

NONINVASIVE ELECTRICAL STIMULATION FOR THE TREATMENT OF RADIOTHERAPY SIDE-EFFECTS

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ABSTRACT

Noninvasive electrical stimulation (ES) may be a safe and effective method for treating mucositis with symptoms of pain, dysphagia and dryness. An original investigation using this new modality for the treatment and prevention of radiation side-effects is presented in an empirical study of ten patients undergoing radiotherapy for carcinoma of the head and neck. Once ES was initiated no interruption of radiotherapy was necessary. In addition those already having symptoms from radiation before ES was begun were markedly palliated.

A retrospective group of 13 patients, randomly selected, who had undergone radiotherapy under similar circumstances were compared to see the extent of radiation side-effects. Nine out of the thirteen patients in this group had to have their radiotherapy interrupted for the symptoms of mucositis.

Pertinent literature and theory for the healing effect of electrical energy are given.

Radiation with megavoltage electron beam therapy has improved greatly over the last three decades. More penetrating radiation has resulted in greater tumor response with less side-effects. In head and neck tumors the overall survival statistics for stage 1 and 2 tumors is about the same using either surgery or radiation alone, and stage 3 and 4 do best with combined therapy.¹ Most cancer centers now carefully weigh each individual patient, considering age, occupation, and medical condition before deciding a therapy regimen.

“ . . . electromedicine is proving to be a safe and effective method for controlling pain as well as for treatment of radiation side effects from inflammation.”

Although the side-effects of radiation have been greatly reduced, they have not been eliminated. Pain, dry mouth, and dysphagia are still present in nearly every patient undergoing radiotherapy, and interruption of treatments for “rest periods” is still the rule for a large percentage of patients. Symptomatic treatment is difficult and has been generally unsatisfactory. It is the intent of this paper to present a new modality for the treatment of these radiation side-effects. We have recently used transcutaneous electrical stimulation in conjunction with radiotherapy in ten consecutive patients.

BACKGROUND

Transcutaneous electrical nerve stimulation (TENS) is a relatively new technique that has been successfully used for the treatment of pain. The effectiveness of TENS has been explained in terms of inhibiting or fatiguing peripheral nerves. Although this may account for some of the pain-relieving effects, the overall response of the body and tissues to electromagnetic stimulation is much more complex and is only now being worked out.² Basset, Pawluk, and Becker demonstrated that bone growth occurs in the vicinity of a negative electrode with currents of less than 3 microamperes, while growth is absent around the corresponding anode.³ Also, electromagnetic radiation has been shown to increase wound healing in animals by 30% to 72% when linear wounds are made down to the dermis of guinea pigs.⁴

METHODS AND MATERIALS

Treatment Population

Ten male patients with squamous cell carcinoma of the

oropharynx undergoing radiation therapy with a 4 megavolt cobalt linear accelerator served as the experimental group for electrical stimulation (ES). The location and classification of the tumors are given in Table One. Some patients were already well into their course of radiation and had side-effects before they were placed on ES.

Control Population

Thirteen subjects were randomly selected from the file patients who had completed radiation for cancer in the oropharynx (see Table Two). The objective in this group was to determine the extent to which patients undergoing radiotherapy of the head and neck had to have their therapy interrupted because of the symptoms of mucositis.

Technique of electrical stimulation (ES)

A pulse generator (Alpha Stim 2000) was used to deliver an alternating current composed of constantly varying biphasic asymmetrical square wave at a frequency of 0.5 Hz and an intensity of 50 to 500 microamperes. The current was delivered to the symptomatic area via surface electrodes. In addition, trigger points in the region of the ear were stimulated. The total duration for each ES was 20 to 60 minutes. The number of radiation treatments administered before ES began ranged from zero through 22 (see Figure One).

“All patients treated with ES had their symptoms reduced to minimal levels during and after the finish of their radiotherapy.”

Patients were electrically stimulated within 4 hours after radiation for the complaints of dryness, pain, and dysphagia. Unfortunately no objective method could be used to visually study the intraoral mucositis when it was present. The number of ES treatments varied and were tailored for each patient. Patient nine requested two ES treatments a day for four days to help bring his symptoms to a minimum. On the other hand patient one could go eight radiation treatments between ES one and two because of no return of symptoms. All patients were treated during each ES session until their symptoms were reduced to zero or close to it. The last day of radiation and ES coincided in most patients, although some did not need stimulation all the way to the completion of their radiotherapy because of the suppression of side-effects.

RESULTS

In the treatment group of ten patients, none needed a rest period from radiation once ES began. Patient seven stopped ES because of transportation difficulties. He subsequently developed severe mucositis causing interruption of his radiation treatments. Patients two and nine had severe mucositis necessitating a rest period before their ES began (see Table one).

By contrast nine out of the 13 patients in the retrospective control group had radiation interrupted because of radiotherapy side-effects (see Table two). Pain with mucositis was the most common complaint.

All patients treated with ES had their symptoms reduced to minimal levels during and after the finish of their radiotherapy. Figure One shows a profile of the decline of symptoms. It shows the level to which the symptoms returned before the next ES was given. It does not give the maximum, immediate effect. One year follow-up indicates that patients remain symptom-free if there is no return of tumor.

CONCLUSION

Electrical stimulation and radiation therapy are two modalities which seem to complement each other. ES apparently enhances the healing process, reducing the side-effects produced by radiation.

An important point that must be addressed is the question, what effect does electrical stimulation have on the tumor itself? The mutagenic effect of electromagnetic phenomenon has been studied by several investigators. At very high frequencies in the mega- and gigahertz range at low intensities there is evidence of chromosomal changes and mutagenesis in plants and animals, but to date there is no evidence of actual cellular toxicity or cellular death; and there are no published reports of induced tumor formation.⁵ In the low frequency and low energy range, which we are using, there is a growing literature of tumor regression and reversibility of tumor cells.^{6,7} Experimental tumors have been inhibited and metastases reduced in hamsters exposed to small direct currents of 500 microamperes.⁸ Basset showed a reduced mortality rate from sarcomas on mice from 80% to zero in mice exposed to electromagnetic-fields.⁹

RADIOTHERAPY SIDE-EFFECTS (Con't)

The mechanism of action is as yet theoretical, but experimental evidence is accumulating which can explain how electromagnetic energy interacts with the cellular membrane. Through a process of non-equilibrium chemical reactions called dissipative energy systems, enzymes in the cell membrane such as adenylate cyclase may be activated which in turn activate cyclic-AMP and intracellular metabolism.^{10,11} Through this action DNA synthesis can be altered.

With advancing technology, electromedicine is proving to be a safe and effective method for controlling pain as well as for treatment of radiation side-effects from inflammation. It should be emphasized that the term electricity is generic. Just as digitalis and codeine are both pills, they are totally different in effect and action. High current amplitude stimulates somatic nerves and muscles and does not seem to have any effect on release of endorphins for pain relief; whereas, low intensity stimulation has the opposite effect of release of endorphins with little effect on sensory nerves.¹² For these reasons future research must carefully define the electrical characteristics and devices which are used.

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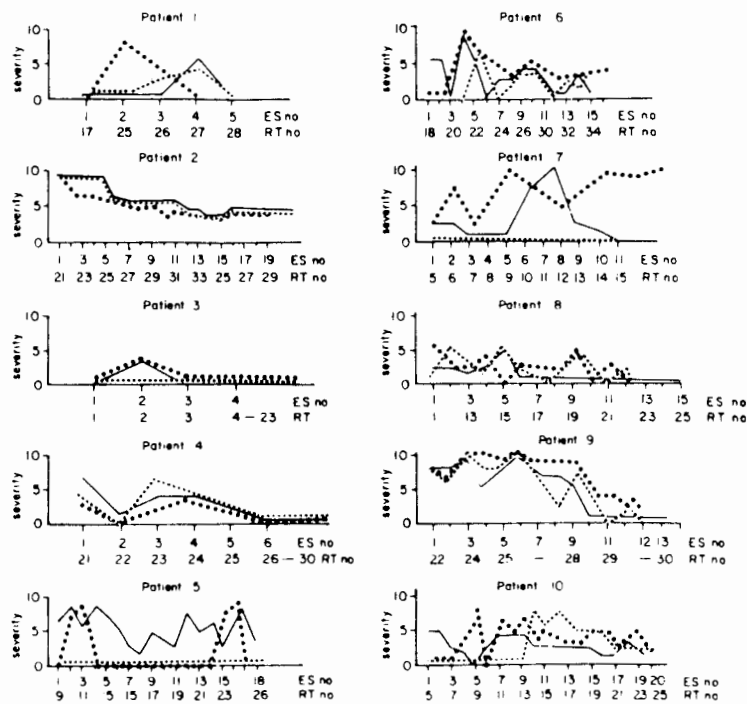
Table Two
RADIATION GROUP
WITHOUT ELECTRICAL STIMULATION

Patient	Site of lesion	T N M stage	Plan of treatment	Total rads	Comments
1	Pharynx	T ₃ N ₁ M ₀	Full course radiation	7100	Mucositis with rest period
2	Oro-pharynx	T ₂ N ₀ M ₀	Full course radiation	5400	Mucositis with 2 rest periods
3	Larynx	T ₁ N ₀ M ₀	Full course radiation	6400	Mucositis with rest period
4	Oro-pharynx	T ₄ N ₃ M ₀	Full course radiation	7000	Mucositis with rest period
5	Larynx	T ₂ N ₀ M ₀	Combined	6600	No rest period
6	Larynx	T ₂ N ₀ M ₀	Combined	6800	Mucositis with rest period
7	Base of tongue	T ₃ N ₀ M ₀	Full course radiation	7000	Mucositis with rest period
8	Hypo-pharynx	T ₄ N ₀ M ₀	Full course radiation	6000	No rest period
9	Base of tongue	T ₃ N ₀ M ₀	Full course radiation	6000	Mucositis with rest period
10	Base of tongue	T ₄ N ₂ M ₀	Full course radiation	5000	Mucositis with rest period
11	Larynx	T ₃ N ₀ M ₀	Combined	5400	No rest period
12	Soft palate	T ₂ N ₀ M ₀	Full course radiation	7000	No rest period
13	Pharynx	T ₂ N ₃ M ₀	Full course radiation	7080	Mucositis with rest period

LEGEND

FIGURE ONE. Graphs demonstrating the severity of symptoms of mucositis (graded 0 to 10). They are plotted as a function of the number of radiation treatments (RT) and the number of electrical stimulation treatments (ES). Not shown is the maximal decrease of symptoms immediately following each ES.

Symptoms of Mucositis *



* Pain * Dry mouth — * Dysphagia - - - - -

Table One
ELECTRICAL STIMULATION GROUP

Patient	Site of lesion	T N M stage	Plan of treatment	Total rads	Total # ES	Comments
1	Larynx	T ₄ N ₀ M ₀	Full course radiation	6000	5	No rest period
2	Larynx	T ₃ N ₃ M ₁	Full course radiation	7000	19	Rest period before ES started
3	Larynx	T ₃ N ₀ M ₀	Combined	6200	4	No rest period
4	Hypo-pharynx	T ₄ N ₀ M ₀	Full course radiation	5800	6	No rest period
5	Tonsil	T ₁ N ₀ M ₀	Full course radiation	7000	18	No rest period
6	Larynx	T ₁ N ₀ M ₀	Full course radiation	7000	15	No rest period
7	Base of tongue	T ₂ N ₁ M ₀	Combined	7800	11	ES stopped, then needed rest period
8	Hypo-pharynx	T ₄ N ₀ M ₀	Full course radiation	5000	15	No rest period
9	Naso-pharynx	T ₃ N ₀ M ₀	Full course radiation	6080	13	Rest period before ES began
10	Larynx	T ₃ N ₀ M ₀	Combined	5000	20	No rest period