

Are the likely treatment benefits worth the potential harm and costs?

When ECT is indicated, eg, for chronic, pharmacotherapy-refractory depression, coadministration of antidepressants was beneficial (NNT=8). Adding nortriptyline was less harmful than adding venlafaxine to ECT or administering ECT alone by effect sizes of 0.2–0.5 in alleviating cognitive adverse effects.

WHAT WILL YOU DO WITH YOUR PATIENT?

Given that there is no systematic review on the topic and that the identified RCT was at low risk of bias and applicable to this patient, we decided to continue the same medication, with due concerns and explanations of possible cognitive adverse effects. Interestingly, the clinical case discussed here is closely related to one of the articles we have selected for this same issue of EBMH, which is about antidepressant treatment after ECT.¹ Please refer to this article to learn what to expect after a successful ECT treatment.

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REFERENCE

1. **Brent DA**, Birmaher B. Antidepressants increase risk of behavioural symptoms in children and adolescents with depression or anxiety. *Evid Based Mental Health* 2014;**17**:4.