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An Evidence-Based Review of Acupuncture in Osteoporosis and Fracture-Related Pain

Jenson Mak and Louise Mak
Rehabilitation Studies Unit, University of Sydney
Department of Geriatric Medicine, Gosford Hospital
Australia

1. Introduction

After 40 years of extensive studies, compelling evidence has been obtained to support acupuncture as a useful tool for treating a spectrum of diseases. In fact, more than 40 disorders have been endorsed by the World Health Organization (WHO) as conditions that can benefit from acupuncture treatment (Han, 2011). A study on 202 subjects attending an Australian university osteoporosis clinic found that almost one-fifth of those using a complementary medicine modality used acupuncture (Table 1: Mak 2010). This chapter begins by looking at the history of documented acupuncture use in osteoporosis. It then utilises an evidence-based approach in appraising relevant clinical trials over the past 10 years of the benefits of acupuncture use in osteoporosis (improvements in bone-mineral density, falls and fracture rates), as well as the efficacy in the treatment of acute fracture-related pain. Finally, it discusses the pathophysiological basis of the efficacy of acupuncture in these conditions. ‘Within the next 5-10 years, clinicians could be routinely recommending acupuncture as a first-line treatment for fracture-related pain. The use of acupuncture in this circumstance bypasses the common problem of systemic side-effects from oral and topical analgesic agents’.

2. Basic bone biology and pathophysiology of fractures

2.1 Osteoporosis

“Osteoporosis” is a term that encompasses both a risk factor for fragility (low bone density) and a condition of fragility (fractures) (Heaney, 1998). About a third of new fractures come to medical attention, suggesting that, in reality, most are either asymptomatic or have tolerable symptoms. Bone strength is based on bone density and other factors, such as remodeling frequency (bone turnover), bone size and area, bone microarchitecture and degree of bone mineralization. While there is a strong inverse relationship between BMD and fracture risk, the rate of bone turnover is also a risk factor for fracture. Cancellous/trabecular bone is more sensitive to high bone turnover. Rapid bone turnover can disrupt the underlying microarchitecture of bone thus affecting bone strength. Because new bone synthesis is a slower process than bone resorption, rapid bone turnover can lead to an imbalance in bone renewal and to loss of connectivity within the trabeculae. Loss of connectivity irreversibly weakens the structural integrity of the bone and is a more serious
consequence than mere thinning of the trabeculae. Such a weakening of bone microarchitecture has been found in early postmenopausal women (Martin, 2008).

Table 1. Patterns of Complementary and Alternative Medicine (CAM) Use in Osteoporosis Clinic Patients According to the Standard CAM Definition (N=104) (from Mak 2010)

2.2 Fractures
Osteoporotic fractures are frequently referred to as fragility fractures or low-trauma fractures, since they occur with minimal or no trauma. The development of osteoporosis and osteoporotic fractures is multifactorial, with skeletal strength factors, such as low bone density and impaired bone quality, and nonskeletal factors, such as falls, playing important roles. The likelihood of a fracture depends on the type of fall (Nevitt, 1993). Hip fractures in the elderly tend to occur with backwards or sideways falls in which the person is unable to break the fall and lands directly on an unprotected hip (Greenspan, 1994). Elderly people who are thinner or taller are at greater risk of a hip fracture because there is less soft tissue to absorb the impact or because the hip axis is longer (Fitzpatrick, 2002).

3. Pathophysiology of osteoporosis and fracture-related pain
Bone pain is a debilitating form of pain emanating from the bone tissue. For many years, it has been known that bones are innervated with sensory neurons. Yet, their exact anatomy
remained obscure due to the contrasting physical properties of bone and neural tissue (McCredie, 2007). However, until recently, it was not determined what types of nerves innervated which sections of bone (Mach, 2002). The sensations from bone tissue are carried by sensory nerves, which mainly supply the periosteum (outer covering of a bone) and the peri-articular (adjacent to a joint) portions of a bone. The nerve supply is also extensively present in vertebrae, which is the reason why vertebral bone pain is more common. Mechanically-induced pain is elicited when these somatic nociceptors are triggered during a fracture, e.g. vertebral collapse or a fractured hip.

3.1 Osteomalacia and pain
Osteomalacia is a generalized bone condition in which there is inadequate mineralization of the bone, caused by insufficient calcium or phosphate. Calcium absorption from the intestine may be reduced because of a deficiency of, or rarely resistance to the action of vitamin D, or less commonly due to a severe lack of dietary calcium (Thacher, 2011). In adults, osteomalacia starts insidiously as aches and pains in the lumbar (lower back) region and thighs, spreading later to the arms and ribs. The pain is symmetrical, non-radiating and is accompanied by sensitivity in the involved bones, and is invariably accompanied by proximal muscle weakness leading to a typical ‘waddling’ gait and difficulty in transfers and stair-climbing. Due to demineralization bones become less rigid. Pathologic fractures due to weight bearing may develop. Most of the time, the only alleged symptom is chronic fatigue, while bone aches are not spontaneous but only revealed by pressure or shocks. (Eisman, 1988).

3.2 Vertebral fractures and pain
Vertebral fractures — deformities of the vertebral bodies identified with imaging of the lateral spine and characterized according to shape — are the most common manifestation of osteoporosis. These fractures are usually identified clinically when a patient presents with back pain, and a spinal radiograph is interpreted as showing a fracture of a vertebral body, most commonly in the thoracolumbar transition zone or mid-thoracic region (Cooper, 1992). However, in contrast with other fracture types, most vertebral fractures do not come to medical attention at the time of their occurrence. Only one quarter to one third of incident radiographically identified vertebral fractures are clinically diagnosed (Fink, 2005). However, clinical vertebral fractures may cause pain severe enough to require hospitalization (Burge, 2002).
In a recent study of 202 patients with vertebral fractures in a randomised-controlled trial of vertebroplasty versus conservative treatment (Vertos II), more than half of the study patients had pain spontaneously decreasing to bearable levels, with a VAS score lower than 5 thereby precluding inclusion, suggesting spontaneous improvement with time. Despite this, the increased pain relief after vertebroplasty remained significant throughout a year of follow-up. This finding is remarkable, since fracture healing in the control group should be completed within several months. However, some patients in the control group developed chronic back pain, possibly because of non-healing of the fracture, and likely inadequate treatment of the initial pain leading to chronic back pain (Klazen, 2010).

3.3 Hip fractures and pain
A recent prospective study by Mak et al (2011) on 415 patients with hip fractures found that multiple variables exist in determining the amount of analgesia used, being a proxy for the
severity of pain, including hip fracture subtype and operative technique. Unstable pertrochanteric fractures (3-4 part intertrochanteric hip fractures) required more analgesia than stable pertrochanteric fractures (2 part) and subcapital fractures in patients with hip fractures at 24 to 36 hours after hip fracture surgery. This is consistent with the theory that the instability of the hip fracture (both the type of hip fracture, SC or trochanteric, and the number of fracture fragments) is a strong determinant for the amount of pain relief required (Table 2).

Table 2. Analgesia Requirements Following Hip Fracture Surgery According to Hip Fracture Subtypes in 415 Patients (from Mak 2011)

<table>
<thead>
<tr>
<th>Postop Analgesia Usage (mg)</th>
<th>Hip Fracture Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subcapital Unplaced Fracture (n = 39)</td>
</tr>
<tr>
<td>0-4 hours</td>
<td>8.3 (24.3)</td>
</tr>
<tr>
<td>6-12 hours</td>
<td>10.3 (24.8)</td>
</tr>
<tr>
<td>13-24 hours</td>
<td>8.8 (18.3)</td>
</tr>
<tr>
<td>24-36 hours</td>
<td>11.3 (17.1)</td>
</tr>
<tr>
<td>0-36 hours</td>
<td>39.6 (77.6)</td>
</tr>
</tbody>
</table>

* Denotes mean ± standard deviation.

Table 2. Analgesia Requirements Following Hip Fracture Surgery According to Hip Fracture Subtypes in 415 Patients (from Mak 2011)

Dasch et al (2008) reviewed a large cohort of elderly patients with hip fracture (1541) over a 21-month period and noted a large fracture-related hip pain prevalence of 13.4%. Patients often focus on the immediate post-operative clinical phase. These studies have revealed shortcomings in the treatment of pain with the consequence that severe pain both at rest and with motion on the first days after the operation delayed early mobilization of the patient, interfered with participation in physical therapy, and led to longer hospital stays (Morrison, 2003). Furthermore, a strong association was found between severe pain in the immediate post-operative phase and higher levels of motor impairment after discharge from hospital, confirmed by other studies (Cree, 2001; Feldt, 2000). The extent to which a previous hip-fracture can be a causal factor in chronic pain in the hip joint area has not been sufficiently studied. Data published to date suggest a high prevalence of hip pain among people with past hip replacement (Herrick, 2004; Linsell, 2006; Morrison, 2003).

Fracture-related pain was reported more frequently in self-rating interviews than in proxy interviews, consistent with the well-known phenomenon that caregivers tend to under estimate the presence of pain in patients (Lungenhausen, 2005). Overall, the severity of the fracture-related hip pain was characterized by 53.4% of the affected patients as moderate (Grades 1 and 2), and by 46.6% as severe to very severe (Grades 3 and 4). This means that after a hip-fracture operation, an unacceptably large proportion of elderly patients suffer from severe pain post-discharge.

4. Evidence for acupuncture and osteoporosis

Acupuncture is a therapeutic intervention characterized by the insertion of fine, solid metallic needles into or through the skin at specific sites (Burge, 2002; Prather, 2007). Internal disharmony among bodily functions and between body and nature is believed to cause blockage of the body’s vital energy, known as qi, which flows along 12 primary and 8 secondary meridians. Blockage of qi is thought to be manifested as tenderness on palpation.
The insertion of acupuncture needles at specific points along the meridians is supposed to restore the proper flow of qi (Figure 1).

A fundamental concept of Traditional Chinese Medicine (TCM) is qi. This is translated as “intrinsic energy”. TCM theory holds that there are invisible channels of energy (Jing Luo) all over the body. These channels conduct the qi to all parts of the body and are connected to vital organs. Qi assists the various organs and fluids of the body to function correctly (Crompton, 1996). Acupuncture treatment regulates qi that further regulates blood to prevent and treat qi and blood problems and maintain a healthy body.
According to the TCM classic “Nei Jing”, the kidney system comprises the kidney, marrow, bone and brain. In this holistic theory, the kidney controls bones in the body. The relationship between the physiology and pathology of the kidney, marrow and brain is associated with pathways made up of channels and collaterals. According to the Jing Luo theory (the theory of Channels and Collaterals) and differential diagnosis, ‘Foot Shao Yin Kidney’ channel, ‘Foot Tai Yang Bladder’ channel, ‘Foot Tai Yin Spleen’ channel and ‘Foot Jue Yin Liver’ channel are all related. A close relationship exists between the ‘Foot Shao Yin Kidney’ and ‘Foot Tai Yang Bladder’ channels. This relationship, in combination with the role of the kidney, as governing bone and marrow and the path of the Bladder channel through the back and hip areas associate weakness in the back and hips with a kidney problem. This supports the TCM view that the occurrence of bone loss and osteoporosis in the region of the lower back and hips (and a high rate of fractures) are associated with TCM kidney. If acupuncture can improve kidney function then bone density may be improved. (Xu, 2003)

A recent review of 57 systematic reviews on the evidence for acupuncture found that it was effective in osteoarthritis pain, neck and low back pain (Ernst, 2011). However, it cautioned about serious complications after acupuncture which continue to be reported. Many are not intrinsic to acupuncture, but caused by malpractice of acupuncturists. The most frequent complications included pneumothorax, and bacterial and viral infections. In the next section, we review the evidence for acupuncture in the different facets of osteoporosis, namely in acute fractures (the most common of which are vertebral and hip fractures), and then onto its possible benefits for bone health.

4.1 Search strategies
The author identified randomised controlled trials (RCTs) and meta-analyses of acupuncture 25 interventions for fractures and bone health that were published from January 2001 to 26 January 2011 by searching electronic databases (MEDLINE, EMBASE and CINAHL) in the 27 English language. The Cochrane Database of Systematic Reviews was searched up to Issue 2, 2011. Search terms were “osteoporosis”, “fractures”, “bone health” together with “acupuncture”. Searches were limited to RCTs and meta-analyses and participants aged 50 years or older. In the absence of an RCT, *the author* searched for large-scale observational and 31 other relevant studies.

All articles were read independently by two assessors *(JCSM and LM)*. Results and data on 33 study quality were recorded on a proforma developed according to Cochrane Collaboration 34 guidelines for assessment of study quality (Higgins, 2011). Disagreements were resolved by 35 a third, independent assessor and a consensus meeting.

4.2 Acupuncture and vertebral fractures
Data from randomized, controlled trials evaluating the efficacy of pain medications in patients with acute vertebral fracture are lacking, but in practice, non-steroidal anti-inflammatory drugs, analgesics (including narcotics and tramadol), transdermal lidocaine, and agents used to relieve neuropathic pain (e.g., tricyclic antidepressants) are commonly used. Although the pain of acute vertebral fracture typically subsides over the course of several weeks, narcotics are often required temporarily to facilitate mobility and avoid prolonged bed rest (Ensrud, 2011). The data from the VERTOS II study (Klazen, 2010) found
that with acute osteoporotic vertebral fractures who have persistent severe pain, vertebroplasty done at a mean 5.6 weeks after onset of symptoms resulted in quicker and greater pain relief than did conservative treatment, suggesting that the benefits of early targeted treatment.

There were no relevant articles on the efficacy of acupuncture in acute vertebral fractures. However, an RCT of 55 older patients (age > 60) on the efficacy of acupuncture for chronic lower back pain patients versus control (not sham acupuncture) found a significant decrease in the modified Roland Disability Questionnaire (RDQ) at week 6 and 9 for subjects treated with five biweekly courses of acupuncture versus usual treatment.

Given the sparsity of evidence, further high-quality RCTs are required in this area comparing with sham acupuncture.

### 4.3 Acupuncture and hip fractures

Again the literature was sparse in this area. However, we found a useful RCT for the use of auricular acupuncture following a hip fracture. Auriculotherapy, or auricular therapy, or ear acupuncture is a form of alternative medicine based on the idea that the ear is a microsystem with the entire body represented on the auricle, the outer portion of the ear. Ailments of the entire body are assumed to be treatable by stimulation of the surface of the ear exclusively. Barker (2006) conducted a randomized, double-blind, sham control study to determine whether auricular acupressure can decrease not only the level of anxiety but also the level of pain in a group of elder patients with acute hip fracture. For the 38 study patients, patients in the true intervention groups had less pain (F = 28, p = 0.0001) and anxiety (F = 4.3, p = 0.018) and lower heart rate (F = 18, p = 0.0001) on arrival at the hospital than did patients in the sham control group. As a result, the patients in the true intervention group reported higher satisfaction in the care they received during the ride to the hospital. The authors encourage physicians, health care providers, and emergency rescuers to learn this easy, noninvasive, and inexpensive technique for its effects in decreasing anxiety and pain during emergency transportation.

### 4.4 Acupuncture and bone health

The literature search revealed no human RCTs but several small animal based and animal research studies on the use of acupuncture in several parameters of bone health.

#### 4.4.1 Animal studies

Zhang (2006) randomised 24 ovariectomised rats into 3 groups (sham: rats were not ovariectomised), model (rats were ovariectomised) and acupuncture groups) and underwent 16 weeks of treatment. Blood and urine were collected to measure serum osteocalcin (OC) and urinary calcium, phosphorus or deoxyripyridinoline (Dpd). After 16 weeks of treatment, all the rats were killed and their tibiae and femora were removed. The tibiae were used for analyses of bone histomorphometry and the femora for a three-point bending test. The acupuncture group gave significant protection against ovariectomy-related decline on femoral strength in the mechanical test, increased the trabecular bone volume and thickness, lowered the trabecular separation of tibiae and restricted the excretion of phosphorus and Dpd, while promoting concentrations of serum osteocalcin as compared with model rats. These results indicate that acupuncture on the points of Pishu
(BL20) and Shenshu (BL23) may promote bone formation but also suppressed the bone resorption induced by ovariectomised in osteoporotic rats. Chen (2010) assessed the effects of acupuncture on the changes in the histomorphometric and mechanical properties of femurs in senescence-accelerated mice strain P6 (SAMP6). Six-month-old male SAMP6 and SAMR1 mice were allocated to 1 of 4 groups: SAMP6 control group (Pc), SAMP6 non-acupoint control group (Pn), SAMP6 acupuncture group (Pa) and SAMR1 control group (Rc). The Pa group was acupunctured at the Shenshu point (BL23) once daily for 8 weeks. After acupuncture treatment, the decreased serum testosterone level in SAMP6 mice increased markedly, whereas the increased OC concentration declined sharply. The bone histomorphometric and mechanical indexes of SAMP6 mice also improved significantly. The values of trabecular thickness, trabecular bone volume, osteoid volume, mineral apposition rate and bone formation rate in Pa mice increased by 20.4, 18.1, 14.1, 9.9 and 14.7%, respectively, compared with Pc mice. The scores for ultimate force, yield force, elastic stress, ultimate stress and energy to yield force for Pa mice were significantly higher than those of Pc and Pn mice. Acupuncture at BL23 was found effective in promoting bone formation, restoring the amount of bone volume, improving bone architecture and reversing osteoporosis in SAMP6 mice to some degree by enhancing the secretion of testosterone and declining bone turnover.

4.4.2 Human studies
Xu (2005) conducted an eight-month paired cross-over study the effects of three traditional Chinese therapeutic strategies (Tai Chi, acupuncture and Chinese herbal medicine) on bone structure and function to prevent bone loss were evaluated. The effects of these modalities were objectively examined through changes in bone material properties and the biomarkers of bone metabolism. Broadband ultrasound attenuation (BUA), a measure of bone structure and density, velocity of sound (VOS), an indicator of the elastic modulus and the breaking forces of bone as provided by ultrasound parameters, were evaluated. The levels of osteocalcin (OSTN) in serum, a biomarker of bone formation and the levels of pyridinoline (PYR) and doxypyridinoline (D-PYR) in urine, which are bone resorption markers were evaluated as parameters of bone metabolism. Traditional Chinese Medicine diagnosis was also used to measure changes in participants’ symptoms resulting from Tai Chi exercise, acupuncture and herbal treatment. Forty menopausal women who completed treatment and testing were divided into three sub groups; 12 into the Tai Chi exercise group, 14 into the acupuncture treatment group and 14 into the herbal treatment group. The groups were then further divided into treatment and control groups. The sub-group for each treatment underwent a four month regime while the control group maintained a normal lifestyle. Three main acupuncture points in the lower legs, KID 3, SP 6 and ST 36 (kidney, stomach and spleen meridians) were used in accordance with the common pattern of disharmony for each of the fourteen participants. Each of the subjects was treated 32 times by the researcher, twice a week for 16 weeks, the duration of each treatment was 30 minutes. Acupuncture of points KID 3, SP 6 and ST 36 tended to increase BUA 8.8% (p=0.005) when comparing the test results of Groups A+B pre and post treatment. The balance between bone formation and resorption improved, OSTN increased 30.9% (p=0.006) which indicates an improvement in bone formation, D-PYR was reduced by 18.5% (p=0.002) indicating a decrease in bone absorption, when comparing the test results of Groups A+B pre and post acupuncture treatment.
Chen (2010) studied the influence of acupuncture on the quality of life, the reproductive endocrine and bone metabolism of postmenopausal women. A total of 65 women with climacteric syndrome were enrolled and randomly assigned to two groups, thirty-three in the treatment group on whom acupuncture was performed with Shenshu (BL23), Sanyinjiao (SP6) and Guanyuan (CV4) as main acupoints, and thirty-two in the control group who were only medicated with a Chinese supplement (Fufuchun Capsule) for a treatment period of 3 months. A further 28 women with childbearing potential and normal regular menstrual cycle were selected and the reproductive endocrine hormone were tested in the ovulatory period as controls. The levels of serum follicle stimulating hormone (FSH) and luteinizing hormone (LH) of postmenopausal women were higher, and serum estradiol (E2) and testosterone (T) were lower than those of normal women (P<0.01). After treatment, the levels of serum E2 in both groups and T in the treatment group were increased, while in the control group the serum E2 increase was more significant than that in the treatment group (P<0.05), and serum T showed no statistical difference. The levels of serum FSH, LH, osteocalcin, calcitonin, parathyroid hormone and alkaline phosphatase were reduced significantly in both groups after treatment (P<0.05). This result suggests that acupuncture enhanced QOL in postmenopausal women and may regulate the hypothalamic-pituitary-ovarian axis to raise the serum E2 level which may be significant in preventing and curing the osteoporosis in postmenopausal women.

5. Conclusion

Acupuncture is an effective strategy to assist with fracture-related bone pain (hip but not vertebral fractures) with few but several importantly rare side effects such as pneumothorax and infection. Whilst there are currently no high-level of evidence RCTs to suggest the benefits of acupuncture in bone health, there are several small animal and human trials suggesting its benefits in improve bone formation and turnover markers, bone structure and density and increase in estradiol levels in post-menopausal women, and testosterone in rats. Given the sparsity of evidence, however, further high-quality RCTs are required in this area comparing with sham acupuncture.

6. References


Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielliebeen AV, Blenk MC, Venmans A, van Rooij WJ, Schoemaker MC,

An Evidence-Based Review of Acupuncture in Osteoporosis and Fracture-Related Pain


Acupuncture is growing in popularity world-wide. Acupuncture and related techniques are useful tools for treating a spectrum of diseases. However, there are still many areas of controversy connected to it due to the fact that mechanisms of action of acupuncture are not entirely clear. Another debilitating element is the absence of a convincing model of sham acupuncture for a control group in clinical trials. Therefore, there are still inappropriate prejudice and unfamiliarity regarding acupuncture. I hope this book can contribute to guide the advance of this ancient medical art. The reader will here find texts wrote by authors from different parts of the world. The chapters cover strategic areas to collaborate with the consolidation of the knowledge in acupuncture. The main objective is to share elements to make acupuncture more and better offered at health systems worldwide.

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