

Acupuncture in Obstetrics and Anaesthesia

Kvorning, Nina 2003 Link to publication

Citation for published version (APA):

Kvorning, N. (2003). *Acupuncture in Obstetrics and Anaesthesia*. [Doctoral Thesis (compilation), Anesthesiology and Intensive Care]. Nina Kvorning, Dep of Anaestesia and Intensive Care, Hospital of Helsingborg, Sweden,.

Total number of authors:

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study

- You may not further distribute the material or use it for any profit-making activity or commercial gain
 You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: https://creativecommons.org/licenses/

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Download date: 17. Dec. 2025

COPYRIGHT: Nina Kvorning LAYOUT: Monica Hallin COVER: Niels Strøbek Gravid. 1976.

Olja och tempera på masonit. 91x74 cm. Ny Carlsberg Fonden, Glyptoteket.

ISBN NUMBER: 91-628-56-40-5
PRINTING WORKS: Holmberg i Malmö AB

CONTENTS

Contents		3
Abbreviations		4
Publications		5
Summary		6
Sammanfattning (Summary in Swedish)		
Background		9
Aims		21
Patients and methods		
Results		31
Discussion		37
Future perspectand personal contracts		43
Conclusions		
Acknowledgements		
Grants		48
References		49
Appendix	Study I Study II Study III Study IV Study V	57 65 75 87 95

ABBREVIATIONS NINA KVORNING

ABBREVIATIONS

AAI A-line ARX Index, technical details, see methods

AEP Auditory Evoked Potentials

Apgar scoring system for the initial clinical evaluation of newborn

infants, the maximal score is 10

ARX autoregression with exogenous input
ASA American Society of Anesthesiologists
BL22-26 lumbar and sacral acupuncture points
BL57 acupuncture point (chengshan), on the leg

CNS central nervous system CSF cerebrospinal fluid

Dechi Chinese word ('arrival of energy') reported by patients as a

characteristic feeling of local pain, heat, numbness or

soreness

DNIC Diffuse Noxious Inhibitory Control

EA electro-acupuncture
EDA epidural analgesia
EEG electroencephalogram

G gauge

GB34 acupuncture point (yanglingquan), on the leg GV20 acupuncture point (baihui), at the top of the head

I-V studies I-V ic intracutaneous im intramuscular iv intravenous

LI4 acupuncture point (hegu), on the hand acupuncture point (taichong), on the foot

MAC minimal alveolar concentration

NA noradrenalin

PC6 acupuncture point (ximen), on the arm

SD standard deviation

SEM standard error of the mean

SP6 acupuncture point (sanyinjiao), on the leg SP9 acupuncture point (yinlingquan), on the leg ST36 acupuncture point (zusanli), on the leg

STRICTA standards for reporting interventions in controlled trials of

acupuncture

TENS transcutaneous electrical nerve stimulation

TP trigger or tender points VAS visual analogue scale

PUBLICATIONS

This thesis is based on the following papers, referred to in the text by their Roman numbers:

- I. Kvorning N, Holmberg C, Grennert L, Åberg A, Åkeson J.
 Acupuncture relieves pelvic and low-back pain in late pregnancy.
 Acta Obstetricia Gynaecologica Scandinavica 2003. In press.
- II. Kvorning Ternov N, Nilsson M, Löfberg L, Algotsson L, Åkeson J. Acupuncture for pain relief during childbirth.Acupuncture and Electrotherapeutic Research 1998;23:19-26.
- III. Kvorning Ternov N, Buchhave P, Svensson G, Åkeson J. Acupuncture during childbirth reduces use of conventional analgesia without major adverse effects: a retrospective study. American Journal of Acupuncture 1998;26:233-239.
- IV. Kvorning N, Christiansson C, Beskow A, Bratt O, Åkeson J. Acupuncture fails to reduce but increases anaesthetic gas required to prevent movement in response to surgical incision. Acta Anaestesiologica Scandinavica 2003. In press.
- V. Kvorning N, Christiansson C, Åkeson J. Acupuncture facilitates neuromuscular and oculomotor responses to skin incision with no influence on auditory evoked potentials during sevoflurane anaesthesia. Acta Anaesthesiologica Scandinavica 2003. In press.

SUMMARY NINA KVORNING

SUMMARY

The aims of the present thesis (I-V) were to evaluate the analgesic and adverse effects of manual acupuncture for low-back and pelvic pain during pregnancy (I) and for labour pain (II, III), and also to study the effects of low-frequency EA on clinical physiological responses to skin incision in anaesthetized patients (IV, V).

Acupuncture in obstetric patients (I-III)

Manual acupuncture in obstetric patients was found to relieve pain in one prospective randomised (I) and two retrospective (II, III) studies.

Low-back and pelvic pain intensity during pregnancy was decreased by acupuncture (I), and parturients receiving acupuncture required fewer of the other analgesic modalities than the women in the control group (II, III). Neither patients in the acupuncture group nor their infants suffered from substantial adverse effects (I-III).

These findings are in agreement with results obtained by other research groups investigating acupuncture during pregnancy and labour, but future studies are desirable to establish the role of acupuncture in obstetrics.

Acupuncture in anaesthetized patients (IV, V)

In contrast to the benificial effects of acupuncture referred above (I-III), two prospective, randomised, placebo-controlled and double-blind studies (IV, V) revealed that low-frequency EA in anaesthetized patients did not attenuate but instead facilitated clinical physiological response to skin incision.

Patients given EA required a higher steady state concentration of sevoflurane to abolish physiological reactions to skin incision (IV). Furthermore, when exposed to the same steady state concentration of sevoflurane, more acupuncture than control patients responded to skin incision with movements of head or limbs, dilation of pupils or divergence of eye axes (V).

Similar results have not been reported elsewhere, although combined high- and low-frequency EA in anaesthetized volunteers was recently reported to have no effect on painful stimulation. In our study, the depth of anaesthesia was not influenced by acupuncture, since the A-line ARX index reflecting AEP activity was found to be similar in the two groups (V). Future studies of the possible mechanisms underlying the effect of EA under general anaesthesia are desirable.

SAMMANFATTNING

Syftet med denna avhandling var att i de tre första undersökningarna (I-III) utvärdera effekterna av manuell akupunkturbehandling, dels vid smärta i bäcken och ländrygg under graviditet (I) och dels vid smärta i samband med förlossningsarbete (II, III) samt i de två sista undersökningarna utvärdera effekterna av elektroakupunktur avseende hur sövda patienter reagerar i samband med ett hudsnitt i buken (IV, V).

Akupunktur i samband med graviditet och förlossning (I-III)

En prospektiv randomiserad undersökning på gravida (I) och två retrospektiva undersökningar avseende förlossningssmärta (II, III) talar för att manuell akupunktur har smärtlindrande effekter under såväl graviditet (I) som förlossning (II, III).

En större andel av de gravida som fick akupunktur under graviditeten upplevde att smärtan avtog under tiden undersökningen fortgick (I). Kvinnor som fått akupunktur p g a förlossningssmärta behövde i mindre utsträckning annan smärtlindring än kvinnor som inte fått akupunktur (II, III). Inga allvarliga biverkningar uppträdde hos de kvinnor som fått akupunktur (I–III) eller hos deras barn (II, III). Våra resultat överensstämmer med tidigare studier av effekter av akupunktur under graviditet och förlossning. Det finns emellertid behov av ytterligare forskning inom området.

Akupunktur i samband med narkos (IV, V)

I motsats till resultaten av ovan nämnda studier (I-III) ökade patienternas reaktioner på snittet i huden om de fått akupunktur under narkosen innan operationen påbörjades. I de båda prospektiva randomiserade undersökningarna av patienter som skulle steriliseras (IV, V) jämförde vi akupunktur med placebo under pågående narkos.

Det visade sig att patienterna som fått akupunktur efter nedsövningen antingen hade ett ökat behov av narkosmedel när de snittades i huden (IV) eller reagerade kraftigare på hudsnittet när samtliga patienter fått samma mängd narkosgas (V). Akupunktur tycks inte förstärka sövda patienters reaktioner vid hudsnitt genom att minska narkosdjupet, eftersom vi registrerade samma elektriska aktivitet i hjärnan som svar på ljudstimulering under narkosen oavsett om patienterna fått akupunktur eller ej (V).

Detta är de första kontrollerade undersökning av akupunktur som genomförts på patienter under narkos, och vi har ännu ingen tillfredsställande förklaring till våra resultat. Nya undersökningar behövs för att kunna klarlägga hur akupunktur verkar i samband med narkos.





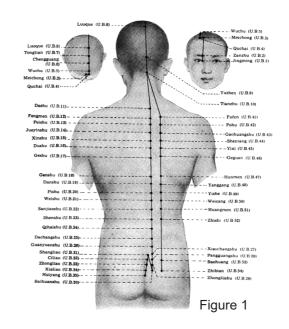




BACKGROUND

Acupuncture was originally developed in China more than 3000 years ago. It is one of several modalities which constitute traditional Chinese medicine. Diagnosis is based, for instance, on inspection of the tongue and bilateral palpation of the radial pulse at three points close to the wrist. After diagnosis, the practitioner determines which therapeutic modality is used. Many Chinese textbooks and articles put forth rigid rules for both diagnosis and treatment. Nevertheless, different rules are often recommended with similar emphasis by other authors.

In traditional Chinese medicine the term acupuncture originally referred to penetration of the skin with needles at specific acupuncture points. Travell and Rinzler noted a close relationship between acupuncture points and TP (Travell and Rinzler 1952). Every TP has a corresponding acupuncture point which, in approximately three fourths of the cases, is used to treat a similar pain syndrome (Melzack et al. 1977).



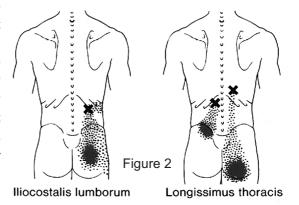


Fig 1.

The bladder meridian. Essentials of Chinese Acupunkture, Beijing, Shanghai, Nanjing College of Traditional Chinese Medicine.

Fig 2.

Trigger points of the lowback. Myofascial Pain and Dysfunction. The Trigger Point Manual by Travell and Simons.

BACKGROUND NINA KVORNING

Mechanisms of action

Nociceptive impulses are transmitted via A ∂ and C fibres and the dorsal root ganglion cells to the dorsal horn of the spinal cord. Stimuli are subsequently processed and transmitted via the spinothalamic tract to the brain stem, thalamus and cerebellum, where spatial and temporal analyses occur, and to the hypothalamic and limbic system, where emotional and autonomic responses originate. At the level of the dorsal horn, motor and sympathetic reflex activity is stimulated and modulation of nociceptive impulse transmission may even occur through several complex supraspinal inhibitory systems (Loeser and Bonica 2001). Nociceptive sensation can also be registered by peripheral sensory Wide Dynamic Range neurons which not only record pain, but also pressure and heat.

The afferent impulses resulting from acupuncture are mainly transmitted via A β and A ∂ fibres (Loeser and Bonica 2001). The interaction between the opioid antagonist naloxone and acupuncture is controversial (Chapman et al. 1983). Divergence of results can arise from activation of other pain modulating systems such as oxytocine (Uvnas-Moberg et al. 1993) which is not inhibited by naloxone.

Experiments with EA in animals and humans suggest that various modes of EA in peripheral acupuncture points may result in the release of different neurotransmitters in the CNS. Han et al. (Han 2003) have posited the existence of two separate pain systems activated by different frequencies of EA and using different neurotransmitters – a pain modulation system activated by 4 Hz and associated with enkephalin and one activated by 200 Hz and associated with dynorphin.

Dorsal horn neuron

2 Hz stimulation	100 Hz stimulation
Arcuate nucleus of hypothalamus	Parabrachial nucleus
Periaquaductal gray	Periaquaductal gray
Medulla	Medulla
Enkephalines - μ and δ receptors	Dynorphin - κ receptors

Dorsal horn neuron

BACKGROUND NINA KVORNING

Naloxone has been found to inhibit analgesia in the rat when 4 Hz but not when 200 Hz EA stimulation was used (Cheng and Pomeranz 1979). The addition of various opioid receptor subtype-specific antagonists showed that low-frequency stimulation mediated analgesia via μ – and δ -receptors, while high-frequency stimulation did so via κ -receptors (Chen and Han 1992). Likewise, low-frequency and high-frequency stimulation induced immunoreactivity of enkephalin and dynorphin specificity, respectively, in radio-immunoassay investigations in humans (Han et al. 1991). The formation of specific neuropeptide-antibody molecules following antibody microinjection has been found to result in defective receptor-binding ability. After such antisera were injected in the CSF, the lack of efficacy of high- and low-frequency stimulation has been used to correlate the type of stimulation with various mediating neurotransmitters such as β -endorphin, enkephalin, endomorphin and dynorphin (Han et al. 1999; He 1990; Huang et al. 2000). In studies in humans, EA has been found to increase the levels of endorphin in the blood (Masala et al. 1983) or the CSF (Clement-Jones et al. 1980).

EA has been reported to be associated with the release of serotonin, NA (Han 1986), oxytocin (Uvnas-Moberg et al. 1993), vasoactive intestinal polypeptide (Dawidson et al. 1998b; Dawidson et al. 1998a) and neuropeptide Y (Bucinskaite et al. 1996; Kim et al. 2001), which might explain the influence of acupuncture on both the sensory, affective and cognitive aspects of clinical pain and other physiological functions.

The release of endogenous opioid antagonists such as NA in brain tissue (Han 1986), CCK-8 (Chen et al. 1994; Zhou et al. 1993), orphanine FQ (Tian and Han 2000), substance P (Bucinskaite et al. 1996) and angiotensin II (Han 2003) has been suggested to be associated with the development of tolerance to acupuncture (Han 1986).

Other possible mechanisms for acupuncture are the Gate Control Mechanism and DNIC. The Gate Control Theory is a hypothesis which explains the pain relief observed when the pain induced by a nociceptive stimulus is decreased by a non-painful stimulus. Large-diameter low-threshold mechanoreceptors inhibit the response of dorsal horn cells to nociceptive inputs (Wall and Melzack 1989) at both pre- and post- synaptic levels (Hongo et al. 1968). Local action and short duration characterize the Gate Control Mechanism. TENS of high frequency persumably exerts its analgesic effect via this neuro-physiological mechanism. DNIC is activated by intensely painful stimulation and inhibits the response of Wide Dynamic Range neurons to local noxious input (Le Bars et al. 1979) by both local segmental inhibition (Fitzgerald 1982) and by loop circuit central inhibition via the brain stem (Le Bars et al. 1979). This inhibitory mechanism, which involves both local and distant pathways, has a short duration of action. Sterile water injections ic are considered to exert their analgesic effects through this mechanism.

Stress-induced analgesia is observed in association with high intensity painful stimulation in animals (Akil et al. 1984) and in man (Willer et al. 1981) as well as in situations of stress induced by social defeat or cold water swim in rats (Grisel et al. 1993). This non-specific effect of e. g. pain stimuli may complicate the interpretation of the results of some of the studies of EA in animals, in which these are exposed to significant amounts of pain or stress for long periods.

Pregnancy

Between 30 and 76 % of pregnant women suffer from pelvic or low-back pain during the last trimester of pregnancy (Bonica 1989; Kristiansson et al. 1996). Such pain is predominantly nociceptive, maximal during sleep, which is often disturbed, and interferes with daily activities as well as with professional work (Young and Jewell 2003). Pelvic or low-back pain during pregnancy is believed to be caused by altered posture, filamentous laxity induced by the release of relaxin from the corpus luteum and by fluid retention in connective tissue (MacEvilly and Buggy 1996). It takes approximately two years after delivery for the prevalence of pain to fall to levels found in non-pregnant women (Ostgaard et al. 1997).

Two prospective randomized studies have evaluated treatments other than acupuncture of pelvic and low-back pain during pregnancy (Kihlstrand et al. 1999; Thomas et al. 1989). One of these studies reported that a special pillow designed to support the pregnant abdomen produced better pain relief than a standard pillow in a crossover study design (Thomas et al. 1989). In the second study, water gymnastics was found to be better than no treatment with respect to pain intensity and sick leave (Kihlstrand et al. 1999).

Alternative modalities for pain relief include analgesics, stabilization of the pelvis by a pelvic-trochanteric belt, regular physiotherapy, TENS and glider-mat. The clinical efficacy of these treatments has not yet been evaluated in randomized studies.

We did not succeeded in finding any controlled studies evaluating acupuncture for pain relief during pregnancy. Nonetheless, acupuncture as well as TENS could theoretically be useful in this context. First, most acupuncturists agree that acupuncture is particularly effective for the management of nociceptive pain of short duration, whereas it is generally considered less efficient in chronic pain and in pain of idiopathic, psychogenic or neuropathic character (Macdonald 1989; Thomas et al. 1992). Second, most pregnant women are unwilling to accept pharmacological and invasive treatments of pain.

BACKGROUND NINA KVORNING

Labour

Labour pain is described as severe to very severe by approximately 50% of parturients and 70-80 % of primiparas (Bonica 1989). During the dilation phase of labour (first stage), visceral pain predominates. Nociceptive stimuli arise from mechanical distension of the lower uterine segment and from cervical dilation (Rowlands and Permezel 1998; Ward 1997). It is possible that high-threshold mechanoreceptors in the myometrium generate nociceptive stimuli in response to uterine contractions, particularly in protracted labours (Faure 1991). During the dilation phase the nociceptive stimuli are predominantly transmitted to the posterior nerve root ganglia at the T10-L1 level (Loeser and Bonica 2001; Ward 1997). The labour pain may progressively be referred to the abdominal wall, lumbosacral region, iliac crests, gluteal areas and thighs (Loeser and Bonica 2001). Up to three fourths of women in labour may also experience contraction-related low-back pain which for some might not abate between contractions (Labrecque et al. 1999; Melzack and Schaffelberg 1987). The perception of pain varies in different women from widespread and diffuse to well defined and localized pain (Melzack et al. 1984). As the pelvic phase of labour progresses during the late first and the second stage, somatic pain from distension of and traction on pelvic structures surrounding the vaginal vault and on the pelvic floor and perineum predominates. These stimuli are transmitted via the pudendal nerve through the anterior rami of S2-S4 (Loeser and Bonica 2001; Ward 1997) and are generally perceived as sharp and well localized pain.

Inhalation of nitrous oxide, systemic administration of opioids, epidural analgesia with local anaesthetics and opioids, pudendal and paracervical nerve blocks, ic administration of sterile water, TENS, hot baths, relaxation and cognitive approaches are all used to relieve labour pain with varying frequencies and results at different delivery centres. The systemic administration of opioids, which is of dubious value in this context (Olofsson et al. 1996) is often withheld, particularly during the last stage of labour, to avoid respiratory depression in the newborn infant and to keep the mother alert and able to cooperate as well as to enable her to keep a clear memory of this important life-event.

Although acupuncture has been reported to reduce delivery pain by various investigators (Deen and Yuelan 1985; Abouleish and Depp 1975; Hyodo 1977; Ledergerber 1976; Umeh 1986; Yanai et al. 1987), few patients were treated in their studies with varied acupuncture regimens under uncontrolled conditions and the information on the effects and adverse effects of acupuncture was insufficient to establish acupuncture as a routine method for pain relief during labour.

Anaesthesia

ING



Incision of the skin results in activation of nociceptive A ∂ and C fibres. From a theoretical point of view acupuncture would thus be useful as an adjuvant under anaesthesia to reduce pain induced by surgery. To our knowledge, there has only been one prospective randomised study published prior to 2002 which was designed to evaluate the perioperative adjuvant effects of acupuncture under anaesthesia in unconscious patients. Less peri-operative fentanyl was used in the treatment than in the control group during retroperitoneal lymph node dissection (Kho et al. 1991). The treatment group received simultaneous EA of the ear and TENS of the back within the dermatomes of the surgical area.

General anaesthesia makes double blinding possible in studies on acupuncture. Insufficient blinding has been a major methodological problem in acupuncture research.

BACKGROUND NINA KVORNING

Methodological problems in acupuncture studies

Sham stimulation

Different forms of sham stimulation have been used in acupuncture research. These range from superficial insertion of a needle at an active point (minimal acupuncture) to superficial insertion or true stimulation at non-acupuncture areas of the skin close to the active point or in regions with minimal acupuncture-meridian density. The use of sham stimulation in acupuncture studies is considerably problematic as reviewed by Lewith and Ryan (Lewith 1984; Lewith and Vincent 1996; Ryan 1999). Sham stimulation might induce DNIC and thereby bring about a non-specific analgesic effect. Consistent with this hypothesis is the observation that acupuncture stimulation relieves pain in approximately 60% of patients with chronic pain, sham stimulation does so in 40-60% of patients and placebo procedures without stimulation in approximately 30% of patients (Lewith and Machin 1983). Thus the future role of sham stimulation in acupuncture studies has been questioned (Lewith and Vincent 1996). A possibly role for sham stimulation is its use in analysis of the precise location of active acupuncture points (Lewith and Vincent 1996).

Placebo with no stimulation

Application of inactivated TENS has been proposed as a useful placebo procedure in acupuncture research. Today inactivated TENS is probably no longer useful as a placebo procedure in Sweden, since TENS is presently well known by many people directly or indirectly through friends and relatives with chronic pain.

Placebo-needles might be a more interesting alternative. Some are placed in rubber rings applied onto the skin thus simulating proper penetration of the skin. Others consist of handles with blunted tips which are placed in a foam cube to pretend penetration of the skin (Fink et al. 2001).

Another possibility is to use the rubber tube, which comes with many of the contemporary acupuncture needles, in the placebo procedure. In the control group the tube is placed onto the skin for a short period of time equal to that used for stimulation of the patients in the acupuncture group. In the acupuncture group penetration of the skin is facilitated by the rubber-tube and the patient hardly, if at all, feels the needle-sting when the needle is pushed through the tube. If periosteal stimulation to Dechi is used, keeping the needle in place for a few seconds only before extracting it is sufficient for the stimulation (Kvorning et al. unpublished data).

When evaluating acupuncture stimulation in body areas invisible to the patient, intradermal needles can be covered by Band-Aids after being inserted into the skin of patients belonging to the acupuncture group, whereas these points can be covered by Band-Aids, solely, in the placebo patients. One study reported that patients did not notice any difference between acupuncture and placebo procedures when acupuncture points of the back were chosen for stimulation (Kotani et al. 2001).

In clinical trials of acupuncture this treatment can also be compared to other relevant treatments or to a non-treatment control group.

Conformity

Most acupuncturists agree that the effect of acupuncture varies between individuals. Such differences are even found in experimental animals treated with acupuncture and subsequently subjected to painful stimulation. Reduced or strong reactions observed in subgroups of animals have been reproducible and species-specific. This has made it possible to divide them into groups of responders and non-responders (Han 1986; Huang et al. 2002). In humans, the study protocols are also complicated by the need for individualized treatments as a consequence of slight differences in the pathological picture. This problem can be partly remedied by defining possible ways to escalate treatment and by adding specified points in a standardized manner. A small number of uniformly trained therapists is important for the reliability of the results in a clinical study, especially when manual stimulation is investigated. A useful measure of stimulation in conscious patients is the achievement of Dechi at all points. In extreme states of pain such as labour pain, it may be difficult to achieve Dechi (personal communication).

Study protocol

To facilitate the interpretation and confirmation of studies, the design of any clinical study of acupuncture should be standardized according to the guidelines recently issued by STRICTA, including the rationales for acupuncture, the acupuncturists' backgrounds, technical details, interventions, co-interventions and control interventions (MacPherson et al. 2002).

If electrical stimulation is used the following data should be reported in detail: mode and intensity of electrical stimulation, duration of treatment and location of the points in which the needles are placed including specification of which points are connected to each pair of cathode and anode.

BACKGROUND NINA KVORNING

Techniques

Acupuncture points can be stimulated with needles through manual stimulation (I-III), electrical stimulation (IV, V) or simply through the act of needle insertion. In chronical pain the patients are usually treated twice a week during the first 2-3 weeks and once weekly after that. In the setting of acute pain, the stimulation can be more vigorous and of longer duration as well as conducted with intervals as frequent as days, hours or minutes. The depth of the penetration differs from superficial ic placement (Macdonald et al. 1983) of the needles to periosteal stimulation (Mann 1987) which is stimulation of bony informations close the acupuncture point (Fig 3).

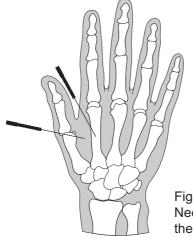


Fig 3.

Needles inserted in the muscle and on the periost.

Manual stimulation

Bone etchings of 1600 B.C. provide the oldest records of acupuncture and the first book of acupuncture, Hungdi Neiging Suwen, was written 200 B.C. (Mann 1987). Manual acupuncture is used more than EA in clinical practice, which is why most practitioners of acupuncture are more interested in evaluations of this technique than of EA. When the question arises as to whether acupuncture could have an effect within a new therapeutic area, it is natural to initiate the trial with manual acupuncture, as it is simple to learn as well as easy and cheap to practice. No technical device is required. Manual acupuncture is however difficult to standardize in clinical research.

Electrical stimulation

Electro-acupuncture was first introduced in anaesthesia for surgery in Shanghai, China, in 1958 (Bonica 1974). Some authors refer to electrical stimulation of TPs, which are not identical with classical acupuncture points and/or were not chosen on the principles of Traditional Chinese Medicine as percutaneous electrical nerve stimulation (PENS).

This is of purely academic interest for evaluation of the studies in this field as long as the anatomy is sufficiently described. When using EA it is possible to account for the electrical parameters in detail, including description of form, frequency, pulse-pattern (Fig 4), location of electrodes and intensity. In our studies (IV, V) we have used either classical low-frequency stimulation or burst stimulation for several reasons.

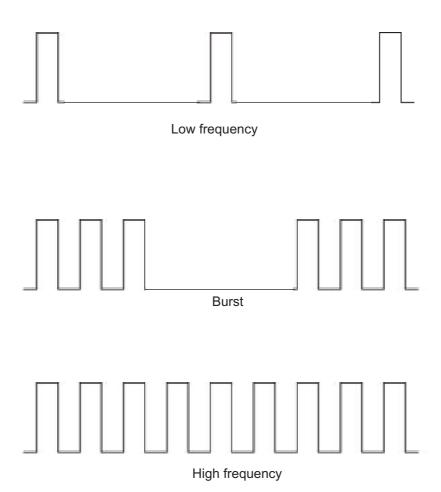


Figure 4. Different modes of electrostimulation.

BACKGROUND NINA KVORNING

These modalities are used in most clinical trials of EA and have been reported to result in a general effect of long duration by activation of μ -receptors as reviewed above. In contrast, high frequency stimulation results in a localized effect of shorter duration and has been found to activate κ -receptors. A third stimulation modality described frequently today is a combination pattern of alternating high and burst stimulation. In spite of the interesting clinical prospects of this mode of stimulation, the simultaneous release of two different forms of endorphins (Han 2003) complicates interpretation of the results in basic studies. In pregnancy, stimulation of the lower abdominal region might theoretically induce cardiac arrhythmias in the foetus, which is why EA stimulation during pregnancy should be performed only by specially trained staff.

Needle insertion

It is unknown whether the efficacy of acupuncture can be improved by placing the needles perpendicularly or obliquely to the skin, intracutaneously or periosteally, for shorter or longer periods, uni- or bilaterally. It is also unknown whether the therapeutic efficacy is improved by heating the needles, rotating them clockwise or counter clockwise or by pushing them up and down.

The practice of inserting needles at acupuncture points, securing them with Band-Aids and leaving them in place for hours or several days with or without initial manipulation has been used mainly in ear-acupuncture which was pioneered by the French doctor Nogier P F M (Nogier 1972). This technique has also been used in other body regions (Kotani et al. 2001) and during delivery, in order to secure the placement of the needle and permit the patient to move freely (Kvorning Ternov et al. 1998).

Acupuncture in obstetrics (I-III)

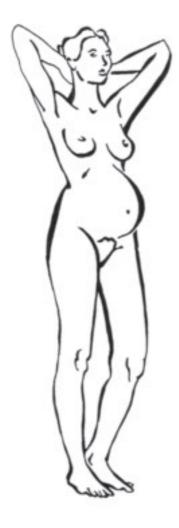
The first part of this thesis was designed

- to determine, whether acupuncture affects pelvic or low-back pain during late pregnancy (I).
- to determine, whether acupuncture affects pain during labour (II, III).
- to determine, whether acupuncture has adverse effects during late pregnancy or labour (I-III).

Acupuncture in anaesthesia (IV, V)

The second part of this thesis was designed

- to determine, whether acupuncture affects requirements for anaesthetic gas in association with surgical incision (IV).
- to determine, whether acupuncture affects clinical physiological responses to surgical incision under standardized general anaesthesia (V).
- to determine, whether acupuncture affects anaesthetic depth during surgery (V).
- to determine, whether acupuncture can be evaluated in a double-blind fashion under general anaesthesia (IV, V).



PATIENTS AND METHODS

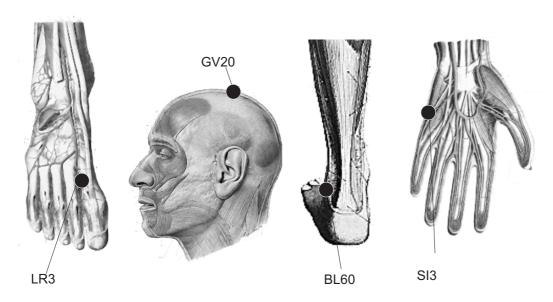
Pregnancy (I)

Patients

We studied 72 pregnant patients with pelvic or low-back pain during the pregnancy weeks 24-37 at three ante-natal clinics in southern Sweden. Of these patients 37 were given acupuncture and 35 comprised a control group. Acupuncture and control patients did not differ significantly in regards to the anatomical location of pain, age, employment, gestational week at the first visit to the ante-natal clinics or total pain during the preceding 24 hours. However, the patients in the acupuncture group had had pain for a longer duration than the patients in the control group, and had visited the ante-natal clinics more frequently. In both groups 20 % of the patients had formerly been treated with acupuncture and 20% reported a negative attitude to acupuncture.

Acupuncture procedures

The acupuncture points LR3 and GV20 together with individual TP were stimulated initially. In case of insufficient response, stimulation of these points was combined with stimulation of BL60, SI3 and/or TPs.



EQUIPMENT

Needles (I-IV)

Stainless steel acupuncture needles

Carbo; EZY-5. Lerna HB, Hollviken, Sweden (I, IV, V)

An Chi Handy Needle, China (II, III)

Dechi was achieved once at up to eight different acupuncture points or TPs on the first visit. On later visits, manipulation of the needle was stopped when Dechi was obvious, but was repeated after 30-60 seconds with the needle left in place, between the two stimulations. After this, the needles were removed and the patient was allowed to rest for at least ten minutes. In the first two-week period patients were given acupuncture twice a week and later on once a week. Between four and eight acupuncture points were used in most patients and the points stimulated most frequently were LR3, local TPs and BL60. Acupuncture was given according to written instructions and periosteal stimulation was used when possible.

Evaluation procedures

Each patient filled out a basic questionnaire upon inclusion in the study and completed follow-up questionnaires weekly during the study period. The midwife filled out another follow-up questionnaire, including information on acupuncture and possible adverse events, each time she met the patient. After delivery, the midwife recorded the Apgar scores of the infant at 1, 5 and 10 minutes. Level of pain was measured with the VAS pain scoring system and pain during physical activity was assessed on a three-point scale (always, at intervals or never).

Labour (II-III)

Patients

In study II, 92 women given acupuncture were compared to the 90 consecutive women with the same pariety at a medium-sized maternity ward (approximately 900 annual births). The groups were similar with respect to age, pariety, gestational age, duration of pregnancy, use of oxytocine and incidence of Caesarean sections.

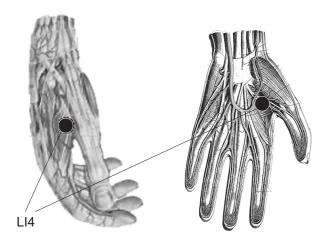
LABOUR ANALGESIA

- · epidural analgesia
- pudendal nerve block
- inhalation of nitrous oxide
- im meperidine
- · local infiltration anaesthesia
- ic sterile water
- TENS

In study III, 1708 women were delivered before (i.e. during the 'first study period') and 1609 women after (during the 'second study period') the introduction of acupuncture at a medium-sized maternity ward (approximately 1500 annual births). Among the 1609 women who delivered after the introduction of acupuncture, 994 received acupuncture while 615 did not. There were no significant differences in terms of patient characteristics except for parity between the women who did and those who did not receive acupuncture during the second study period.

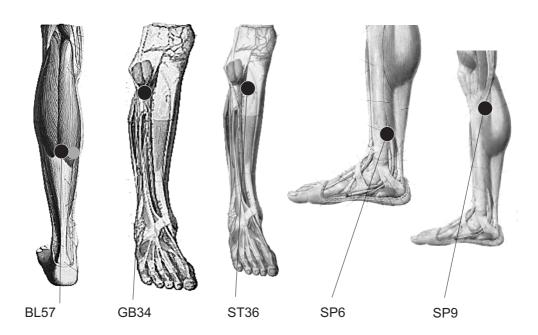
Acupuncture procedures

Stimulation was initiated once the cervix was dilated for 3 cm or more (II) or without consideration for the extent of cervical dilation (III). The stimulation was delivered initially at GV20 for approximately three minutes and in most cases the needle was left in position throughout labour (II, III).



The treatment was continued at the point LI4 during every contraction for approximately half an hour or until the woman was satisfied with the analgesia (II).

During most deliveries the point LR3 was stimulated along with one or several other acupuncture points as mentioned below (III).



In cases of persisting pain, some of the points BL60, BL57, SI3, GB34, ST36, SP6, SP9 or local TP in muscles of the low-back or girdle were stimulated (II, III). Alternatively, and in patients who did not respond to stimulation of the points listed above, long needles were inserted and stimulated bilaterally on the back along the bladder meridians, in the dermatomes of maximal pain and/or in tender areas of the inguinal regions as well as in TPs in muscles of the low-back and girdle (III). In both studies stimulation was individualized according to the progress of delivery pain and no more than five (II) or ten (III) needles were used simultaneously.

Evaluation procedures

The analgesic effect of acupuncture was assessed by comparing the total use of traditional forms of labour analgesia in parturients not given acupuncture with that of parturients given acupuncture (II, III). Questionnaires were completed by women of the acupuncture group included in both studies, 100% in study II and 89% in study III. Parturients and midwifes also recorded adverse effects suspected to be related to acupuncture (III).

EQUIPMENT

Electro stimulator (IV, V)

ACUS II stimulator (CEFAR, Lund, Sweden)



AEP Monitor and electrodes (V)

Alaris Medical Sysems Inc., San Diego, USA silver/silver chloride electrodes, A-Line®, Danmeter AS, Odense, Denmark



Anaesthesia (IV, V)

Patients

Ninety-two healthy patients scheduled for laparoscopic sterilisation at a large Swedish county hospital were randomized to receive either EA (n=46) or sham procedures (n=46) between the induction of general anaesthesia and the start of surgery. Exclusion criteria, apart from ASA physical status III or IV, were daily use of analgesics, body mass index >35 kg/m² or language difficulties. Body mass index and the duration of EA or sham procedures did not differ significantly between the two groups. The first 46 randomised patients were included in study IV and the remaining 46 patients in study V. The patients were similar in age (IV) or slightly older in the control group (V). One patient was excluded for technical reasons (V). Auditory evoked potentials were recorded in the last 35 patients (V) and analyzed in 16 acupuncture and 16 control patients.

Acupuncture procedures

Adhesive, transparent dressings with securing tape were applied to the skin at all acupuncture points stimulated after induction. Once anaesthetized the patients were stimulated with EA at three pairs of acupuncture points – LI4 and PC6, ST36 and SP9 and LR3 and SP6. Treatment was continued for approximately 20 minutes after which needles were removed and all acupuncture points were covered with Band-Aids.

In the first of the studies (IV) the patients were stimulated at these acupuncture points on the right side of their body with a low frequency (2Hz) current of 2.5 mA intensity (Fig 4). In the second study (V) the patients were stimulated bilaterally with burst of low frequency of 2,0 m A intensity (Fig 4).

Sham procedure

The electrodes were taped onto the skin at the same points as in the acupuncture group but were disconnected from the EA device. The patients received simulated stimulation during approximately 20 minutes, after which the electrodes were removed and all acupuncture points were covered with Band-Aids.

Anaesthetic procedures

The patients were prepared for surgery according to the clinical routines of the department. A drape was used to prevent the anaesthesia nurse, positioned by the patient's head, from observing the rest of the patient. Induction was performed by facemask with 6–8 % of sevoflurane in 6 l/min of oxygen. After the patients had completed the investigation, surgery was carried out according to the established local guidelines at the department. In the first study (IV) the steady state level of sevoflurane used in each patient was determined from the response to surgical incision of the preceding patient from the same group, according to Dixon's up-and-down method for determination of MAC (Dixon 1965). The first patient of each study group was exposed to 1.8 % of sevoflurane at the incision. For the next patient of the same group the concentration of sevoflurane was increased or decreased by 0.2% depending on the motor response to surgical incision in the previous patient of that group. The MAC value of sevoflurane in each group was defined as the mean steady state concentration of that group. In the second study (V) the concentration of anaesthetic gas was adjusted to reach a steady state concentration of 1.8% in all patients.

EEG analysing procedure

Auditory evoked potential is a method developed to evaluate anaesthetic depth by continuously measuring and analysing EEG potentials. Bilateral click sound stimuli of 65 decibel, 2 ms duration and 9 Hz repetition rate were delivered through a pair of headphones. Auditory evoked potential signals were detected by three silver/silver chloride electrodes placed on the median forehead (positive), the left mastoid (negative) and the left forehead (reference) and were continuously recorded with an AEP monitor. Mid-latency 40 Hz AEP signals were extracted from the EEG by ARX modelling (Alpiger 2002; Litvan 2002). Changes in mid-latency AEP, reported to correlate with the depth of anaesthesia (Alpiger 2002; Litvan 2002; Kurita 2001; Thornton 1991), are reflected by the AAI. Evaluation was done by subtracting the average AAI level before incision from the maximal value immediately after incision.

Evaluation procedures

In the first study (IV), the MAC at which 50% of the patients reacted to pain stimulation was used as the primary measure of EA. In the second study (V), the proportion of patients

All studies (I-V)

neck or limbs (IV, V).

Statistics

The statistical analyses of parametric data in each of the studies were carried out by comparing means between groups with unpaired two-sided Student's t-test. Differences in non-parametric (continuous and discrete) variables were analyzed with Fisher's exact, Chi-2 or the Mann-Witney U-test. The level of statistical significance was set at p<0.05.

Before study I was carried out, a minimal number of 34 patients in each group had been calculated to be required to confirm statistically, with 80% power and 95% probability, a 30% difference in proportion of patients with decreasing pain intensity during the study period between the acupuncture and control groups. Based on this analysis we included 50 patients in each group to allow for a 30% exclusion. Two investigators (NK, JÅ) independently recorded visual analogue scale (VAS) assessments of pain intensity and physical activity scores for each patient. Inter-observer variability was determined by calculating weighted kappa coefficients with 95% statistical confidence intervals (Brennan and Silman 1992).

Before study IV was carried out power calculations showed that 84 patients were required to confirm statistically a difference in MAC of 0.25±0.4% (mean±SD) with 95% accuracy and 80% power at steady state. We intended to include 92 patients to allow for 10% dropouts.

Ethical considerations

All the studies were approved by the Medical Faculty Ethics Committee at Lund University, Sweden. In study I, patients presenting with low-back or pelvic pain were provided with oral and written information during their initial visit. In studies IV and V, patients received written and oral information at home in advance via mail and telephone, and gave written consent to participate in the studies.



RESULTS

Pregnancy (I)

A larger proportion of women in the acupuncture group experienced a reduction in pain during pregnancy compared with the control group (Fig 5) in spite of reduced use of other analgesic methods (Table 1). Two acupuncture and no control patients were pain-free during their last three weeks of pregnancy. Pain associated with physical activity decreased more in acupuncture patients than in control patients during the study period. In addition, a significantly smaller proportion of women in the acupuncture group experienced an increase in pain during pregnancy than women in the control group.

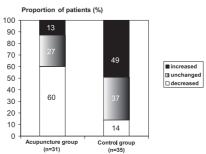


Figure 5.

Changes in pain intensity over time in acupuncture and control patients during the study period.

	Acupuncture group	Control group	р
Analgesic drugs	0	5	<0.05
TENS	0	6	<0.01
Pelvic-trochanteric belt	4	15	<0.01
Physiotherapy	0	6	<0.01

Table 1.

Use of other analgesic methods during the study period.

More than 60 % of the reported adverse effects were local pain, a feeling of heat or sweating (which might actually represent Dechi). Birth weight and Apgar scores of the infants were similar in the two groups.

RESULTS NINA KVORNING

Labour (II, III)

In both studies acupuncture patients used less additional analgesia than control patients.

In the first labour study (II), 60% of women in the acupuncture group compared to 13 % in the control group endured labour without additional analgesia. The uses of nitrous oxide, intramuscular meperidine and pudendal nerve block were all reduced. Likewise, the uses of nitrous oxide, intramuscular meperidine, local infiltration anaesthesia and ic sterile water were all reduced during the second labour study (III) after the introduction of acupuncture.

In the second labour study there was no difference in the use of Caesarean section between the women given or not given acupuncture during the second study period. The total number of Caesarean sections was approximately 20% higher during the second study period compared with the first study period. Epidural analgesia was used more in acupuncture patients during the second study period, in which primiparas comprised almost half of parturients in the acupuncture group compared with only one fourth in the control group (III).

No serious complications or adverse effects were reported (II, III). Adverse effects possibly related to acupuncture were recorded in 7.1% of women given acupuncture (III) (Table 2). Of these, 65 % were recorded as rapid delivery without specification of whether this was considered a positive or negative adverse effect of acupuncture and 27% had experienced local pain from the needles. All infants were healthy with no Apgar score below 8 (II). Apgar scores and the referral rate to the neonatal intense care unit were not different before as compared to after the introduction of acupuncture (III).

Adverse effects	Number (%)
Rapid delivery	41 (4.6)
Local pain from needles	17 (1.9)
Dizziness or fatigue	3 (0.3)
Sensation of heat	1 (0.1)
Tension	1 (0.1)

Table 2.

Adverse effects registered in the acupuncture group during labour (III)

In questionnaires filled out by the parturients after the delivery, 94% of the parturients reported that they would consider acupuncture in future deliveries (II), 58 reported satisfaction with their pain relief and 78% reported that they would reconsider acupuncture in future deliveries (III).

Anaesthesia (IV, V)

In the first of the anaesthesia studies (IV), the MAC of sevoflurane at which reaction to incision occurred in 50% of the patients was higher in the acupuncture than in the control patients (Fig 6).

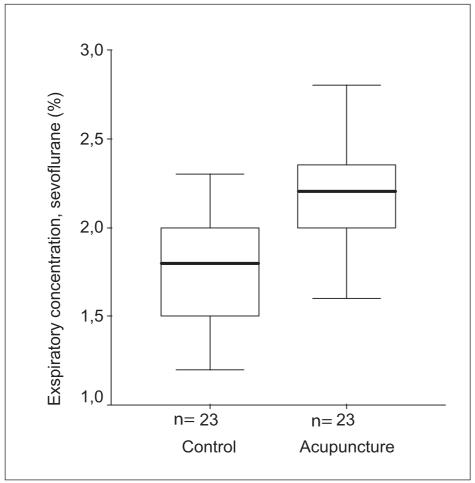


Figure 6.

The mean arterial pressure was unaffected by incision in acupuncture patients but increased significantly after incision in control patients. Changes in pupil size, orientation of eye axes and heart rate were similar in the two groups.

RESULTS NINA KVORNING

In the second anaesthesia study (V), skin incision was associated with head or major limb movements in more acupuncture than control patients (Fig 7).

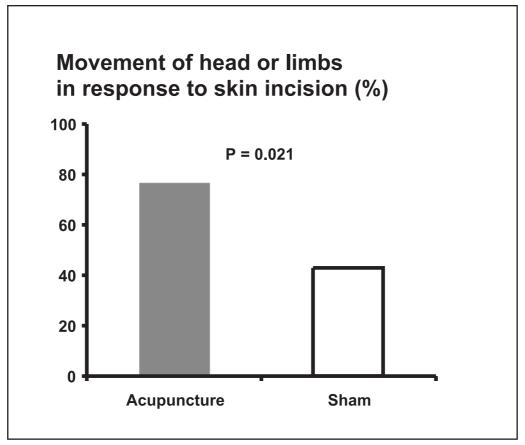


Figure 7.

Pupil dilation and divergence of eye axes also occurred more frequently in the acupuncture group (V).

There was no difference in median AAI change in response to skin incision between acupuncture and control patients. No differences appeared in the responses of mean arterial pressure and heart rate to skin incision (V).

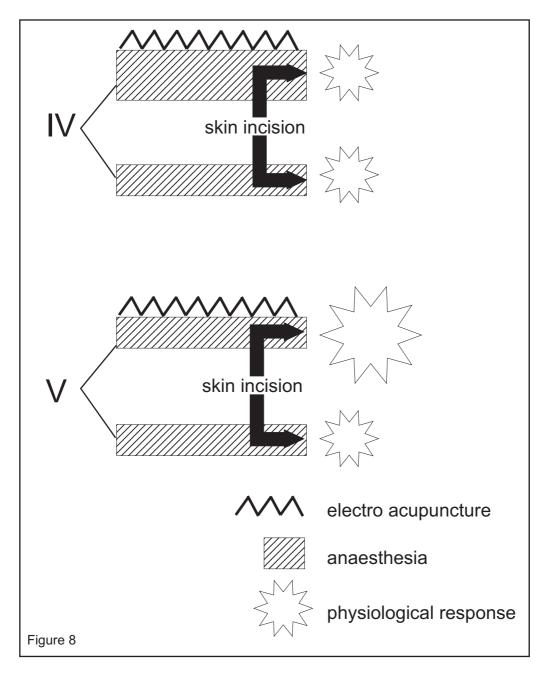


Figure 8
A higher steady state concentration of sevoflurane (IV) is counteracted by facilitation of physiological response to skin incition (V) when the patients were stimulated with EA in the two studies.



DISCUSSION

Acupuncture during pregnancy (I)

Study design

As already mentioned above, double-blinding is impossible in studies on acupuncture in conscious patients. This is a major drawback in the interpretation of results on effects and adverse effects obtained in various studies on acupuncture. Single blinding has been proposed to be possible in awake patients or subjects (Fink et al. 2001; Kotani et al. 2001).

In the present study, an open randomised design was chosen since it was considered unethical to subject the pregnant women in the control group to unnecessary visits at the ante-natal clinic. Many women try to fullfill all the duties of their professional, social and private lives without restriction in spite of the burden of pregnancy. A visit to the maternity ward is yet another obstacle in a full schedule. The evaluation of the placebo effect is under discussion (Kienle and Kiene 1997). It has previously been considered to be a purely negative, distracting factor in the evaluation of the precise magnitude of treatment effects. The placebo effect depends on the treatments (Kienle and Kiene 1996) and the therapists involved (Benedetti 2002). A potent placebo effect would add to the specific effect of a treatment, especially in pain of short duration. The study of pain during pregnancy is fraught with certain unique problems. The duration of the pain episode is relatively short, the date of delivery is uncertain and the psychosocial factors play a nontrivial role in pain perception of great variation between individuals. These factors complicate both the randomization and evaluation processes. On the other hand the pain is purely nociceptive and is characterized, by a reasonably uniform anatomical distribution as well as by a nocturnal increase and exacerbations brought on by certain activities.

Effects

Pain intensity, pain associated with physical activity and the use of analgesic drugs or non-acupuncture analgesic techniques were all found to decrease more over the study period in acupuncture patients than in control patients.

Recently, acupuncture has also been reported to reduce low-back and pelvic pain better than physiotherapy in a prospective randomised study of 28 pregnant patients (Wedenberg et al. 2000) and to reduce low-back and pelvic pain in a retrospective study of 167 pregnant patients (Kvorning Ternov et al. 2001).

DISCUSSION NINA KVORNING

Adverse effects

In 38% of the patients given acupuncture in this study adverse events were reported during one of their treatments. The major problem, reported in more than half of these patients, was local pain, sweating or a feeling of heat, i.e. symptoms consistent with Dechi.

In other studies, approximately 600 acupuncture procedures in 91 pregnant women resulted in no maternal or obstetrical side effects (Carlsson et al. 2000; Knight et al. 2001; Kvorning Ternov et al. 2001; Wedenberg et al. 2000). We recorded all possible adverse effects in our study. This attention to detail could explain the high number of possible adverse effects of acupuncture.

Acupuncture during labour (II, III)

Study design

Both studies reported here are retrospective, which makes evaluation and interpretation of effects and adverse effects more difficult. At the time these studies were planned, it was important to investigate potential adverse effects of acupuncture and publish this information, as acupuncture was getting popular and adequate safety information was lacking. It was possible to evaluate data retrospectively.

Effects

In both of our studies the use of acupuncture during labour was found to be associated with decreased use of other analgesic methods for labour pain (II, III).

These findings are in agreement with results obtained in two prospective studies where pregnant patients given acupuncture had similar (Ramnero et al. 2002) or lower (Skilnand et al. 2002) levels of pain according to VAS assessments, compared with patients given placebo stimulation or no treatment, respectively. In the first of these studies, anxiety was also reduced in acupuncture patients (Ramnero et al. 2002), whereas acupuncture patients had shorter delivery time in the other study (Skilnand et al. 2002). In our studies rapid delivery was recorded by midwives as an adverse effect of acupuncture in approximately 5%, not indicating if the short delivery time had been of benefit to the patient or not (III). Reduced duration of labour in patients given acupuncture has also been proposed by others (Deen and Yuelan 1985; Hyodo 1977).

Adverse effects

The main question we sought to answer through our studies of the effects of acupuncture on labour pain (II, III) was whether acupuncture would cause adverse effects in women in labour. Obstetric follow-up should be meticulous since acupuncture has previously been strongly discouraged during pregnancy due to the fear of serious side effects (Low 1990). The fact that potential complications constitute a risk for both mother and child was another important issue. As in our second labour study, no adverse effects were registered in the two prospective, randomized studies of labour pain, in which an equal number of complications were registered in both groups. The high rate, 7.1%, of adverse effects reported by patients given acupuncture in labour (III) could be caused by the active interrogation for and careful reporting of any kind of discomfort or sensation during and after each stimulation. The large number of women included in our studies makes it also more likely that adverse effects are recorded than in the two prospective studies, which included relatively few women.

Acupuncture under anaesthesia (IV, V)

Study design

During anaesthesia, double blinding of acupuncture treatment is possible. All interventions can be standardised. The level of the intensity of the current used during our two studies, which was tested on a number of our colleagues, was found to be under the pain threshold, thereby eliminating the risk for stress-induced analgesia as an explanation for potential analgesic benefits. This feature of the investigational treatment also facilitated ethic considerations on behalf of the investigators. We chose a minimum of 20 minutes for our stimulation as it had been shown that the pain threshold is raised after 20 minutes of low frequency-stimulation (Kitade et al. 1988; Romita et al. 1997). Stimulation was stopped just prior to the entrance of a blinded observer and a few minutes before incision. This short interval should have insured that even a short-term acupuncture effect was maintained. Anti-nociception after low frequency electrical stimulation has been shown to persist for 30 minutes or more beyond the cessation of stimulation (Chung et al. 1984a; Romita et al. 1997; Chung et al. 1984b).

DISCUSSION NINA KVORNING

Effects

In both studies of acupuncture under anaesthesia, acupuncture was shown to facilitate the response to skin incision. In one study, a higher MAC was needed to prevent movement in the acupuncture group than in the control group (IV). In the other study, in which all patients were exposed to the same concentration of sevoflurane, EA patients reacted more to skin incision than control patients (V).

In contrast, a lower (Taguchi et al. 2002) or similar (Morioka et al. 2002) concentration of desflurane was found to be required in volunteers subjected to acupuncture, compared with sham procedures, for similar physiological responses to noxious electrical stimulation in two recent, double-blind and randomized cross-over studies. The volunters were given either combined high- and low-frequency EA administered at acupuncture points close to the region of noxious stimulation (Morioka et al. 2002) or manual acupuncture at acupuncture points of the ear (Taguchi et al. 2002). The MAC was determined using Dixon's up and down method in both of these studies, as in one of ours (IV).

Differences in study design may explain the divergence of results.

Different gases, acupuncture points, stimulation patterns as well as intensities and location of pain stimuli (close to or far from the acupuncture points which were stimu-lated) were used in the studies. The results of the four studies could be summarized as follows:

- low frequency EA far from the noxious stimulus facilitated the reaction to skin incision (IV, V).
- Combined high- and low-frequency EA close to the noxious stimulus did not change the reaction to skin incision (Morioka et al. 2002).
- manual acupuncture at the ear and far from the noxious stimulus reduced the reaction to skin incision (Taguchi et al. 2002).

Simultaneous use of alternating bursts of low- and high-frequency stimulation, as in the study by Morioka et al. (Morioka et al. 2002), should lead to release of both enkephalins and dynorphines. Low frequency EA (2 Hz) has been found to mediate analgesia predominantly by activation of μ -and δ receptors, whereas high frequency EA (100 Hz) mainly activates κ -receptors in studies on EA in animals (Chen and Han 1992; Huang et al. 2002), and, using TENS, in humans (Han et al. 1991). Different neurophysiological mechanisms are obviously involved in high- and low-frequency EA. Under anaesthesia transmitter systems with opposing effects might be activated simultaneously by the two

NO.

different types of stimulation. Another possibility is that a local Gate Control Mechanism of anti-nociception, activated by high-frequency EA, neutralized a nociceptive effect of low frequency EA of more generalized character. Nociception could be mediated by release of endogenous opioid antagonists, as EA has been shown to release several of these compounds in animal studies (Han 2003). The combination of high- and low-frequency stimulation might thus have opposing effects on nociception under anaesthesia, although high- and low-frequency stimulation presumably has additive anti-nociceptive effects in non-anaesthetized individuals.

One of the four studies reported that manual acupuncture of the ear decreased physiological reactions to nociceptive stimulation (Taguchi et al. 2002). These results, opposite to ours, might well reflect activation of a completely different mechanism of pain modulation, since the outer ear is innervated by afferents of the trigeminal and vagal cranial nerves, in contrast to the spinal nerves stimulated by AE in the three other studies (IV, V) (Morioka et al. 2002). Consistent to the results found by Taguchi et al. (Taguchi et al. 2002) TENS of high frequency close to the ear reduced reaction to noxious stimulation during anaesthesia (Greif et al. 2002).

In our last study, differences between the groups regarding major movements of head or limbs, dilation of pupils and divergence of eye axes in response to skin incision, were found not to have been associated with a corresponding difference in the AAI level, reflecting AEP activity. It has recently been shown, that an AAI value below 30 is associated with an anaesthetic level of sevoflurane found to abolish neuromuscular response to surgical skin incision in virtually all patients (Kurita et al. 2001). Provided that AEP activity, reflected in the AAI, reliably reflects the depth of sevoflurane anaesthesia (Alpiger et al. 2002; Kurita et al. 2001; Litvan et al. 2002; Thornton 1991), there is no considerable interaction of EA with the anaesthetic effect of sevoflurane. These results indicate that the increase in movement and oculomotor response to nociceptive stimulation, found in patients given EA under general anaesthesia (V), is not caused by interaction of acupuncture with anaesthetic depth.

Adverse effects

We found no adverse effects in the 45 anaesthetized patients given acupuncture, except for a haematoma at LI4 which resolved on its own within a week. No adverse events have been associated with EA under anaesthesia in the other studies on EA reported here.



FUTURE PERSPECTIVES AND PERSONAL CONSIDERATIONS

Obstetrics (I-III)

The positive effects of acupuncture on pain in pregnancy and labour, reported in this thesis, should lead to further evaluations to determine whether acupuncture ought to be a standard analgesic modality offered to obstetric patients. Considering that acupuncture is still a new therapeutic method, future evaluations should include both prospective randomized (preferably placebo controlled) studies and an effective recording system for the adverse effects and complications of patients given acupuncture presently in both ante-natal clinics and labour wards.

Many problems of pregnancy and labour could be of interest in this evaluation:

- · unwanted infertility
- · emesis
- · low-back and girdle pain
- nocturnal cramps of the calves
- insufficient placental blood flow
- labour pain
- · placental retention
- · postnatal cramps
- mastitis
- influence on lactation immediately postpartum

Anaesthesia (IV, V)

The investigation of acupuncture in man is frustrated by difficult methodological problems. In anaesthetized patients, it was possible to both standardize all conditions and secure perfectly blinded conditions, for both the patient and the personnel, aside from the acupuncturist.

Our model could be used to gain basic knowledge of the effects of:

- · different EA stimulation modalities
- · potency of individual acupuncture points
- importance of timing of treatment related to occurrence of effect

Based on our two studies, it should be possible to predict the number of patients needed for the future investigations of points of similar potency to those used in our studies.

An equal design could be used to evaluate, in a double-blind fashion, the effect of an acupuncture or placebo procedure given the day before the operation (without interaction of anaesthesia), on reaction to interoperative pain. This procedure might determine the delayed effect of acupuncture often seen in clinical practice.

We have in our studies obtained blood samples before the start of anaesthesia, immediately before incision and 30 minutes after incision (IV, V). These should be analyzed for stress hormone and endorphine levels, to evaluate eventual influences of acupuncture on these modalities. Furthermore, the patients have recorded pain intensity, nausea and tiredness during the first 3 days after the operation and these data should be analyzed to estimate eventual postoperative benefits of the acupuncture treatment.

My personal interest in acupuncture for the management of problems during pregnancy and labour evolved from favourable experiences with this treatment during my three pregnancies. When I expected my first child, I concentrated my attention on TENS. Professor Pecka Pöntinen had told me, that acupuncture didn't work, but TENS was efficient in reducing labour pain. I realized that in my case TENS was certainly good when it came to reducing the peak intensity of labour cramps, but it didn't relieve the permanent low-backache. During my last delivery, the midwives gave me two times four ic sterile water paples with an approximate one hour interval between treatments, which resulted in a very good effect on the low-backache. The combination of TENS, during labour cramps, with this treatment resulted in a very decent analgesia. It seemed important to investigate whether acupuncture could also reduce one or more of these types of pain during labour.

While expecting my second child I was convinced that I had a severe attack of ischias, a diagnosis which was contradicted by the fact that a few needles in a few TPs of the medial gluteal muscle cured me. After my third pregnancy, I cured post-labour cramps of quite some dignity. A mastitis, which had been resistant to all conventional treatment and of which I had a few hours history for not only local redness, tenderness, increased skin temperature as well as increased consistency of a quadrant of the left breast, but also fever, was cured by one stimulation of HT3. All local symptoms, except for the redness of the skin, disappeared instantaneously upon treatment. As I trust in my perception and experience, I concluded that it was important to investigate the potency of acupuncture for the treatment of the pain and other adverse effects of pregnancy.

ING

CONCLUSIONS

Manual acupuncture in obstetric patients (I-III)

- reduces pelvic and low-back pain during late pregnancy, since pain intensity reflected in VAS assessments and pain associated with physical activity both decreased over time in significantly more acupuncture than control patients (I).
- probably reduces pain during labour, since use of other kinds of labour analgesia was found to be lower in patients given acupuncture than in those not given acupuncture (II, III).
- is associated with few and minor adverse effects in the third trimester of pregnancy and during labour, since we found no serious complications in patients or infants, although this finding does not exclude the possibility of more uncommon and serious problems (I-III).

Low-frequency electro-acupuncture in anaesthetized patients (IV, V)

- increases requirements for anaesthetic gas during general surgery, since significantly more sevoflurane was found to be required to allow skin incision without limb or neck movement in acupuncture patients than in sham patients (IV).
- facilitates clinical and physiological reactions to surgery, since significantly more patients subjected to acupuncture than to sham procedures were found to respond to skin incision with head or limb movements, dilation of pupils or divergence of eye axes under identical conditions of general anaesthesia (V).
- · does not affect anaesthetic depth during surgery, since there was no significant difference in AAI level between patients subjected to acupuncture or sham procedures while being exposed to the same steady-state concentration of sevoflurane (V).
- enables potential effects of acupuncture to be studied in a double-blind fashion, since the double-blind study design proved to be useful in comparing patients subjected to acupuncture or sham procedures with respect to their physiological responses to surgery under general anaesthesia (IV, V).

Jan Åke Nilsson, for statistical advise, and a clear perception of which parts of the work should be done by me - in spite of my spontaneous wishes.

Monica Hallin, for her fine graphic work and edition of this book as well as Gull-Britt Dahlman for her help with references – and the energy and immense support in the final process of this book, which I got from you both. 'My' secretary Carina Olofsson, however she finds all lost material in the computer, I will never know? Cecilia Holm for finding all mistakes in the figures of the last three articles and doing the good-looking pirate-copies of these. Eric Dryver for his meticulous correction of my English and text, but also his generous attitude. Hans Olsson for instructions in mental training, which brought me through this.

My family in which it was always an obvious duty and privilege to do ones best, even when this had obvious flaws, and to my kids such dear inspiration, but lately even reliable whenever I needed you – you really know what a deal is! I'm happy to be so closely related to you.

GRANTS NINA KVORNING

GRANTS

Thorsten Birger Segerfalks Stiftelse, Stiftelsen Thelma Zoégas Fond, Stig and Ragna Gorthons Stiftelse.

REFERENCES

- Abouleish, E. and Depp, R., Acupuncture in obstetrics, Anesth Analg, 54 (1975) 82-8.
- Akil, H., Watson, S.J., Young, E., Lewis, M.E., Khachaturian, H. and Walker, J.M., Endogenous opioids: biology and function, Annu Rev Neurosci, 7 (1984) 223-55.
- Alpiger, S., Helbo-Hansen, H.S. and Jensen, E.W., Effect of sevoflurane on the mid-latency auditory evoked potentials measured by a new fast extracting monitor, Acta Anaesthesiol Scand, 46 (2002) 252-6.
- Benedetti, F., How the doctor's words affect the patient's brain, Eval Health Prof, 25 (2002) 369-86.
- Bonica, J.J., Anesthesiology in the People's Republic of China, Anesthesiology, 40 (1974) 175-86.
- Bonica, J.J., Labour pain. In: P.D. Wall and R. Melzack (Eds.), Textbook of Pain, Churchil Livingstone, Edinburgh, 1989, pp. 482-499.
- Brennan, P. and Silman, A., Statistical methods for assessing observer variability in clinical measures, Bmj, 304 (1992) 1491-4.
- Bucinskaite, V., Theodorsson, E., Crumpton, K., Stenfors, C., Ekblom, A. and Lundeberg, T., Effects of repeated sensory stimulation (electro-acupuncture) and physical exercise (running) on open-field behaviour and concentrations of neuropeptides in the hippocampus in WKY and SHR rats, Eur J Neurosci, 8 (1996) 382-7.
- Carlsson, C.P., Axemo, P., Bodin, A., Carstensen, H., Ehrenroth, B., Madegard-Lind, I. and Navander, C., Manual acupuncture reduces hyperemesis gravidarum: a placebo- controlled, randomized, single-blind, crossover study, J Pain Symptom Manage, 20 (2000) 273-9.
- Chapman, C.R., Benedetti, C., Colpitts, Y.H. and Gerlach, R., Naloxone fails to reverse pain thresholds elevated by acupuncture: acupuncture analgesia reconsidered, Pain, 16 (1983) 13-31.
- Chen, X.H. and Han, J.S., Analgesia induced by electroacupuncture of different frequencies is mediated by different types of opioid receptors: another cross- tolerance study, Behav Brain Res, 47 (1992) 143-9.
- Chen, X.H., Han, J.S. and Huang, L.T., CCK receptor antagonist L-365,260 potentiated electroacupuncture analgesia in Wistar rats but not in audiogenic epileptic rats, Chin Med J (Engl), 107 (1994) 113-8.

Cheng, R.S. and Pomeranz, B., Electroacupuncture analgesia could be mediated by at least two pain- relieving mechanisms; endorphin and non-endorphin systems, Life Sci, 25 (1979) 1957-62.

- Chung, J.M., Fang, Z.R., Hori, Y., Lee, K.H. and Willis, W.D., Prolonged inhibition of primate spinothalamic tract cells by peripheral nerve stimulation, Pain, 19 (1984a) 259-75.
- Chung, J.M., Lee, K.H., Hori, Y., Endo, K. and Willis, W.D., Factors influencing peripheral nerve stimulation produced inhibition of primate spinothalamic tract cells, Pain, 19 (1984b) 277-93.
- Clement-Jones, V., McLoughlin, L., Tomlin, S., Besser, G.M., Rees, L.H. and Wen, H.L., Increased beta-endorphin but not met-enkephalin levels in human cerebrospinal fluid after acupuncture for recurrent pain, Lancet, 2 (1980) 946-9.
- Dawidson, I., Angmar-Mansson, B., Blom, M., Theodorsson, E. and Lundeberg, T., The influence of sensory stimulation (acupuncture) on the release of neuropeptides in the saliva of healthy subjects, Life Sci, 63 (1998a) 659-74.
- Dawidson, I., Angmar-Mansson, B., Blom, M., Theodorsson, E. and Lundeberg, T., Sensory stimulation (acupuncture) increases the release of vasoactive intestinal polypeptide in the saliva of xerostomia sufferers, Neuropeptides, 32 (1998b) 543-8.
- Deen, P. and Yuelan, H., Use of acupuncture analgesia during childbirth, Journal of Traditional Chinese Medicin, 5 (1985) 253-255.
- Dixon, W.J., The up and down method for small samples, American Statistical Association Journal, dec (1965) 967-978.
- Faure, E.A., The pain of parturition, Semin Perinatol, 15 (1991) 342-7.
- Fink, M., Gutenbrunner, C., Rollnik, J. and Karst, M., Credibility of a newly designed placebo needle for clinical trials in acupuncture research, Forsch Komplementarmed Klass Naturheilkd, 8 (2001) 368-72.
- Fitzgerald, M., The contralateral input to the dorsal horn of the spinal cord in the decerebrate spinal rat, Brain Res, 236 (1982) 275-87.
- Greif, R., Laciny, S., Mokhtarani, M., Doufas, A.G., Bakhshandeh, M., Dorfer, L. and Sessler, D.I., Transcutaneous electrical stimulation of an auricular acupuncture point decreases anesthetic requirement, Anesthesiology, 96 (2002) 306-12.
- Grisel, J.E., Fleshner, M., Watkins, L.R. and Maier, S.F., Opioid and nonopioid interactions in two forms of stress-induced analgesia, Pharmacol Biochem Behav, 45 (1993) 161-72.
- Han, J.S., Electroacupuncture: an alternative to antidepressants for treating affective diseases?, Int J Neurosci, 29 (1986) 79-92.

ING

- Han, J.S., Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies, Trends Neurosci, 26 (2003) 17-22.
- Han, J.S., Chen, X.H., Sun, S.L., Xu, X.J., Yuan, Y., Yan, S.C., Hao, J.X. and Terenius, L., Effect of low- and high-frequency TENS on Metenkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF, Pain, 47 (1991) 295-8.
- Han, Z., Jiang, Y.H., Wan, Y., Wang, Y., Chang, J.K. and Han, J.S., Endomorphin-1 mediates 2 Hz but not 100 Hz electroacupuncture analgesia in the rat, Neurosci Lett, 274 (1999) 75-8.
- He, C.a.H., JS, Attenuation of low- rather high-frequency electro-acupuncture analgesia following microinjection of beta-endorphin antiserum into the periaqueductal grey rats, Acupunct. Sci. Int. J., 1 (1990) 94-99.
- Hongo, T., Jankowska, E. and Lundberg, A., Post-synaptic excitation and inhibition from primary afferents in neurones of the spinocervical tract, J Physiol, 199 (1968) 569-92.
- Huang, C., Wang, Y., Chang, J.K. and Han, J.S., Endomorphin and mu-opioid receptors in mouse brain mediate the analgesic effect induced by 2 Hz but not 100 Hz electroacupuncture stimulation, Neurosci Lett, 294 (2000) 159-62.
- Huang, C., Wang, Y., Han, J.S. and Wan, Y., Characteristics of electroacupuncture-induced analgesia in mice: variation with strain, frequency, intensity and opioid involvement, Brain Res, 945 (2002) 20-5.
- Hyodo, M.a.G., O, Use of acupuncture anesthesia for normal delivery, American Journal of Chinese Medicin, 5 (1977) 63-69.
- Kho, H.G., Eijk, R.J., Kapteijns, W.M. and van Egmond, J., Acupuncture and transcutaneous stimulation analgesia in comparison with moderate-dose fentanyl anaesthesia in major surgery. Clinical efficacy and influence on recovery and morbidity, Anaesthesia, 46 (1991) 129-35.
- Kienle, G.S. and Kiene, H., Placebo effect and placebo concept: a critical methodological and conceptual analysis of reports on the magnitude of the placebo effect, Altern Ther Health Med, 2 (1996) 39-54.
- Kienle, G.S. and Kiene, H., The powerful placebo effect: fact or fiction?, J Clin Epidemiol, 50 (1997) 1311-8.

Kihlstrand, M., Stenman, B., Nilsson, S. and Axelsson, O., Water-gymnastics reduced the intensity of back/low back pain in pregnant women, Acta Obstet Gynecol Scand, 78 (1999) 180-5.

- Kim, E.H., Kim, Y., Jang, M.H., Lim, B.V., Kim, Y.J., Chung, J.H. and Kim, C.J., Auricular acupuncture decreases neuropeptide Y expression in the hypothalamus of food-deprived Sprague-Dawley rats, Neurosci Lett, 307 (2001) 113-6.
- Kitade, T., Odahara, Y., Shinohara, S., Ikeuchi, T., Sakai, T., Morikawa, K., Minamikawa, M., Toyota, S., Kawachi, A., Hyodo, M. and et al., Studies on the enhanced effect of acupuncture analgesia and acupuncture anesthesia by D-phenylalanine (first report)—effect on pain threshold and inhibition by naloxone, Acupunct Electrother Res, 13 (1988) 87-97.
- Kitade, T., Odahara, Y., Shinohara, S., Ikeuchi, T., Sakai, T., Morikawa, K., Minamikawa, M., Toyota, S., Kawachi, A., Hyodo, M. and et al., Studies on the enhanced effect of acupuncture analgesia and acupuncture anesthesia by D-phenylalanine (2nd report)—schedule of administration and clinical effects in low back pain and tooth extraction, Acupunct Electrother Res, 15 (1990) 121-35.
- Knight, B., Mudge, C., Openshaw, S., White, A. and Hart, A., Effect of acupuncture on nausea of pregnancy: a randomized, controlled trial, Obstet Gynecol, 97 (2001) 184-8.
- Kotani, N., Hashimoto, H., Sato, Y., Sessler, D.I., Yoshioka, H., Kitayama, M., Yasuda, T. and Matsuki, A., Preoperative intradermal acupuncture reduces postoperative pain, nausea and vomiting, analgesic requirement, and sympathoadrenal responses, Anesthesiology, 95 (2001) 349-56.
- Kristiansson, P., Svardsudd, K. and von Schoultz, B., Back pain during pregnancy: a prospective study, Spine, 21 (1996) 702-9.
- Kurita, T., Doi, M., Katoh, T., Sano, H., Sato, S., Mantzaridis, H. and Kenny, G.N., Auditory evoked potential index predicts the depth of sedation and movement in response to skin incision during sevoflurane anesthesia, Anesthesiology, 95 (2001) 364-70.
- Kvorning Ternov, N., Buchhave, P., G, S. and J, Å. Acupuncture During Childbirth Reduces Use of Conventional Analgesis Without Major Adverse Effects: A retrospective Study, American Journal of Acupuncture, 26 (1998) 233-239.

- Kvorning Ternov, N., Grennert, L., Åberg, A., Algotsson, L. and Åkeson, J., Acupuncture for Lower Back and Pelvic Pain in Late Pregnancy: A Retrospective Report om 167 Consecutive Cases, Pain Medicine, 2 (2001) 204-207.
- Labrecque, M., Nouwen, A., Bergeron, M. and Rancourt, J.F., A randomized controlled trial of nonpharmacologic approaches for relief of low back pain during labor, J Fam Pract, 48 (1999) 259-63.
- Le Bars, D., Dickenson, A.H. and Besson, J.M., Diffuse noxious inhibitory controls (DNIC). I. Effects on dorsal horn convergent neurones in the rat, Pain, 6 (1979) 283-304.
- Ledergerber, C., Electroacupuncture in obstetrics, Acupuncture & Electro-Therapeut. Res. Int. J., 2 (1976) 119-125.
- Lewith, G.T., How effective is acupuncture in the management of pain?, J R Coll Gen Pract, 34 (1984) 275-8.
- Lewith, G.T. and Machin, D., On the evaluation of the clinical effects of acupuncture, Pain, 16 (1983) 111-27.
- Lewith, G.T. and Vincent, C., On the evaluation of the clinical effects of acupuncture: a problem reassessed and a framework for future research, J Altern Complement Med, 2 (1996) 79-90; discussion 91-100.
- Litvan, H., Jensen, E.W., Galan, J., Lund, J., Rodriguez, B.E., Henneberg, S.W., Caminal, P. and Villar Landeira, J.M., Comparison of conventional averaged and rapid averaged, autoregressive-based extracted auditory evoked potentials for monitoring the hypnotic level during propofol induction, Anesthesiology, 97 (2002) 351-8.
- Loeser, J.D. and Bonica, J.J., Bonica's management of pain, Philadelphia; Lippincott Williams and Wilkins,, 2001, xxii, 2178 pp.
- Low, R., Acupuncture in gynaecology and obstetrics. An essential guide for practitioners and students., Thorsons, London, 1990.
- Macdonald, A., Acupuncture analgesia and therapy. In: P.D. Wall (Ed.), Textbook of pain, Churchill Livingstone, Edinbutgh, 1989, pp. 906-919.
- Macdonald, A.J., Macrae, K.D., Master, B.R. and Rubin, A.P., Superficial acupuncture in the relief of chronic low back pain, Ann R Coll Surg Engl, 65 (1983) 44-6.
- MacEvilly, M. and Buggy, D., Back pain and pregnancy: a review, Pain, 64 (1996) 405-14.

MacPherson, H., White, A., Cummings, M., Jobst, K.A., Rose, K. and Niemtzow, R.C., Standards for Reporting Interventions in Controlled Trials of Acupuncture: the STRICTA recommendations, J Altern Complement Med, 8 (2002) 85-9.

- Mann, F., Textbook of acupuncture, Heinemann Medical, Oxford, 1987.
- Masala, A., Satta, G., Alagna, S., Zolo, T.A., Rovasio, P.P. and Rassu, S., Suppression of electroacupuncture(EA)-induced beta-endorphin and ACTH release by hydrocortisone in man. Absence of effects on EA-induced anaesthesia, Acta Endocrinol, 103 (1983) 469-72.
- Melzack, R., Kinch, R., Dobkin, P., Lebrun, M. and Taenzer, P., Severity of labour pain: influence of physical as well as psychologic variables, Can Med Assoc J, 130 (1984) 579-84.
- Melzack, R. and Schaffelberg, D., Low-back pain during labor, Am J Obstet Gynecol, 156 (1987) 901-5.
- Melzack, R., Stillwell, D.M. and Fox, E.J., Trigger points and acupuncture points for pain: correlations and implications, Pain, 3 (1977) 3-23.
- Morioka, N., Akca, O., Doufas, A.G., Chernyak, G. and Sessler, D.I., Electroacupuncture at the Zusanli, Yanglingquan, and Kunlun points does not reduce anesthetic requirement, Anesth Analg, 95 (2002) 98-102.
- Nogier, P.F.M., Treatise of auriculotherapy, Maisonneuve, Moulinles-Metz (1972).
- Olofsson, C., Ekblom, A., Ekman-Ordeberg, G., Hjelm, A. and Irestedt, L., Lack of analgesic effect of systemically administered morphine or pethidine on labour pain, Br J Obstet Gynaecol, 103 (1996) 968-72.
- Ostgaard, H.C., Zetherstrom, G. and Roos-Hansson, E., Back pain in relation to pregnancy: a 6-year follow-up, Spine, 22 (1997) 2945-50.
- Ramnero, A., Hanson, U. and Kihlgren, M., Acupuncture treatment during labour—a randomised controlled trial, BJOG, 109 (2002) 637-44.
- Romita, V.V., Suk, A. and Henry, J.L., Parametric studies on electroacupuncture-like stimulation in a rat model: effects of intensity, frequency, and duration of stimulation on evoked antinociception, Brain Res Bull, 42 (1997) 289-96.
- Rowlands, S. and Permezel, M., Physiology of pain in labour, Baillieres Clin Obstet Gynaecol, 12 (1998) 347-62.
- Ryan, D., Toward Improving the Reliability of Clinical Acupuncture Trials:

 Arguments Against the Validity of "Sham Acupuncture" as

 Controls, American Journal of Acupuncture, 27 (1999) 105-109.
- Skilnand, E., Fossen, D. and Heiberg, E., Acupuncture in the management of pain in labor, Acta Obstet Gynecol Scand, 81 (2002) 943-8.

- Taguchi, A., Sharma, N., Ali, S.Z., Dave, B., Sessler, D.I. and Kurz, A., The effect of auricular acupuncture on anaesthesia with desflurane, Anaesthesia, 57 (2002) 1159-63.
- Thomas, I.L., Nicklin, J., Pollock, H. and Faulkner, K., Evaluation of a maternity cushion (Ozzlo pillow) for backache and insomnia in late pregnancy, Aust N Z J Obstet Gynaecol, 29 (1989) 133-8.
- Thomas, M., Arner, S. and Lundeberg, T., Is acupuncture an alternative in idiopathic pain disorder?, Acta Anaesthesiol Scand, 36 (1992) 637-42.
- Thornton, C., Evoked potentials in anaesthesia, Eur J Anaesthesiol, 8 (1991) 89-107.
- Tian, J.H. and Han, J.S., Functional studies using antibodies against orphanin FQ/nociceptin, Peptides, 21 (2000) 1047-50.
- Travell, J. and Rinzler, S.H., The myofascial genesis of pain, Postgraduate Medicine, 11 (1952) 425-434.
- Umeh, B.U., Sacral acupuncture for pain relief in labour: initial clinical experience in Nigerian women, Acupunct Electrother Res, 11 (1986) 147-51.
- Uvnas-Moberg, K., Bruzelius, G., Alster, P. and Lundeberg, T., The antinociceptive effect of non-noxious sensory stimulation is mediated partly through oxytocinergic mechanisms, Acta Physiol Scand, 149 (1993) 199-204.
- Wall, P.D. and Melzack, R., Textbook of pain, Churchill Livingstone, Edinburgh, 1989, 1064 pp.
- Ward, M.E., Acute pain and the obstetric patient: recent developments in analgesia for labor and delivery, Int Anesthesiol Clin, 35 (1997) 83-103.
- Wedenberg, K., Moen, B. and Norling, A., A prospective randomized study comparing acupuncture with physiotherapy for low-back and pelvic pain in pregnancy, Acta Obstet Gynecol Scand, 79 (2000) 331-5.
- Willer, J.C., Dehen, H. and Cambier, J., Stress-induced analgesia in humans: endogenous opioids and naloxone- reversible depression of pain reflexes, Science, 212 (1981) 689-91.
- Yanai, N., Shalev, E., Yagudin, E. and Zuckerman, H., The Use of Electroacupuncture During Labor, American Journal of Acupuncture, 15 (1987) 311-312.
- Young, G. and Jewell, D., Interventions for preventing and treating pelvic and back pain in pregnancy (Cochrane Review), The Cochrane Library (2003).

Zhou, Y., Sun, Y.H., Shen, J.M. and Han, J.S., Increased release of immunoreactive CCK-8 by electroacupuncture and enhancement of electroacupuncture analgesia by CCK-B antagonist in rat spinal cord, Neuropeptides, 24 (1993) 139-44.

I. Kvorning N, Holmberg C, Grennert L, Åberg A, Åkeson J. Acupuncture relieves pelvic and low-back pain in late pregnancy. Acta Obstetricia Gynaecologica Scandinavica 2003. In press.

