

# Depressed patients perception of the efficacy of electroconvulsive therapy and venlafaxine therapy

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Submitted: October 8, 2007

Accepted: October 24, 2007

*Key words:* ECT; venlafaxine; depressive disorder; self-report inventories; bipolar depression

Neuroendocrinol Lett 2007;28(6):889–894 PMID: 18063943 NEL280607A09 © 2007 Neuroendocrinology Letters • [www.nel.edu](http://www.nel.edu)

## Abstract

**BACKGROUND:** The aim of our study was to evaluate the efficacy of electroconvulsive (ECT) and venlafaxine therapy from the patient's point of view.

**METHODS:** We used a retrospective chart review from 22 inpatients who underwent ECT and 22 patients treated with venlafaxine due to resistant unipolar or bipolar depression. We used bilateral ECT in a median of 8 (IQR 7–9.7) sessions and venlafaxine therapy with a median daily dosage of 225 mg (IQR 150–225 mg) for a median of 4 (IQR 4–5) weeks. The main outcome was change in a self-evaluation scale – Short Form of the Beck Depression Inventory (BDI-SF). The response was defined as the decreasing of the BDI-SF score by ≥50%, remission as decreasing of BDI-SF score ≤4.

**RESULTS:** We did not find significant differences between sex, age and BDI-SF before therapy in both groups. The reduction of BDI-SF score was significantly higher in the ECT group than in venlafaxine group ( $p=0.025$ ). Significantly more patients treated with ECT reached response than patients treated with venlafaxine (68% vs. 23%;  $<0.01$ ). The remission rate after ECT was not significantly higher than venlafaxine therapy (27% vs. 5%;  $p=0.094$ ). The number needed to treat (NNT) of ECT for BDI-SF response was 3 (CI95% 1.4 to 5.2) and NNT for BDI-SF remission was 5 (CI95% 2.3 to 45.8).

**DISCUSSION:** After the median of 3 failed antidepressant trials, ECT was more effective than venlafaxine in the short term therapy in some parameters according to our patients. We suggest that the fact that mental state was evaluated by patients themselves is an important pro-argument in the discussion about ECT.

## Abbreviations

BAI	- Beck Anxiety Inventory
BDI-SF	- Beck Depression Inventory Short Form
CORE	- the Consortium for Research in ECT
CUC	- Columbia University Consortium
ECT	- Electroconvulsive Therapy
EPS	- Extra Pyramidal Syndrom
ICD-10	- International Classification of Diseases, 10 <sup>th</sup> edition
i.m.	- intra muscular
i.v.	- intra venous
NNT	- the number need to treat
PPC	- Prague Psychiatric Centre
rTMS	- repetitive Transcranial Magnetic Stimulation
STEP-BD	- Systematic Treatment Enhancement Program for Bipolar Disorder
STAR*D	- The Sequenced Treatment Alternatives to Relieve Depression
SSRI	- Selective Serotonin Reuptake Inhibitor

## INTRODUCTION

Unipolar depressive disorder and bipolar disorder are the fourth and the sixth-leading cause of disability worldwide [24], thus determining the best treatment algorithm for both disorders is the subject of many studies. The first results of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) were recently published. This results did not show an adjunctive effect of paroxetine or bupropione, as compared with the use of mood stabilizers in the short treatment of bipolar depression [37]. Adjunctive lamotrigine to mood stabilizers was better in some parameters than treatment with adjunctive inositol or risperidone in patients with bipolar depression who were not responsive to a combination of adequate doses of established mood stabilizers [26].

Another large STAR\*D trial (The Sequenced Treatment Alternatives to Relieve Depression) tested a multistep algorithm of depression treatment on the sample of 3,671 patients [34]. After the first step – citalopram treatment – 36.7% of patients remitted. In the second step, the remission rate was 30%. The overall remission rate of the third and the forth step was 13.7% and 13% [34]. No one from the above mentioned studies included electroconvulsive therapy (ECT) to treatment algorithmus. According to McCall [22] the fact that in STAR\*D two successive steps were not effective in approximately one third of patients should open a serious discussion about how many unsuccessful treatments should be pushed before ECT will be introduced.

ECT is considered to be the most effective acute intervention for severe depression [25]. The effect of ECT seems to be similar in unipolar and bipolar depression [5,9]. According to three meta-analyses, ECT is more effective than sham stimulation and significantly more effective than pharmacotherapy including tricyclic antidepressants, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors and lithium [7,15,27]. The ECT response rate according to Prudic [31] is greater in non-resistant patients (69%) than in resistant patients (42%). Other authors did not find difference between resistant and non-resistant patients [16,42], but

the duration of the index episode can play an important role [16].

More recently, complete symptom remission has been proposed as a more stringent goal for the acute phase treatment of depression [12,41]. Two multisite collaborations – the Consortium for Research in ECT (CORE) and the Columbia University Consortium (CUC) studies reported remission rates after ECT between 55–86% [10,13,36].

Despite proven efficacy and relative safety, ECT is widely stigmatized as a last-resort treatment. This image is largely the result of professional and public preoccupations with the effects of ECT on memory and the failure to fairly consider the treatment's benefits compared with alternative treatments [8].

The aim of our study was to compare the efficacy of electroconvulsive and venlafaxine therapy from inpatients' points of view. We chose venlafaxine for comparison because it was not included in previous ECT meta-analyses [7,15,27] and at least two meta-analyses detected that venlafaxine was more effective than SSRI's [29,41].

We have assumed that even while using one of the most modern antidepressant, venlafaxine, treatment with ECT will still be more effective.

## METHODS

### *Population*

We used a retrospective chart review of inpatients hospitalized in an open ward of the Prague Psychiatric Centre (PPC) who underwent ETC for depression over the period from January 2003 until December 2004. The group treated by ECT included twenty two patients (12 women) with a diagnosis of depressive disorder or recurrent depressive disorder or a depressive phase of bipolar affective disorder (n=3). Two patients suffered from psychotic depressive disorder. Data about this group were published previously [19]. To compare the efficacy of ECT with venlafaxine therapy we searched the archives of PPC (years 2001–2005) with the criterion of diagnosis (as mentioned above), pharmacoresistance – insufficient response to treatment with at least one antidepressant [40], treatment with a minimal dose of 150 mg of venlafaxine and continued treatment for at least three weeks. The control group treated by venlafaxine included twenty two patients (11 women) with a diagnosis of depressive disorder, recurrent depressive disorder or a depressive phase of bipolar affective disorder (n=3). No patient from venlafaxine group had psychotic depressive disorder. Diagnoses were made according to the ICD-10 criteria. Study protocol was approved by the Ethical Committee of the Prague Psychiatric Center.

### *Assessment of psychopathology*

The change of depressive symptoms was evaluated with a self-evaluation scale – Beck Depression Inventory Short Form (BDI-SF) [2] which is filled out by inpatients

with a diagnosis of depression in PPC every week. The correlation between BDI-SF and the full version of BDI is 0.89–0.97. BDI-SF thus may be accepted as a replacement of the full version BDI [3]. BDI-SF contains 13 items, each is scored by 0–3 points and the maximum score is 39 points. The recommended cut off scores for assessing mild, moderate and severe depression are 5, 8 and 16 points respectively [2]. The correlation between BDI-SF and Hamilton Depression Rating Scale is  $r=0.68$  [39].

We used records of patient's BDI-SF scores before initialization and after completion of venlafaxine therapy and ECT sessions. Response to therapy was defined as a decrease of BDI-SF score by 50% or more. The remission was defined as achievement of BDI-SF score  $\leq 4$  [2,21].

We used a self-evaluation scale – Beck Anxiety Inventory (BAI) to evaluate severity of anxiety before treatment in both groups [4].

#### Electroconvulsive therapy

Electroconvulsive therapy was administered using Thymatron™ DGx device which delivers brief bipolar pulses. We used bitemporal ECT application. Intensity was assessed according to patients' age. Treatments were given under anesthesia with sodium thiopental (200–300 mg i.v), muscle relaxation with suxamethonium chloride (1 mg/kg) and premedication with atropine (0.5 mg i.m). Therapy was administered three times a week, with a median of 8 (IQR 7–9.75) sessions. Eighteen patients received pharmacologic antidepressant treatment along with electroconvulsive treatment. During ECT treatment patients used anxiolytics: alprazolam (n=4), clonazepam (n=1), mood stabilizers: lithium (n=1), lamotrigine (n=1), adjunctive antidepressant: clomipramine (n=5), venlafaxine (n=2), sertraline (n=3), trazodone (n=1), dosulepine (n=3), maprotiline (n=2), bupropion (n=1), citalopram (n=2), escitalopram (n=1) or adjunctive low dose of new antipsychotic: olanzapine (n=3), risperidone (n=3), ziprasidone (n=1).

#### Therapy with venlafaxine

Venlafaxine was administered in the median of 4 weeks (IQR 4–4.75) with median daily dosage 225 mg (IQR 150–225 mg). Patients used anxiolytics: alprazolam (n=8), hydroxyzine (n=5), drugs for insomnia: zolpidem (n=10), nitrazepam (n=2), mood stabilizers: lithium (n=1), lamotrigine (n=1), adjunctive antidepressants: clomipramin (n=1), bupropion (n=1), amitriptylin (n=1) or adjunctive low dose of new antipsychotic: seroquel (n=1), amisulpride (n=1).

#### Statistical analysis

Data distribution was not normal (Shapiro Wilk test) therefore non parametric tests were used. We used the Wilcoxon pair test for within group analysis and the Mann Whitney U test for between group analysis. Fisher exact test was used for category variables (response, remission). The significance level was  $p<0.05$ . The ef-

fect size was calculated using the difference of the mean divided by the average of standard deviations.

## RESULTS

#### Efficacy of electroconvulsive therapy

There was a significant reduction of BDI-SF score (Wilcoxon Matched Pairs Test  $Z=3.37$ ,  $p<0.001$ ) after ECT (Table 2). Sixty-eight percent of patients treated with ECT responded ( $\Delta$ BDI-SF  $\geq 50\%$ ) and 27% achieved remission (BDI-SF  $\leq 4$ ).

#### Efficacy of venlafaxine therapy

There was a significant reduction of BDI-SF score after venlafaxine treatment (Wilcoxon Matched Pairs Test  $Z=3.35$ ,  $p<0.001$ ). Twenty-three percent of patients treated with venlafaxine responded, and 5% achieved remission.

#### Electroconvulsive vs. venlafaxine therapy

The group of patients treated by ECT did not differ significantly from the group treated by venlafaxine in regard to sex, age, patients with psychotic depressive disorder or with bipolar depression (Table 1), and intensity of depressive symptoms using BDI-SF before treatment (Mann-Whitney U test,  $Z=-0.312$ ,  $p=0.75$ )

**Table 1.** Demographic characteristic.

	ECT (n=22) median (IQR)	venlafaxine (n=22) median (IQR)	p-value
<b>age</b>	49 (30.5–52.2)	50.5 (37–55.0)	n.s.+
<b>men / female</b>	12 / 10	11 / 11	n.s.*
<b>number of previous trials during current episode</b>	3 (2–4)	3 (1–4.7)	n.s.*
<b>unipolar depression/ bipolar depression</b>	19 / 3	19 / 3	n.s.*
<b>psychotic depressive disorder</b>	2	0	n.s.*
<b>patients using anxiolytic</b>	5	13	0.03*
<b>patients using hypnotic</b>	0	12	0.005*
<b>patients using concomitant antidepressants</b>	20	3	0.000*
<b>patients using concomitant antipsychotic</b>	7	2	n.s.*
<b>patients using mood stabilizer</b>	2	2	n.s.*

IQR - interquartile range, +Mann-Whitney U test,

\*Fischer exact test - two tails

**Table 2.** BDI-SF scores and efficacy of treatment.

	<b>ECT (n=22)</b> median (IQR)	<b>venlafaxine (n=22)</b> median (IQR)	<b>p-value</b>
<b>BDI-SF - I</b>	20 (18–21.7)	20.5 (15.5–25.5)	n.s.+
<b>BDI-SF - II</b>	8 (4.2–16.2)	15.5 (10–21.7)	0.061+
<b>BAI</b>	21 (12–27)	18 (11.3–28.8)	n.s.+
<b>BDI-SF Score reduction</b>	11 (5.2–14.5)	3.5 (2.0–6.7)	0.025+
<b>Responders</b>	15	5	0.0058*
<b>Remissions</b>	6	1	0.094*
<b>Treatment duration (weeks)</b>	2.8 (2.3–3.3)	4 (4–5)	<0.001+

IQR - interquartile range, BDI-SF- I - Beck Depression Inventory

Short Form before treatment, BDI-SF- II - Beck Depression Inventory

Short Form after treatment, BAI - Beck Anxiety Inventory before

treatment, +Mann-Whitney U test, \*Fischer exact test - two tails

or anxiety using BAI before treatment (Mann-Whitney U test,  $Z=0.113$ ,  $p=0.91$ ). The reduction of scores was significantly higher in the ECT group than in the venlafaxine group (Mann-Whitney U test,  $Z=2.22$ ,  $p=0.025$ ). The ECT response rate (68%) was significantly higher than venlafaxine response rate (23%) (Fisher exact test,  $p<0.01$ ). The ECT remission rate (27%) was non-significantly higher than the venlafaxine remission rate (5%) using two tales Fisher exact test ( $p=0.098$ ). The final BDI-SF score after ECT was non-significantly lower than after venlafaxine (Mann-Whitney U test,  $Z=-1.86$ ,  $p=0.061$ ). The ECT treatment was significantly shorter than the venlafaxine treatment (Mann-Whitney U test,  $Z=-5.02$ ,  $p<0.001$ ). The antidepressive effect size of ECT compared to venlafaxine was  $d=0.54$ . The number needed to treat (NNT) for BDI-SF response was 3 (95% confidence interval (CI95%) for the NNT ranges from 1.4 to 5.2) and NNT for BDI-SF remission was 5 (CI95% from 2.3 to 45.8).

## DISCUSSION

In our study, ECT was more effective than venlafaxine therapy when comparing the number of responses or reduction of score. It is important to emphasize that the evaluation of depressive symptoms has been performed on the self-rated scale, thus ECT has been found significantly more efficient in the reduction of subjectively perceived depressive symptoms from the patient's point of view. The STAR\*D trial also used self-rated scale – the QIDS-SR16 (The 16-Item Quick Inventory of Depressive Symptomatology) [34].

The response rate after venlafaxine treatment (25%) in our study is comparable with the venlafaxine response rate (28.2%) in the second step of STAR\*D [35], but remission rate in our study (5%) is lower than presented in STAR\*D (25%). The differences could be explained by the shorter treatment period in our study. Treatment duration with venlafaxine in STAR\*D was 9.3 weeks. In our study 13% of the patients were treated for 6 weeks, following 18% for 5 weeks, 60% 4 weeks and 9% for 3 weeks. We also included patients using venlafaxine only 3 weeks. A recent meta-analysis showed that during 6 weeks of study, the maximum treatment response occurred during the first 4 weeks, and only 10% of patients responded during last 2 weeks [30]. In fact when we had excluded two patients with 3 weeks of treatment, we lost the patient who reached remission after venlafaxine therapy. The mean time to reach remission was between 5–8 weeks during the various steps in STAR\*D [35]. It is thus probable that more patients would have responded if treated longer. Some patients could reach remission later during outpatient treatment, but we did not detect them because we evaluated only inpatient records, which is a limitation in this study.

The number of remissions after ECT (27%) from the patients' point of view is quite low in our study when comparing it to previously reported remission rates in CORE and CUC studies 55–86% [10,13,36]. This discrepancy may be due to use self-evaluation scale, different ECT parameters or differences in the patient population. The patients were recruited from an open psychiatric ward where most patients suffered from pharmacoresistant, subchronic moderate depressive disorder rather than acute severe depressive disorder. Our results are close to other recent ECT studies with remission rates between 20–46.7% [32,33]. ECT remission rate and final BDI-SF were not significantly different from venlafaxine treatment but indicate a trend of better efficacy. The failure to find a significant difference in remission rate and final BDI-SF score could be due to a relative small sample size.

More patients in the ECT group took antidepressants as co-medication than in the venlafaxine group. In some patients we continued with unsuccessful medication, and in another we started new medication during ECT treatment, so in this cases patients took antidepressants only one or two weeks. There was no evidence that combining ECT with antidepressant or lithium therapies, or with atypical antipsychotics increases clinical efficacy or cognitive impairment [1,16]. More patients treated with venlafaxine used anxiolytic and hypnotics what reflect restriction of benzodiazepines and hypnotic in ECT group than higher occurrence of anxiety in venlafaxine group. On the other hand, in our previous study, we detected not only significant antidepressant, but anxiolytic effects, of ECT also [19].

The treatment of ECT was significantly shorter than treatment with venlafaxine, which is an important characteristic for patients and can minimize the need for long

inpatient care. Our results agree with reported quick antidepressant effect onset of ECT [10].

A limitation of our study is the fact that patients treated with venlafaxine therapy were not treated in exactly the same time period as patients with ECT. We choose a wider period for patients treated with venlafaxine to have the same sample as in ECT group.

Our study can not answer the clinically useful question of what is the best time to use ECT but showed that ECT is more effective than treatment with venlafaxine after three unsuccessful trials. Using data from STAR\*D where efficacy during the third antidepressant trial decreases we can hypothesize, that the best time to use ECT is after two antidepressant failures. The STAR\*D trial did not use all the possible alternatives to treat patients with resistant depression. A recently published meta-analysis confirmed that augmentation of antidepressants with atypical antipsychotics in patients with resistant depression is more effective than placebo augmentation [28]. On the other hand this approach could be associated with antipsychotic induced EPS, akathisia, galactorrhea or metabolic syndrom [14,17,18,20,43]. Another novel therapy such rTMS shows in some studies the same efficacy as ECT [6,11] and a better effect for cognitive function [38], but other studies did not find cognitive or cost-effect benefits of rTMS over ECT [23,33].

We suggest that early use of ECT during sequenced treatment of depression can be a more effective treatment.

## CONCLUSION

The results of our study partially confirmed the hypothesis that ECT is more efficient than venlafaxine therapy of resistant depression from inpatients' point of view. We suggest that the fact that mental state was evaluated by patients themselves is an important pro-argument in the discussion about ECT.

## ACKNOWLEDGEMENTS

This work was supported by the research project MSM0021620816 and CNS 1M0517 from Ministry of Education, Youth and Sports, the Czech Republic. The authors thank Tricia Hahn, PhD. for the help with the final revisions of the manuscript.

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