Journal of Affective Disorders 150 (2013) 686–690

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Brief report

Do benzodiazepines moderate the effectiveness of bitemporal electroconvulsive therapy in major depression?

Verònica Gálvez [a,b,c], Colleen K. Loo [d,e,f,h,*], Angelo Alonzo [d,f], Ester Cerrillo [a,b,c], José Manuel Menchón [a,c,g], José Manuel Crespo [a,c,g], Mikel Urretavizcaya [a,c,g]

[a] Neuroscience Group, Bellvitge Biomedical Research Institute (IDIBELL), Barcelona, Spain
[b] Mood Disorders Clinical and Research Unit & ECT Unit, Psychiatry Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain
[c] University of Barcelona (UB), Barcelona, Spain
[d] School of Psychiatry, University of New South Wales, Sydney, NSW 2031, Australia
[e] St. George Hospital, Sydney, NSW, Australia
[f] Black Dog Institute, Sydney, NSW, Australia
[g] Mood Disorders Clinical and Research Unit, Psychiatry Department, Bellvitge University Hospital, L'Hospitalet de Llobregat, Barcelona, Spain
[h] CIBERSAM—Ciber en Salud Mental, Barcelona, Spain

ARTICLE INFO

Article history:
Received 20 November 2012
Received in revised form
27 March 2013
Accepted 27 March 2013
Available online 11 May 2013

Keywords:
Electroconvulsive therapy
Bitemporal
Major depression
Benzodiazepines
Efficacy

ABSTRACT

Background: Electroconvulsive therapy (ECT) is the most effective treatment for depression. However, the use of concomitant medications during ECT is controversial, especially benzodiazepines, as some past evidence suggests these may reduce the efficacy of ECT. This study analysed the effect of benzodiazepines on treatment outcomes in a group of depressed patients treated with bitemporal (BT) ECT.
Methods: 90 patients with major depression who received BT ECT were analysed. Clinical, demographic and ECT data were extracted from clinical records. Mood improvement was rated by trained psychiatrists using the Hamilton Depression Rating Scale (HDRS-21) at baseline and after the final ECT treatment. The association between benzodiazepine dose and mood outcomes over the ECT course was examined with regression analyses, controlling for variables that may affect ECT efficacy.
Results: Hierarchical multiple regression analysis found only current episode duration ($t=-4.77$, $p<0.001$) was a significant predictor of change in HDRS. Benzodiazepine dose was not associated with a change in HDRS ($p>0.05$, $R^2=0.39$).
Limitations: This was a retrospective study. The use of the half-age dosing method for ECT did not permit examination of the effects of benzodiazepines on seizure threshold.
Conclusions: Benzodiazepines did not affect the efficacy of BT ECT with the dosing method used. However, these results may not generalise to other forms of ECT, ECT given with other methods of dose determination or to other populations less responsive to ECT.

1. Introduction

Electroconvulsive therapy (ECT) is the treatment of choice for pharmacotherapy-resistant and severe depression (NICE Clinical Guidelines, 2009). However, severe depression is often accompanied by agitation and/or anxiety, for which benzodiazepines are often prescribed. Benzodiazepines, though, have been demonstrated to have anticonvulsant properties (Shader and Greenblatt, 1979), elevate seizure threshold (APA, 2001; Ottosson, 1985) and shorten seizure duration (D'Elia, 1982; Standish-Barry et al., 1985; Stromgren et al., 1980). Thus, benzodiazepines may affect the efficacy of ECT when co-administered. The majority of clinical practice guidelines (e.g., US, Spain, Australia, UK) recommend gradual cessation or reduction of benzodiazepines prior to ECT, regardless of unilateral (UL) or bitemporal (BT) electrode placement (APA, 2001; Consenso Español sobre la TEC, 1999; ECT: Minimum Standards for Practice in New South Wales, 2011; The ECT Handbook, Royal College of Psychiatrists, 2005).

Past research has also suggested benzodiazepine use should be minimized during ECT (for review see Greenberg and Pettinati (1993)). However, the majority of studies contain methodological limitations that preclude definitive conclusions. Most were retrospective, some used seizure duration as the main outcome measure, which is not a good marker of efficacy (Abrams, 2002; Sackeim et al., 1991), and information regarding doses of benzodiazepines, ECT stimulus dosage and depression subtype was either incomplete or absent.

* Corresponding author at: Black Dog Institute, Hospital Road, Randwick, 2031, Sydney, Australia.
Tel.: +61 2 9113 2039; fax: +61 2 9113 3734.
E-mail address: colleen.loo@unsw.edu.au (C.K. Loo).

0165-0327/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jad.2013.03.028

It is nonetheless possible, though, that the impact of concurrent benzodiazepines may depend on the type of ECT given with the strongest evidence of benzodiazepines affecting ECT outcomes found in UL ECT. In a retrospective study by Pettinati et al. (1990) comprised of 48 patients (70% on benzodiazepines) receiving UL ECT, there was a higher percentage of responders in the non-benzodiazepine group (93% vs. 62%). Jha and Stein (1996) reported similar results in a retrospective study of 124 patients treated with UL or BT ECT, while receiving benzodiazepines and 124 control ECT patients not on benzodiazepines. The presence of benzodiazepines reduced the response rate of UL, but not BT ECT.

This study aimed to assess the impact of benzodiazepine use on the efficacy of BT ECT taking into account the drug dosage used and using structured rating scales to measure clinical response.

2. Methods

2.1. Study design

All in-patients at the Psychiatry Department of Bellvitge University Hospital who received ECT in 2007–2012 were retrospectively screened for inclusion. Clinical, demographic and ECT treatment-related data were extracted from clinical files. The study was approved by the ethics committee of the Bellvitge University Hospital.

2.2. Participants

Inclusion criteria were: DSM-IV Major Depressive Episode, unipolar type, age ≥18 year old and clinical indication for ECT. Exclusion criteria were: Axis I diagnoses other than major depressive disorder (MDD), substance abuse, Axis II disorders, ECT treatment in the previous 3 months and concomitant treatment with anticonvulsants. From a total number of 190 patients screened, 90 met the inclusion criteria and were included. Medication resistance was assessed prior to the start of the ECT course through the Thase and Rush staging method (Thase and Rush, 1997). (See Table 1).

2.3. Treatment issues

2.3.1. Medication

Psychotropic medications during the ECT course were as prescribed by the patient's psychiatrist. Benzodiazepines used were of intermediate to long half life (lorazepam, lormetazepam, clonazepam, alprazolam, diazepam, flunitrazepam, clorazepate, ketazolam) and were administered one to three times daily. Patients did not receive any medication the morning prior to ECT.

Of a total of 90 patients, 15 were benzodiazepine-free during the ECT course (16.7%). The average daily benzodiazepine dose over the ECT course, expressed as diazepam mg equivalents (Ashton, 2002), was 17.95 mg (SD 20.30, range 0–105). (See Table 1).

2.3.2. ECT procedure

Bitemporal ECT (standard Bifrontotemporal, APA, 2001) was administered 2 or 3 (mean 2.74, SD 0.48) times per week using a Thymatron System IV device (Somatics Inc, Lake Bluff, Ill). Anaesthesia given was thiopental (2–2.5 mg/kg) or propofol (0.5–1.5 mg/kg) and succinylcholine (0.5 mg/kg). Initial charge was determined using the half-age method (Petrides and Fink, 1996). Charge was increased in increments of 50.4 mC over the ECT course as needed to maintain seizures of EEG≥15 s and adequate morphology (Krystal et al., 1998).The number of ECT sessions was determined by the patient's psychiatrist, according to clinical response. (See Table 1).

Table 1
Demographic, clinical and treatment related data.

N.	90
Demographical variables	
Age (yr), mean (SD)	65.7 (12.7)
Gender: male, *n* (%)	35 (38.9%)
Illness course variables	
First episode, *n* (%)	7 (7.8%)
Recurrent, *n* (%)	83 (92.2%)
Melancholic features, *n* (%)	85 (94.4%)
Psychotic features, *n* (%)	42 (46.7%)
Current episode duration (wk), mean (SD)	48.7 (99.8)
Treatment resistance (Thase), *n* (%)	
Resistance 0	7 (7.8%)
Resistance 1	18 (20%)
Resistance 2	13 (14.4%)
Resistance 3	41 (45.6%)
Resistance 4	11 (12.2%)
Resistance 5	0 (0%)
Onset age (yr), mean (SD)	45.8 (16.8)
Previous depressive episodes, mean (SD)	3.3 (2.6)
Previous ECT, *n* (%)	31 (34.4%)
Current episode data	
HDRS score pre-ECT, mean (SD)	30 (6.3)
Days of hospitalization, mean (SD)	41 (14.7)
HDRS post-ECT, mean (SD)	3.99 (3.2)
Concurrent medications	
Antidepressants taken during ECT course, *n* (%)	90 (100%)
Increase in the dose, *n* (%)	35 (38.9%)
Change in the antidepressant, *n* (%)	23 (25.6%)
Benzodiazepines taken during ECT course, *n* (%)	75 (83.3%)
One benzodiazepine taken, *n* (%)	48 (53.3%)
Two benzodiazepines taken, *n* (%)	23 (25.6%)
Three benzodiazepines taken, *n* (%)	4 (4.4%)
Antipsychotics taken during ECT course, *n* (%)	46 (51.1%)
Lithium taken during ECT course, *n* (%)	5 (5.6%)
Anaesthetic used	
Thiopenthone, *n* (%)	86 (95.6%)
Propofol, *n* (%)	4 (4.4%)
ECT treatment parameters	
Number of ECT treatments received, mean (SD)	11.1 (2.9)
Dose first ECT (mC), mean (SD)	175.8 (55.5)
Dose last ECT (mC), mean (SD)	259.3 (108.6)
Average dose (mC) across treatments, mean (SD)	223.3 (78.0)
ECT PW used	
1 ms, *n* (%)	65 (72.2%)
0.5 ms, *n* (%)	25 (27.8%)
Average EEG duration across treatments (s), mean (SD)	30.7 (7.6)

Resistance 0 (no adequate treatment); Resistance 1 (no response to one adequate treatment); Resistance 2 (no response to 2 adequate treatments with different profiles); Resistance 3 (no response to 2 adequate treatments with different profiles +no response to potentiation/resistance to ATCs*); Resistance 4 (no response to 2 adequate treatments with different profiles+no response to potentiation/resistance to ATCs*+no respond to 2nd potentiation/resistance to IMAOs*); Resistance 5 (no response to 2 adequate treatments with different profiles+no response to potentiation/resistance to ATCs*+no response to 2nd potentiation/resistance to IMAOs*+no response to bilateral ECT). SD (standard deviation), MDD (major depressive disorder), wk (weeks), ECT (electroconvulsive therapy), HDRS (Hamilton Depression Rating Scale),*ATCs (tryciclic antidepressants), *IMAOs (selective inhibitors of monoamine oxidase A), mC (miliColoumbs), PW (pulse width), ms (miliseconds), mg (miligrams), sec (seconds).

2.4. Clinical evaluations

Mood ratings were collected by a trained psychiatrist using the HDRS-21 scale at baseline and weekly over the ECT course until treatment termination. Remission was defined at ≤7 (Riedel et al., 2010) and response as 50% reduction from baseline scores to the end of the ECT course.