Exciting matters in electroconvulsive therapy : studies on seizure thresholds

Waarde, J.A.. van

3

Exceptionally high initial seizure threshold in a catatonic patient treated with electroconvulsive therapy

Jeroen A. van Waarde
Michael E.M.T. Müller
Bastiaan Verwey
Rose C. van der Mast

Journal of ECT 2009;25:121-124

Abstract

Background: Seizure threshold in electroconvulsive therapy (ECT) is generally defined as the smallest electrical stimulus dose that produces a generalized seizure of at least 25 to 30 seconds on electroencephalogram. Seizure thresholds vary considerably among patients, and some patients have an exceptionally high initial seizure threshold. We describe a patient with catatonia who showed an initial seizure threshold exceeding 500 milliCoulombs (mC). The literature was searched for other reports on this phenomenon.

Methods: A systematic review was conducted using MedLine from 1966 to January 2008 and PsychINFO (2007), cross-referencing ECT and (excessively high) seizure threshold, as well as standard works on ECT. The literature was scrutinized for reports on high initial seizure threshold and associated demographic and clinical characteristics.

Results: Besides our patient, 6 articles were found reporting on 9 severely depressed, mostly elderly patients (aged 45-85 years; 5 males, 2 females, 2 persons with unknown sex) with excessive initial seizure thresholds ranging from 335 to 896 mC, and most with cardiovascular compromise. Strategies to lower seizure thresholds in ECT included manipulation of stimulus parameters, adjustment of anesthetics, and augmentation with proconvulsant agents.

Conclusions: Because reports on exceptionally high initial seizure thresholds in ECT are rare, no definite conclusions can be drawn regarding its possible risk factors and management. However, since high initial seizure thresholds can complicate ECT, it is clinically important to further investigate this phenomenon.

Introduction

In clinical practice, some patients treated with electroconvulsive therapy (ECT) show exceptionally high initial seizure thresholds. At the first ECT session, a high stimulus dose is then needed to induce a seizure of sufficient length in case a stimulus titration method [1] is used, or a subconvulsive stimulus is the result of the initial "age-based estimated dose method". Seizure threshold in ECT is generally defined as the smallest electrical stimulus dose that results in a generalised seizure of at least 25 to 30 seconds on electroencephalogram (EEG).[2,3] Seizure thresholds vary greatly among patients, and no consistent relationship has been found with the antidepressant response, except in unilateral ECT.[4,5] Induction of any seizure activity is thought to be imperative for effectiveness of ECT,[2] whereas it has also been reported that subconvulsive stimulation can be dangerous for the patient because of harmful bradycardia or asystole.[6] Exceptionally high seizure thresholds may therefore complicate ECT, due to the increased risk of inadequate treatment, especially in countries where the maximum stimulus dose of ECT devices is limited.[7]

In this report we describe ECT in a catatonic patient who needed an exceptionally high initial stimulus dose to induce an adequate seizure. The literature was searched for other reports on this phenomenon paying special attention to clinical and treatment characteristics and to strategies for management of high initial seizure threshold.

Case report

A 76-year-old patient with a history of recurrent depressive disorder with psychotic features and personality disorder for more than 20 years was referred for ECT because of catatonia during the last two months. She had a history of diabetes mellitus type 2, myocardial infarction, and ischemic cerebral infarction; in addition a moderate to severe aortic stenosis and aortic insufficiency had recently been diagnosed. During the previous year symptoms of cognitive impairment had emerged, probably due to cerebral cardiovascular disease. At admission, she almost exclusively showed severe muscle rigidity and mutism. On the Bush-Francis Catatonia Rating Scale (CRS), a score of 18 (from a maximum of 69 points) was rated.[8] The patient's clinical condition deteriorated quickly because she could not eat or drink. ECT was considered to be the treatment with the least risks and the highest probability to achieve improvement of her condition. In line with the clinical diagnosis of catatonia, apart from dehydration with uremia and masked

anemia, no abnormalities were found in blood tests. Cerebral MRI showed generalized atrophy with central and peripheral liquor spaces and bilateral periventricular white matter lesions. No signs of infarction were found.

At the first ECT session, anesthesia was induced with 10 mg etomidate intravenously (IV). Because the patient had been immobile for a prolonged period muscle relaxation was initiated with 8 mg mivacurium IV, instead of succinylcholine, to inhibit release of large amounts of potassium. In addition, 0.5 mg methylatropine IV was given to prevent bradycardia. Metoprolol was administered to prevent tachycardia and hypertension; in patients with aorta stenoses the latter conditions are potentially fatal. Standard bilateral (bifrontotemporal) ECT was administrated with the Thymatron IV (constant current, 0.9 Ampère; brief pulse; Somatics, Lake Bluff, Ill., USA). Seizure duration was monitored by EEG and motor activity by electromyography using the cuff method.

At the first stimulus, a dose of 223.2 milliCoulombs (mC; frequency, 70 Hz; pulse width, 0.25 milliseconds; stimulus duration, 7.2 seconds; static impedance, 1620 Ω; dynamic impedance, 270 Ω) was administered. This dosage was considered to be well above the age-based estimated seizure threshold. However, no muscle contractions occurred, and no seizure activity was registered on the EEG; the patient continued to have a regular heart rate and normal blood pressure. After 30 seconds, a second dose of 497.8 mC (frequency, 140 Hz; pulse width, 0.25 milliseconds; stimulus duration, 8 seconds; static impedance, 1460 Ω; dynamic impedance, 270 Ω) was given, again without any motor or EEG convulsive activity. While the patient was still adequately paralyzed and anesthesia was maintained, a third stimulus of 760.8 mC (frequency, 70 Hz; pulse width, 0.75 milliseconds; stimulus duration, 8 seconds; static impedance, 1350 Ω; dynamic impedance, 260 Ω) could be given. This stimulus resulted in 22 seconds of motor activity, and 29 seconds of EEG seizure activity.

Because of the patient's clinical condition, ECT was administered daily. During treatments, the stimulus doses and etomidate doses were kept identical resulting in adequate seizures with duration of motor activity ranging from 20 to 38 seconds. After 6 ECT sessions, the Catatonia Rating Scale score declined to 6 points, and after the 10th ECT session, the score was only 1 point. Clinically, the patient could speak, eat and drink again, and the catatonic features were no longer present. Unfortunately, after the 10th session, the patient suddenly developed paralysis of the left side of her face and mouth for several hours. After 3 days, the CT scan did not show infarction of the brain. However, ECT was discontinued because a transient ischemic attack was suspected, and it was considered that there was a

substantial risk of inducing more (severe) vascular incidents. The catatonia did not recur, and the patient was transferred back to the long-stay facility where she lived before admission to the hospital.

Literature search

We made a systematic search of the literature for other reports on patients with this phenomenon using Medline from 1966 to January 2008 and PsychINFO (2007), cross-referencing ECT and (excessively high) seizure threshold. The references of the articles found were hand searched for any additional reports. Furthermore, standard works on ECT were consulted.[2,3,9] We were especially interested in demographic and clinical factors that might enhance the initial seizure threshold and in strategies for its prevention. The abstracts of the articles found were scrutinized for reports on patients with high initial seizure thresholds in ECT, associated demographic and clinical characteristics, and recommendations for its management. Articles that did not describe any patient characteristics or descriptions of initial seizure thresholds were excluded.

Only 6 articles reporting on 10 patients with excessive initial seizure thresholds were found (Table 1).[7,10-14] The highest seizure threshold (3,226 mC) was described in a patient treated with ECT for status epilepticus,[14] although ECT is normally not indicated in such a condition. The other 5 case reports described high initial seizure thresholds (ranging from 335 to 896 mC) in severely depressed, mostly elderly patients (age range, 45-85 years; 5 males, 2 females; in 2 patients, data on age and sex were lacking). In 5 patients, comorbid somatic diseases were described, mostly of cardiovascular origin. In the literature, several factors influencing the seizure threshold could be identified, of which many were present in our patient (see Discussion). Some of the methods reported to lower seizure thresholds are given in Table 2.[2,12,15-24]

Table 1 Characteristics of patients (n= 10) with exceptionally high initial seizure thresholds, reported in the literature

Reference	Sex	Age (years)	Indication for ECT	Comorbidity	Initial seizure threshold*
[10]	Female	45	Major depression	Hypertension; diabetes mellitus type 2; dialysis-dependent renal failure; cardiomegaly; peripheral neuropathy; retinopathy	576 mC
	Female	74	Major depression	Dementia due to small-vessel cerebrovascular disease; hypertension; urinary incontinence; organic heart disease	RUL: 576 mC
[11]	Male	'elderly'	Psychotic depression	-	BL: 672 mC
[7]	Male	70	Bipolar depression	Renal insufficiency; hypertension; diabetes mellitus; atrial fibrillation	BL: 840 mC
	Male	85	Recurrent major depression	Cardiovascular diseases	RUL: 896 mC
[13]	-	-	Major depression	-	BL: 428 mC (n=1)
	-	-	Major depression	-	BL: 335 mC (n=2)
[12]	Male	54	Major depression	-	RUL: 840 mC
	Male	80	Major depression	-	BL: 576 mC
[14]	Male	36	Status epilepticus	Partial left posterior frontal resection	Modified (right frontotemporal + left anterior-frontal): 3,226 mC

*In milliCoulombs (mC); RUL: right unilateral electrode placement (d'Elia); BL: bifrontotemporal placement.

Table 2 Methods used to overcome high seizure threshold in patients undergoing ECT

Manipulation of stimulus parameters	**Reference**
(Switch to, or provide) unilateral ECT d'Elia.	[27]
Raise the stimulus dose Provide longer stimulus duration with same dosage Lower stimulus frequency Lower the frequency of treatments	[2,17,18]
Adjustments made by the anesthesiologist	
Switching anesthetic (administration of etomidate is advised as first-line in patients with high seizure thresholds; administrating ketamine or combining methohexital with alfentanil may prolong seizure duration)	[15]
Hyperventilation before stimulation, which lowers the carbon oxide level thereby raising neuroexcitability	[2,19]
Administer antagonist (flumazenil) if concomitant benzodiazepines are used	[12,20]
Augmentation strategies during ECT	
Caffeine augmentation significantly increases seizure duration, but does not decrease the seizure threshold	[19]
Theophiline augmentation	[19]
Concomitant use of an antipsychotic (chlorpromazine and clozapine have a relatively high seizurogenic potential).	[21]
Concomitant use of an antidepressant use (maprotiline, clomipramine, bupropion) is inconclusive	[21]
Augmentation strategies during ECT	
If possible, advise the patient to stop using or lower the use of anticonvulsants, benzodiazepines (also hypnotics), and antihypertensive medication (e.g. beta-blockers and calcium antagonists)	[2,16]
Advise sleep deprivation the night before ECT	[22]
Advise the patient to stop drinking alcohol	[23]
Encourage weight loss in an obese Chinese patient	[24]

Discussion

We have described bilateral ECT in a 76-year-old female catatonic patient with an exceptionally high initial seizure threshold. Because 2 preceding subconvulsive stimuli may have lowered the seizure threshold, her initial threshold might have been even higher.[25] A literature search revealed only 10 other cases with excessively high initial seizure thresholds. Compared with our patient, in most other cases, even higher seizure thresholds had to be overcome in order to elicit an adequate seizure. Several factors might have played a role in the occurrence of the exceptionally high seizure threshold in our patient, including, higher age, pre-existent dementia, large medical burden (in particular of cardiovascular origin), dehydration, use of metoprolol before ECT, bilateral electrode placement, lower dynamic impedance (260-270 Ω), and higher pulse frequency (70-140 Hz). Malnutrition for several months may have further contributed to the excessively high seizure threshold of our patient. It has been shown in young rats that a low-carbohydrate diet produces a significant increase of the seizure threshold.[26] On the other hand, female patients generally have a lower seizure threshold than males,[27] and the stimulus parameters used in our patient (i.e., long stimulus duration and short pulse width) may have contributed to lowering her seizure threshold.[18] Etomidate has been recommended as the first-line anesthetic for patients with very high seizure thresholds.[15] Because we routinely administer etomidate, lowering the seizure threshold by switching to another anesthetic was not an option with our patient. The cardiovascular condition of our patient was severely compromised as shown by the transient ischemic attack during the treatment period. Earlier, higher severity scores for cardiac illness and other forms of vascular diseases have been associated with higher seizure thresholds.[12] Concomitant use of antihypertensives and antiarrhythmics may have raised the seizure threshold in our patient who was given metoprolol before the first ECT because of aortic stenosis to prevent severe tachycardia and hypertension.[16,28]

In conclusion, patients with an exceptionally high seizure threshold at their first ECT are rare. Until now, besides our patient, very few have been reported in the literature. Several factors are known to raise the seizure threshold, thereby complicating ECT. Some of these factors might be managed clinically, with the aim to improve treatment and hopefully the outcome in individual patients. Further research may help to identify patients with exceptionally high seizure thresholds, to better understand their underlying causes, and to better deal with such phenomena.

Acknowledgments
The authors thank J.H.A.M. Tuerlings, MD, PhD, for critically reviewing the manuscript.

References

(1) Malitz S, Sackeim HA, Decina P. ECT in the treatment of major affective disorders: clinical and basic research issues. Psychiatr J Univ Ottawa 1982;7.
(2) Abrams R. Electroconvulsive Therapy. Fourth edition. New York, NY: Oxford University Press; 2002.
(3) Coffey CE. The Clinical Science of Electroconvulsive Therapy. Washington DC: American Psychiatric Press Inc; 1993.
(4) Abrams R. Stimulus titration and ECT dosing. J ECT. 2002;18:3-9.
(5) Sackeim HA, Prudic J, Devanand DP et al. Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. N Engl J Med 1993;328:839-846.
(6) Welch CA, Drop LJ. Cardiovascular effects of ECT. Convuls Ther 1989;5:35-43.
(7) Lisanby SH, Devanand DP, Nobler MS, et al. Exceptionally high seizure threshold: ECT device limitations. Convuls Ther 1996;12:156-164.
(8) Bush G, Fink M, Petrides G, et al. Catatonia. I. Rating scale and standardized examination. Acta Psychiatr Scand 1996;93:129-136.
(9) American Psychiatric Association. The Practice of Electroconvulsive Therapy. Second Edition. Washington DC: American Psychiatric Association; 2001.
(10) Lurie SN, Coffey CE. Caffeine-modified electroconvulsive therapy in depressed patients with medical illness. J Clin Psychiatry 1990;51:154-157.
(11) Sackeim HA. Are ECT devices underpowered? Convuls Ther 1991;7:233-236.
(12) Boylan LS, Haskett RF, Mulsant BH et al. Determinants of seizure threshold in ECT: benzodiazepine use, anesthetic dosage, and other factors. J ECT 2000;16:3-18.
(13) Shapira B, Lidsky D, Gorfine M, et al. Electroconvulsive therapy and resistant depression: clinical implications of seizure threshold. J Clin Psychiatry 1996;57:32-38.
(14) Lisanby SH, Bazil CW, Resor SR, et al. ECT in the treatment of status epilepticus. J ECT 2001;17:210-215.
(15) Khalid N, Atkins M, Kirov G. The effects of etomidate on seizure duration and electrical stimulus dose in seizure-resistant patients during electroconvulsive therapy. J ECT 2006;22:184-188.
(16) Luchowska E, Luchowski P, Wielosz M, et al. Propranolol and metoprolol enhance the anticonvulsant action of valproate and diazepam against maximal electroshock. Pharmacol Biochem Behav 2002;71:223-231.
(17) Girish K, Gangadhar BN, Janakiramaiah N, et al. Seizure threshold in ECT: effect of stimulus pulse frequency. J ECT 2003;19:133-135.
(18) Kotresh S, Girish K, Janakiramaiah N, et al. Effect of ECT stimulus parameters on seizure physiology and outcome. J ECT 2004;20:10-12.
(19) Datto C, Rai AK, Ilivicky HJ, et al. Augmentation of seizure induction in electroconvulsive therapy: a clinical reappraisal. J ECT 2002;18:118-125.
(20) Krystal AD, Watts BV, Weiner RD, et al. The use of flumazenil in the anxious and benzodiazepine-dependent ECT patient. J ECT 1998;14:5-14.
(21) Pisani F, Oteri G, Costa C, et al. Effects of psychotropic drugs on seizure threshold. Drug Saf 2002;25:91-110.
(22) Gilabert E, Rojo E, Vallejo J. Augmentation of electroconvulsive therapy seizures with sleep deprivation. J ECT 2004;20:242-247.
(23) Hillbom M, Pieninkeroinen I, Leone M. Seizures in alcohol-dependent patients: epidemiology, pathophysiology and management. CNS Drugs 2003;17:1013-1030.
(24) Chung KF. Determinants of seizure threshold of electroconvulsive therapy in Chinese. J ECT 2006;22:100-102.
(25) Swartz CM. Stimulus dosing in electroconvulsive therapy and the threshold multiple method. J ECT 2001;17:87-90.
(26) Bough KJ, Valiyil R, Han FT, et al. Seizure resistance is dependent upon age and calorie restriction in rats fed a ketogenic diet. Epilepsy Res 1999;35:21-28.

(27) Sackeim HA, Decina P, Portnoy S, et al. Studies of dosage, seizure threshold, and seizure duration in ECT. Biol Psychiatry 1987;22:249-268.
(28) Mueller PS, Barnes RD, Varghese R, et al. The safety of electroconvulsive therapy in patients with severe aortic stenosis. Mayo Clin Proc 2007;82:1360-1363.