The use of cranial electrotherapy stimulation in the management of chronic pain: A review

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Cranial Electrotherapy Stimulation (CES) has a growing history of applications in the treatment of anxiety, depression, and insomnia. CES gained its first major application in the field of addiction treatment and rehabilitation. By the mid-1980s research was showing CES to be highly effective in the treatment of chronic pain patients. It may be elevating the pain threshold but does not relieve pain when anxiety and depression are reduced to normal levels. Modern theories of pain mechanisms in the central nervous system provide an additional basis for understanding CES mechanisms in the control of pain-related disorders.

1. Introduction

Cranial Electrotherapy Stimulation (CES) is the application of a small amount of current, usually less than one milliamper, to the head via a pair of electrodes. It came to the United States in the late 1960s and early 1970s under the term “electrodespine.” It had been developed in the U.S. S.R. in 1954, and had spread from the former Eastern Bloc, then into Europe and much of the West. It was already in use in Japan where it is called a “Seez.” It had been used in animal and human subjects at several universities in the United States in the 1960s. By the latter 1960s, it was being researched in both animal and human subjects at several U.S. universities. Studies at the University of Miami and the University of California [1, 2, 3] summarized the progress of CES in American medicine.

2. Research in Rehabilitation Medicine

2.1. Rehabilitation of addictions persons

The first research and subsequent use of CES in rehabilitation medicine began in the early 1970s, when research reports began coming out of the District of Columbia’s 600-bed outpatient Rehabilitation Center for Alcoholics (6), and Veterans Administration Hospitals (7, 8). Following the publication of these double-blind, placebo-controlled studies (9, 10), the Complare Corporation, then the largest rehabilitation facility in the US, at the request of the study, was to put CES into their own treatment program throughout the nation. Unfortunately, there was no manufacturer of CES devices available at the time that could supply that heavy a demand for products to the point that they were discontinued. CES continued to be used in addiction treatment, however, with many facilities using both the CES Group and other major addiction treatment drugs making widespread use of CES in their clinical treatment protocols.

2.2. The use of CES in postoperative and quasi-psychiatric patients

What kind of feedback do CES devices carry is a common question asked about CES devices. It can be assumed that they are used as much in the postoperative period as they are used in the rehabilitation of patients with addictions. CES was found to be effective in reducing pain and postoperative complications. It was also found to be effective in reducing anxiety and depression symptoms in patients with addictions. CES was also found to be effective in reducing anxiety and depression symptoms in patients with addictions. CES was also found to be effective in reducing anxiety and depression symptoms in patients with addictions.
subsequently employed in the hospital treatment protocol, with the physical therapists, especially, commenting that patients often had much better morale during muscle exercise training when they used a CES device during the midmorning, postprandial exercise sessions. They completed the sessions with little or no complaining, crying, or other emotional negativity and acting out.

2.5. The use of CES in closed head injured patients

One of the first reports of the use of CES in closed head injured (CHI) patients appeared in 1996. It was a clinical case presentation of two CHI patients, the major focus being on their post-traumatic amnesia and subsequent cognitive deficits. It was found that following 40 minutes of CES treatment daily for three weeks, the first patient had a 55% improvement in immediate recall and a 56% increase in delayed recall. The second patient had improved 20% on immediate recall and 79% on delayed recall [12].

A subsequent double-blind, placebo-controlled study of CHI patients was published in 1994 [13]. While the major focus of the study was anxiety and depression in these patients, a side issue was the seizure disorders suffered by the patients, all of whom were on anti-seizure medications. It was known at the time what effect CES might have on seizures. While earlier studies of addiction patients in one rehabilitation center had selectively eliminated patients known to have had withdrawal seizures, another large rehabilitation center had deliberately and successfully treated similar patients with CES to prevent withdrawal seizures [14].

During the study, one patient was observed to have a seizure and was immediately removed from further participation in the study. Following the study it was discovered that the seizure patient had been a sham-treated control and had received no stimulation. The researchers reported that when that subject’s parents saw the results in the CES treated group they insisted that their son receive CES treatment. This was done, with no further seizure activity reported in this or any of the other patients who had undergone CES treatment during the study.

2.4. The use of CES in physical therapy

In an early CES study in the US, 23 patients who had been diagnosed with hemiplegia, paraplegia and muscle spasm following traumatic injuries, were given CES treatments of one hour each day for ten days in an open clinical trial. Muscle spasticity was tested with an EMG device before and just following the CES treatment. A clinically significant improvement in muscle spasticity was found in all patients [15].

Another study had a serendipitous finding when researchers designed a study to test whether or not it was possible to actually put patients to sleep. Among 15 patients in this open clinical trial were two patients suffering from Parkinson’s disease and one diagnosed with dystonia musculorum. Different types, intensities and amounts of CES current were given over several weeks of experimentation, at the end of which an unexpected finding was that the involuntary movements in the three patients with muscle dyskinesias were changed in character during the passage of current, and eventually completely eliminated, as measured by EMG [16].

In another study, researchers found that at least some types of patients, muscle tremor can be associated with the underlying level of psychological stress. While measuring muscle tremor in 55 withdrawing alcoholics, researchers found that patients who were under the most psychological stress actually had fewer tremors than those who were under only moderate stress. Following 40 minutes of CES, those who formerly were under greater psychological stress began to tremor more, presumably as their stress level was reduced, while those who began under moderate levels of stress actually tremored less as their stress level fell back toward normal. Psychological stress was measured by the Minnesota Multiphasic Personality Inventory and tremor was measured with the Lafayette Instrument Steadiness Tester. It was found that benzodiazepines, 25 mg. t.i.d. and 30 mg. h.s., for three to five days had no similar effect in altering the tremor of these patients, such as was found with the 40 minute CES treatment [17].

In a study of 20 children with mild to severe spastic cerebral palsy, aged 2.5 months to 12 years, CES or sham CES was given twice a day for ten minutes each time for six weeks in a crossover design. The results were evaluated on the Mallet Gross Motor Rating Scales I, II, and III, and the Advanced Gross Motor Skills Scale. There was significant improvement in total gross motor performance in each group following the active but not the sham treatment. The authors concluded that using children with spastic cerebral palsy with CES in addition to physical therapy is superior to conventional treatment alone [18].

In the latest such study to appear in the CES literature, 10 patients diagnosed with minimal cerebral dysfunction, cerebral palsy and spastic quadriplegia were given either occupational therapy (OT) alone, CES
3. Research in chronic pain patients

While CES treatment became much more evident in pain management programs in the mid-1990s, it was often brought in as an adjunct to pain management with the Alpha-Stat microcurrent stimulation device, which also provided CES capability. In this regard, one review noted: "CES is a primary modality effective for controlling anxiety, depression, insomnia and generalised stress (which is ubiquitous in pain patients)" [20].

3.1. Research in spinal pain

In 1999, a neurosurgeon used CES in an open clinical trial on spinal pain patients who were waiting in line for the implantation of dorsal column stimulators. In his study, CES was provided with Alpha-Stat SCS units applied daily for one hour a day for three weeks. The results were so impressive that he then conducted a double-blind, placebo-controlled study [21]. In the 38 patients studied, the effects of CES in reducing pain scores measured as "pain at best", "pain at worst", and "pain in general" were dramatic and significant. No positive placebo effect was found among the sham treated patients. The results of both phases of his study are compiled in Fig. 1.

The researcher currently plans to replicate the study with a greater number of patients, since he feels that this is a seminal finding in the treatment of chronic spinal pain patients. A replication of this study is also just getting under way in Bangalore, India [22].

3.2. Research in fibromyalgia

In 1999 a research protocol was developed for a multi-center study of the use of CES in fibromyalgia patients. The protocol provided for double-blind, placebo-controlled studies in larger clinical settings and for open clinical trials in smaller treatment centers. In the double-blind protocol, the patients were to receive either CES treatment below perception threshold at 100 microamperes of current intensity, for 5 hours on a 5-day-daily cycle, or sham treatment via devices set exactly like the first, but using electrodes that would not pass any current. The placebo-controlled patients were to sit out the three weeks without access to the CES device, to serve as controls for any placebo effect in the sham-treated patients. The physician, other therapists and the psychiatrist were to remain blind to the treatment conditions, as was the statistician who would evaluate the study results. Patients were to be randomly assigned to each of the research groups. All subjects were to sign patient consent forms, and each study would be run under the supervision and guidelines of a local investigative Review Board to assure compliance with local community standards in human subjects research.

Due to the strictness of the protocol, only one-third of the subjects in each study would receive actual CES treatment for their fibromyalgia. Accordingly, it was suggested that in those research centers where CES treatment was shown to be effective, any of the untreated, two-thirds of the patients who served as controls should be offered three weeks of CES treatment one hour per day, in an open clinical format, following the double blind phase of the study. They would then receive treatment at higher current intensity since there would be no need to treat their below sensation level and they could set the intensity to any level they chose. The treatment results of those who agreed to a third testing following this treatment could then be included in the report as controlled, clinical data.

The first double-blind study to be completed involved 50 patients in a large private rheumatology practice in New Jersey [23]. The principal investigator had served on the national panel that developed the diagnostic protocol for fibromyalgia, and the protocol was approved by the Investigational Review Board of the Newark Wood-Ridge Medical School. Measures included the physician's evaluation of each patient's tender points pre and post study, and the patient completed ten pain self rating of their overall level of pain, their quality of sleep, their feeling of well being and their quality of life. They also completed...
the Profile of Mood States, a standardized psychological test of depression, anxiety, fatigue, and cognitive function among other factors.

It was found that the CES treated patients improved significantly on every measure following three weeks of CES treatment. Neither the sham-treated patients nor the placebo control patients showed improvement on any area measured. These results are given in Fig. 2, where it can also be seen that the patients who received open clinical treatment following the double-blind phase of the research, all at self chosen current intensity settings, actually fared better than those who received the pre-set submaximal level treatment, as would be expected.

A large clinical practice in Southern California chose to complete their research with the open clinical protocol [24]. Again, patients received CES treatments, one hour per day for three weeks. All tests and measures were as described above. They halted the study after the first 20 patients had completed it to see what the results had been. These results can be seen in Fig. 3. The researchers were so impressed that they decided to run the study for an additional 12 months, and are in that process as of this writing.

Researchers at the Louisiana State University Medical School pain clinic are currently implementing the thrombolyxan study double-blind protocol [25], and several other clinics and hospitals are reviewing the protocol for possible participation.

4.1. Research in headaches

Perhaps the earliest US study on headache was done as a Masters Degree thesis at North Texas State University in Denton. In that double-blind, placebo-controlled study, 18 migraine headache patients were divided into three groups of 6 each. In the treated group, CES was given for 15 minutes daily for 15 days, Monday through Friday. Over a two week period immediately following the study it was found that CES treated patients, but not the sham-treated or placebo control patients, reported significant reductions in both headache intensity and duration [26].

In another study of migraine headaches, this time a doctoral dissertation research project, 38 patients were assigned to biofeedback (BF), CES, or biofeedback combined with CES. Eight treatment sessions of 15 minutes each were given over a two to three week period. The patients measured the frequency and intensity of headaches daily during the eight days of therapy, then over a one month, a two month and a three month period following the treatments.

There was no difference between the groups at the end of the eight treatment sessions, but a steady increasing cumulative improvement took place over the three month period following the study, as shown in Fig 4. This biofeedback group had an accumulative improvement of 70% while the combined BF/CES group, the group that did best over all, had an accumulative improvement of 400% by the end of the third month [27].
3.4. Research on dental pain

In a double-blind dental study, 50 patients were divided into two groups, 30 receiving CES and 20 receiving sham CES treatment. They were randomly assigned to procedures including oral surgery, restorations, tooth extractions, root planing, gutta-percha, and temporomandibular joint therapy. It was found that 24 of the 30 CES patients (80%) were able to undergo dental procedures without other anesthesia, while 15 of the 20 sham treated patients (75%) requested anesthesia. In the operative groups, 13 of 14 CES patients (93%) did not require anesthesia, while 4 of 7 sham-treated patients (43%) did. All patients required anesthesia for endodontic procedures. All CES patients stated that the use of CES would be their first choice in future dental visits [30].

Another dentist used CES in 600 dental procedures over a 12-month period. 76% of the patients reported a 99% or greater reduction in pain with CES and did not require additional anesthetics. When the results were broken down by procedure, 83% of the patients who underwent scaling and prophylactic procedures did not ask for additional anesthesia, compared with 76% of those undergoing 473 operative procedures, and 55% of those undergoing 49 crown preparations.

A serendipitous, but not surprising finding was that all patients reported feeling more relaxed than usual while in the dental chair [31].

4.5. Chronic pain, type unspecified

In a study of the neurochemistry of depression, CES researchers found that among the patients in their study were 14 who were listed as unresolved chronic pain patients, and 9 other chronic pain patients who considered their condition hopeless. Following two weeks of daily CES treatment, given 20 minutes a day, the 23 chronic pain patients reported a significant reduction of 44% or more in their pain intensity [32].

In a survey of clinicians who use the Alpha-Stim CES device in their practice, it was reported that 260 of 360 chronic pain patients (72%) reported significant relief following CES treatments. Among those treated for headaches, 136 of 151 patients (90%) reported significant reduction in headache pain, and 245 of 259 patients (95%) who reported pain related muscle spasms reported significant relief [33].

4. Studies of anesthetic equivalency

There have been two studies that assessed the equivalency of CES to various types of anesthetics. In a rather straightforward study in which he compared CES with various concentrations of N\textsubscript{2}O, Stanley gave a group of 90 urological patients and 30 abdominal surgery patients either 5% ± 2.5% or 5% N\textsubscript{2}O alone or a similar concentration of N\textsubscript{2}O plus CES. After 20 minutes of
treatment, patients were given a painful stimulus with a Keele stump clamp on the second catch and applied in their upper, inner thighs for one minute. Measurements of pain included patient movement, systemic blood pressure, heart rate, respiratory rate and minute ventilation.

It was found that CES increased the potency of N2O by approximately 37% at each level, being between 0.3 and 0.5 MAC in anaesthetic potency when compared with N2O. The authors also noted that the CES group experienced prolonged analgesia after recovery of consciousness.

In a somewhat more elaborate study, CES equivalence to the narcotic fentanyl was studied on patients undergoing surgery. Fifty patients who were undergoing anesthetic procedures were divided into two groups to receive either CES or sham CES in addition to normal anesthetic procedures. All patients received induction with droperidol (0.20 mg/kg IV), diazepam (0.2 mg/kg IV), and pancuronium (0.6 mg/kg IV). Anaesthesia was maintained during the surgical procedure with fentanyl given in 100 microgram IV increments every three minutes if necessary to maintain the patient at the required level of anesthesia.

It was found that an average of 99% less fentanyl was required in patients who simultaneously received CES treatment.

5. Discussion

While the above studies represent an entire range of study design from open clinical trials to double-blind, placebo-controlled studies, in every instance treatment with CES has been accompanied by a dramatic reduction in the perception of pain in every pain category studied.

It is not clear why putting microncurrent electrical stimulation across the head would reduce pain in the body. While some would point to a possible increase in endorphins, no studies that looked for this did not find it, although we did find an increase in serotonin and a decrease in cholecystokinin [32]. The other study found an increase of MAO-B in blood platelets and an increased concentration of GABA in the blood following CES treatments, but did not find an increase in serotonin, dopamine or beta-endorphins in the blood [36].

Pizzo's animal studies indicate that CES is apparently effective in bringing neurotransmitters back into homeostatic balance when that balance is deliberately disrupted [37]. It would be possible that when the brain's normal homeostasis has been shifted into a stress pattern, it is a period of time, an occurrence suggested by Selye's theories to be somewhat frequent in our day and age [38], CES may be effectively putting it back into a pre-stress homeostasis, accompanied by a reduction in stress related hormones such as cortisol, which is known to play a role in increased pain perception.

There is also increasing evidence for a central pain neuraxis, which is responsible for processing pain messages throughout the body, even in the absence of perceivable pathologies or the body parts themselves as in the examples of phantom limb pain or pain patterns persisting after the removal of tumors. The neuraxis is thought to change under certain conditions such as physical trauma of various kinds that interrupt normal incoming stimulation. Notable researchers such as Ronald Melzack are now theorizing that the pain neuraxis may be more important in producing chronic pain states than previously considered [39]. It is known that CES stimulates every area of the brain, and therefore would include the area in which the pain neuraxis is thought to reside [40, 41]. It is unlikely to speculate on what the effect of that stimulation might be, but if it is found it will almost certainly be a balancing, or normalizing effect on the cerebral cortex.

From a different perspective, researchers at the St. Vincent Medical Center in Connecticut have found what appears to be occult damage in the lower medullatory sensory and motor pathways in complex regional pain syndromes such as fibrositis and RSD. A theory, "We suggest that bilateral symmetrical and centrencephalic deficits, with a conspicuous pallidal hemineglect and hemiparesis, bilateral cranial nerve dysfunction and lack of other concomitant pain, left-handedness, and other symptoms are compatible with dysfunction of lower medullatory sensory and motor pathways," that trauma was reported by 51% of the 145 patients studied, among which was a high incidence of whiplash injury, falls, and physical assault [42].

Again, it is not clear what the effect of CES stimulation of the medulla or other than that it provides a biologically symmetrical stimulus into the area over time, varying only by the treatment parameters chosen in each instance.

Furthermore, that certain types of CES stimulation, applied to the body, reduced the Fast Fourier Transform mean square (RMS) of the EEG significantly, lowering the peaks normally found in pain patients, and changing the EEG into the normal pattern normally found in pain-free patients as shown.

Fig. 5. Fast Fourier Transform of the EEG in a typical pain-free patient. FFTs are based on 2 minute averaged EEG RMS amplitudes on the vertical axis, and EEG frequency on the horizontal axis.

Fig. 6. FFT of a typical chronic pain patient. The patient has degenerative joint disease for more than 2 years causing at least 8 hours of pain daily.

Figs 5, 6 and 7. The patients rated their pain as significantly less acutely, resolving to the spectral smoothing of the EEG (43). We also found a significantly decreased chaotic correlation dimension in the EEG following CES suggesting a heightened organization of a formerly disorganized EEG in pain patients. This also was accompanied by a reduction in pain and stress symptoms (44).

Many pain clinics across the United States, and now the world, are using the Alpha-Stim 100's CES capability in addition to its available probe and self-adhesive electrodes which are used at or near pain sites on the body of their patients. The use of CES with pain patients is increasingly being supported by the outcome of well-designed research protocols. It’s proven efficacy in controlling the anxiety, depression and insomnia ubiquitous in pain patients is a significant added benefit. Side effects are rare, primarily minor self-limiting problems, such as headaches (1 in 450) and electrode burns (1 in 811). As a cost-effective, non-medication treatment for the reduction of pain, especially in chronic pain patients, cranial electrotherapy stimulation usage can only increase as practitioners be-
Fig. 7. FFT of the EEG of the same patient in Fig. 6 following 10 sessions of Alpha-Brain CES treatment.

References


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