RELIEF OF PRIMARY DYSENORRHEA BY TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

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Abstract. In this study we describe the use of high-frequency transcutaneous electrical nerve stimulation (TENS)(100 Hz) and low-frequency TENS (lf-TENS) (2 Hz trains) compared with placebo-TENS (p-TENS) in a group of 21 patients suffering from primary dysmenorrhea. Naloxone, a relatively pure opiate antagonist, was an additional test administered to 6 volunteer patients who had experienced an alleviation of pain with TENS. As will be seen, 14 out of 21 patients receiving high-frequency TENS (hf-TENS) experienced a pain reduction exceeding 50% of its original intensity. During lf-TENS or p-TENS, only 7 and 5 patients, respectively, obtained pain relief exceeding 50%. In 4 out of 6 volunteer patients, the relief of pain obtained with lf-TENS was counteracted by naloxone, whereas the relief experienced with hf-TENS in the same patients was, in general, unaffected by naloxone.

Key words: Dysmenorrhea, TENS, naloxone

Dysmenorrhea is a very common complaint, being presented by about 10% of females in their late teens and early twenties. The pain is often so severe that the women has to stay in bed for one or two days, thereby often occasioning absence from work.

Evidence indicates that prostaglandins regulate myometrial contractility leading to ischemia, which may be the underlying cause of primary dysmenorrhea (27). Interestingly, elevated levels of F2α prostaglandins and metabolites have been found in the menstrual fluid of dysmenorrheic women and the levels of these in endometrium and plasma seem to correlate very well to the presence of pain (14). It has been reported that the degree of potency of analgesics in alleviating dysmenorrhea is related to their effectiveness in depressing prostaglandin synthesis or its action. Also, Ca²⁺ antagonistic agents such as nifedipine and verapamil have been shown to reduce prostaglandin-induced uterine hypercontractility, thereby relieving menstrual pain (2, 9, 20). Other drugs that have been used in the treatment of primary dysmenorrhea are hormonal preparations that inhibit ovulation (4, 5, 8, 24). However, a non-pharmacological method for the alleviation of dysmenorrhea can be of great value especially in patients suffering from various side effects from the drugs used. One of the most widely used non-pharmacological methods for the relief of pain is transcutaneous electrical nerve stimulation, TENS. In several studies this method has proved to be an effective measure against a number of pain conditions of varying origin (3, 6, 7, 19, 22, 26).

In this paper we describe the use of hf-TENS (100 Hz) and lf-TENS (2 Hz trains; 6, 7) as compared with p-TENS in a group of 21 patients suffering from primary dysmenorrhea. Naloxone, a relatively pure opiate antagonist, was an additional test administered to 6 volunteer patients who had experienced an alleviation of pain with both hf-TENS and lf-TENS.

MATERIAL AND METHODS

The study was performed on 21 patients suffering from primary dysmenorrhea who had been referred because of symptomatic pain treatment. All of the patients complained of pain localized to the lower back (bilaterally) during menstrual flow. In 7 patients the pain began a day before menses. In 16 patients the pain was colicky and in the remaining 5, continuous. The intensity of the pain was so great that it compelled the patients to stay home from work. Also, 10 of the patients had to stay in bed for 2 days. All the patients who were examined underwent a gynecological exam, were informed of their diagnosis and asked if they wanted to take part in the experiments. Those willing to participate were informed about their role in the trial treatments. Furthermore, the patients were told that they might or might not experience pain relief — or even exacerbated pain during stimulation, but every effort was made to avoid any suggestion as to the effect. The patients were told that they could stop the stimulation treatment at any time. Their history of pain ranged from 18 months to 9 years. The mean age of the 21 patients was 22 years (15–29). All who had previ-
ously undergone various therapies which had resulted in unsatisfactory alleviation of pain, or various side effects.

Before treatment, the patients were asked to describe the location of their pain and its characteristic qualities, using a modified McGill pain questionnaire (cf. 15). They were also asked to describe drug intake, intake of alcohol, smoking habits, physical activity levels, effects of the pain in relation to daily behavior patterns and what made the pain increase or decrease. The patients also rated their subjective pain intensity before each stimulation session using a visual analogue scale. The words “no pain” and “worst pain ever” were placed at the left and right extreme end, respectively, of a 10 cm long horizontal line. The patients were instructed to mark the line at a point representing their pain. After stimulation, the patients were again asked to rate their subjective pain intensity.

While receiving treatment with TENS or p-TENS the patients rated their subjective pain intensity using a mechanical device with a graphic rating scale, connected to an in-writer out of sight of the patient (12, 18). No verbal communication took place with the patient during treatment.

Experimental protocol for treatment
The patients were randomly assigned to one of three groups, each group consisting of seven patients. All patients were treated during separate cycles with hf-TENS, If-TENS, or p-TENS, making a total of two TENS sessions and one placebo treatment.

Treatment groups
Group 1 received If-TENS during the first trial, hf-TENS during the second trial, and p-TENS during the last treatment cycle.

Group 2 received p-TENS during the first trial, If-TENS during the second trial, and hf-TENS during the last treatment cycle.

Group 3 received hf-TENS during the first trial, p-TENS during the second trial, and If-TENS during the last treatment cycle.

TENS in comparison with naproxen and verapamil
Following the end of the three different treatment cycles the patients were asked during which cycle they experienced the most effective pain alleviation. The type of stimulation used during this cycle was termed the "mode of choice". In the next cycle the patients were given one treatment with the respective "mode of choice" stimulation. On the following day, if pain persisted, they were given 500 mg naproxen and asked to rate its effect on the visual analogue scale. Finally the patients were asked to compare the effect of naproxen with that of the "mode of choice" stimulation. The same procedure was repeated during the next cycle, with the difference that the patients were given 120 mg verapamil instead of naproxen.

Effect of naloxone
Naloxone hydrochloride was given intravenously in a 0.4 mg/ml solution. In 4 patients, two test injections of 1.0 mg were first administered while experiencing alleviation of pain from treatment. If the pain returned within 10 min, a double-blind experiment was always performed with a series of six intravenous injections at 30-min intervals. In 2 patients, however, the double-blind procedure was performed directly. Sterile saline of the same volumes was used as placebo. The pain intensity was scored continuously on the graphic rating scale. Changes in pain intensity of less than 10% 10 min after injection were considered uncertain (cf. 22).

High-frequency TENS
The TENS apparatus used (Electroform 4C) produced monopolar square wave pulses with a duration of 0.2 msec and a frequency of 100 Hz. A pair of rubber electrodes, each with a surface area of 36 cm², were applied to the skin in the painful area. The stimulus intensity was just below the pain threshold (low intensity). At the first treatment session, TENS was applied to the area of pain for 20 min. If a pain-relieving effect was obtained, the treatment was continued for a further 25 min at the same point. If the patient did not report a reduction of pain after 20 min of treatment the electrodes were moved to some other place, e.g. a trigger point, if this was localized outside of the area of pain, proximal to the area of pain, along the peripheral nerve or to an acupuncture point close to the area of pain. If no reduction was obtained at any of these points the electrodes were applied for 25 min within the painful area (16).

Low-frequency TENS
The TENS apparatus used (Electroform 4C) produced trains of monopolar square wave pulses with a duration of 0.2 msec. Each pulse train (8 pulses) had a total duration of 80 msec and was delivered at 2 trains per second (2 Hz). The intensity used produced muscular contractions in the stimulated area (high intensity). The electrodes used, their placement and the procedure used were the same as for hf-TENS.

Placebo
Placebo-TENS was performed using the same type of apparatus as during TENS treatment, but the apparatus had no electrical output to the electrodes. The patients were told that they were given an “ultra-high frequency” TENS treatment and that some people may not experience any cutaneous sensations during stimulation.

RESULTS

The McGill Pain Questionnaire
The McGill pain questionnaire was used as a means of assessing the pain profile of patients suffering from dysmenorrhea. Factorial investigations of the questionnaire provided for a distinction between affective and sensory descriptors (dimensions). Forty-three per cent of the patients checked words (fearful—terrifying and wretched—blinding), describing emotional or affective aspects of the pain, which may reflect the negative attitude held by many women towards their period pains. Sixty-eight per cent of the patients checked sensory descriptors. Two components of sensory descriptors were derived — one related to dullness, and the other to cramping. In conclusion the pattern of scores emerging from the ques-
Table I. Mean pain intensity scores before treatment sessions.

<table>
<thead>
<tr>
<th>Treatment session</th>
<th>Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4.6</td>
<td>5.2</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>4.4</td>
<td>3.7</td>
<td>5.1</td>
<td></td>
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<tr>
<td>III</td>
<td>4.9</td>
<td>4.5</td>
<td>3.9</td>
<td></td>
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<tr>
<td>IV</td>
<td>5.1</td>
<td>4.7</td>
<td>4.3</td>
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<tr>
<td>V</td>
<td>4.2</td>
<td>3.8</td>
<td>4.6</td>
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<tr>
<td>VI</td>
<td>4.7</td>
<td>4.2</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>3.7</td>
<td>5.1</td>
<td>3.9</td>
<td></td>
</tr>
</tbody>
</table>

questionnaire indicate the significance of the emotional or affective aspect of the pain.

Pain intensity score
As indicated in Material and Methods all patients were asked to rate their pretreatment pain on a visual analogue scale. The mean pain intensity score of the three groups is given in Table I. As seen, there was no significant difference between the three groups.

Site of stimulation
Eighteen of the patients reported that the best point of stimulation was the painful area on the back (Th10−L1). Three patients reported that the best site was located on the abdomen (segmentally related to the painful area).

Pain-reducing effect of peripheral stimulation
The diagrams in Fig. 1 summarize the effects of the different modes of stimulation used in the present study. As can be seen, TENS stimulation at 100 Hz (high frequency) (hf-TENS) was clearly superior to 2 Hz TENS (low frequency) (lf-TENS) or placebo-TENS (p-TENS).

When treated with hf-TENS stimulation, 16 out of 21 patients experienced relief of pain. Increased pain was experienced by 3 patients, and 2 patients reported no change in pain intensity.

Of all 21 patients, 9 women obtained a reduction of their pain with lf-TENS. Low-frequency TENS caused an increase in pain in 3 patients and left 9 patients unaffected by the treatment.

During placebo ‘stimulation’ 7 patients experienced pain alleviation, while 14 patients obtained no reduction in pain. Out of these 14 patients, 3 women reported an increase in pain. It is interesting to note that the same 3 patients also reported an increase in pain during TENS stimulation.

The diagram in Fig. 2 summarizes the effect of the various TENS modes of treatment and placebo, the numbers in the circles indicating the number of patients experiencing pain relief for each mode of treatment and placebo. In all, 17 of the 21 patients experienced pain relief; 8 of these patients experienced a re-

Fig. 1. Effects of TENS and p-TENS on subjective pain intensity. Pain increase (+), no changes in pain intensity (0), pain reduction 50% or less (50), pain reduction 50−100% (100); hatched area, complete relief of pain.

Fig. 2. Number of patients obtaining relief of pain from hf-TENS, lf-TENS, and p-TENS.

Fig. 3. Effect of hf-TENS in a 19-year-old patient. TENS applied for 45 min in the painful area. Abscissa: time, in minutes; ordinate: subjective pain intensity; zero indicates pain intensity before hf-TENS. Downward deflection, pain reduction, 100% indicating complete relief of pain.
Induction time for maximal pain reduction

The data obtained from measurements of the time necessary for maximum pain suppression from the records as illustrated in Fig. 3 are summarized in Fig. 4. As seen, approximately the same time for stimulation was required for If-TENS and p-TENS in order to obtain maximal pain suppression. On average, pain was completely suppressed with these modes of stimulation within 20–25 min. High-frequency TENS had in general a faster pain-suppressing effect, pain relief being obtained in most patients after about 10 min.

Duration of pain relief

It is well known that TENS treatment can produce pain suppression which sometimes lasts for several hours. It was therefore of interest to measure the duration of effect of the two types of TENS and p-TENS in the present study. As seen in Fig. 5, there is no significant difference in this respect between the different modes of TENS or p-TENS.

Comparison with naproxen and verapamil

The results of the comparison of the pain-alleviating effect of “mode of choice” stimulation as compared with naproxen or verapamil are presented in Table II. Out of 17 patients experiencing pain relief, 5 patients treated with hf-TENS rated the pain-relieving effect of stimulation (“mode of choice”) as better than that of naproxen. Four of the patients, 2 women treated with hf-TENS (“mode of choice”) and 2 treated with If-TENS (“mode of choice”) reported that naproxen and the “mode of choice” were about equally effective in relieving their pain. Eight patients, 6 of whom treated with hf-TENS (“mode of choice”), 1 patient treated with If-TENS (“mode of choice”), and 1 patient with p-TENS (“mode of choice”) rated 500 mg of naproxen as most effective. Four out of the 5 patients who did not obtain relief of pain when treated with TENS reported pain relief from taking naproxen. Out of 17 patients experiencing pain relief, 7 (6 treated with hf-TENS and one patient treated

Fig. 4. Induction time for maximal pain reduction in the patients experiencing pain relief.

Fig. 5. Duration of pain relief after treatment.
Table II. Comparison of "mode of choice" stimulation vs. naproxen and vs. verapamil.

<table>
<thead>
<tr>
<th>No. of</th>
<th>&quot;Mode of choice&quot; stimulation</th>
<th>Compared with naproxen</th>
<th>Compared with verapamil</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Better</td>
<td>Equal</td>
</tr>
<tr>
<td>13</td>
<td>High TENS</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Low TENS</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>Placebo-TENS</td>
<td>1</td>
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</tbody>
</table>

with If-TENS) rated the pain-relieving effect of stimulation ("mode of choice") as more pronounced than that of verapamil. Six of the patients, 4 women treated with hf-TENS ("mode of choice"), one woman with If-TENS ("mode of choice") and one with p-TENS ("mode of choice") reported that verapamil and the "mode of choice" were about equally effective in relieving their pain. Four patients, 3 of whom were treated with hf-TENS ("mode of choice") and one treated with If-TENS ("mode of choice") reported 120 mg of verapamil as most effective. Two out of the 5 patients who did not obtain any relief of pain when treated with TENS reported pain relief when taking verapamil.

Effect of naloxone

During the previous treatment cycles the 6 volunteer patients had experienced relief of pain with both high- and low-frequency TENS. During the additional cycles they were treated with hf-TENS or If-TENS and subjected to naloxone. The results from the 6 patients when receiving hf-TENS and naloxone can be seen in Fig. 6. Here the patients' reactions to test doses of naloxone are denoted by open circles and the reactions to saline or naloxone administered in double-blind fashion are illustrated as filled circles.

The reactions to saline are shown in the left part of the diagram and those to naloxone are shown on the right-hand side. It can be seen that none of these patients consistently experienced any inhibition of pain reduction from naloxone. However, one patient (No. 3) reported inhibition of pain alleviation from four out of six injections, containing either saline or naloxone. In Fig. 6 the corresponding results are shown for If-TENS treatment. Patients 1, 2, 4, and 5 systematically experienced inhibition of pain relief from naloxone, but not from saline. Patient No. 3 indicated inhibition of pain alleviation both from naloxone and saline administration. Patient No. 6, on the other hand, did not experience any changes in the pain relief after If-TENS from naloxone or saline injections.

DISCUSSION

Transcutaneous electrical nerve stimulation has been extensively used in recent years for the relief of a variety of pain syndromes. Although it has been known that TENS can effectively suppress pain, this method appears not to have been widely used in clinical practice for the alleviation of dysmenorrhea. However, recent observations on the pain-suppressive effect of hf-TENS in patients suffering from dysmenorrhea...
menorrhea have focused attention on this mode of treatment as an alternative pain-alleviating measure in dysmenorrhea (13).

In the present study we have compared the pain-reducing effects of hf-TENS, lf-TENS and p-TENS with that of naproxen and verapamil. Each patient was subjected in random order to the various TENS modes of treatment. About 70% of the patients experienced pain reduction when treated with hf-TENS. Low-frequency TENS was clearly less effective and relieved only about 45% of the patients. Moreover, even though 9 out of the 21 patients experienced pain relief from lf-TENS, only 3 rated it as “mode of choice”. This would seem to imply that the pain relief scores should be interpreted with caution as to which mode of treatment to use. In all, about 75% of the patients (16 women) reported that they experienced some relief of pain during one or several of the sessions of peripheral stimulation. Of these 16 patients, 5 treated with naproxen and 7 treated with verapamil rated TENS as more effective than naproxen/verapamil, whereas 8 patients treated with naproxen and 4 patients with verapamil rated the effect of naproxen/verapamil as superior to TENS. This would appear to suggest that in the choice between naproxen and verapamil the latter mode of treatment is to be preferred for the treatment of dysmenorrhea. However, TENS appears to be more effective than verapamil in relieving patients from dysmenorrhea and about equally effective with naproxen. This would appear to suggest that TENS can be used for the symptomatic treatment of dysmenorrhea and especially in patients suffering from the side effects of the drugs used. In the choice of treatment of dysmenorrhea, both hf-TENS and naproxen and verapamil therefore merit consideration. Also, TENS can be administered by paramedical personnel once the appropriate point or area of stimulation has been located and can even be self-administered by the patients.

The present results indicate that a non-opioid pathway mediates the relief of pain obtained with hf-TENS, whereas the relief of pain obtained with lf-TENS appears to involve endogenous opioids. This is in agreement with previous results of Sjölund and Eriksson (22). On what basis then is the pain-suppressive effects obtained by hf-TENS? Since the presentation of the gate control theory, the neurophysiological basis of the theory has been questioned. Still, evidence is available (10) that activity in pain-carrying fibers is subjected to modulation from other sensory inputs and from descending influences from supraspinal areas. Furthermore, there is increasing evidence that non-opioid pathways, especially descending serotonergic pathways, suppress pain in animals (1, 11, 21, 25).

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