Safety of acupuncture for osteoarthritis of the knee – a review of randomised controlled trials, focusing on specific reactions to acupuncture

Hitoshi Yamashita, Shoko Masuyama, Kuniharu Otsuki, Hiroshi Tsukayama

Abstract
In order to assess how many reported adverse reactions to acupuncture are truly associated with the physiological mechanisms of acupuncture, we performed a literature review of published RCTs of acupuncture for osteoarthritis of the knee. We searched for reports of RCTs using two data sources: PubMed and Japana Centra Revuo Medicina (Igaku Chuo Zasshi). Of the twelve RCTs located, seven included information on adverse events. No serious adverse events were reported. Joint swelling, local inflammation, haematoma and back pain occurred more frequently in the dummy electroacupuncture or minimal acupuncture group. We confirmed the possibility that many adverse reactions to acupuncture treatment reported in RCTs, at least for the knee OA, are non-specific, and that not all reported events should be attributed to the mechanism of action of acupuncture. It is likely this is also true for RCTs of acupuncture in other conditions, and for prospective surveys on adverse events of acupuncture.

Keywords
Acupuncture, safety, adverse event, randomised controlled trial, systematic review.

Introduction
In this paper, we define 'adverse event' as an unfavourable medical event which occurs during or after treatment regardless of proven causal relationships. This definition is in accord with the definition used in clinical evaluation of drugs. Therefore, adverse events include not only side effects (adverse reactions) caused by the physiological mechanisms of acupuncture, and medical errors caused by the acupuncturist, but also symptoms or accidents in which acupuncture was just suspected as the cause.

Reviewing published case reports on adverse events during or after acupuncture treatment for osteoarthritis (OA) of the knee, there are some serious cases such as Candida arthritis, mycobacteriosis, pseudoaneurysm of the popliteal artery, and necrotising fasciitis in Asian countries. However, assessing safety on the basis of published case reports has some limitations. First, because of publication bias, only rare and serious cases are likely to be published. Secondly, because a case report is basically retrospective, there is a substantial recall bias. Thirdly, because the total number of acupuncture sessions (the denominator needed for calculating incidence) is not known, we cannot know how rarely or how frequently the reported adverse event happens.

Nevertheless, discussions on the safety of acupuncture until recently were generally based solely on retrospective case reports or case series. Since the late 1990s, reports on prospective observational surveys regarding adverse events of acupuncture have been published. These reports confirm that serious adverse events are rare in standard practice if the acupuncture is performed by a competent therapist. The reports also suggested to us that there are some cases of negligent practice which could have been prevented. In other words, acupuncture stimulation is inherently safe, but the safety of the practice depends on the quality of the acupuncturist. This brings us to the fourth limitation in the usual methods of assessing the safety of acupuncture.
Safety

Without a control group, it is difficult to be sure that an adverse event is actually caused by acupuncture, ie by its physiological mechanism of action. By analogy, in interpreting the effectiveness of acupuncture from a controlled clinical trial, the specific effectiveness is considered to be the difference between the effects of real and sham acupuncture. Similarly, we consider that the specific adverse events that can be truly attributed to the physiological mechanism of action of acupuncture are also shown by the difference between the adverse events in real and control groups.

In Figure 1, we present a classification of adverse events reported as a ‘side effect of acupuncture’ or ‘adverse reaction to acupuncture’. The adverse events which are reported as side effects actually include non-specific reactions to penetration of the skin, nocebo effects, spontaneous changes, and other events which have no causal relationship with acupuncture. If we compare the reported adverse effects of real acupuncture with that of control acupuncture, we would theoretically be able to estimate the proportion of specific adverse reactions to real acupuncture. Clearly, the non-specific reactions to skin penetration need to be included when assessing the overall safety of acupuncture. Therefore, in order to assess how many specific adverse reactions to penetration of the skin are included in reported adverse events in prospective observational surveys, we performed a literature review of published randomised controlled trials (RCTs) of acupuncture for osteoarthritis (OA) of the knee.

Methods

We searched for papers on RCT of acupuncture for knee OA, using two data sources: PubMed and Japana Centra Revuo Medicina (Igaku Chuo Zasshi) in November, 2006. Keywords used for PubMed were ‘acupuncture’, ‘electroacupuncture’, ‘osteoarthritis’, ‘knee’, ‘gonalgia’ and ‘gonarthrosis’. Those used for Japana Centra Revuo Medicina were ‘hari (acupuncture)’, ‘hiza (knee)’ and ‘henkei-sei hiza kansetsu-sho (knee OA)’. The type of article was limited to RCT.

We read all the papers located and selected only those which have sham or no treatment as a control group and those which included information on adverse events. We extracted the descriptions regarding adverse events in treating knee OA.

Results

After excluding one paper reporting an RCT on osteoarthritis of any joint,10 one secondary analysis of RCT data already published,11 one report of an RCT comparing unilateral with bilateral treatment,12 and one report of an RCT on knee pain not caused by osteoarthritis,13 we located 12 RCTs for inclusion in the review.14-25 Of those, seven included information on adverse events.14;18;21-25 All papers published after 2003 reported adverse events, while many of the earlier papers and a Japanese domestic paper did not.

In Table 1, we show the extracted adverse events reported in the seven papers. Adverse events already judged to have no causal relationship by the authors of each paper are excluded. Only adverse events in acupuncture, sham, and/or no treatment group are shown. Some papers report local bruise (contusion) or subcutaneous haemorrhage as an adverse event while others did not. Some papers show the number of patients, while others show the number of events. Because of such heterogeneity of reporting style, we did not synthesise the data.

No serious adverse events are reported in the included studies. Some adverse events occurred more often in the control group: joint swelling in a dummy...
Safety

Table 1  Adverse events Reported in RCTs of acupuncture for OA knee

<table>
<thead>
<tr>
<th>First author (Year of publication)</th>
<th>Acupuncture group</th>
<th>Sham or no treatment group (intervention used)</th>
<th>N</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christensen (1992)</td>
<td>3 patients: worsening of pain, nausea, or dizziness</td>
<td>(no treatment)</td>
<td>32*</td>
<td>9</td>
</tr>
<tr>
<td>1 patient: a large haematoma (no sequela)</td>
<td>2 patients: joint swelling (dummy electroacupuncture)</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 patient: vaso-vagal attack</td>
<td>21 patients (reported as 45%): local contusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sangdee (2002)</td>
<td>1 patient: joint swelling</td>
<td>'No side effects... were noted' (acupuncture and medication)</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>21 patients (reported as 45%):</td>
<td>No events (Streitberger needle)</td>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>local contusion</td>
<td>'... did not statistically significantly differ...' (sham acupuncture)</td>
<td>190</td>
<td>189</td>
<td></td>
</tr>
<tr>
<td>6 events: others, such as needleling pain</td>
<td>1 event: local inflammation (minimal acupuncture)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 events: bone pain</td>
<td>10 events: bone pain</td>
<td>18 events: haematoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 events: haematoma</td>
<td>11 events: back pain</td>
<td>8 events: joint lock (minimal acupuncture)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 events: back pain</td>
<td>8 event: joint lock</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 events: joint lock</td>
<td></td>
<td></td>
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</tbody>
</table>

* cross-over study

Discussion

The present literature review suggests that a large proportion of the cases reported as an ‘adverse event’ or ‘side effect’ in uncontrolled case reports and prospective surveys are actually unrelated to the physiological mechanism of action of acupuncture. They might be ‘non-specific’ reactions to penetration of the skin, nocebo effects, spontaneous changes, or events unrelated to acupuncture treatment.

There are some limitations of the safety assessment based on RCT papers. First, because of the small sample sizes compared with large-scale prospective surveys, we may not be able to detect important side effects which occur infrequently. Secondly, because the style for reporting adverse events in acupuncture treatment is not uniform, we cannot conduct meta-analysis in this field. Thirdly, because the acupuncture points used and needling method applied are usually restricted in RCTs, the observed adverse events may differ somewhat from those in daily acupuncture practices. Fourthly, there are some differences in efficacy studies and safety studies. For example, anecdotal evidence from a case report is important in terms of safety assessment because side effects may be induced because of a patient’s idiosyncrasy.

Considering these limitations, we should use multiple research methodologies in assessing the safety of acupuncture: retrospective case reports for detecting the rare side effect, large-scale prospective survey for calculating incidence, and RCTs or a systematic review of RCTs for estimating the proportion of specific reaction associated with the physiological mechanism of action of acupuncture. Needless to say, causal relationship should be carefully assessed in every research methodology. In the present review, we could confirm the possibility that many ‘non-specific’ adverse events that are unrelated to penetration of the skin are reported in RCTs of acupuncture, at least for knee OA. We believe that this may be also true for RCTs of acupuncture for other conditions and for prospective surveys on adverse events of acupuncture.
Safety

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Reference list