Cranial Electrotherapy Stimulation for the Treatment of Chronically Symptomatic Bipolar Patients

Mostafa Amr, MD, Mahmoud El-Wasify, MD,* Ahmed Z. Elmaadawi, MD,† R. Jeannie Roberts, MD,‡ and Rif S. El-Mallakh, MD‡*

Objective: The aim of this study was to determine if cranial electrotherapy stimulation (CES) is beneficial in chronically symptomatic bipolar (CSBP) subjects.

Methods: A retrospective chart review of all consecutive CSBP subjects who were prescribed CES collected demographic and clinical information.

Results: The Clinical Global Impression improved significantly [mean (SD), 2.7 (0.6) at baseline vs 2.0 (0.0), $t = 0$, $P < 0.001$], but mood symptoms change minimally. There were very few adverse effects of CES.

Conclusions: Patients with CSBP continue to experience symptoms with CES but also are modestly improved.

Key Words: bipolar disorder, cranial electrical stimulation, chronically symptomatic bipolar patients, depression, mania

(*J ECT* 2013;29: e31–e32)

Dear Editor:

Subsyndromal symptoms are common in bipolar disorders.[1] Subsyndromal symptoms occupy 14.8% of the lives of type I bipolar patients and 15.7% of type II patients.[1] Anxiety disorder may co-occur with bipolar disorder in more than 90% of patients.[2] High rates of co-occurrence of personality disorders, substance abuse disorders, and attention deficit disorder are also notable.[2]

These issues conspire to create a significant fraction of bipolar patients who are chronically or frequently symptomatic. These groups of patients are clinically challenging and frequently require extensive polypharmacy. Despite aggressive treatment, chronically symptomatic bipolar patients (CSBP) continue to exhibit cycling, mixed polarity, and subsyndromal symptoms.

Cranial electrotherapy stimulation (CES) was approved by the US Food and Drug Administration for treating anxiety, depression, and insomnia in 1979. Its use in CSBP has not been examined.

METHOD

Design

This was a retrospective chart review of naturalistic use of CES in CSBPs. Chronically symptomatic bipolar patients have variable psychiatric symptoms that do not meet syndromal levels. These patients are not rapid cycling because they do not meet syndromal criteria but are chronically symptomatic. Seven consecutive patients met inclusion criteria of a diagnosis of bipolar type I or type II and chronic symptoms not responsive to ongoing medication. Data were collected for 8 weeks.

All patient used the AlphaStim SCS (Electromedical Products International, Inc, Mineral Wells, Tex). Each patient was instructed to set the current between 10 and 500 μA and a frequency of 0.5 Hz, with pulse duration of 2 milliseconds, for 1 or 2 daily sessions ranging from 20 to 60 minutes each. The electrical current was delivered by 2 surface wet electrodes that were clipped to both ear lobes.

Data collected from the charts included the Global Assessment of Function, Clinical Global Impression (CGI), the Montgomery Asberg Depression Rating Scale, and the Young Mania Scale.

Data Analysis

Differences were examined using paired *t* tests.

RESULTS

Five women and 2 men participated. The mean (SD) age was 42.3 (6.4) years. Four had type II illness, and 3 had type I. All patients were on anticonvulsant mood stabilizers or lithium and a second-generation antipsychotic. Most were also on other medications that addressed anxiety (gabapentin, propranolol, prazocin, or a benzodiazepine), sleep disturbance (trazadone, ropinirole), or attentional problems (methylphenidate). The mean number of psychotropic medications was 4.25 (compared with the overall clinic mean of 3.0 psychotropics). The patients titrated their duration and current strength to their perceived optimal level. Nearly always this corresponded to a setting of 4 (approximately 350 μA), for 30 minutes daily. Two patients used the maximum setting of 6 (approximately 500 μA), for 1 hour daily. Most patients varied the length of the sessions on a daily basis, usually in response to their level of distress on that particular day, so that an accurate duration could not be determined. Clinical Global Impression significantly decreased (Table 1). Most measured variables also improved nonsignificantly (Table 1). The effect size of the improvement in depressive symptoms was small 0.1. The power of the current study for capturing a difference of that effect is moderate at 0.48. A sample of approximately 20 patients would be required to show that the improvement is significant. There were very few adverse consequences. Four reported mild light-headedness or dizziness, which was not sufficient to discontinue treatment. Four subjects thought that the improvement was sufficient to warrant purchasing the device.

DISCUSSION

In this naturalistic retrospective chart review of CSBPs, the use of CES was associated with a small effect in symptom improvement. A significant improvement was seen in CGI, which improved nearly 25% ($P < 0.001$; Table 1). Depressive symptoms improved some 34%, and manic symptoms improved

From the *Department of Psychiatry, Mansoura Faculty of Medicine, Mansoura, Egypt; †Department of Psychiatry, Mayo Clinic, Rochester, MN; and ‡Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Louisville, Louisville, KY.

Received for publication January 2, 2012; accepted June 28, 2012.

Reprints: Rif S. El-Mallakh, MD, Mood Disorders Research Program, Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Louisville, Medcenter One, 501 E Broadway, Suite 340, Louisville, KY 40202 (e-mail: rselma01@louisville.edu).

Conflicts of interest: Dr El-Mallakh is on the speaker's bureau of Astra Zeneca, Bristol Myers Squibb, Merck, and Novartis. There are no other potential conflicts to report.

DOI: 10.1097/YCT.0b013e31828a344d

TABLE 1. Mean Scores of the Study Outcomes at the Baseline and End of Treatment

	Baseline, Mean (SD)	End of Study Week 8, Mean (SD)	Significance Test	Percent Changes
MADRS	17.3 (2.9)	11.5 (3.5)	$t = 2.6$, $P = 0.122$	34% decrease
YMS	4.8 (4.1)	3.8 (2.9)	$t = 0.6$, $P = 0.635$	21% decrease
CGI	2.7 (0.6)	2.0 (0.0)	$t = 0$, $P < 0.001$	24.8% decrease
GAF	68.3 (5.8)	71 (7.9)	$t = 1$, $P = 0.5$	3.7% increase

GAF, Global Assessment of Function; MADRS, Montgomery Asberg Depression Rating Scale; YMS, Young Mania Scale.

21% (both not significant; Table 1). The lack of significant improvement in mood symptoms suggests that the CGI effect may have been driven by improvements in anxiety or other factors, which were not measured in these patients.

These results are in line with previously reported effects of CES. A survey in 2002 showed that 66% of patients with depression had greater than 50% improvement, and 31% of patients reported greater than 75% improvement.[3] More than 35% of patients with anxiety alone (n = 128) reported greater than 75% improvement, but only 29% of patients with both anxiety and depression (n = 58) had greater than 75% improvement.[3] However, survey studies may overestimate the efficacy of treatment modalities, the results are, nonetheless, important to consider.

Even with a small effect size, CES may be a reasonable intervention because it has very few adverse effects (AEs).[4] Adverse effects are uncommon, headache (0.20%) and local skin irritation (0.11%) are the more frequent but are generally mild. Other rare AEs include vertigo, dizziness, disorientation, seizures, nausea, and electrical skin burns at the site of the electrodes. Many of these AEs can be modified by reduction in treatment intensity. In our patients, AEs were very rare and mild.

The mechanism of CES is not known. It is believed that CES may stimulate the vagus nerve, causing a parasympathetic response and resultant relaxation. Much of the effect is believed to be mediated by brain stem nuclei that radiate widely through the central nervous system.[5] This includes all the systems believed to be important in mood and anxiety disorders (dopamine, serotonin, and norepinephrine). Cranial electrotherapy stimulation has been shown to increase synchronous activity on electroencephalogram.[5] This may increase the antidepressant or anxiolytic activity of endogenous systems.[5]

This study has several limitations. First, this was a retrospective naturalistic study without a sham group. Second, the small study sample did not allow for adequate power for the effect size of improvement with CES. Despite these limitations, this study demonstrates that nearly half of CSBP patients feel the improvement in symptoms is worth the financial investment in the device. A larger sample size, a longer intervention period of CES, and the addition of a sham group need to be used in future studies of CES in CSBP.

REFERENCES

1. Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. *Arch Gen Psychiatry.* 2003;60:261–269.
2. Keck PE Jr, Kessler RC, Ross R. Clinical and economic effects of unrecognized or inadequately treated bipolar disorder. *J Psychiatr Pract*. 2008;14(suppl 2):31–38.
3. Smith RB. Microcurrent therapies: emerging theories of physiological information processing. *NeuroRehabilitation*. 2002;17:3–7.
4. Gilula MF, Barach PR. Cranial electrotherapy stimulation: a safe neuromedical treatment for anxiety, depression, or insomnia. *South Med J.* 2004;97:1269–1270.
5. Zaghi S, Acar M, Hultgren B, et al. Noninvasive brain stimulation with low-intesity electrical currents: putative mechanisms of action for direct and alternating current stimulation. *Neuroscientist*. 2010;16:285–307.

