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# **Intramuscular or periosteal acupuncture for patients with chronic musculoskeletal pain in the neck and low back – effects on pain, physical and psychological functioning**

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## ABSTRACT

**Background:** Periosteal acupuncture has shown promising results in the clinic. No studies of effects in patients with chronic pain in the neck and low back are today available.

**Aims:** The main purpose was to compare intramuscular and periosteal acupuncture. The specific aims were to compare three groups of patients suffering from chronic musculoskeletal pain in the neck and/or low back, one with intramuscular acupuncture, one with periosteal acupuncture and a third information control group with respect to clinically relevant pain relief, intake of analgesics, and physical functioning (Study I) and to psychological functioning and quality of sleep (Study II).

**Material:** Consecutive patients in primary care with nociceptive pain in the neck and/or low back of unspecific origin for >3 months, aged 18-70 years were included. The patients were alternately allocated to intramuscular acupuncture, periosteal acupuncture and an information control group.

**Methods:** Eight acupuncture treatments were administered during a five week period with two voluntary additional treatments after one month. All patients were encouraged to stay active.

Pain was estimated in a pain diary employing standard visual analogue scales (VAS) three times a day for seven days. Average pain during the last week was also estimated on a similar VAS. Study I. Clinically relevant pain relief was defined as a reduction of pain comparable with a 30% decrease of the initial value. Intake of analgesics was recorded from the pain diary. Study I. Physical functioning was assessed with the Disability Rating Index. Study I. Psychological functioning was evaluated with the Hospital and Anxiety Scale. Study II and Sleep and mood at awakening were evaluated on a VAS. Study II.

All estimations were made one week prior to treatment, one week, one, three and six months after termination of treatment. An additional estimation of actual level of pain, intake of analgesics, sleep, and mood at awakening were recorded in the pain diary in the middle of the treatment period.

In the control group the estimations were made at corresponding times (similar intervals), but only for one month after termination of treatment. Non-parametric statistics were used.

**Results:** 144 patients, 59 in the intramuscular group, 55 in the periosteal group and 30 in the control group were included in the analysis.

Before treatment there were no differences between the three groups regarding pain, intake of analgesics and psychological functioning. No differences were found between the acupuncture groups regarding any of the outcome variables. There were differences between each of the two acupuncture groups compared with the control group on all test occasions up to one month after treatment with respect to pain diary, one week after treatment with respect to pain last week, and one month after treatment with respect to anxiety. Clinically relevant pain relief with respect to pain diary was obtained in 29 intramuscular acupuncture patients, 25 periosteal acupuncture patients and 5 patients in the control group. The proportions of non-cases with respect to anxiety increased in the intramuscular acupuncture group from 39 to 47, in the periosteal acupuncture group from 37 to 49, and in the control group from 15 to 16. Six months after end of treatment, 46% of the patients in the intramuscular acupuncture group and 45% of the patients in the periosteal acupuncture group had obtained clinically relevant pain relief in terms of pain diary. The corresponding figure for pain last week was 29% of the patients in each group. Reduced anxiety was observed in both acupuncture groups up to three months after end of treatment i.e. the number of non-cases increased with four in the intramuscular acupuncture group and with seven in the periosteal acupuncture group.

**Conclusion:** Periosteal acupuncture is equally effective as intramuscular acupuncture. One month after end of treatment more patients in both acupuncture groups had obtained clinically relevant pain relief and reduced anxiety compared with patients in the control group. Six months after treatment 45% of the patients in both acupuncture groups had obtained a clinically relevant pain relief. The effect on anxiety remained up to three months for both acupuncture groups.

Keywords: Acupuncture, Chronic nociceptive pain, Neck pain, Low back pain Non-parametric statistics

## SAMMANFATTNING

**Bakgrund och syfte:** Periosteal akupunktur har visat lovande resultat. Idag finns inga studier avseende dess effekt på patienter med långvarig smärta i nacke och ländrygg.

**Syfte:** var att jämföra effekten av intramuskulär och periosteal akupunktur och att jämföra tre grupper av patienter med långvarig smärta i nacke och ländrygg, en som erhållit intramuskulär, en som erhållit periosteal akupunktur och en kontrollgrupp avseende kliniskt relevant smärta, konsumtion of analgetika och fysisk funktion samt psykisk funktion och sömnkvalitet.

**Material:** patienter i primärvården med nociceptiv smärta i nacke och/eller ländrygg av ospecifik karaktär, som varat längre än 3 månader, och i åldrar mellan 18-70 år inkluderades konsekutivt. Patienterna allokerades alternativt till intramuskulär akupunktur, periosteal akupunktur och en kontroll grupp. Åtta akupunkturbehandlingar gavs under fem veckor med tillägg av två ytterligare frivilliga behandlingar efter en månad. Patienterna i de tre grupperna uppmuntrades att vara aktiva. Smärta utvärderades med smärtdagbok innehållande VAS tre gånger per dag i sju dagar. Medelsmärta under senaste veckan värderades med liknande VAS. (Study I). Klinisk relevant smärtlindring definierades som motsvarande 30 % minskning av initiala värdet. Analgetika konsumtion registrerades från smärtdagboken och fysisk funktion värderades med Disability Rating Index (Study I). Psykisk funktion värderades med Hospital and Anxiety Scale (Study II). Sömn samt stämningsläge på morgonen värderades med VAS (Study II). Alla skattningar genomfördes en vecka före behandling, en vecka, en, tre och sex månader efter avslutad behandling. En ytterligare mätning av aktuell smärta, konsumtion av analgetika, sömn samt stämningsläge på morgonen registrerades i smärtdagboken i mitten av behandlingsserien. I kontrollgruppen genomfördes mätningar på motsvarande tidpunkter men enbart en månad efter behandlingsseriens slut. Icke parametrisk statistik användes.

**Resultat:** 144 patients, 59 i intramuskulära gruppen, 55 i periosteal gruppen och 30 i kontrollgruppen inkluderades i analyserna. Före behandling förelåg inga skillnader mellan de tre grupperna med avseende på smärta, konsumtion av analgetika, samt psykologisk funktion. Ingen skillnad förelåg mellan de båda akupunkturgrupperna i någon utvärderingsvariabel. Skillnader förelåg mellan vardera akupunkturgrupp och kontrollgruppen vid samtliga testtillfällen fram till en månad efter behandlingsslut med avseende på smärtdagbok, en vecka efter med avseende på smärta senaste veckan, en månad efter med avseende på ångest. Klinisk relevant smärtlindring med avseende på smärtdagbok uppnåddes av 29 intramuskulär patienter, 25 periosteal patienter samt 5 patienter i kontrollgruppen. Andelen non-cases med avseende på ångest hade ökat i intramuskulära gruppen från 39 till 47, i periosteal gruppen från 37 till 49 och i kontrollgruppen från 15 till 16. Sex månader efter behandlingsslut hade 46 % i intramuskulär gruppen och 45% i periosteal gruppen klinisk relevant smärtlindring med avseende på smärtdagboken. Motsvarande siffror för smärta senaste veckan var 29 % för båda grupper. Minskad ångest registrerades i båda akupunkturgrupperna fram till tre månader efter behandlingsslut. Tre månader efter behandling hade antalet non-cases ökat med fyra i intramuskulär gruppen och sju i periosteal gruppen.

**Konklusion:** Periosteal akupunktur är lika effektiv som intramuskulär akupunktur. En månad efter behandlingens slut hade fler patienter i båda akupunkturgrupperna uppnått klinisk relevant smärtlindring och reducerad ångest jämfört med kontrollgruppen. Sex månader efter behandlingsslut hade 45 % av patienterna i båda akupunkturgrupperna fått klinisk relevant smärtlindring. Effekten på ångest kvarstod fram till tre månader efter behandlingsslut.

**Nyckelord:** akupunktur, långvarig nociceptiv smärta, nacksmärta, ländryggsmärta, icke parametrisk statistik.

## LIST OF PUBLICATIONS

This thesis is based on the following publications, which are referred to in the text with their Roman numerals

I Hansson Y., Carlsson C., and Olsson E. Intramuscular and periosteal acupuncture in patients suffering from nociceptive musculoskeletal chronic neck and/or low-back pain - an evaluator blind, controlled study.

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II Hansson Y., Carlsson C., and Olsson E. (2007) Intramuscular and periosteal acupuncture for anxiety and sleep quality in patients with chronic musculoskeletal pain - an evaluator blind, controlled study. *Acupuncture in Medicine* 25, 148-157.

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## LIST OF ABBREVIATIONS

<b>DRI</b>	Disability Rating Index
<b>GENMOD</b>	Generalized linear models
<b>HAD</b>	Hospital Anxiety and Depression Index
<b>IASP</b>	International Association for the Study of Pain
<b>ICF</b>	Int Classification of Functioning, Disability, and Health
<b>IMA</b>	Intramuscular acupuncture
<b>PA</b>	Periosteal acupuncture
<b>PD</b>	Pain Diary
<b>PLW</b>	Pain Last Week
<b>SAS</b>	Statistical Analysis Software
<b>TENS</b>	Transcutaneous Electrical Nerve Stimulation
<b>VAS</b>	Visual Analogue Scale

## **1. INTRODUCTION**

### **1.1 Pain**

Pain is an essential signal that alerts us to the presence in the environment of damaging stimuli [1]. It is a common reason for seeking medical help. Pain involves the whole individual and has great consequences that are clearly stated in the definition by the International Association for the Study of Pain (IASP): “Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue-damage, or described in terms of such damage” [2].

Pain can be classified as nociceptive (associated with tissue-damage), neuropathic (associated with damages in the peripheral or the central nervous system), psychogenic (associated with major psychiatric disorder), or unknown (sometimes previously called idiopathic) without known aetiology [2]. Pain is often categorized between acute and chronic pain, the latter defined as pain persisting during the expected healing-period, often up to three or six months and accompanied with complex disturbances in the nervous system [3, 4].

As stated in the definition by IASP, pain is a subjective experience often

influenced by affective components and can only be assessed indirectly [4, 5].

Women have shown a lower tolerance for pain and a higher prevalence of painful disorders than men [6, 7].

#### **1.1.1 Musculoskeletal pain in the neck and low back**

Musculoskeletal pain in the neck and low back is a common problem among people in the industrialized countries [8]. The estimates varies depending on the type of question asked [9, 10]. In a population study performed in the northern part of Sweden 16-22% of the population reported neck pain with a duration of more than six months [11]. Thus, chronic musculoskeletal pain is a major problem which has consequences for both individuals and society [9, 12].

Pain in the neck and low back without gross pathology is defined as non-specific [13, 14]. It is often accompanied with an impaired physical functioning, as well as a lowered level of psychological functioning [15-18]. Low psychological functioning is a poor prognostic factor which in persons with neck and low back pain can lead to an increased consumption of care [17, 19]. The term psychological functioning is here used as a broader concept including psychological distress or mild to moderate mood disturbances.

Sleep is essential for health and well-being [20] Sleep can be impaired by somatic or mental disorders as well as by lifestyle factors [20, 21]. Experimental, clinical, and population based studies have shown a relationship between poor sleep and pain [22-24]. Sleep disturbances in pain patients are independent of mood-disturbances [22].

### **1.2 Physiotherapy**

The theoretical frame of physiotherapy is the study of movement in a broader meaning. This perspective includes a movement continuum with movements within the body at one end and movements of the body in the environment at the other [25]. Broberg stated that “physiotherapy involves knowledge in and investigation of the human being in movement referred to perceive, utilize and control the body...” [26]. The International Classification of Functioning,

Disability, and Health (ICF) provides a systematic classification of health and health related domains often used within physiotherapy, where all conditions of health are determined by body functions and body structures, activities and participation, together with interacting environmental factors [27]. The domain impairment deals with body structures and body functions such as pain, sleep, anxiety and depression. The domain disability/activities deals with different physical activities e.g. activities of daily living, the domain participation deals with the ability to participate in different aspects of life, and the domain environment factors deals with the influence of the environment on the individual [27].

Thus, pain on the impairment level and its consequences on the disability and participation levels are seen as a health problem which impairs the capability for movements. The goal of physiotherapy is to alleviate pain and restore function. This applies especially to patients with chronic pain [28] and chronic musculoskeletal pain, who often seek physiotherapy [29].

### **1.2.1 Physiotherapy for patients with chronic neck and low back pain**

For this large group the treatment options are numerous although during recent years, evidence for more active treatment strategies is growing [28, 30, 31]. There is strong evidence for using an active exercise programme for patients with chronic low back pain [28, 30, 31]. However, for neck pain the evidence for exercise programme is conflicting [32, 33]. There is no evidence for using manual therapy for patients with chronic low back pain [34, 35]. However, there is strong evidence for using manual therapy combined with active exercise for patients with chronic neck pain [32, 36]. Today there is no clear recommendations about using transcutaneous electrical stimulation, electrotherapy, massage, low level laser therapy and braces as single therapy for patients with chronic low back and neck pain due to inconsistency of the results or lack of high quality studies [37-43]. The evidence for the effects of back-schools and education are also limited for these patients [44, 45]. However, there is strong evidence that multidisciplinary programmes including physical restoration are effective for patients with chronic low back pain [46, 47].

### **1.3 Acupuncture**

Acupuncture is an ancient method for healing originally from China where the methods were used together with other modalities to prevent and treat disease [48, 49]. The word acupuncture derives from acus i.e. a sharp instrument and puncture to puncture [48, 49]. It means practically "Insertion of fine needles (made of steel, gold or other metals) through specific points at the skin and then twirling them for some time at a slow rate. The needles may also be left in place for varying periods of time." [48]. The points denoted as acupoints are often in muscles near motor-points or so called trigger points [48]. According to traditional Chinese medicine (TCM), the needle stimulation should give rise to a specific sensation, De Qi' which is experienced as numbness, heaviness and radiating paraesthesia, a sensation close to deep muscle pain, and a sign of the activation of thin nerve fibres [49]. Acupuncture has been used for treatment of a variety of diseases and symptoms including pain of different aetiology [50].

The physiological mechanisms behind the pain relieving effects are to some extent explained by peripheral events with increased blood flow and substances that promote healing. [51-54]. Activation of central mechanisms that result in alterations in levels of monoamines and endorphins as well as gate control are also responsible for the pain relieving effect of acupuncture [55]. Studies of the living brain with imaging techniques have revealed that acupuncture modulate structures in the brain involved in pain perception and affective states on healthy volunteers and patients with chronic pain [56-58]. These results demonstrate that acupuncture and placebo have some mutual influence on the brain but also that a stimulation specific component exists [59]. Thus, in acupuncture as well as in all other treatments for pain the so called placebo effect or non specific effects are of importance and contribute to the positive effects [55, 60]. No satisfactory explanation for the long term effects seen in some patients is yet published since much of the explanations of the positive effects of acupuncture rely on experimental animal studies or studies on healthy voluntaries with focus on short lived effects [55].

Intramuscular acupuncture with eliciting of the characteristic needle-sensation De Qi is the most common form of acupuncture stimulation in both clinical as well as in experimental investigations [61]. From the numerous clinical studies on the effects of acupuncture for pain relief the following conclusions can be drawn. The pain alleviating effect is comparable to routine care, superior to no treatment or inactive treatment and is a useful complement to routine care for patients with chronic low back and neck pain [62-73] or routine physical therapy [74]. The effect on physical functioning is modest and short lived for patients with chronic low back pain [62, 63, 65], and in patients with chronic neck pain conflicting with positive results in some studies [68, 70, 72]. A retrospective study of the long term effects of acupuncture in patients with mixed types of chronic pain revealed a more pronounced relief in those with nociceptive pain than in those with neurogenic or psychogenic pain [75].

The Swedish County Council on Technology Assessment in Health Care found strong evidence for using acupuncture for pain relief in patients with chronic low back pain. However, for chronic neck pain the evidence was limited [76].

Since pain is often associated with lowered psychological functioning it is of interest to know if the pain relief obtained by acupuncture is associated with an increase of psychological functioning. Promising results have been registered in a few clinical studies [70, 74]. Pilkington and collaborators concluded that acupuncture had a positive effect on anxiety related disorders. However, the authors would like to see more well designed adequately powered studies [77]. A recently performed literature review showed that the positive effects on depression were conflicting [78-80].

Positive effects of acupuncture on the quality of sleep for patients with chronic musculoskeletal pain were reported in a few clinical investigations [67, 70]. However, it can be concluded that the effect is unclear when investigating acupuncture for a variety of sleep disorders and more studies of high quality are needed [81, 82].

### **1.3.1 Periosteal acupuncture**

Some clinicians have a hypothesis that a deeper stimulation, referred to as periosteal acupuncture, first introduced by Mann may give rise to a more pronounced effect in some patients [83]. The method is mentioned in Chinese

literature to treat deceases in bones and joints, but is not in regular use in China. It involves a brief stimulation of small areas on or very close to the periosteum, following which the needles are withdrawn . Mann described treatment of different forms of pain mostly of musculoskeletal origin. He denied the specificity of certain acupoints and mentioned tender areas which could be recognised after careful palpation. [83]. In an experimental comparison of different types of sensory stimulation, electrical stimulation of the periosteum was the only form that could raise the pain threshold in the musculature and periosteum [84]. We have found no answer in the scientific literature to why stimulation of the periosteum should give rise to better clinical results in some patients. Thomas and co-workers tested the method in patients with idiopathic pain where two out of twelve had significant pain relief [85].

To our knowledge no studies comparing intramuscular and periosteal acupuncture for patients with chronic nociceptive pain in the neck and low back have appeared with respect to pain, physical, and psychological functioning, so we hypothesized that periosteal acupuncture has a more pronounced pain relieving effect than intramuscular acupuncture.

## 2 AIMS

The main purpose of this thesis was to compare intramuscular and periosteal acupuncture.

The specific aims were to compare three groups of patients suffering from chronic musculoskeletal pain in the neck and/or low back, one with intramuscular acupuncture, one with periosteal acupuncture and a third information control group with respect

- to clinically relevant pain relief, intake of analgesics, and physical functioning (Study I) and
- to psychological functioning and quality of sleep (Study II).

### **3 METHODS**

#### **3.1 Patients**

The study group comprised all patients seeking primary care for musculoskeletal neck and/or low-back pain referred to physical therapy during the period 1996-2000 in the community of Krokoms, a sparsely populated municipality in the northern part of Sweden. A standard clinical examination including a neurological status gave a basis for inclusion and exclusion to the study. It was made by personnel blinded to group affiliation.

Inclusion criteria were pain originating from the cervical and/or lumbar column with a duration of more than 3 months, that could be provoked by active or passive movements and an age between 18 and 70 years.

Exclusion criteria were treatment with acupuncture within 3 months prior to enrolment in the present study, pregnancy, fibromyalgia, symptoms of neurogenic pain e.g. signs of disturbances of sensation and neurological deficits within distribution of the area of pain [2], a coagulation disorder, serious medical conditions, treatment with anticoagulants or antidepressants, a diagnosed addiction to drugs or alcohol, and/or inability to speak and read Swedish.

Initially the patients were divided into three groups according to pain location i.e. neck pain, low back pain or both and in each group alternately allocated to an intramuscular (IMA) and a periosteal acupuncture (PA) group. We originally calculated that 50 patients in each group would be sufficient to detect a clinically meaningful difference in pain scores between groups, using parametric statistics. After the first 41 patients had been allocated this way, the research team was revised and a control group (CG) was added, as the new team considered this as a way to strengthen the quality of the study. No results were available at that stage; no new power calculation was conducted. For the subsequent three years every third presenting patient regardless of location of pain was assigned to the control group. When the treatment groups had reached a sufficient number of patients an additional 14 consecutive patients were included as controls in order to make this group sufficiently large as well. The patients were neither charged for acupuncture nor did they receive compensation for participating in the trial.

#### **3.2 Treatment**

##### **3.2.1 Information**

On all test occasions all patients were encouraged to live an active life as normally as possible and to maintain and increase mobility particularly in the painful parts of the body. The control group also had the possibility to get added information and encouragement from the evaluating physical therapist.

##### **3.2.2 Acupuncture**

All acupuncture treatments were administered by one physiotherapist (YH), twice during each of the first three weeks and once during each of the following two weeks for 30 minutes at each session. One month after the series of treatments were completed and evaluated, the patients were offered a maximum of two follow-up treatments of the same kind one week apart. The study was single-blind with respect to type of acupuncture stimulation. All patients were treated in a lying position chosen by

themselves. Chinese stainless steel disposable needles (Hegu and Hwato), with diameter 0,3mm in diameter and length 30-50mm were used. On points on the back the same types of needles with diameter 0,4 and length 50-75mm were used.

#### **Intramuscular acupuncture**

Standard De Qi intramuscular acupuncture was utilised with individualised point selection of acu-points within the painful area [67, 75]. When the practitioner felt the characteristic resistance at a depth of insertion of usually 1-3 cm, the needle was twirled until the patient felt the characteristic needle sensation i.e. numbness, soreness or slight pain. De Qi was elicited two additional times during each session. The number of needles inserted was successively increased from four to twelve according to the patient's response to the treatment.

#### **Periosteal acupuncture (PA)**

The needles were inserted in tender areas (not always standard acupoints) and the underlying periosteum was pecked for approximately ten seconds 2-4 times per second, where all of our patients felt a radiating sensation. In this study the needles remained inserted just outside the periosteum for another 30 minutes, without further stimulation. The number of needles employed was increased successively from two to eight. Each patient was checked at least twice during each session.

In both types of treatment the selection of acu-points was individualized and the number of needles was increased successively in accordance with the patient's response to the treatment. Fig 1.

The treating physiotherapist (YH) is expert in orthopaedic manual therapies with university courses in acupuncture and has performed more than 2000 treatments of each type before study start.

### **3.3 Evaluation methods**

The methods of evaluation were classified according to the ICF [27].

The present study emphasizes the levels impairment and physical activities.

**Physical functioning is used synonymously with physical performance.**

#### **3.3.1 Pain (Study I)**

**The current pain by pain diary (PD)** was estimated by the patient in a pain diary employing a standard visual analogue scale (VAS) with the anchor points "no pain" and "worst imaginable pain" [86] three times a day for seven days. From the maximal values for each day the median VAS value for the entire week was calculated. The pain diary is often used in pain clinics and in scientific studies as pain ratings consisting of numerous ratings have shown good reliability [87].

**Average pain during the last week (PLW)** was also estimated on a similar VAS. Jensen and co-workers showed that a single rating of pain had sufficient psychometric strength to be useful comparing relatively large groups of individuals with chronic pain [87]. PLW is often used in primary care.

#### **3.3.2 Intake of analgesics (Study II)**

Intake of analgesics was registered daily by the patient and recorded from the pain diary. Analgesics were categorized as simple analgesics (e.g. anti-inflammatory drugs, paracetamol), weak opioids (e.g. dexopropoxifen,

codeine), and others (e.g. muscle relaxant and combinations of simple analgesics and weak opioids). Consumption (yes or no) was registered weekly during every seven-day evaluation period. Two tablets or less during the evaluation period was ignored.

### **3.3.3 Physical functioning (Study I)**

Physical functioning was tested using the Disability Rating Index (**DRI**) [88]. The capacity level of each of the 12 variables of this self-administered questionnaire is marked on a scale between endpoints 0="without difficulty" and 100="not at all". The variables are organized into common activities, more demanding activities and work-related activities. Reliability and validity of the DRI were found to be good when tested in relevant patient groups [88-90].

### **3.3.4 Psychological functioning (Study II)**

Psychological functioning was tested with the **Hospital and Anxiety scale (HAD)** [91-93]. It is a self administered questionnaire, designed for non-psychiatric patients and independent of somatic symptoms. A 14-item scale contains seven items each for anxiety and depression scored on a four point Likert scale (0-3). Low scores indicate better psychological functioning. The scores within each of the subscales are added and the following categories are defined: non case =0-7, doubtful case =8-10 and definite case 11-21. Good reliability and validity in patients with musculoskeletal pain have been registered [16, 18, 94].

#### **Sleep (Study II)**

Sleep was evaluated on a VAS with the anchor points 0= (slept extremely well) and 100= (slept extremely poorly).

**Mood at awakening** as a reflection of alertness or energy in the morning was estimated on a similar VAS with the anchor points 0= thoroughly rested and 100= tired. Sleep and Mood estimations were scored in a diary immediately after awakening for seven days for each observation period. A median-value for each of these two variables, for each patient, and for each test occasion was calculated.

All estimations were made one week prior to treatment (T1) and one week after treatment (T2) and one month (T3), three months (T4), and six months (T5) after termination of treatment. An additional estimation of actual level of pain, intake of analgesics, sleep, and mood at awakening was recorded in the pain diary (PD) in the middle of the treatment period, i.e., between the fourth and fifth treatments (T1,5). In the control group the estimations were made at corresponding times (similar intervals), but only for one month after termination of the series of treatments. Table 1. The first three evaluations were carried out in the clinic, whereas the three- and six-month evaluations were based on questionnaires delivered by mail. All questionnaires were handled by personnel blinded for group assignment.

## **3.4 Handling of data and Statistical methods**

Initially all data were analysed with parametric statistics. During my research education there was an increasing interest and a trend towards using non-parametric statistics especially for the VAS. According to the research which support the idea that VAS as well as other scales and scores

have the mathematical properties as for ordered categorical data [95, 96] we chose to utilise this type of statistics.

#### **3.4.1. Pain and intake of analgesics (Study I)**

On the initial evaluation the patients were categorized according to severity of pain for each of the two pain variables, with low pain indicated by less than 30 mm, medium pain between 30 and 60 mm and high pain more than 60 mm on the VAS, respectively. Farrar et al showed in large samples of patients with chronic pain that a 30% or two-step decrease in pain evaluated on an eleven-step numerical rating scale, could be regarded as clinically relevant [97, 98]. We defined a clinically relevant pain relief for those with low pain as a reduction of 10 mm or more, for those with medium pain as a reduction of 20 mm or more and for those with high pain as a reduction of more than 30 mm on a VAS. The Chi square test and sign tests were used for analyses of pain and intake of analgesics [99].

#### **3.4.2 Physical functioning**

The DRI variables were organized into three groups: common, more demanding, and work related activities, respectively [88]. The Mann-Whitney test, the Kruskal-Wallis test and Friedman's Anova by ranks were used for analyses [99].

#### **3.4.3 Psychological functioning**

The items in HAD e.g. anxiety and depression, were added separately and formed the categories non-case =0-7, doubtful case =8-10 and definitive case 11-21 [91, 92]. ANOVA by ranks followed by multiple comparisons between groups based on ranks were used to compare the HAD, sleep and mood at awakening scores for the IMA, PA and CG. For analysis of variation between repeated estimations, Friedman's ANOVA by ranks, followed by the multiple comparisons between visits based on ranks, were performed [99]. Sign tests were also used to analyze anxiety and depression. In order to analyse the interaction between the group- and time effects we fitted a generalized estimating equations (GEE) model with the GENMOD procedure in SAS® [100]. This ordinal response ranging from 1 to 3, according to HAD and 1 to 4 according to VAS was subsequently analysed with a proportional odds model for repeated measurements, using the GEE procedure. A statistician performed part of this analysis. For analyses the SPSS 12.0 (Statistical Package for Social Science) and the SAS system were used. The level of significance was set to  $p < 0.05$  for between-group comparisons and to  $p < 0.01$  for within group comparisons. The analyses with parametric statistics served as a basis for discussion.

### **3.5 Ethical considerations**

All patients gave their written and verbal consent to participate in the study and were free to withdraw without stating any reason. All studies were approved by the Ethics Committees of the Universities of Gothenburg and Umeå, as well as of the Karolinska Institutet in Stockholm.

## **4 RESULTS**

### **4.1 Patients**

A total of 154 patients who fulfilled the criteria and agreed to participate in the study were allocated to intramuscular (n=59), periosteal (n=55) or control (n=30) groups. Ten patients (6,5%), equally distributed between the groups, did not accomplish the first evaluation and were therefore excluded. Accordingly, 144 patients 59 in the IMA-group 55 in the PA-group and 30 in the control group were included in the analyses. Table 2. Before the three-month evaluation there were no drop outs in either group. The rates of dropout at the time of the six-month evaluation were 12 % and 7% for the IMA and the PA groups, respectively. Reasons for drop out were other medical condition or injury, not related to acupuncture.

### **4.2 Intergroup analyses**

Before treatment there were no differences between the patients in the three groups regarding any of the outcome variables except for demanding activities (DRI) where both treatment groups scored lower function compared with the control group. Tables 3,4.

After treatment there were no differences between the two treatment groups regarding any outcome variable. Tables 3-5. One month after termination of treatment clinically relevant pain relief with respect to pain diary was obtained in 29 IMA patients, in 25 PA patients, and in 5 patients in the control group. Corresponding figures for pain last week were 25, 24, and 3, respectively. A lower level of anxiety was also registered in each acupuncture group compared with the control group.

### **4.3 Intragroup analyses**

#### **4.3.1 Pain (Study I)**

Six months after end of treatment, 46% of the IMA patients and 45% of the PA patients had obtained clinically relevant pain relief in terms of PD. The corresponding figure for PLW was 29% of the patients in each group. Table 5.

#### **4.3.2 Intake of Analgesics (Study I)**

Three months after end of treatment 55% of the patients in the PA-group had finished or decreased their intake of analgesics. Corresponding number for the IMA group one month after treatment was 38%. There were no differences in intake in the CG. Table 4. No strong opioids were used.

#### **4.3.3. Physical functioning (Study I)**

The patients in the IMA group increased their physical capacity in both demanding activities, from 41 to 29, and work-related activities, from 64 to 53 up to six months after treatment. Lower scores indicate better function. The PA patients increased their capacity in demanding activities up to three months from 54 to 32, and in work-related activities from 57 to 45 up to one month after treatment. Table 4.

#### **4.3.4 Psychological functioning (Study II)**

Regarding anxiety the number of non-cases increased with four in the IMA group and with seven in the PA-group indicating that anxiety was less frequently reported at the

three month test by both treatment groups. The level of depression was lower at one week after end of treatment in the IMA group. (Data not shown).

Sleep improved up to six months for the IMA group, from 34 to 18, and up to three months for the PA-group, from 31 to 17.

Mood at awakening improved up to six months for both treatment groups, for the IMA-group from 52 to 28, and for the PA-group from 48 to 33. Table 4.

No correlations were observed between the level of initial pain and response to acupuncture (Data not shown).

Calculations performed with parametric statistics did not differ from those performed with non-parametric statistics. (Data not shown).

## 5 DISCUSSION

### 5.1 Main findings

For the first time it is shown that periosteal acupuncture is equally effective as intramuscular acupuncture in obtaining clinically relevant pain relief in patients with chronic musculoskeletal pain in the neck and low back. Moreover, we found that the two acupuncture groups were superior to the information control group in obtaining clinically relevant pain relief and reducing anxiety.

Our intention to study the *intake of analgesics* was to exclude that any pain relief obtained in a treatment group was an effect of an increase in intake of analgesics. However, we did not find any differences between the three groups, which is in accordance with Weiner and co-workers who compared periosteal acupuncture and sham acupuncture in patients with osteoarthritis of the knee and found no reduction in medicine consumption [101]. On the other hand a significant decrease in intake of analgesics was observed in the PA group up to three months after end of treatment. We did not have the possibility to restrict the use of analgesics to certain medicines and doses, a routine commonly used in studies of acupuncture [68, 71], which might explain the lack of differences between the three groups.

No effect on *physical functioning* was found in the present study. A reason may be that we added four activities together and calculated a median value for each patient and evaluation occasion. It had the disadvantage that differences in individual activities were not registered. Before treatment the control group scored better in demanding activities than the treatment groups, which made interpretation of the result more difficult. Our results are, however in accordance with Weiner and co-workers, who found a reduction of pain but no improvement in physical functioning [101]. In other studies of acupuncture in the relevant patient group the positive effects on physical functioning were negligible and short lived [62, 63, 65, 71].

*Anxiety* was reduced in both acupuncture groups, which was not the case regarding *depression* or *mood at awakening*. Similar results were obtained in other studies of patients with chronic low back and neck pain [70]. Leibing et al did not separate anxiety and depression which made interpretation difficult [74]. In a study by He et al both anxiety and depression decreased [70]. The rate of depression was low in populations recruited in primary care [17], which was also the case in our study. In studies of acupuncture for patients with depression the literature still shows conflicting results [78-80].

Only small differences in *sleep* in the middle of the treatment period were registered for the acupuncture groups compared with the control group, significant only in the IMA group.

In a study on the same population as in this study a reciprocal time relationship between sleep and pain was found in the acupuncture groups e.g. only patients who had decreased pain in the evening improved their sleep the following night. Moreover, patients who reported improved sleep had decreased pain in the next morning [102].

*Our hypothesis*, that stimulation of the periosteum might be a stronger type of stimulation since deeper stimulation gives access to more nerve fibres provided that the same number of needles with the same size and equally amount of stimulation is applied, was based on clinical experience. This was later supported by Graven-Nielsen

et al who showed that stimulation of the periosteum gave rise to a stronger sensation than stimulation of muscles in healthy volunteers [103]. The considerable overlap between myotomes and sclerotomes makes it obvious that stimulation of one point affects at least in some areas more segments [104]. Unfortunately, we found no differences between the two acupuncture groups in any of the outcome variables. This is in accordance with other studies comparing two types of acupuncture [67, 72, 105]. There are several possible reasons for this. The *mechanisms* for intramuscular and periosteal acupuncture might be the same, since experimental studies on animals and humans have revealed that periosteum and musculature contain mainly the same types of nerve fibres i.e. fibres with substance-p and calcitonin gene-related peptide (CGRP [106-110]. Another reason why our hypothesis was not accepted, may be the relative similarity in dosage with more needles and stimulation of the needles, three times, in the IMA group compared with fewer needles and only stimulation of the needles once in the PA group. A far more important explanation, though, is the clinical fact that the optimal dosage of stimulation shows a major intra- and inter-individual variation [111, 112]. Thus, consecutive allocation or randomisation of patients into different types of acupuncture or doses of acupuncture is not optimal and accordingly not in consequence with clinical experience and good practise of acupuncture.

*The long term effect* of the treatment was most pronounced six months after end of treatment in clinically relevant pain relief which was obtained by 46% of the patients in the IMA group and 45% of the patients in the PA group. Corresponding figures for PLW were 29% for both IMA and PA groups. The effects on physical functioning and sleep were in general of a somewhat shorter duration with a tendency to be more pronounced for patients in the PA group. On the other hand, a higher proportion of patients in the PA group had decreased their intake of analgesics three months after end of treatment compared with before treatment. No such improvement was registered in the IMA group at that time. In both acupuncture groups the positive effects on anxiety remained up to three months after end of treatment and the improvement of mood at awakening remained up to six months after end of treatment. The positive effects on sleep remained up to six and three months for the IMA and PA groups, respectively. In other studies of acupuncture for patients with chronic musculoskeletal pain the positive effects remained up to three and six months or even longer after end of treatment [64, 67, 70, 72].

The main findings in this study were a reduction of pain and anxiety in the acupuncture groups compared with the control group. Thus, the effects of acupuncture seem to reflect mainly on the impairment level according to ICF. There is a similarity in the patterns of anxiety and pain that is reflected in the variable PLW. Table 4.5. Linton and colleagues also found an association between pain and anxiety evaluated at the same occasion [113]. If the relief of pain relieves anxiety or if acupuncture influences both of the states is a question for forthcoming studies.

## **5.2 Methodological considerations**

The study was started as a pilot study with allocation of the patients to alternately one of two types of acupuncture. In connection with a change of supervisor a control group and a larger number of patients were introduced. No results were available at that stage and all statistics were performed after the end of the study. A correct randomisation would have been preferable and would have strengthened

the results. Patients were blinded with respect to type of acupuncture but not if they were allocated to the control group.

In recent years the special problems in acupuncture research have been in focus. Blinding of subjects, specificity of acu points, choice of control intervention, and adequacy of treatment have been discussed [60, 114, 115]. An often used control intervention is shallow insertion of needles in non acupuncture points [60, 114, 115]. Haker and co-workers showed a physiological effect of shallow needling [116] This method is, thus, not physiologically inert and accordingly not suitable for controlling for unspecific effects [114, 115, 117]. An optimal control for nonspecific effects would have been some sort of inactive treatment without a physiological effect [114, 115]. Sham transcutaneous electrical stimulation was often used and recommended when our study was planned [115, 117]. However, the limited access to acupuncture and TENS naïve patients prevented us to use this method [115, 117]. The placebo needle first introduced by Streitberger and co-worker would have been an acceptable alternative but was not commercially available at that time [118]. A few years later White and co-workers showed that nearly 40% of the patients could distinguish between the real needles and the Streitberger needles [119]. They also found that the patients whose therapists elicited less De Qi were less likely to distinguish between real needles and placebo needles [119]. As periosteal acupuncture often yields a clear radiating sensation, it is likely that our patients could distinguish between real treatment and placebo.

The study would have benefited from a scale of global improvement. As the discussion about clinically relevant pain relief and the debate whether the VAS has properties as for ordered categorical data were actualised after our study was planned, we made calculations according to Farrar to take these important topics into consideration.

[97]. We therefore defined clinically relevant pain relief for those with initial pain  $\leq 30$ mm as a reduction of 10mm or more, for those with pain  $>30 \leq 60$ mm as a reduction of 20mm or more and for those with pain  $>60$  as a reduction of 30mm or more. This method of calculation was not formally validated. However, just recently the VIII International forum for Primary Care Research on Low Back pain recommended that a minimally important change should be defined as a change of 15-20mm on a VAS [98].

In Study II we performed the statistical analyses with the GENMOD procedure in the SAS system [100]. The method is designated to find changes of classes for groups of individuals and is most effective when there are established cut points in the variables. Since the literature provides no basis on which to categorize VAS results, we also chose to divide the median values of the ratings for sleep and mood at awakening for all of our patients into four ranges in an attempt to minimize the risk that minor changes would give rise to statistical significances.

We chose to set the level of significance for the intra-group comparisons to  $p < 0,01$  in order to minimize the risk for type-I error. A less stringent significance would increase the risk of rejecting a true null hypothesis, i.e. of concluding that acupuncture has a more long lasting effect, when in fact it does not.

We have performed calculations with both parametric statistics and several forms of nonparametric statistics with similar results.

Taken all this into consideration it is not probable that our results would have changed, if different forms of parametric or another type of nonparametric statistics had been

utilized. Anyway, according to recent research we find it theoretically more correct to use non parametric statistics in scales and scores used in our study [95, 96].

Encouragement to stay active was a common first intervention in primary care when this study was started and therefore an adequate type of control intervention. It is still recommended for this group of patients, but is not sufficient to regain them to an active life [30]. Today some sort of supervised exercise programme would be recommended [28, 31].

### **5.3 Future studies**

It would be of interest a) to combine acupuncture with exercise and a behavioural intervention for patients with chronic musculoskeletal pain, and to study if pain relieving effects are associated with positive effects on psychological and physical functioning, b) to develop guidelines to find the optimal stimulation parameters for the individual patient, c) to experimentally investigate peripheral and central effects of periosteal acupuncture, d) to study if effects on the autonomous nervous system differ between the two acupuncture methods, and finally e) to further explore the relationship between pain and sleep in patients with chronic musculoskeletal pain.

## **6 CONCLUSIONS**

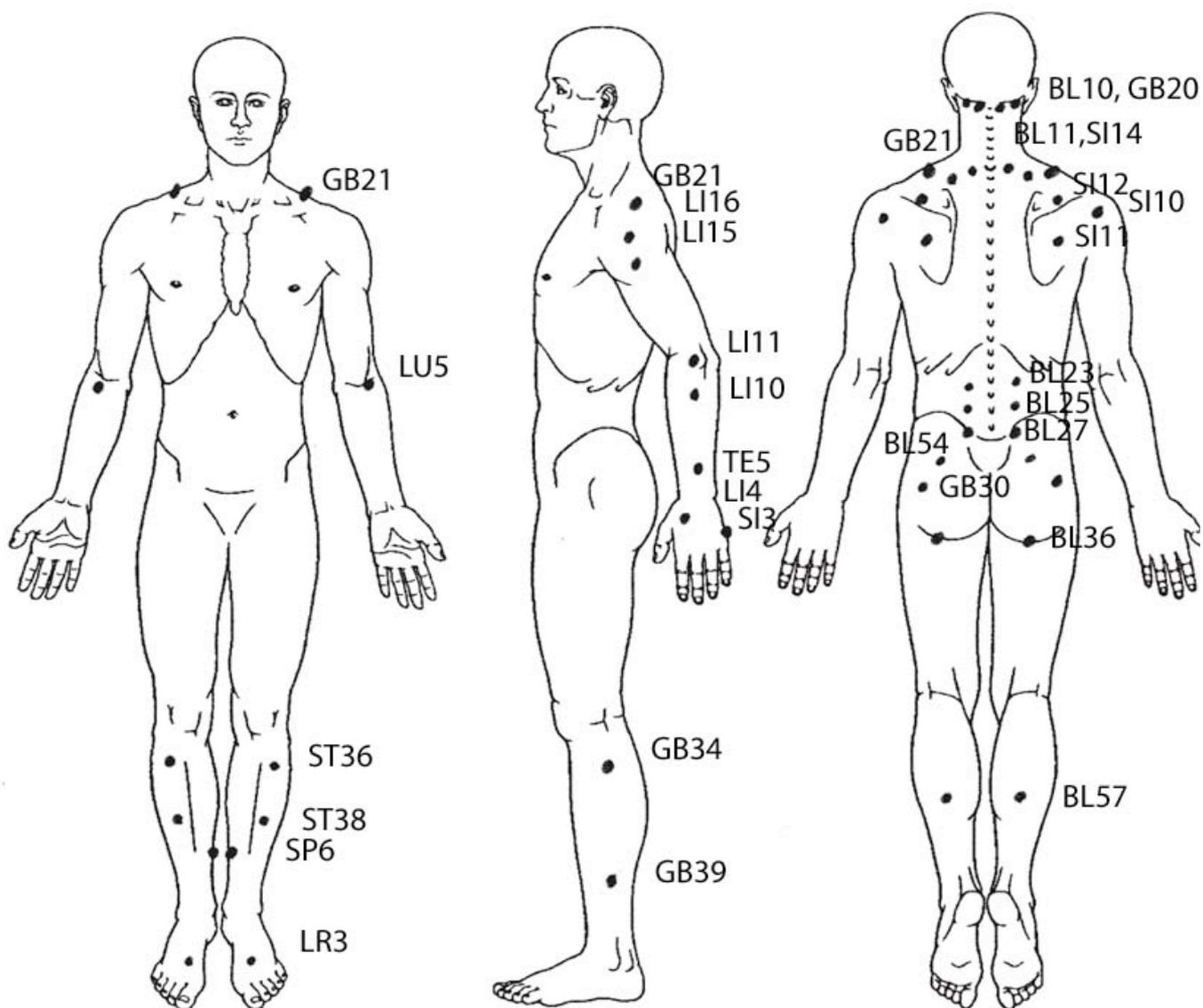
Intramuscular and periosteal acupuncture are equally effective for patients with chronic musculoskeletal pain in the neck and low back.

One month after treatment more patients in both acupuncture groups had clinically relevant pain relief and reduced anxiety than those in the control group.

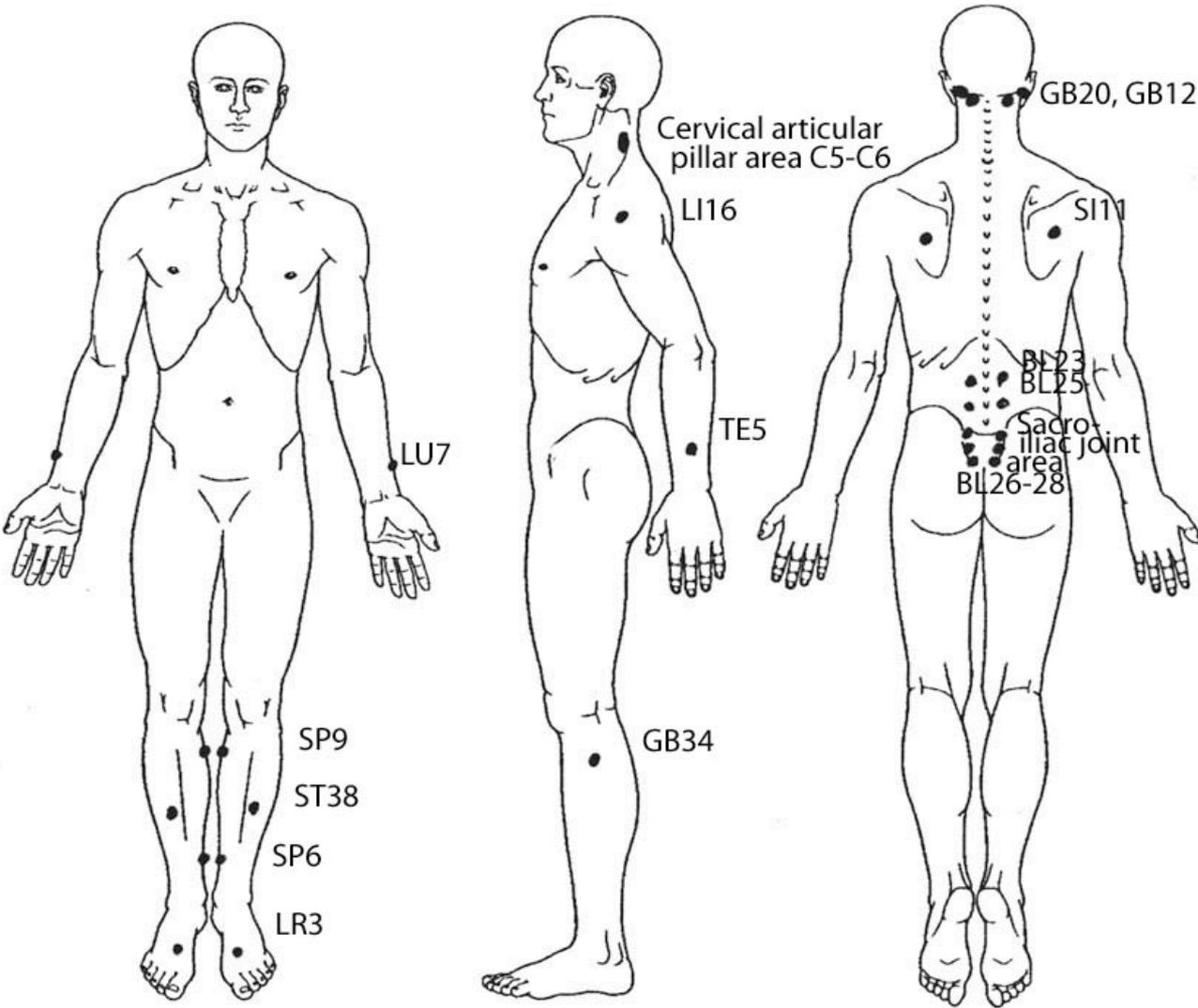
Six months after treatment 45% of the patients in both acupuncture groups had obtained a clinically relevant pain relief.

7 FIGURE and TABLES

Fig 1.A The sites at which needles were inserted in connection with intramuscular acupuncture



**Fig.1B. The sites at which needles were inserted in connection with periosteal acupuncture. Stimulation was performed in near periosteal areas.**



**Table I. Study design.**

Evaluation methods	Before Treatment	Middle of treatment	1 week after	1 month after	3 months after	6 months after
<b>Acupuncture groups</b>						
Pain diary	X	X	X	X	X	X
Pain last week	X		X	X	X	X
Analgesics	X	X	X	X	X	X
DRI	X		X	X	X	X
HAD	X		X	X	X	X
Sleep	X	X	X	X	X	X
Mood	X	X	X	X	X	X
<b>Control group</b>						
Pain diary	X	X	X	X		
Pain last week	X		X	X		
Analgesics	X	X	X	X		
DRI	X		X	X		
HAD	X		X	X		
Sleep	X	X	X	X		
Mood	X	X	X	X		

**Table 2. Demographics**

	Intramuscular acupuncture (n=59)	Periosteal acupuncture (n=55)	Control group (n=30)
Women/Men	40/19	37/18	18/12
Age mean (SD)	50 (9.8)	49 (11.8)	45 (13)
On sick leave >50%	24	16	16
Unemployed	4	1	2
Retired >65years	1	8	0
Retired <65 years or 100% or disablement	10	7	4
Location of pain			
Neck/shoulder region	19	20	12
Lumbar region	14	11	4
Both	26	24	14
Duration of pain			
3-11 months	7	10	6
>1 year	52	45	24
Accepted the two extra treatments	9	14	

**Table 3. Initial level of pain with Pain Diary and Pain last week categorized into low, medium and high pain**

	<b>IMA</b>	<b>PA</b>	<b>CG</b>
<b>Pain Diary</b> N=	58	55	29
Low <=30	6	7	5
Middle >30<=60	20	21	15
High >60	32	27	9
<b>Pain Last Week</b> N=	59	55	28
Low <=30	15	8	10
Middle >30<=60	20	28	12
High >60	24	19	6

IMA = Intramuscular acupuncture PA = Periosteal acupuncture CG = control group

**Table 4. Number of patients in the three groups, who do not take analgesics, their physical and psychological functioning, and sleep quality. Only variables where differences were obtained.**

	Prior to treatment	Middle of treatment	One week	One month after termination of treatment	Three months	Six months
<b>INTRAMUSCULAR ACUPUNCTURE</b>						
<b>No analgesics</b>	19/53	23/55	27/56	30/55	29/54	27/53
		n.s	p<0.05	p<0.01	p<0.05	P<0.05
<b>Demanding</b>	59		59	59	57	52
Median	41		29.5	28	39.5	29.5
			p<0.001	p<0.001	p<0.001	p<0.001
<b>Work</b>	59		58	58	57	52
Median	64		49.2	41.2	57.5	53.2
			p<0.01	p<0.001	p<0.01	p<0.01
<b>Anxiety</b>						
Non-case	39/59		44/59	47/55	43/55	35/52
			n.s	(p<.05)	n.s	n.s
<b>Sleep</b>	58	58	58	57	56	53
Median	34	19	21	18	19	18
		p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
<b>Mood at Awakening</b>	58	58	58	58	55	53
Median	52	28	30	26.5	35	28
		p<0.01	p<0.001	p<0.001	p<0.001	p<0.001
<b>PERIOSTEAL ACUPUNCTURE</b>						
<b>No analgesics</b>	21/55	30/52	35/53	39/53	33/51	27/50
		p<0.01	p<0.001	p<0.001	p<0.01	n.s
<b>Demanding</b>	55		55	55	52	53
Median	54.5		32.5	28.5	31.8	35.5
			p<0.001	p<0.001	p<0.01	n.s.
<b>Work</b>	53		54	55	49	53
Median	57.5		42	45.5	47.5	46
			p<0.001	p<0.01	n.s.	(p<0.05)
<b>Anxiety</b>						
Non-Case	37/54		46/55	49/55	44/52	39/53
			n.s	p<.001	(p<.05)	n.s
<b>Sleep</b>	55	55	53	54	52	53
Median	31	19	17	15.5	17	19
		p<(0.05)	p<0.001	p<0.001	p<0.001	p<(0.05)
<b>Mood at Awakening</b>	55	55	53	54	52	53
Median	48	30	25	26.5	32.5	33
		p<0.01	p<0.001	p<0.001	p<0.001	p<0.01

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**CONTROL GROUP**

<b>No analgesics</b>	13/29	15/29	16/28	15/28
		n.s	n.s	n.s
<b>Demanding</b>	28		30	30
Median	24.5		31.5	32.5
			n.s.	n.s.
<b>Work</b>	28		30	30
Median	46		50.2	53.5
			n.s.	n.s.
<b>Anxiety</b>				
Non-case	15/26		18/30	16/30
			n.s	n.s
<b>Sleep</b>	29	29	30	30
Median	30	22	15	17.5
		n.s	n.s	n.s
<b>Mood at</b>	29	29	30	30
<b>Awakening</b>				
Median	46	35	31	31
		n.s	n.s	n.s

n.s. = not significant (p<0.05) is not significant

Demanding =More demanding activities High scores indicates low function

Work =Work-related activities

**Table 5. Number of patients with clinically relevant painrelief**

	Middle	One week	One month	Three months	Six months
<b>Intramuscular acupuncture group</b>					
Pain Diary	57	57	57	54	52
Responder PD	27	29	29	27	24
	47%	51%	51%	50%	46%
Pain Last Week	n.r.	59	59	55	52
Responder PLW	n.r.	22	25	21	15
		37%	42%	38%	29%
<b>Periosteal acupuncture group</b>					
Pain Diary	55	55	54	52	53
Responder PD	20	28	25	23	24
	36%	51%	46%	44%	45%
Pain Last Week	n.r.	53	55	52	51
Responder PLW	n.r.	28	24	18	15
		53%	44%	35%	29%
<b>Control group</b>					
Pain Diary	28	29	29		
Responder PD	4	5	5		
	14%	17%	17%		
Pain Last Week	n.r.	28	28		
Responder PLW	n.r.	3	6		
		11%	21%		

PD =Pain diary PLW =Pain last week n.r. = not relevant

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