Study protocol

Effectiveness of mid-frequent electrotherapy StimaWELL® in patients with chronic neck- and low-back pain

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Summary

Transcutaneous electrical nerve stimulation (TENS) is widely used in everyday clinical practice for both acute and chronic pain. One of the main indications for the use of TENS is musculoskeletal pain (Johnson and Martinson, 2007). Especially in chronic low-back pain (Shimoji et al, 2007; Pop et al, 2010; Buchmuller et al, 2011; Facci et al, 2011; Ratajczak et al., 2011) and Cervicalgia (Maayah and Al-Jarrah 2010) the effectiveness of TENS has been shown several times in the literature, although no clear benefit could be proven in larger systematic reviews or meta-analyses, neither for cervical syndrome (Machado et al, 2009; Kroeling et al., 2013), nor for lumbargia (Khadilkar et al., 2008; Van Middelcoop et al. , 2011). In the use of TENS with sufficiently high stimulation intensities, a reduced need for opioids and less opioid-induced adverse reactions have been observed (Wang et al., 1997; Chen et al, 1998).

The aim of this study is to assess the effect of the application of regular, mid-frequent electrotherapy on chronic neck- or low-back pain. This electrode mat used in the study is larger than the electrode patches of conventional TENS devices, and covers the entire spine. The patients are interviewed anamnestically and physically examined before and after the application of the device regarding the subjektive pain sensation (Numeric pain rating scale, Shortform-Mc Gill Pain Questionnary incl. Visual analogue scale) and the functionality in everyday life using questinnonaires (Roland-Morris Disabilty Questionnaire, Neck Disability Index). Furthermore, the spine mobility (i.e. the range of motion) of the cervical and lumbar region is also determined before and after the sessions.

Type of the study

The study is a prospective, monocentric, double-blind, randomized and controlled study.

Primary outcome:

- Is there a significant difference in the Visual Analogue Scale (VAS)/Numeric rating scale (NRS) of patients with neck- and low-back pain before and after application of StimaWELL® between verum, control group, and control of the control group)?

Secondary outcomes:

- Is there a significant difference in the individual pain qualities (SF-MPQ), in the Roland-Morris Disabiltiy Questionnaire, in the Neck Disability Index, in the spinal range of motion (ROM) in chronic neck- or low-back pain patients after application of StimaWELL® compared to the control group and control of control group?

- Are there gender-specific differences regarding the effect of StimaWELL® regarding. SF-MPQ, in the Roland-Morris Disability Index, Neck-Disability Index or ROM?

- Does the use of StimaWELL® change the need for painkillers (WHO level II, WHO level III drugs)?

Material and methods

The study will test 125 patients (equivalent to 50 patients in the verum group, 50 patients in the control group, as well as 25 patients in control of the control group) in the pain outpatient clinic of the University Clinic for Anesthesia, General Anesthesia and Special Pain Therapy. The patients are recruited from the respective outpatient clinics, by extramural ordinations or libraries by means of flyers, and were asked to contact the e-mail address studie_elektrotherapie@hotmail.com for preliminary examination. As a next step they are randomized into three different groups: “Verum group” with superliminal mid-frequency stimulation for 30 min after device calibration, “control group” with Sham treatment with device calibration only without consequent electrostimulation, or “control of the control group” without any stimulation. During the preliminary examination, all patients, regardless whether they have been recruited by public libraries or extramural ordinations, are examined by trained medical staff in respect to the inclusion and exclusion criteria. Patients who are eligible to participate in the study are then assigned to the six-time weekly sessions for 30 min each, and for follow-up examination.

The recruitment of patients were performed in the pain clinic of the University Clinic for Anesthesia, in the University Clinic for Physical Medicine and Rehabilitation in the Medical University of Vienna, as well as by the following extramural ordinations and public libraries by means of advertising flyers:

- University Library of the Medical University of Vienna

- Entrance hall/pinboards on level 5 and pinboards on level 4, levels 7 and 8 of the Medical University of Vienna
- Orthopaedics Donauzentrum Dr. Bernhard Gisinger/Dr. Michaela Huber, Donaustadtstraße 1, 1220 Vienna
- Dr. Christoph Katzenschlager, ENTObere Landstraße 3, 3500 Krems
- Dr. Susanne Kuta, Jägerstraße 41/1, 1200 Vienna, +43-1-3327029
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The calculation of the number of cases is based on the primary endpoint. To achieve a power of 80%, using the t-test for unpaired samples, n-number of 37 patients per group is needed for the verum and control group, respectively, assuming that the difference in the change in the VAS/NRS score between the two groups is exactly 10 (VAS) or 1 point (NRS), and n-number of 10 in the control of control group, assuming that there is no significant change in the VAS/NRS score before and after the sessions. Based on the study by Pop et al. 2010, a standard deviation of 1.5 (for NRS) was assumed. In order to correct for possible drop-outs (about 30 %), the number of cases is increased to 50 patients per in the verum and control group each, and to 25 patients in the control of control group. The statistical evaluation is carried out with the help of SPSS.

There is no payment of the study patients provided. All study participants are insured via Zürich Versicherungs-Aktiengesellschaft, policy number 07229622-2.

Inclusion criteria

- Women and men aged at least 18 years, who have been suffering from pain and/or tension in the cervical, thoracic or lumbar spine for at least 3 months without radicular involvement or pain radiating into the arms or legs.

- From a scale of 0 to 10, the subjectively perceived pain intensity (numeric pain rating scale, NRPS) should be > 5.

- Current laboratory values incl. complete blood count and inflammation values, as well as an X-ray of the spine (anterior/posterior and lateral, functional images), each not older than max. 3 months, should be used to ensure the work diagnosis (myalgia, spondylarthrosis, spondylolistheses, sacroileitis, etc.) and to verify the exclusion criteria.

- The pain medication must have remained constant 2 weeks before the start of the study and must not be changed during the study period.

- Non-oral pain therapies such as physiotherapy, physical therapy, acupuncture, manual therapy, osteopathy, etc. must be completed at least 2 weeks before the start of the study and may not be carried out additionally during the study period.

- None of the following exclusion criteria should apply:

Exclusion criteria

- Pregnancy
- Participation in other studies (anamnestic query)
- Pretreatment with TENS (transcutaneous electrical nerve stimulation; for the purpose of risk of unblinding)
- Ongoing pension procedure (in order to avoid bias due to pretension of illness; anamnestic query)

- Neuropathic, radicular pain (anamnestic query)
- Acute instabilities and/or surgical indication in the spine (e. g. sudden loss of strength, acute problems with urination or defecation, riding pants hypoesthesia)
- Previous spine surgery
- Infections/abscesses/skin lesions in the spine or the surrounding area
- Malignant diseases or secondary blastomas in the spine or in the surrounding area
- Change in the pain therapy the last 4 weeks (e. g. intravenous infusions, local infiltrations, peridural anesthesia or other invasive procedures in the close vicinity of the spine, physical treatments, change of the oral drug therapy)
- Cardiac arrhythmias, implanted pacemaker or defibrillator, previous heart surgery
- Epilepsy

Managementof complications and aftercare

Patients receive a written information sheet with the contact details of the study leaders in order to be able to report any undesirable effect.

Benefits for study participants

The advantage of the patients is the intensified medical and physical care during the study, as well as the option to receive further treatments with StimaWELL® in the Pain Outpatient Clinic after the study partcipation.

Ethical considerations

StimaWELL® is a form of electrotherapy, based on the TENS device widely used in everyday clinical practice, and ist not-invasiv,cost-effective, easy to perform, low side effect, and takes only approx. 30 minutes per application. Analogous to the TENS device, a painkiller requirement reducing effect is expected after repeated application.

The duration of the total examination ofabout one hour and follow-up evaluation of 60 minuteseach, as well as 6 therapy units of 30 minutes per patient at weekly intervals, can be regarded as less stressful.

There are no additional invasive measures beyond the normaln outpatient measures (e.B. X-ray examination, bloodsampling). For these reasons, no risks for the study participants are to be expected.

The consent ofthe study participants is given by means of an information sheet and detailed oral information.

Time shedule

All examinations (anamnesis incl. personal data collection and assessment of the past medical history, physical examination, quesionnaires about the funcionality in daily life, quality of life, and measurement of the spine mobility) can be carried out within about an hour in total. The application of StimaWELL® does not exceed about an hour (about 30 minutes on average).

Actionn	**Number of treatments/sessions**	**Required time**
anamnesis	1x	about 10 minutes
Survey of the subj. Pain perception by means of questionnaire (SF-MPQ incl. VAS)	2x (before and after 6 units StimaWELL®)	about 10 minutes
Survey of functionality in everyday life by means of questionnaires (Roland-Morris Disability Questionnaire, Neck Disability Index)	2x (before and after 6 units StimaWELL®)	about 20 minutes
Examination of the spinal mobility (ROM)	2x (before and after 6 units StimaWELL®)	about 10 minutes
Application of StimaWELL® or Sham treatment	6x	about 30 minutes
Evaluation of medication intake	2x (before and after 6 units StimaWELL®)	about 5 minutes

Time Shedule

	Week 1	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 8**
First contact in the outpatient clinic, patient recruitment	Basic investigation (SF-MPQ incl. VAS/NRS, ROM, RMDQ, NDI, medication)							Final investigation (SF-MPQ incl. VAS, ROM, RMDQ, NDI, medication)
		Session 1 (verum/ control/ control of control)	Session 2 (verum/ control/ control of control)	Session 3 (verum/ control/ control of control)	Session 4 (verum/ control/ control of control)	Session 5 (verum/ control/ control of control)	Session 6 (verum/ control/ control of control)	

Study-related measures

At the beginning of the study, a detailed explanation is performed by means of an information sheet and an informed consent is obtained. After a basic investigation (anamnesis inkl. collection of personal data and medical history, physical examination and quesionnaires), patients were randomized into one of the three gourps (verum, control, control of control). Weekly sessions withor without electrostimulation for 30 min each and six times in total are then performed. In the end, the same investigations performed at the beginning of the study are repeated and patients were asked for any unvoluntary effects during the study. The basic, as well as the final investigation consist of the following:

Evaluation of personal data and medical history

- Collection of personal data
- Evaluation of the actual pain state (in rest, under activity, average in the last 4 weeks, minimum, maximum) using NRS
- Current or previous illnesses or surgeries
- Concomitant medication

Questionnaires for recording the quality of life (QoL), subjective pain perception and functionality

The survey of the quality of life,the subjective sensation of pain, as well as the functionality in everyday life is carried out with the means of validated questionnaires (SF-MPQ: subjective pain relief; Roland-Morris Disability Questionnaire/Neck Disability Index: Questioning functionality in everyday life). The mobility (range of motion) of the cervical and lumbar spine is based on validated tests (modified-modified Schober: Williams et al., 1993; Tousignant et al., 2005; Performance Attainment Associates CROM: see Tousignant et al., 2000; Williams et al., 2010).

Application of StimaWELL®

StimaWELL® is a multidimensional, dynamic deep stimulation device from Schwa-medico, which is an electrode mat consisting of 12 bilateral stimulation bars. Mid-frequent electrotherapy (2-6 kHz) can be applied, also in comination with heat application and mechanical stimulation (massage) if desired. According to the company, StimaWELL® can be used in acute and chronic pain in the spine with or without degenerations detectable in X-ray or MRI such as osteochondrosis, spondylarthrosis, spondylolisthesis, intervertebral disc protrusions, lumbar spinal canal stenosis, as well as in osteoporosis.
In accordance with the Medical Devices Directive 93/42/EEC, the device bears the CE marking CE0482. StimaWELL® Is used in the study according to the indication specified by the manufacturer, namely pain treatment in the spine area, in consideration of the contraindications (see exclusion criteria).

Patients who have been assigned into the verum group receive a suprathreshold stimulation for 30 minutes in each session, which remains subjectively clearly noticeable. In the control group, the device is initially set for device calibration and then switched off (= sham therapy), in the control of control group, the device is kept inactivated from start to finish of the session; to avoid unblinding of the patient, the display is covered with a blanket after device setting so that it can't be seen by the patients.

Statistical analysis

Data is evaluated using Sigma Plot version 12.0 from Systat Software GmbH and SPSS® version 19 from IBM. The demographic data are divided into the following variables and presented:

- Qualitative variables (e.B. gender): absolute frequency in %, calculated separately for verum control and control of the control group
- Quantitative variables (e.B. age, NRS, VAS, ROM): mean + standard deviation, median, minimum, maximum; calculated for verum and control and control of the control group

Primary parameters:

Is there a difference in VAS/NRS between the verum and control groupn after the application of StimaWELL®?

Mean and standard deviation, minimum, maximum and median for the difference between the pre- and post values are calculated separately for all groups. Statistically significant difference is checked with the help of the t-test for unpaired samples. A significance level of alpha = 5% (two-sided) is used.

Secondary parameters (e.B. differences in the individual pain qualities in the SF-MPQ; gender-specific differences in SF-MPQ, Roland-Morris Test/Neck Disability Index, ROM; Change in drug dosage) are analyzed using RM-One Way ANOVA and Bonferroni correction.

The data of the patients used are pseudonymized. The completeness of the entries (e.B. patient number and initials on each sheet of the CRF) is controlled after testing and transfer to the online form (Clincase) or to Excel developed by the Statistics Institute. The data is transferred to Excel sheets, backed up electronically 2 times at least and printed out once. An interim evaluation in half of the study is planned to check the statistical fluctuation and the dropout rate.

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