OTHER PAIN (N VADIVELU AND A KAYE, SECTION EDITORS)



The Role of Acupuncture in Pain Management

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Published online: 20 February 2016

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Abstract Acupuncture is a traditional Chinese practice of medicine that has gained popularity in Western culture and around the world. It involves the insertion of thin needles into the skin to stimulate nerves, muscles, and connective tissues throughout the body with the goal of alleviating pain, tension, and stress. More broadly, acupuncture is actually a family of different procedures. Conceptually, it is believed to stimulate the body's meridians, or energy-carrying channels, in an attempt to correct imbalances and to restore health. These benefits are thought to be derived from the proximity of acupoints with nerves through intracellular calcium ions. This lesson outlines a brief history of acupuncture and how it may be used to treat various types of physical and emotional pain and specific conditions, including overactive bladder and psoriasis. Acupuncture has been demonstrated to enhance endogenous opiates, such as dynorphin, endorphin, encephalin, and release corticosteroids, relieving pain and enhancing the healing process. There are associated risks; however, serious side effects are rare. When compared to traditional methods of pain management, more studies are warranted in order to establish the efficacy of acupuncture and its place in pain management.

 $\begin{tabular}{ll} \textbf{Keywords} & Acupuncture \cdot Analgesia \cdot Pain management \cdot \\ Alternative therapy \cdot Pain relief \end{tabular}$

This article is part of the Topical Collection on Other Pain

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Introduction and History

Acupuncture is the practice of inserting needles into the body to reduce pain or induce analgesia. There are a number of different approaches to diagnosis and treatment in American acupuncture that incorporate medical traditions from China, Japan, Korea, and other countries. The postulated mechanism of stimulation of acupuncture points during an acupuncture procedure consists of penetration of the skin by thin, solid, metallic needles that can be manipulated manually or by electrical stimulation.

Acupuncture dates back more than 2500 years to Chinese doctors who believed that illness was due to imbalances in energy. It was brought to the West by the Jesuits in the seventeenth century. In the 1970s, acupuncture gained popularity in the USA when President Nixon visited China. Nixon toured medical facilities where acupuncture was widely used, and during the trip, a reporter, Scottie Reston, required an emergency appendectomy and received acupuncture for the treatment of postoperative pain. He found acupuncture very effective and wrote about his experience upon arriving home [1].

Acupuncture is conceptually thought of as stimulating the body's meridians, or energy-carrying channels, to correct these imbalances and to restore health. It is hypothesized that these benefits derive from the proximity of the acupoints to nerves. Stimulation of these points can supposedly allow the nerves (close to the point of needle entry) to release endorphins that can ameliorate pain.

The physiology of how acupuncture works is not yet understood. Research suggests that neural signaling, opioid peptides, glutamate, and adenosine calcium are all likely involved in the process. Molecular imaging studies have shown that mechanical movements of the acupuncture needle itself are important for the release of aforementioned signaling molecules, all of which can alleviate pain [1].



Ancient Chinese culture created the notion of an organic unity of the universe and the human body as one. It believed in two fundamental forces: yin, which represents a female energy, the moon, and is dark, sinister, concealed, and hidden, while yang represents a masculine energy and is bright, open, and outgoing. The two forces work together and in balance. In the body, this duality is expressed in the qi (yang) and the blood (yin) as two separate circulation systems. Blood is pumped by the heart and circulates through arteries, veins, and capillaries, which helps the lungs generate qi. Qi through invisible tracts called jin-luo (meridians) in the body.

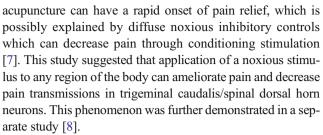
Meridians are defined as conductive pathways supporting the circulation of qi and are fundamental for the circulation of energy throughout the body [2]. Blood and qi are interconnected and mutually supportive or can be considered counterbalancing, like yin and yang. Blood, qi, the meridians, and the five elements are the foundation of the basic physiology and pathology of traditional Chinese medicine. Jin may be translated as *channel* with luo as the multiple branches so that the body surface is all under the jin-luo influence. Along the meridians are a large number of *points* on the surface of the body. Three hundred sixty-five points were numbered (probably corresponding to the calendar days) in the first century B.C. and over 400 in late twentieth century. But for practical purpose, fewer than 50 are normally employed [1].

The 2007 National Health Interview Survey demonstrated increasing acceptance and utilization of acupuncture for treatment and health promotion. The study found that over 14 million Americans have used acupuncture as part of their health care, which was an increase from 8 million in 2002 [3]. Acupuncture has been used successfully to treat migraine, knee and back pain, chemo-induced nausea, vomiting, and hot flash among other disorders. Taken together, all of these data suggest that more individuals are accepting acupuncture treatment as part of their current health-care regimen.

Acupuncture to Alleviate Pain

The 2002 National Health Interview Survey study showed that the majority of patients used acupuncture for a specific condition. Almost half of patients sought this therapy because conventional treatments had failed. The study also revealed that some patients use acupuncture to achieve general wellness, enhance energy, and improve immune function.

The exact mechanism of action of acupuncture is unclear and has been explored since the 1970s [4]. Early research studies suggested that endogenous opioids may play a role in how acupuncture exerts its effects due to the antagonistic effects of naloxone on electro-acupuncture analgesia (EAA) [5]. Endogenous opioids have also been measured in the plasma and cerebrospinal fluid of patients that received EAA treatment [6]. Anecdotal reports from patients suggest that



Dowson et al. demonstrated in his study that acupuncture was 20 % more effective than placebo in relieving headaches, but results were not statistically significant [9]. In regards to chronic pain, Vickers et al. conducted an individual meta-analysis of 17,922 patients on the effect of acupuncture on head/neck pain, osteoarthritis, and shoulder pain [10]. The authors found that acupuncture is superior to both sham and no-acupuncture control groups in each subset of patients and could be effectively used to treat chronic pain. They concluded that acupuncture is more than placebo, given the statistical significant findings they observed.

According to the National Institutes of Health (NIH), acupuncture can be utilized as an alternative form of treatment when a conventional therapy is ineffective or as an adjunct in patients who suffer from the side effects of medications. In 1997, the NIH proclaimed the efficacy of acupuncture for postoperative pain, nausea and vomiting secondary to chemotherapy, and dental pain.

Diseases for which treatment has been promising but further research is indicated include acne vulgaris, insomnia, cancer pain, obesity, herpes zoster, polycystic ovarian syndrome (PCOS), female infertility, temporomandibular joint (TMJ) disorders, and whooping cough. Diseases where only individual trials have had positive results or other conventional therapies have failed include chloasma, neuropathic bladder in spinal cord injury, and small airway obstruction, among others. The final category of diseases, in which only specialized medical personnel would consider using acupuncture, includes comatose patients, infants with encephalitis/convulsions, and coronary artery disease.

Acupuncture for Physical Pain

Cancer Pain

The World Health Organization (WHO) recommends using alternate therapies in addition to pharmacological treatment for management of pain. Low levels of substance P and upregulation of beta-endorphins in the blood result in analgesia from acupuncture.

A Cochrane systematic review of acupuncture for cancer pain yielded insufficient evidence to prove its efficacy due to small sample sizes of the studies and poor reporting and analysis [11]. Individual pain studies with small sample sizes have shown positive findings. Alimi et al. in 2003 compared



auricular acupuncture using semi-permanent needles with two placebo groups: auricular acupuncture using semi-permanent needles at non-acupuncture placebo points and non-invasive auricular seeds at non-acupuncture placebo points in patients with chronic pain related to cancer [12]. Pain scores at 1 and 2 months were reduced in the 29 patients treated with acupuncture. A 36 % decrease in pain intensity as measured by visual analogue scale (VAS) scores was observed after 2 months of auricular therapy in the acupuncture group [11]. A pilot study of 19 patients by Crew et al. demonstrated improved functional ability and decreased joint symptoms after acupuncture in breast cancer patients treated with aromatase inhibitors. Aromatase inhibitors are frequently used in the treatment of breast cancer and are implicated in joint pain [13]. Randomized, blinded, sham-controlled trials done by the same author concluded the effectiveness of true acupuncture in lowering pain scores in women with aromatase inhibitor-induced arthralgia [14].

Acupuncture for Dysmenorrhea

Acupressure at matched points of Hegu (L1–4) and Sanyinjiao (Sp6) has been shown to reduce pain, distress, and anxiety due to primary dysmenorrhea. Menstrual pain was reduced by acupressure at a single point—Hegu—after a 6-month follow-up in the same study [15]. Wang et al. demonstrated increased levels of nitric oxide and a decrease in menstrual symptoms in the auricular acupressure group [16]. A decreased serum concentration of nitric oxide is associated with more severe muscular and vascular contractions of the uterus [17].

Acupuncture for Labor Pain

Acupuncture is effective for pain control during the first stage of labor. It does not reduce the intensity of uterine contractions. Most commonly used acupoints are Sp6 (Sanyinjiao) and L1–4 (Hegu). Acupressure at Sp6 releases oxytocin from the pituitary gland, which stimulates uterine contractions and enhances the labor process [18••]. Acupressure at Hegu (L1–4) decreases pain. One explanation, although somewhat controversial, may be found in the gate control theory in which stimulating large myelinated fibers block the smaller-diameter pain fibers from transmitting painful stimuli [15]. Acupressure at Hegu also has an effect on the release of endogenous opioids and subjective pain scores [18••].

Mucuk et al. conducted a pilot study including 78 women to evaluate the effectiveness of Hegu acupressure on labor pain and adrenocorticotropic hormone (ACTH) and cortisol levels. The VAS scores, cortisol levels, and ACTH levels were lower in the acupuncture group when compared to the control group; however, the results were not statistically significant [19]. Levett et al. reviewed four review articles on this subject.

Study groups required less pharmacologic analgesia, had lower instrumental deliveries, and achieved greater pain satisfaction scores [18••]. These therapies are useful adjuncts in managing labor pain and minimize adverse effects with conventional pharmacologic analgesia.

Acupuncture for Migraine

Acupuncture has been used for treating and preventing migraine attacks that affect 18 % of women and 5 % of men in the USA. The trigeminal nucleus caudalis receives a trigeminal sensory pain input from cranial vessels and the dura mater. Acupuncture by its inhibitory effect on the trigeminal nucleus caudalis and dorsal horn can relieve migraine [20]. Molsberger in 2012 postulated that "acupuncture is at least as effective as prophylactic drug therapy for migraine and it is safe, long lasting and cost effective" [21].

A Cochrane review in 2009 included 22 trials with 4419 participants. In 6 trials, after 3–4 months of acupuncture treatment, patients had fewer headaches and treatment was superior to no prophylactic treatment or routine care only. Fourteen trials compared true to sham acupuncture. Both groups reported fewer headaches than before treatment; however, there was no statistically significant result showing the superiority of true acupuncture. Four trials comparing acupuncture to proven migraine prophylaxis drug treatment showed fewer side effects and a slightly better outcome [22]. Consideration for using acupuncture for migraine should be offered to patients.

Acupuncture for Emotional Pain and Anxiety Disorders

Anxiety, Depression, and Schizophrenia

Acupuncture use in anxiety and depression is increasing. Anxiety is a collection of conditions as per DSM-IV and includes panic attacks and disorders, phobias, obsessivecompulsive disorders, post-traumatic stress disorders, generalized anxiety, acute stress, substance-induced stress, anxiety disorders due to a medical condition, or anxiety disorders not otherwise specified. One percent of all disability-adjusted life years lost worldwide are due to post-traumatic stress disorder, obsessive-compulsive disorder, and panic disorder combined as per the World Health Organization statistics in 2004 [23]. A systematic review in 2007 included 12 controlled trials utilizing acupuncture for anxiety and anxiety disorders. As per this review, the use of auricular acupuncture for short-term anxiety such as perioperative anxiety is effective when compared to sham acupuncture. Interpretation of RCTs for acupuncture use in generalized anxiety disorders or anxiety neurosis is difficult to interpret as acupuncture was compared to several different modalities of anti-anxiety intervention including sham acupuncture, behavioral desensitization, and drug therapy [23].



A 2010 study found acupuncture to be safe and effective in treating major depressive disorders and post-stroke depression [24]. Wu et al. concluded acupuncture to be a potentially effective monotherapy for depression and a safe adjunctive treatment with antidepressants [25]. A review of 30 trials in 2010 by Smith et al. failed to recommend the use of acupuncture for depression, as the risk of bias was high in most trials [26]. Two mechanisms related to sleep and emotion explain the positive effects of acupuncture in improving the quality of life in depression and schizophrenia. An indirect mechanism involves improving the quality of sleep by acupuncture. Disturbances in sleep have been found in patients with schizophrenia and depression. Improving cognitive function and reducing daytime somnolence with acupuncture therapy improve the quality of life. A second positive effect is seen by reducing depressive symptoms post therapy. Less anxiety and a better disposition were observed in patients with schizophrenia after therapy [27••].

Acupuncture for Anorexia Nervosa

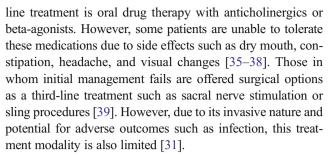
Acupuncture should be used only as an adjunct and not as a first-line therapy for anorexia nervosa. Moreover, there is only weak evidence for the improvement in bingeing even when used as an adjunct. Practice guidelines for acupuncturists developed by Fogarty and Ramjan dwell on these key points [28•]. A pilot study concluded that participants undergoing acupuncture in addition to existing treatment reported reduced anxiety levels, less depression, and better quality of life [29].

Acupuncture for Specific Conditions

Overactive Bladder

Overactive bladder (OAB) is defined by the International Continence Society (ICS) as "the presence of urinary urgency (both daytime and nighttime), usually accompanied by increased frequency and nocturia with or without urge, urinary incontinence in the absence of a urinary tract infection or other obvious pathology." Overactive bladder syndrome affects 17 % of men and women in the USA (National Overactive Bladder Evaluation study) and 12–17 % in six European nations [30]. OAB has a major impact on the quality of life related to social and sexual functions that may lead to anxiety and depression and may be associated with lower quality of life scores than patients with hypertension, depression, diabetes, and asthma [31–33].

Conventional treatments for OAB as defined by the American Urological Association (AUA) include conservative behavioral modifications for a first-line therapy such as pelvic floor exercises, delayed voiding, bladder training, and restriction of fluid intake. However, favorable outcomes rely on patient investment of time and effort [34, 35]. A second-



Acupuncture is an alternative therapy for OAB that is minimally invasive and causes few side effects [40, 41]. There are two approaches. The segmental approach can be applied by the use of needling points such as BL28 and BL30 (S2-S4) that invokes a parasympathetic response at a spinal level. Alternatively, acupuncture can be applied to all tissues supplied by the nerve at this level, which may have a calming effect on involuntary bladder contractions [42]. The therapeutic benefits of acupuncture on OAB are achieved through increases in maximum bladder capacity, suppression of detrusor muscle activity, reduction of maximum bladder contraction pressure, and decreases in peak urinary flow rate [16, 43]. Several clinical studies have shown that acupuncture could reduce micturition over 24 h and urgency episodes over 24 h and improve the quality of life. Acupuncture should be considered as a potential alternative to current regimens [44–48].

Benign Prostatic Hypertrophy

Benign prostatic hypertrophy (BPH) is a non-malignant enlargement of the prostate that commonly affects men as they age. It is estimated that at least 40 % of men have BPH during their 50s, increasing to 90 % of men in their 80s [49]. BPH is inconsequential in many men; however, if the enlargement narrows the urethral passage from the bladder, patients experience urinary difficulties. BPH can cause lower urinary tract symptomatology including obstructive symptoms (weak urinary stream, hesitancy, intermittency, incomplete bladder emptying, terminal urine dribbling, and abdominal straining) and irritative symptoms (urinary frequency, urgency, and nocturia) [50]. The International Prostate Symptom Score (IPSS) is used to measure the burden of these symptoms. Traditionally, treatment options for BPH include minimally invasive therapy, surgery, and medical therapy with alphablockers, 5-α-reductase inhibitors, and phosphodiesterase inhibitors [50].

The frequency of BPH in Chinese men is comparable to the estimates observed in Western countries [51]. However, in China, the use of acupuncture to treat BPH-related urinary symptoms is common. Traditional Chinese medicine theorizes that acupuncture can strengthen the human body's vital essence, called "qi," and remove blockages in channels. According to Chinese medicine, acupuncture needles are inserted and hand-manipulated at very specific *acupoints*.



Electro-acupuncture (EA) is a variation of this technique in which needles are inserted at these assigned points and briefly hand-manipulated to stimulate the flow of energy along body meridians, and then a low electric current is run through the needles to continue the stimulation for a prescribed period. The reasoning behind this is that hand manipulation is subject to fatigue whereas electric current is consistent [16].

A 2013 study found that administering EA at the proper acupoint improved IPSS scores significantly over random needling. The acupuncture point was UB33, which is located on the sacrum directly over the third posterior sacral foramen. EA was applied with disperse-dense waves at 20 Hz bilaterally to UB33 with obliquely inserted acupuncture needles. However, there were no differences in post-void residual (PVR) urine or maximum urinary flow rate (Q_{max}) . Interestingly, this study showed improvement in the quality of life in spite of no difference in physiologic urinary function (retention of urine and maximum flow). This lends itself to the researchers' theory that EA at point UB33 is effective for the treatment of BPH [16]. Although the exact mechanism of EA treatment for BPH is unknown, some researchers are inclined to "believe that the effects of acupuncture are less likely to be related to histological changes of the prostate," than to brain function, because "...the human brain is closely involved in the sensation and control of the lower urinary system" [16].

Chronic Urticaria

Urticaria is a heterogeneous group of skin diseases involving the onset of pruritic wheals, angioedema, or both [52]. The diagnosis of chronic urticaria is made when recurrent crops of urticarial skin lesions continue for more than 6 weeks. It is a common disease with a prevalence of 0.5–1 % and affects nearly 20 % of people at least once during their lifetime [53]. Women encounter urticaria twice as often as men, and there is increased frequency among individuals between the ages of 20 and 40. The itching and physical discomfort during outbreaks negatively influences the quality of life [52].

The goal of urticaria treatment is to alleviate symptoms. Conservative first-line measures include elimination of potential underlying causes and eliciting triggers. The second-line therapy is medications such as non-sedating histamines and short-term corticosteroids for exacerbations [52, 54].

Asia has historically embraced the use of acupuncture for the treatment of urticaria. The most commonly used acupuncture points are L11, Sp10, Sp6, and S36. Chronic urticaria has proved challenging for medical therapy. However, several acupuncture methods have overcome the shortcomings of medications. Based on uncontrolled studies, the efficacy of acupuncture in chronic urticaria was reported to range from 30 to 50 %. The addition of specific points on the ears to the normal points in standard practice increased the efficacy to 96 % [55].

Acupuncture may suppress the immunological reaction. Studies in animals and humans demonstrated that acupuncture can decrease the pruritic and inflammatory effects of histamine, modulate the function of the immune system, and decrease the adhesion molecule [56]. Although current research has clinical limitations, acupuncture may provide an effective alternative for the treatment of urticaria, particularly in those refractory to medical therapy.

Psoriasis

Psoriasis is a chronic, recurrent inflammatory skin disease that presents as discrete bright red macules, papules, or patches covered with lamellated silvery scales. Psoriasis affects 1–3 % of individuals worldwide with 7.5 million patients in the USA alone [57]. Psoriasis affects males and females equally, and its onset is usually in the second to fourth decades of life. Psoriasis has a negative impact on the quality of life and can be psychosocially debilitating [58]. Psoriasis places patients at increased risk of psoriatic arthritis, obesity, dyslipidemia, hypertension, diabetes mellitus, and cardiovascular disease [59].

Psoriasis is an immune-mediated disease caused by genetic and environmental factors requiring a long-term therapy due to its chronic and intermittent nature. The standard treatment of psoriasis includes systemic therapy (e.g., methotrexate, cyclosporine, acitretin, photochemotherapy) and biological agents (e.g., efalizumab, etanercept, infliximab, adalimumab) [60]. However, medical therapy merely leads to temporary remission of symptoms and most patients are dissatisfied with treatment due to side effects and cumulative toxicity [61]. Thus, more effective treatment strategies are in demand [62].

In recent years, acupuncture has been widely tested as an alternative treatment. One study demonstrated that acupuncture alleviates erythema, scales, and local thickening of maculae in some patients [63]. Acupuncture may be helpful due to the relaxation effect of the therapy combined with traditional Chinese medicine approaches of eliminating the "heat" and "dampness" in the meridians (energy pathways in the body) associated with psoriasis. However, this topic warrants further research, as there is no consensus as to its effectiveness or safety.

Risks and Adverse Events Associated with Acupuncture

There are associated risks. Although acupuncture is generally considered safe, an adverse reaction can occur. A 2010 study revealed that 75 (6.8 %) subjects described negative short-term acupuncture reactions which included feelings of *pain* (37, 3.4 %), tiredness (24, 2.2 %), and dizziness (9, 0.8 %).



Another study reported that of 229,230 patients receiving on average 10.2 ± 3.0 acupuncture treatments, 19,726 patients (8.6%) reported experiencing at least one adverse effect and 4963 (2.2%) reported one which required treatment [64]. The most commonly occurring adverse effects were bleeding or hematoma (6.1% of patients, 58% of all adverse effects), pain (1.7%), and vegetative symptoms, meaning weight loss, fatigue, decreased appetite, and depression (0.7%). In a separate study, where 9408 patients completed 3-month post-treatment questionnaires, 682 patients reported at least one adverse event over 3 months, a rate of 107 per 1000 patients (95% CI 100 to 115). Three patients reported a serious adverse event [65]. The most common events reported were severe tiredness and exhaustion, pain at the site of needling, and headache.

Nevertheless, side effects are rare and there are generally no serious adverse events reported in peerreviewed studies [66]. Most patients report positive outcomes [66]. The most common positive short-term acupuncture reaction was that of a relaxed feeling in 472 (43.1 %), followed by 90 (8.2 %) who acknowledged a feeling of less pain, 16 (1.5 %) felt energized, 16 (1.5 %) experienced tingling, and a sensation of heat or coldness was reported by 10 (0.9 %) [66]. Posttreatment positive short-term acupuncture reactions were 12 times higher than those of the negative short-term reactions. Overall, subjects were comparatively satisfied with the acupuncture treatment. Furthermore, if acupuncture treatment is administered by an experienced practitioner and is conducted in accordance with established guidelines, it is considered to be a safe treatment method to treat patients with pain [66].

Comparison of Acupuncture with Traditional Pain Management

Acupuncture treatment, whether traditional or auricular, showed pain alleviation in headache, trigeminal neuralgia, and retro-auricular pain, but no significant difference was seen between groups. Prospective, well-controlled, and relevant protocols using multimodal strategies to define the roles are needed [67].

A recent publication reported 1763 participants in a study comparing acupuncture to sham acupuncture, no treatment or usual care for osteoarthritis. Acupuncture use was associated with significant reductions in pain intensity (mean difference (MD) -0.29, 95 % CI -0.55 to -0.02, I^2 0 %, 10 trials, 1699 participants), functional mobility (standardized MD -0.34, 95 % CI -0.55 to -0.14, I^2 70 %, 9 trials, 1543 participants), and health-related quality of life (standardized MD -0.36, 95 % CI -0.58 to -0.14, I^2 50 %, 3 trials, 958 participants). Significant reductions in pain intensity and improvement in functional mobility and quality of life were demonstrated [68].



Acupuncture is a generally safe procedure for the treatment of pain and conditions where pain is a side effect. While there are risks associated with acupuncture, general consensus suggests that the benefits of acupuncture outweigh the drawbacks. Informed consent and education about the procedures are important. If patients are interested in exploring acupuncture, it is the responsibility of the health-care provider to understand the potential of acupuncture treatment and how it may affect additional pain treatments or medications and quality of life.

Compliance with Ethical Standards

Conflict of Interest Shilpadevi Patil, Sudipta Sen, Matthew Bral, Shanthi Reddy, Kevin K. Bradley, Elyse M. Cornett, Charles J. Fox, and Alan David Kaye declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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