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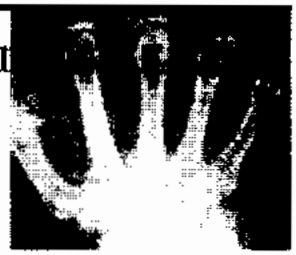

The Treatment of Fibromyalgia with Cranial Electrotherapy Stimulation

Alan S. Lichtbroun, Mei-Ming C. Raicer, Ray B. Smith

In cranial electrotherapy stimulation (CES), microcurrent levels of electrical stimulation are passed across the head via electrodes clipped to the ear lobes. After successful clinical use of CES with fibromyalgia patients in our clinic, it was decided to test these results with a double-blind, placebo-controlled study in which 60 randomly assigned patients were given 3 weeks of 1-hour-daily CES treatments, sham CES treatments, or were held as wait-in-line controls for any placebo effect in the sham-treated patients. Treated patients showed a 28% improvement in tender point scores, and a 27% improvement in self-rated scores of general pain level. The number of subjects rating their quality of sleep as poor dropped from 60% at the beginning of the study to 5%. In addition, there were significant gains in the self-rated feelings of well-being and quality of life, plus gains in six stress-related psychological test measures. No placebo effect was found among the sham-treated controls. A theoretical role of CES in affecting the brain's pain message mechanisms and/or neurohormonal control systems is discussed. It is concluded that CES is as effective as the drug therapies in several trials, with no negative side effects, and deserves further consideration as an additional agent for the treatment of fibromyalgia. **(J Clin Rheumatol 2001;7:72–78)**

Key words: Fibromyalgia, CES, Electrotherapy, Microcurrent

Cranial electrotherapy stimulation (CES) is a U.S. Food and Drug Administration–recognized, drug-free treatment for anxiety, depression, and insomnia. CES typically involves the passage of microcurrent levels of biphasic electrical stimulation across the head for from 20 minutes to an hour daily for a few days to a few weeks, depending on the disorder being treated. The stimulation levels applied in double-blind research studies are always below sensation level, and are also often at this level during the normal clinical use of CES.

Since CES arrived in the United States in the late 1960s, over 125 human and animal studies have been completed (1). Most of the animal studies were performed to elicit mechanisms of action, patterns of electrical current transfer through the brain, and related physiologic concomitants to the stimulation. The studies by Pozos et al. in dogs at the University of Tennessee Medical Center yielded strong inferential evidence that CES worked to bring neurotransmitters in the brain back into homeostatic balance, once he had mechanically disrupted that balance (2).

Whereas many earlier clinicians doubted that an electric current of such small intensity actually entered the brain, rather than just spreading around the scalp tissue and hair, researchers at the University of Wisconsin Medical School used monkeys to show that 42% of the current applied at the skin surface traveled throughout the brain, canalizing especially across the limbic system (3).

Early CES research on anxiety and depression often used inpatient populations of addicts who were experiencing the drug abstinence syndrome. It was in these studies that CES was found invaluable in inducing medication-free reductions in anxiety and depression while simultaneously improving sleep (4, 5). It was also during these studies that the benefits of CES in improving cognitive dysfunction were found (6–8). For example, it was discovered that the 24 months of total sobriety that were normally required to bring an alcoholic patient's cognitive function back to normal could be accomplished with 3 weeks of 45- 60-minute-daily CES treatments. Cognitive recovery findings were later

Robert Wood Johnson Medical School, East Brunswick, NJ (ASL); Real World Health, Wall, NJ (M-MCR); Electromedical Products International, Mineral Wells, TX (RBS).

Address correspondence to: Mei-Ming C. Raicer, MS, Research Clinician, Real World Health, 1414 Francis Drive, Wall, NJ 07719. Fax: 732-280-5991.

extended to other clinical groups such as patients with closed head injuries (9) and children and adults with attention deficit disorder (10). Electroencephalographic studies in patients with insomnia have found CES effective in reducing sleep onset time, number of awakenings during the night, time spent in stage IV (delta) sleep, and patient report of feeling rested upon awakening (11). Most recently, it has been noted that CES is associated with an increase in insulin-like growth factor-1 (IGF-1) levels in older female patients (12).

Perhaps because of its use in the treatment of various stress disorders, CES is finding an ever-greater use in the treatment of several pain syndromes (13). Many clinicians believe that the pain threshold tends to lower in response to stress and rise as stress is reduced. Schuster states, "Patients' psychological states influence their perceptions of pain; anxiety can decrease patients' pain thresholds. Increased anxiety . . . can increase pain" (14). Bennett agrees, saying, "there is . . . overwhelming evidence that psychologic factors do affect perception of pain. . ." (15).

The fibromyalgia literature has documented problems in fibromyalgia patients that involve many of the areas in which CES has been found effective. One reviewer found studies in which insomnia was a major contributing problem in fibromyalgia (16), and Wolfe found that more than 75% of patients with fibromyalgia experience a nonrestorative sleep pattern (17). Another reviewer noted that in addition to sleep problems, the fibromyalgia patients also suffered from marked anxiety and depression (18). Another study has found consistently low levels of IGF-1 levels in fibromyalgia patients when compared with nonfibromyalgia controls (19).

Although we have treated a large number of fibromyalgia patients in our clinic over the years, we only recently became aware of the CES research findings. Once this research was brought to our attention, we completed a successful open clinical trial of CES treatment of our fibromyalgia patients. After that, we decided to perform a double-blind, placebo-controlled study to see if these effects were attributable to the CES treatment or to placebo effect alone.

PATIENTS AND METHODS

After approval of the study protocol by the Investigational Review Board of the Robert Wood Johnson Medical School, 60 patients from our large fibromyalgia practice signed volunteer consent forms to participate in the study. The first author (ASL), a physician, had previously diagnosed them as having fibromyalgia, using the criteria set forth by the American College of Rheumatology (20). The subjects' age range was 23 to 82 years (mean, 50); there were two men and 58 women including two African Americans and one Asian American. They had suffered with fibromyalgia from 1 to 40 years, with an average of 11 years. No change was made in the medical treatment regimen then underway of any subject in the study.

The subjects were randomly assigned into three separate groups by an office secretary who drew their names, which were on separate, sealed slips of paper in a container. Groups I and II were assigned to CES devices that would provide either subsensation treatment or sham treatment. Group III served as wait-in-line placebo controls, to control for any placebo effect experienced by the sham-treated group. The Alpha-Stim CES device was used (Electromedical Products International, Inc., Mineral Wells, TX). Each device was preset to provide 1 hour of 100-μA, modified square-wave biphasic stimulation on a 50% duty cycle at 0.5 Hz, and to automatically turn off at the end of the hour. To prevent the subjects from increasing the current from the 100-μA presetting, once the current level had been set, the current setting dial was removed from the device and the space that it occupied was permanently sealed. All treatment was given via electrodes clipped to the ear lobes. Sham treatment was provided by identical ear clip electrodes that did not pass current. All ear clip electrodes had a number etched on them, identifying each as real or sham treating, and the code was kept in a sealed envelope away from the study site.

All subjects, the staff, the examining physician, and the psychometrician remained blind to the treatment conditions. After the study, the staff opened the code envelope and separated the patient evaluation forms into treatment, sham treatment, or placebo control groups. The statistician who evaluated the final study results remained blind to the treatment conditions, working from three identical groups of study data during the data analysis. The above procedures rendered the study essentially quadruple-blind.

Just prior to beginning the treatment phase of the study, the study physician pretested all patients on nine bilateral tender points and three bilateral sham tender points. The sham points were on the biceps, the abdomen, and the gastrocnemius. Any scores obtained at these points were subtracted from the total tender point score. The patients then completed self-ratings of overall pain, quality of sleep, feeling of well-being, and quality of life, all on 10-point self-rating forms that were provided. Finally, the patients completed the Profile of Mood States (POMS) (Educational and Industrial Testing Service, San Diego, CA), a standardized paper and pencil psychological test measuring the following mood factors: tension/anxiety, depression/dejection, anger/hostility, energy/vigor, fatigue/inertia, and confusion/bewilderment. An overall total mood disturbance

score could also be computed with a formula given in the POMS user's manual.

Following the pretests, subjects in groups I and II were taught how to use the CES unit, and they were instructed to use it every day for 1 hour over a 3-week period. At the end of that time, they returned to the clinic for posttreatment evaluations as above. Group III subjects were given no CES device, but they were told to return in 3 weeks for retesting.

All subjects were told that those sham-treated and placebo-controlled patients who did not receive treatment during the study would be provided CES treatment after the conclusion of the double-blinded part of the study if they wished. That treatment would be in an open, non–double-blind clinical trial in which each patient would be provided an Alpha-Stim CES unit to use at home, and they would be allowed to adjust the stimulation intensity to maximum comfort level.

During the study, a clinical staff member called each member of groups I and II once a week to check on compliance. It was checked again when subjects came in for final study evaluations.

RESULTS

No differences were found on the 12 pretest measures among the three study groups at the beginning of the study. The question sometimes arises in studies of this kind if the study outcome might be attributed to differences in patient medications in the various study groups. We did not control specifically for that, assuming that the randomization of patients into the three groups would scatter this effect more or less equally across the groups. These results indicate that the assumption was correct.

The double-blind condition depended on the stimulation current being below sensation threshold in most patients so that the patients would not know whether or not they were actually receiving treatment. CES electrodes contain a felt covering that is thoroughly wetted prior to placing it on the patient, and many patients experience the cold covering as stimulation, and they report a feeling of tingling, even after the moistened felt has warmed to skin temperature. Because sham-treated patients have been just as likely to report this sensation as have treated patients in past studies, we did not ask for this information from the patients. After the study, however, four patients volunteered the information that they had felt a tingling sensation from the electrodes during the study. Two were later found to be sham treated and two had received actual treatment.

The double-blind treated group had significant mean gains on tender point score ($t = 2.27$, $p < 0.01$), self-rated pain ($t = 3.04$, $p < 0.002$), quality of sleep ($t = 2.05$, $p < 0.02$), feeling of well-being ($t = 1.67$, $p < 0.05$), and quality of life ($t = 1.92$, $p < 0.03$). There were 38 degrees of freedom on each analysis. The sham-treated and placebo-controlled groups had no positive gains during the study.

Since subsensation CES at 100 μA is a very small level of stimulation, it was decided also to compare the treated subjects in the double-blind study against those in the poststudy open clinical group who reported having used an intensity of stimulation that was above sensation level.

Only 23 of the 40 control patients opted for actual CES treatment after their participation in the double-blind part of the study. When the test scores of those who came in for the additional treatment were compared with those of the group not asking for additional treatment, no differences were found on their 12 pretest measures except on the self-rated quality of life, in which those requesting treatment had significantly lower scores ($t = 2.48$, $df = 38$, $p < 0.02$).

The four groups that were analyzed are shown in Figure 1, where it can be seen that there was no positive placebo effect among the sham-treated patients on the scores presented. One-tailed analyses were performed to see if the observed mean reductions of the scores among the treated groups were significant.

The open clinical group had significant gains on tender point scores ($t = 3.27$, $p < 0.001$), self-rated pain ($t = 1.68$, $p < 0.05$), qual-

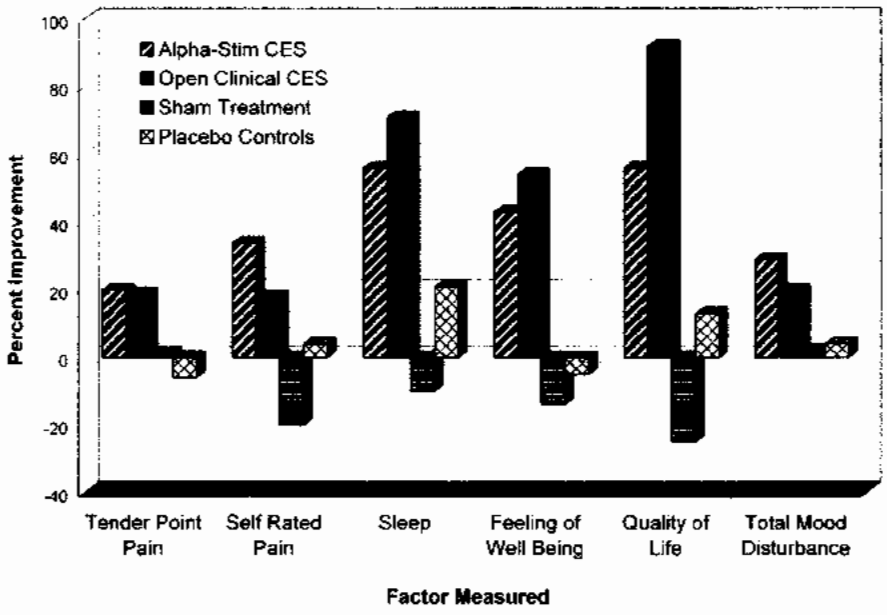

FIGURE 1. *Response of patients on various measures.*

ity of sleep ($t = 3.89, p < 0.001$), feeling of well-being ($t = 5.33, p < 0.001$), and quality of life ($t = 5.23, p < 0.001$). There were 44 degrees of freedom in each analysis.

Figure 2 shows the distribution of pre- and posttreatment self-rated pain scores for all study subjects, who ultimately received CES treatment during the study, either double-blind or open clinical. It can be seen that the pain scores dropped off in intensity fairly dramatically for many of the subjects after treatment. Overall, there was a 27% reduction in self-rated pain scores among the treated group and a 28% decrease in the tender point scores.

Among the areas tested, the self-rated sleep score was the one that showed the greatest improvement from the open clinical treatment, which provided a higher level of stimulation intensity. Figure 3 shows that fewer than 5% of the patients in this group ended the study reporting little or no sleep, whereas over 60% of the study group reported little or no sleep on entering the study. Again, there was no significant placebo effect on sleep from the sham treatment.

There were fairly dramatic improvements on all of the psychological factors measured among the subjects receiving double-blind CES treatment, as can be seen in Figure 4. Because of wide variation among scores across all subjects, parametric testing could only find significance on the vigor score ($t = 2.97$; $p < 0.01$, two-tailed) and fatigue score ($t = 1.93$; $p < 0.03$, one-tailed $p < 0.06$ two-tailed; $df = 38$).

Although no attempt was made to measure medication use among patients during the study, it was noted that several of the patients who had received actual treatment, but none of the untreated controls, told members of the research team that they had completely eliminated all pain and sleeping medication by the end of their 3 weeks of treatment.

DISCUSSION

We closely approximated Wolfe's finding of sleep pattern disturbances in 75% of the fibromyalgia patients he studied (17). Sixty percent of our patients had a similar complaint going into the study. Others have also noted this problem and report that it is most likely because of intrusion of faster alpha waves during non–rapid-eye-movement sleep (21). Studies cited above have shown that CES tends to normalize the electroencephalogram after several treatment sessions (11). In the present study, the patients responded as if this might be so, with the vast majority of them reporting little or no restful sleep going into the study and fewer than 5% of them persisting in this complaint after CES treatment. Meanwhile, their pain associated with fibromyalgia was significantly reduced.

Leventhal concluded his review of 34 studies of drug treatment and 12 studies of nondrug

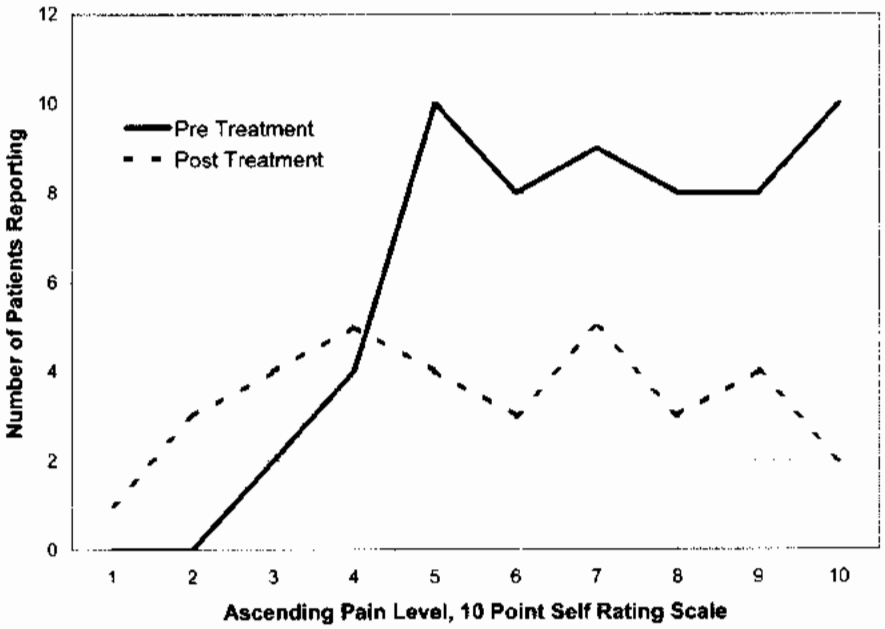

FIGURE 2. *Pre- and posttreatment pain score distribution.*

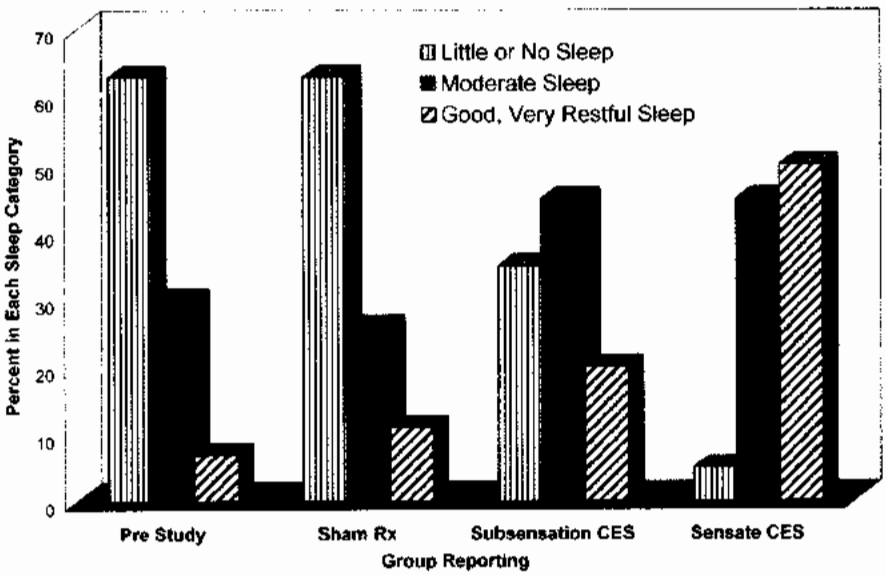

FIGURE 3. *Sleep pattern of study groups.*

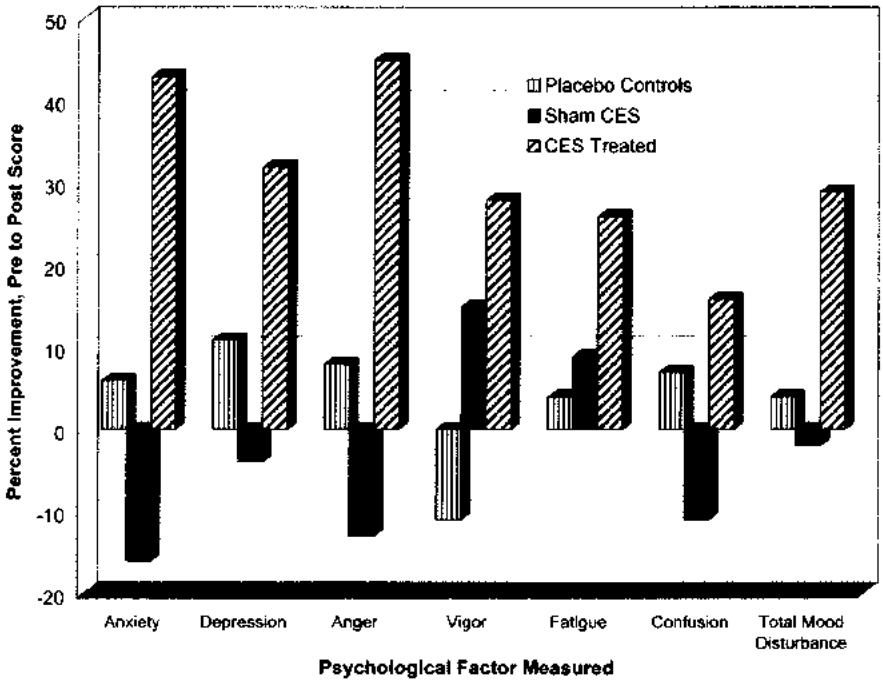

FIGURE 4. *Changes in psychological scores pre- to posttreatment.*

treatment of fibromyalgia patients by saying, "Overall, clinical evidence suggests that the most effective agents in managing the pain of fibromyalgia are those that affect neurotransmitter metabolism at the receptor site" (16). CES has been long thought to have as one of its major effects a normalizing of the neurotransmitter homeostasis in the brain (2).

Another study cited above concluded that a subset of fibromyalgia patients have a dysfunction traceable to the brain's hypothalamic pituitary axis (19). CES is almost certainly stimulating that axis when it engenders increases in IGF-1 production in low–IGF-1–producing females (12).

As to whether CES might prove to be an acceptable therapeutic approach to use with fibromyalgia patients, Leventhal also noted that fibromyalgia patients in one study were found to be 91% more likely to pursue alternative therapies than were the nonfibromyalgia controls (16).

Among alternative treatments that have been considered, biofeedback in combination with exercise training and relaxation training resulted in a significantly greater benefit and longer lasting improvement over the use of any of those therapies alone in the fibromyalgia patients studied (22). It is interesting to speculate that CES might be a meaningful addition to such alternative therapeutic procedures. In our experience, patient acceptance of this therapy has been very high, and CES has been shown to dramatically potentiate the effects of biofeedback therapy when the two are given together (23).

As another nondrug alternative therapy, acupuncture has lately been the topic of a National Institutes of Health consensus report that stated, "acupuncture may be useful as an adjunct treatment or an acceptable alternative or may be included in a comprehensive management program" (24). In that connection, the Alpha-Stim 100 provides probe electrodes that are often used by acupuncturists practicing electroacupuncture, a therapy that has been rated as good and sometimes superior to needle acupuncture alone. Reasons for the preference of noninvasive electroacupuncture are the following: it eliminates the effects of tissue damage caused by manual insertion and twirling of needles, it avoids the possibility of transmitting diseases such as acquired immunodeficiency syndrome or hepatitis, and it reduces treatment time on each treatment point from 20 minutes to 10 to 12 seconds (25). It can also be done by a trained paramedic or by the patient alone (26).

Insofar as all of these are nondrug therapies, their use in a multimodality treatment program could avoid, to a large extent, most or all of the major adverse effects listed in Leventhal's review that resulted from the various drug therapies. Those adverse effects were experienced by up to 20% of patients using them (16). On the other hand, patients in those studies improved up to 28% at best, a figure similar to that found in the present study whose patients experienced no significant negative side effects. Unlike medication, there is no ongoing cost to the patient with CES therapy other than the initial acquisition of the device and training in its clinical application.

There was some question among the research staff as to why the sham-treated subjects tended to become worse on most of the parameters measured whereas their wait-in-line placebo- controlled subjects did not. Although the research protocol was not designed to answer that question, there is a strong possibility that patients who thought they might be receiving CES treatment did not wish to use other treatment strategies that might interfere with its possible effectiveness during the study. Meanwhile, the placebo-controlled subjects were typically doing everything they could to ameliorate their pain symptoms while waiting their turn for the CES treatment.

In this study, we have shown that CES is an effective treatment for several important elements in the syndrome of fibromyalgia. Because the study was double-blind, treatment of very low intensity for only 1 hour a day was given. The

control group participants who later received greater stimulation in the open clinical phase after the double-blind study experienced greater gains in several of the areas measured.

This study was a first of the use of CES in fibromyalgia. Additional research will be needed to validate these results and to learn how CES can best be fit into the larger fibromyalgia treatment milieu. Future studies might also explore the effects of extending both the number of treatments per day and/or the number of days in the duration of treatments, either or both of which could possibly result in greater reductions in symptoms among their fibromyalgia patients.

For now, because of the limitations of time and space in a typical office practice, physicians can possibly best use CES by instructing the patient in the correct application of the electrodes and adjustment of the stimulation level and time controls, then prescribing it for home use. These instructions are provided in the patient information booklet that comes with the CES device. The ear clip electrodes used in this study were placed as high on the ear lobe as possible and as close to the cheek as possible, as is shown in Figure 5. The patient should be followed every week or so until the physician feels confident that the patient is using it correctly and positive results are being obtained.

Since CES can potentiate the effects of some medications, the patient should be monitored more closely when a new medication is prescribed or any change in the dosage of presently prescribed medications is contemplated. The patient should also be monitored more closely if he or she requests to be allowed to use the CES device to reduce or eliminate the use of any given medication.

The physician should not be concerned that the patient might overuse the CES device at home, since some hospitals withdraw patients from benzodiazepines by treating them with CES 24 hours a day for 10 days (except when they are in the shower) and then reevaluating their symptoms prior to adjusting the treatment level. No negative side effects have been reported from this use (27). In addition, cancer patients are clinically reported to have used CES from 2 to 16 hours a day to control or eliminate pain throughout the body for months at a time (M. Waddington, personal communication, October 2000).

FIGURE 5. *Ear clip electrode placement on patients in the study.*

The physician and patient working together can usually come up with the best plan for the use of CES as the patient gains more experience with the device and acquires skill in reporting its effect.

ACKNOWLEDGMENTS

The manufacturer loaned the treatment devices used in the study. They were returned to the manufacturer after the study. Dr. Smith, the manufacturer's Director of Science, assisted in the development of the study protocol and completed a blind analysis of the study data, the results of which were given to the study team while he remained blind to patient treatment condition. He was not involved in any of the study's patient interactions or data collection.

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COMMENTARY

This article is certainly intriguing. The results are so positive in such a difficult-to-treat population that one becomes skeptical. Nonetheless, positive results in a double-blind controlled study need to be taken seriously.

I wonder if this study can be replicated. I have often thought that therapies that help fibromyalgia patients in the short run—therapeutic massage, physical therapy techniques, and the like—do not seem very helpful in the long run. Long-term follow-up of these patients, especially in a controlled double-blind setting, would be useful.

It is hard for me to think that a therapy as innocuous and simple as this one can realign neurotransmitters. However, it is hard to dispute the present data. The fact that 90% of the patients treated with the cranial electrotherapy stimulation reported improvement in quality of life compared with a 20% reduction in patients receiving a sham treatment is truly amazing.

Robert S. Katz, MD
Chicago, Illinois