The Ethics Committee for Non-Medical Experiments involving human subjects at the Faculty of Natural Sciences, Medicine and Dentistry

The Hebrew University

הפקולטה לרפואה
THE FACULTY OF MEDICINE

האוניברסיטה העברית בירושלים
THE HEBREW UNIVERSITY OF JERUSALEM

Subject: **Your Research on: "Use of the Medkey device, an electrotherapy device, to treat musculoskeletal pain: a retrospective cohort study of existing data"**

The Ethics Committee for Human Research in Non-Medical Fields at the Faculty of Natural Sciences, Medicine and Dentistry has reviewed your request for approval to conduct the aforementioned research.

I am pleased to inform you that the committee has approved the conduct of your research, which meets the criteria for ethical research. This approval is valid for two years from the date of receipt.
The researcher is responsible for conducting the research in accordance with the ethical guidelines presented in the request. Any changes must be reported and approved.

Please cite the approval number 14082024 in all correspondence or publications related to this research.

We wish you success in your research.
Sincerely,

Dr. Ne'ama Kashet
Chairman of the Ethics Committee

RESEARCH:

Use of the Medkey device - an electrotherapy device to treat musculoskeletal pain

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A retrospective cohort study of existing data.

Research Sponsor: Avidor Medical Ltd. – Foot Health Center, May 2024
Conducted by Prof. Amnon Lahad, MD, MPH, August 2024

Content:

1. Background

The use of muscle stimulation as a therapeutic measure for musculoskeletal pain is very common, especially as part of treatments Transcutaneous electrical nerve stimulation (TENS) is the accepted method. Physiotherapists

Regarding TENS, there are many articles and several meta-analyses with inconsistent results. A Cochrane review on neck pain [I] found a small pain reduction effect that was not significant in two studies. In rheumatic pain, one type of TENS [AL-TENS] demonstrated a decrease in pain and increase in gross strength based on 3 small studies [II]. A review study of Cochrane meta-analyses found 51 randomized studies that included a total of 2895 in low-quality studies [the meta-analyses were good but the studies within them less so]. The authors felt that it could not be concluded that TENS is an effective treatment. [III]

Due to the inconsistency of the research, devices were later developed that use the same principle of nerve/muscle stimulation but at different intensities and with the ability to measure alongside muscle stimulation.

The Medkey device, made in Germany [identical to the InterX device made in the USA] is an electrotherapy device that transmits energy through the skin adaptively [transcutaneous electrical stimulation]. The device reads skin resistance [which depends on the muscular response beneath the skin] and adapts to it a response of electrical muscle stimulation similar to TENS.

Only a small number of controlled studies have examined the effect of operating the device:

- A study that randomly examined 60 elderly patients after hip fracture surgery who were divided into a treatment group and a control group demonstrated significantly less pain [VAS of 4.0 versus 7.3], an increase in range of motion of 25° more flexion in the treatment group, and also an increase in walking ability. [IV]
- The same group examined 60 patients aged 20-60, after bimalleolar ankle fracture who were divided in a controlled manner into two groups. In the treatment group, the pain decreased by an average of 1.9 points more [out of 10]. Also, the decrease in edema in the surgical leg was 32% greater and so was the ability to flex the ankle, which was 18° higher in the intervention group. The difference in all outcomes was significant [$p<0.001$]. [V]
- Another study involving 61 participants after knee replacement surgery [TKR], divided the participants randomly into a regular treatment group and an intervention group that also received 8 treatments with the InterX device. In the intervention group, pain decreased by 2.2 points more [on a VAS scale of 10] than in the control group, $P=0.002$. Also, the range of motion was greater in the intervention group. [VI]
- Another controlled study examined 104 patients with plantar fasciitis who were divided into a regular treatment arm and an arm that was also treated with InterX. At 12 weeks follow-up, both pain levels and use of anti-inflammatory drugs were significantly lower in the intervention group. [VII]

- There is another controlled study that has so far only been published as a poster at conferences and showed an advantage for the device in treating shoulder problems in athletes.

In summary – there is good evidence from several controlled studies regarding the ability of Medkey/InterX treatment to reduce pain and improve range of motion and ability to function. There is still a lack of information regarding different effects in subgroups (men/women, differences in age and weight, as well as many additional indications). In addition, there is a lack of research on a large number of patients in conditions that are not controlled studies.

The Medkey device was imported to Israel by Avidor company and received Ministry of Health approval.

The device is in commercial use as part of treatments offered only by physiotherapists in a framework called Q-Room. To date, over 3,000 patients have been treated with the device in Israel for a fee. In Germany, Australia, and the Netherlands, tens of thousands more.

As part of the treatment system, data was collected, without planned research intent, regarding users that included age, sex, and the organ with the problem, and additional administrative data. In addition, all patients filled out a pain scale – VAS before starting treatment and upon completion, usually after 4 weeks of weekly treatment.

Therefore, it makes sense to examine the response among patients in Q-Room.

2. **Research Objective**

Comparison of subjective pain levels among patients treated by the Medkey device before and after treatment.

Research questions:

- What is the difference in average and absolute pain levels between the start and end of treatment? By how much?
- Is there a different effect according to the organ that was the reason for starting treatment?
- Does the effect differ by age, sex, and weight?
- What is the effect of the number of treatments? And is there an optimal number of treatments?
- Is there a difference in response in people in relation to the number of treatments?

3. **Methods**

This is a study using existing data. The data was collected for operational purposes of the pain rooms (Q-room) and not for research purposes. This is a study in which the participants are identified as members of Clalit Health Services. The study is in a before and after method. In this method, each person is compared to themselves.

4. **Data**

Data will be taken on the last 1,500 patients from Avidor's operational system in Q-room. For each patient, the following variables will be collected:

- Age
- Sex
- Weight
- Organ with pain and because of which they came for treatment
- Number of treatments
- Treatment frequency
- Whether the patient underwent surgery in the pain area
- VAS pain scale before starting treatment
- VAS pain scale after completing treatment

The data will be collected in an EXCEL file by the treating physiotherapist from the treatment information system. Each patient will be given an identifying number. Only the therapists [who are not part of the research team] will have an identifying key of the patients.

The file will be transferred to the principal investigator, without name, ID number, address, phone number, or identifying data except those specified above.

5. Statistical Analysis

The data will be processed using SPSS for Windows 29.0. The outcome will be the difference in pain according to the VAS scale. This is a continuous scale with a distribution that can be normalized [in most studies of this type at the beginning of the study the pain is high and mostly above 5, but still with a distribution that allows logarithmic conversion creating a normal distribution].

Comparison between variables will be performed using t-tests between groups [sex, after surgery], ANOVA regarding comparison of continuous variables [weight, age, number of treatments].

Subsequently, linear regression will be performed to quantify the effect of each variable given the other variables.

6. Interim Results

a. Nominal decrease in VAS according to pain areas:

Painful Area Treated	Number of Patients in Sample	Level of Decrease in VAS	Significance
1. Neck	70	4.3	< 0.01
2. Back	293	4.0	< 0.01
3. Foot and Achilles tendon	838	4.6	< 0.01
4. Leg & Knee	174	4.6	< 0.01
5. Hip	34	4.9	< 0.01
6. Shoulder	54	4.7	< 0.01
7. Hand & Arm	37	4.7	< 0.01

b. For all subjects, relative VAS decrease – reduced to 4 areas:

1. Neck, shoulder, hand. 2) Foot, ankle. 3) Leg 4) Back

i. Improvement in area: Neck & Shoulder & Hand: Sample - 161 random patients.

Level of Improvement in %	Number of Patients	% of 161 Patient Sample	Treatment Success	Notes
0	3	1.9	Unsuccessful	No patient reported worsening
22-10	19	11.8	Low success	
23-50	29	18	Successful	
50-100	110	68.3	Very successful	Significant success in treatment 86.3%

ii. Improvement in area: Back: Sample - 293 random patients.

Level of Improvement in %	Number of Patients	% of 293 Patient Sample	Treatment Success	Notes
0	22	7.5	Unsuccessful	No patient reported worsening
22-11	25	8.5	Low success	
23-50	66	22.5	Successful	
50-100	180	61.4	Very successful	Significant success in treatment 83.9%

iii. Improvement in area: Foot ankle: Sample - 834 random patients.

Level of Improvement in %	Number of Patients	% of 834 Patient Sample	Treatment Success	Notes
0	37	4.4	Unsuccessful	No patient reported worsening
17-11	33	3.8	Low success	
50-18	184	22.0	Successful	
51-100	584	69.9	Very successful	Significant success in treatment 91.9%

iv. Improvement in area: Leg: Sample - 208 random patients.

Level of Improvement in %	Number of Patients	% of 208 Patient Sample	Treatment Success	Notes
0	10	4.8	Unsuccessful	No patient reported worsening
25-13	9	4.3	Low success	
50-18	32	15.4	Successful	
51-100	157	75.5	Very successful	Significant success in treatment 91.9%

7. Conclusions

a. Average VAS decrease for all 1,500 subjects in the sample: 4.47.

b. Men responded slightly better - 0.28 VAS, a significant result.

c. Weight and age were found to have no significant effect.

d. The more treatments, the better the response: a decrease of 0.25 for each treatment beyond

e. Generally, a reduction of 2 points on the VAS scale is considered a successful treatment. In light of this, the Medkey treatment, which achieved an average of 4.7 or about 67% reduction in the pain level with which the patient started the treatment, has been proven significantly to contribute to pain reduction. This is in a test sample of 1,500 random patients.

f. Many aspects of Q-room activity were not examined in this retrospective study and are recommended for future research, such as:

- i. The duration of stability of the pain improvement achieved and the level of pain recurrence and/or alternatively the need for maintenance treatments.
- ii. Effects of combining the additional technologies implemented in Q-room.
- iii. Examination of more precise syndromes and pain areas. It was not possible to separate in this study as we defined that a minimal sample for a pain area is 30 patients.

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