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Transdermal Transcutaneous Electric Nerve Stimulation for Pain: The Search for an Optimal Waveform

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Abstract. A search has been made for an optimal wave form for transcutaneous nerve stimulation for pain. The effect of electrical stimulation of sympathetic nerves was studied as a model because (1) this system has small diameter axons, as do nociceptive fibers, and (2) alteration of activity in sympathetic fibers may be evaluated objectively by observing the effects upon circulation. A transcutaneously applied waveform was found which influenced circulation maximally, suggesting that sympathetic nerves were affected by the transdermal stimulation. The hypothesis that these stimulation parameters might be optimal for pain relief was tested. Relief of 40% or more was obtained in 68% of 2,800 patients suffering from chronic pain of diverse origin, utilizing this waveform.

Introduction

Numerous publications on electric stimulation by the transcutaneous route have appeared [2–5, 13, 16, 17]. Experimental proof of an optimal waveform for transcutaneous stimulation remains controversial [17], perhaps because of the many types of chronic pain which have been treated by electrical stimulation.

The diameter of nerve fibers has been reported to correlate with the effects of electric stimulation [1, 6, 18, 19]. Since the diameter of nociceptive and sympathetic fibers are similar, we thought that a study of the effect of transcutaneous stimulation upon sympathetic nerves might be profitable. The influence of the activity in these nerves is objectively mea-

Appl Neurophysiol 44(5-6): 330-337, 1981 surable by assessing peripheral vasomotor tone [10]. Using the stellate ganglion as a target, we evaluated the effects of various waveforms of the electrical stimulus applied, and evaluated whether the optimal waveform of a transcutaneously applied stimulus for the sympathetic nervous system should also influence pain perception.

Methods

40 normal volunteers and 50 patients who were receiving a stellate ganglion block for therapeutic reasons were subjected to what might be called an 'electric stellate block' [10], by manually applying a small electrode to an area of skin directly overlying the stellate ganglion anteriorly. This hemispheral electrode of finely polished aluminium had a surface area of 0.5 cm^2. For satisfactory skin contact, electrode paste (EKG-sol) was used. The cathode was applied on the back adjacent to the dorsal spines of the 6th and 7th cervical and 1st and 2nd thoracic vertebrae. The surface of this cathodal electrode, consisting of a lead plate in a foam rubber envelope (moistened in tap water), measured 100 cm^2.

The stimulus source was a multipurpose generator (model 'Impulsator' by Dr. *Schuhfried*, Vienna) which allowed wide variations in waveform. Polarity, monophasic versus biphasic stimulation, sequence of stimuli in groups, interstimulus intervals, amplitude, frequence and rise and fall time of each stimulus could be selected at will (fig. 1).

Circulatory effects were observed by the impedance method. Either both arms or both halves of the head were cleansed at sites where electrodes usually are applied for peripheral rheograms [12] or rheoencephalography [8]. 3M electrode tape (M 6001) was applied around the proximal circumference of the upper arm and the distal circumference of the lower arm to obtain longitudinal peripheral rheograms of the arms. Frontal (glabella) and bilateral retromastoid sites, for the conductive 1.6 cm^2 silicone electrodes, were used to obtain rheoencephalograms. The semiquantitative evaluation was carried out according to *Jantsch and Schuhfried* [7]. The effect of a stellate block by injection of a local anesthetic was documented [8]. Any changes observed were expressed as percentage of prestimulation (control) value of the respective record (left or right side) for each patient.

Results

A retrospective record (fig. 1) reveals the influence of transdermal stimulation on pulsatile head impedance. On the side of transdermal stimulation of the stellate ganglion, the rheographic amplitude increases 100%. This change of amplitude (which should be calculated from at least 10 pulse cycles) differed widely with various stimulus waveforms, as did

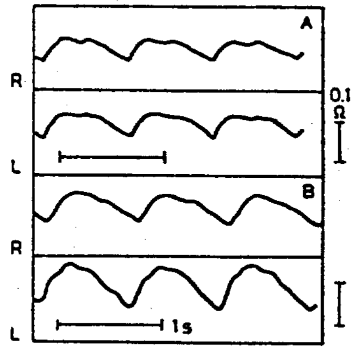

Fig. 1. Rheographic tracings recorded before (A) and just after (B) a 20 min session of electric stimulation of left stellate ganglion (left electric stellate block) using impulses of IG 50/70. Signal = 0.1 Ω; paper transport speed = 25 mm/s (time mark = 1 s); larger response on side of stimulation represents a 100% increase of amplitude of tracing. L = left and R = right rheoencephalogram. Writeout from dual beam scope memory.

the duration of rheographic changes after cessation of stimulation. Only two waveforms influenced the sympathetic nerves in such a way that the rheographic or rheoencephalographic changes remained for many months. These changes averaged (in 50 patients) 175%, with a range from 44 to 345%, if a series of five stimulations were given on consecutive days, each lasting for 20 min. These rheographic changes corresponded well to the known [8] effects of a stellate block by injection of local anesthetics.

Each type of stimulus was tested on 10 volunteers (table I) and the changes of the amplitude of the tracing (from which the so-called relative pulse wave volume was calculated, correcting for the differences in pulse frequency [7]) noted. The percentile change of relative pulse wave volumes for each side of each volunteer (columns R and L for each stimulus type) is listed for 4 different types of stimuli (designation of stimuli given in second horizontal line). Mean, standard deviation and statistically significant differences between comparable results are also presented in table I. From table I it is evident that the greatest changes on the stimulated (right) side were observed following transcutaneous stimulation of the stellate ganglion using IG-50 stimuli. These stimuli are characterized by: duration of single stimuli of 0.1 msec; interval of 10 msec between stimuli; groups of stimuli with waxing and waning amplitudes; amplitude of cen-

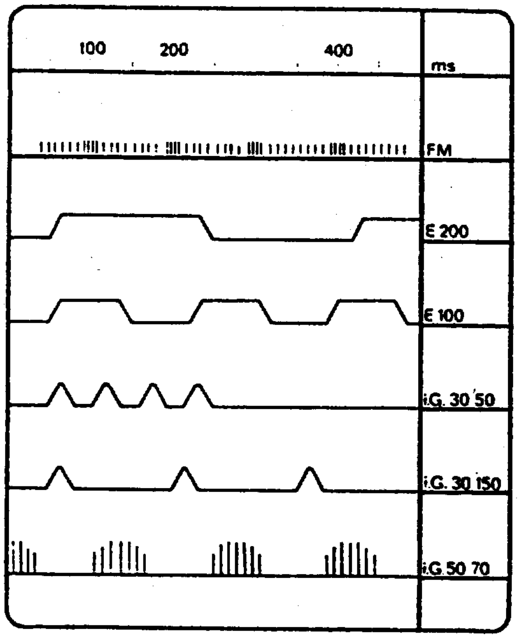

Fig. 2. Several waveforms selected from the many tested. Upper line: time in milliseconds. Waveforms are designated on right margin of graph as: FM = frequency modulated single stimuli; E 200 = exponential impulses with duration of impulses and pauses of 200 ms; E 100 = same, but duration of impulses and pauses of 100 ms; IG 30/50 (30/150) = exponential impulses of 30 ms duration with pauses of 50 (150) ms duration; IG 50/70 = group of single stimuli of very short (0.1 ms) duration and waxing and waning amplitudes (voltage peak levels of 180 V) with duration of group of impulses of 50.5 ms and pauses of 70 ms.

tral stimulus of each group of stimuli of 180 V; duration of each group 50.5 ms and of intervals between groups of stimuli 70 ms. A diagrammatic presentation of this optimal stimulus is given in figure 2, which also shows characteristics of other stimuli whose results are compiled in table I. From this table it may be seen that the effect of the optimal stimulus is statistically significantly different not only from ineffective stimuli but also from the second best stimulus (IG-30).

In order to see whether these waveforms showed a noticeable effect on the reduction of chronic pain, transdermal stimulation, using various forms of stimuli, was applied in patients. The preliminary observations were that those two waveforms referred to above (IG-50 and IG-30) also

Table I. Percentile changes of relative pulse wave volumes

Group stim. side	A							
	E-100		E-200		IG 30		IG 50	
	R	L	R	L	R	L	R	L
1	10	00	30	10	60	40	120	8
2	30	15	40	15	35	20	90	60
3	15	05	20	05	75	60	85	45
4	00	00	15	00	25	05	140	85
5	05	00	25	05	60	20	75	40
6	−10	−05	05	00	35	15	170	110
7	20	10	10	00	40	25	95	50
8	00	00	20	10	70	30	140	70
9	−05	00	15	00	20	00	120	55
10	10	05	25	10	55	15	70	35
Mean	7.5	3.0	20.5	6.0	47.5	23.0	110.5	63.0
SD	12.07	5.86	10.12	5.16	19.03	17.35	32.78	23.35
sd	1.2	7.8			1.3	7.9	2.3	8.9

Percentile changes of relative pulse wave volume (compared to prestimulation control value as 100%; increase indicated by no sign, decrease by –) calculated from rheoencephalograms of volunteer subjects, recorded immediately after end of 20 min-stimulation period of right stellate ganglion (A) and 1 h later (B). Code as in figure 2 for 4 waveforms used for stimulation. After one experiment, the volunteer subject had to refrain from any experiment for a 2-month period. Statistical

were the most effective ones in relieving chronic pain [9]. Pain profile scoring matrices were calculated after *Ray* [16] for each patient before, immediately after and at monthly intervals up to 1 year after the end of the stimulation period and showed a decrease in these indices of 68% (average value of all 2,800 patients, including 410 with chronic pain due to malignancies).

Discussion

Ray and Maurer [17] state '... experimental proof of the appropriate generator waveform for transdermal stimulation impulses remains

B								A		B	
E-100		E-200		IG 30		IG 50					
R	L	R	L	R	L	R	L	R	L	R	L
05	00	05	00	20	15	100	70				
10	05	10	05	15	10	75	45				
00	-05	00	-05	50	35	80	35				
-05	00	10	00	20	05	125	75				
00	00	05	-05	40	05	60	35				
05	00	00	00	15	10	155	100				
10	05	00	-05	25	15	85	45				
00	-05	05	00	45	15	125	55				
00	-05	00	00	05	00	105	45				
00	00	05	00	25	10	65	25				
2.5	-0.5	4.0	-1.0	26.0	11.0	97.5	53.0	46.5	22.5	32.5	15.87
4.85	3.68	3.94	3.16	14.49	10.21	30.39	22.63	44.75	27.89	42.47	25.36
4.5	10.11			4.6	10.12	5.6	11.12	13	13	14	14
								A	B	A	B

analysis $\bar{x}$ = mean; SD = standard deviation; sd = significant differences between columns marked with identical numbers; columns on right side of table, with figures only in statistical values indicate changes for all experiments (summary), separating right and left sides only; here, identical letters stand for no significant differences (between left A and B or right A and B).

controversial . . .' and '. . . much effort has been expended in an attempt to determine the optimum stimulating waveform for transcutaneous and implant applications with little success.'

Our study suggests that the effect of stimulation will be best when one applies a small electrode as the anode over the nerve to be stimulated. The cathode may either be on opposite surface of the body from the anode or, in exceptional cases, peripheral to the anode along the course of the nerve to be stimulated (e.g., trigeminal nerve). Brief, low frequency stimuli appear to be more effective. Each stimulus never should exceed a pulse width of 0.2 ms. We have observed that changes of the rheographic or rheoencephalographic tracings were minimal or absent when stimuli of relatively high frequency were used. Our study suggests that selection of frequency of stimulation by the patient may not be optimal for relief of symptoms.

Summary

The search for an optimal waveform for transcutaneous electric stimulation was carried out using sympathetic nerves with their known modifying influence on circulatory changes as test objects. With our model, we could select an optimal waveform among the various stimuli applied for transcutaneous stimulation of sympathetic fibers on 40 normal subjects and test it on 50 patients requiring therapeutic stellate blocks. We also found this same wave form to be optimally useful in relieving chronic pain in 2,800 patients suffering from various conditons.

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