Are homeopathic remedies clinically and cost effective in the treatment of migraine and osteoarthritis?

What is an evidence note

Evidence notes are rapid reviews of published secondary clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions and are produced in an approximately 3-month period. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The reports are subject to peer review. Evidence notes do not make recommendations for NHSScotland, however the Scottish Health Technologies Group (SHTG) produce an Advice Statement to accompany all evidence reviews.

Definition

Homeopathy: A therapeutic system founded over 200 years ago that involves treatment using very low dose preparations of various substances selected by matching a patient’s symptoms with the symptoms that those substances produce in healthy people. Homeopaths predominantly prescribe individualised homeopathy selected to treat the patient as an individual rather than treating a particular health condition.

Literature search

A systematic search of the secondary literature was carried out between 22 July 2013 and 24 July 2013 to identify systematic reviews, health technology assessments and other evidence based reports. Medline, Medline in process, Embase, Cinahl and Web of Science databases were searched for systematic reviews.

Key websites were searched for guidelines, policy documents, clinical summaries and economic studies. Websites of organisations related to this topic, for example National Center for...
Introduction

Homeopathy is available to patients in Scotland through primary care where some general practitioners (GPs) have a qualification in homeopathy or patients can ask their GP for a referral to a homeopathic GP. In 2003–2004 an estimated 12% of GPs in Scotland prescribed homoeopathic remedies. Homeopathy is also available to patients at the discretion of local NHS boards through contracts with local homeopaths in the private sector and referral to regional National Health Service (NHS) clinics and the Centre for Integrative Care (CIC) (formerly Glasgow Homeopathic Hospital), based at Gartnavel General Hospital, the latter through a service-level agreement with NHS Greater Glasgow & Clyde. The CIC accepts referrals from all healthcare professionals however GPs are the main source, as shown in Table 1 (ISD Scotland. Personal Communication, 27 September 2013).

On referral to the CIC, patients are seen at an outpatient clinic and, while the centre mainly provides outpatient care, patients with more complex problems may be offered admission to the inpatient unit to undergo assessment.

The CIC is not a therapy-specific service. Even if a referrer requests a particular therapy such as homeopathy the centre provides each patient with an individualised care plan, which may or may not include homeopathy among other integrative therapies. An audit conducted in 2013 showed that around 80% of patients referred to the CIC did receive homeopathy.

NHS provision of homeopathic services is controversial. A House of Commons Committee on Science and Technology report published in 2010 concluded that the NHS should cease funding for homeopathy on the basis that there is no evidence that it works beyond the placebo effect. In Scotland, an estimated £660,000 was invested in homeopathy in 2012 although not all boards provide funding and investment varies widely among those that do. In 2013, the gross ingredient cost for homeopathic preparations dispensed in the community in Scotland was approximately £115,000.

In recent years, individual NHSScotland health boards have begun to review their funding for homeopathy services. In 2010, NHS Highland withdrew financial support for homeopathy services following representations by the Director of Public Health based on insufficient evidence of clinical benefit. In 2012, NHS Lothian conducted a public consultation on the continued provision of homeopathy services, having established that the service cost the board an estimated £240,000 per year. The board took the decision to discontinue funding homeopathy, instead offering patients assessment by their GP, while not ruling out consideration of referral to the CIC in exceptional cases (A McMahon, Director of Strategic Planning, Performance Reporting & Information, NHS Lothian. Personal Communication, 7 May 2014). In 2013, the NHS Lanarkshire Homeopathy Review Group concluded, on reviewing the evidence on therapies provided by the CIC, that there was insufficient evidence of effectiveness to allow the board to continue to support referrals to the centre. NHS Lanarkshire is now conducting a public consultation to inform a decision on whether the board should retain current services or cease new referrals.

Table 1 Referral source and outpatient attendance at the CIC in 2012

<table>
<thead>
<tr>
<th>Referral source</th>
<th>New outpatient</th>
<th>Follow-up/return outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community health service</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>GP</td>
<td>904</td>
<td>6,798</td>
</tr>
<tr>
<td>Consultant at this NHS health board</td>
<td>91</td>
<td>130</td>
</tr>
<tr>
<td>Consultant from another NHS health board</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Self referral</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Other (includes armed forces)</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Dental practitioner</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,031</strong></td>
<td><strong>6,960</strong></td>
</tr>
</tbody>
</table>
Service users have subsequently challenged health boards’ decisions to withdraw funding for homeopathy. NHS Lothian’s decision is under judicial review with a first hearing in June 2014 (A McMahon, Director of Strategic Planning, Performance Reporting & Information, NHS Lothian. Personal Communication, 7 May 2014). Through its appeal process, NHS Highland is currently considering requests from individual patients for referral to the CIC for treatment of migraine and osteoarthritis (N O’Neill, Public Health Scientist, NHS Highland. Personal Communication, 13 August 2013).

This evidence note, undertaken in response to an enquiry from NHS Highland, summarises clinical and cost-effectiveness evidence from published secondary sources comparing homeopathy with placebo or standard therapy for the treatment or prophylaxis of migraine, and for the treatment of osteoarthritis.

**Health technology description**

Homeopathy is a therapeutic system founded over 200 years ago\(^1\). Its first principle is that ‘like should be cured with like’, according to which patients with particular signs and symptoms are treated with homeopathic remedies, or medicines, prepared using substances that produce those same signs and symptoms in healthy people\(^9,11\). Homeopathic medicines can be prepared from a wide variety of substances including plant and animal extracts, minerals and chemicals\(^1,10\). The second principle of homeopathy is that the biological activity of a substance in a solution retains activity after repeated dilution and vigorous shaking (succussion)\(^1,10,11\). Homeopathic remedies are prepared by serial dilution of the substance in water and alcohol usually in steps of 1 in 10 (X) or 1 in 100 (C): for example, 30C potency means that the substance has undergone a series of 30 consecutive dilutions of 1 part medicine to 99 parts water or alcohol\(^1\). The more stages of dilution and succussion the preparation goes through, the more potent it is (for example, a 30C medicine is more potent than a 6C medicine)\(^1\). In higher dilutions the original substance is diluted to a very low concentration such that preparations with the highest potency are unlikely to contain any molecules of the original substance\(^10,11\).

There are two main approaches to prescribing homeopathic medicines, namely classical and clinical\(^10,11\). In classical homeopathy, the practitioner, or homeopath, prescribes a single homeopathic medicine that best corresponds with the presentation (symptoms) and medical history of the individual patient as well as other aspects of their ‘general constitution’\(^10,11\). In clinical homeopathy, the homeopath prescribes one or more homeopathic medicines to treat a particular clinical condition or the most prominent presenting symptoms\(^11-13\). The term complex homeopathy refers to treatment using more than one homeopathic preparation combined in a single medicine, formulated to cover symptomatic variation, to treat patients with the same clinical condition and, therefore, usually prescribed on the basis of a pre-defined indication\(^12\).

Research studies of homeopathy are often categorised according to whether prescribing was individualised to each participant (including individualised prescribing from a limited range of pre-defined medicines) or involved non-individualised prescribing of the same medicine to all participants\(^13\).

**Epidemiology**

**Migraine**

Migraine is a common recurring and temporarily disabling neurological condition with an estimated prevalence among adults in the UK of 15% (7.6% of men, 19.1% of women)\(^14\). Migraine headaches, as defined by the International Headache Society (IHS) diagnostic criteria, are idiopathic (spontaneous, cause unknown) and last for 4–72 hours\(^15\). They are typically of moderate to severe intensity, associated with nausea, phonophobia (sensitivity to sound), photophobia (sensitivity to light) or a combination of these, and aggravated by routine physical activity\(^15\). Migraine headaches are classified as occurring with or without visual or sensorimotor aura (visual disturbance or numbness or tingling)\(^14,15\).

Acute medication options for migraine include analgesics (such as non-steroidal anti-inflammatory drugs (NSAIDs)), anti-emetics and migraine-specific drugs including triptans\(^16\). A range of drugs developed to treat other conditions can be used to prevent migraine.
attacks, including beta-blockers, antiserotonergic drugs, tricyclic antidepressants, NSAIDs, calcium channel blockers and anticonvulsants16.

**Osteoarthritis**

Osteoarthritis is the most common form of arthritis and is caused by degenerative changes in the cartilage and bone of the joints. It is the most common musculoskeletal condition affecting older people, women more than men, and increases with age largely as a result of damage to the joints through ‘wear and tear’17. Osteoarthritis can affect any joint but the most commonly affected are the knee and hip, and joints in the foot, ankle, hand and wrist17. Around a third of people in the UK aged 45 years and over seek treatment for osteoarthritis17. In Scotland, an estimated 83,800 patients aged 45 years and over (52,500 women, 31,300 men) consulted a GP or practice nurse at least once for osteoarthritis in the year 2012–1318. This corresponds to rates per 1,000 population of 16.9 for women and 9.8 for men aged 45–54 years; 36.8 women and 28.2 men aged 54–64 years; 56.1 women and 39.2 men aged 65–74 years; and 70.5 women and 50.4 men aged 75 years and over18.

The main symptom of osteoarthritis is pain, which together with reduced mobility in affected joints can impact on many areas of day-to-day life17. There is no cure therefore treatment aims to ease symptoms and improve quality of life. This can involve exercise and lifestyle changes as well as analgesics and, in severe cases, joint replacement surgery17.

**Clinical effectiveness**

**Migraine**

The literature search identified three systematic reviews published in 201319, 200420 and 199921. All three reviews included the same four placebo-controlled randomised controlled trials (RCTs) published between 1991 and 1997. One of the RCTs was published twice, in 1997 and again, in a different journal, in 2000.

All four RCTs evaluated individualised homeopathy, selected from a choice of six to 60 pre-defined remedies (the trials excluded patients whose condition did not correspond with the pre-defined remedies). None of the systematic reviews differentiated treatment from prophylaxis. Two RCTs reported using IHS criteria to define migraine, one did not define the criteria used, and one RCT used IHS criteria but included patients with tension headaches as well as patients with migraine and did not report results for migraine separately21. Study duration was either 3 or 4 months and, in total, the RCTs included 286 participants for analysis. The systematic reviews used various instruments to assess and score the quality of the RCTs.

All three systematic reviews showed that one RCT found homeopathy to be superior to placebo on all of the outcomes reported, including frequency, severity and duration of pain, whereas the other three RCTs found no statistically significant difference between homeopathy and placebo. The quality of the trials varied. Only one provided an adequate description of randomisation. The reviews consistently indicated that the RCT which reported superior results for homeopathy had the lowest quality score.

One systematic review used meta-analysis to combine results from the RCTs to obtain a pooled estimate of treatment effect that showed no statistically significant difference between homeopathy and placebo (relative risk (RR)=1.58; 95% confidence interval (CI) 0.8 to 3.1; p=0.187)19. The outcome measure used was the proportion of patients assessed as improved in each study (S Saha, Central Council for Research in Homeopathy, Government of India. Personal Communication, 2 May 2014) on the basis that this could be dichotomised19 but whether improvement was defined in the same way in all four studies was unclear.

A recent report of a comprehensive literature search for RCTs of homeopathy found no other relevant placebo or active treatment controlled trials published to early January 201213 and a review of systematic reviews commissioned by the Australian National Health and Medical Research Council (NHMRC) found no other reviews of homeopathy for migraine published in English to January 201322.

**Osteoarthritis**

The literature search identified two systematic reviews published in 201123 and 200124. The more recent review23 was conducted to inform an Arthritis Research UK report on complementary and alternative medicines25, which also drew on evidence from the earlier review. Both reviews
included the same three RCTs published between 1983 and 2000. The earlier review included an additional RCT published in 1998 (a total of four RCTs)\(^24\). Another systematic review published in 2000 was excluded because it only included the osteoarthritis RCT published in 1983 and pooled its results with results from trials in rheumatoid arthritis, fibromyalgia and myalgia\(^26\).

All four RCTs included in the two systematic reviews compared non-individualised homeopathy preparations with alternative treatments for osteoarthritis of the knee (three trials) or hip and knee (one trial). Two trials compared oral homeopathic preparations with paracetamol or fenoprofen (an NSAID); the latter also included a placebo group comparator. One trial compared a topical preparation with topical piroxicam (an NSAID), and one compared a homeopathic preparation administered by intra-articular injection with intra-articular injection of hyaluronic acid (a component of articular cartilage). In total, the RCTs included around 384 participants in the analysis (for one RCT the actual number was unclear) and study duration ranged from 2–5 weeks. Both systematic reviews used the Jadad instrument\(^27\) to assess and score the quality of the RCTs.

The systematic reviews showed that the RCT comparing oral homeopathy with paracetamol found no statistically significant difference in the proportion of patients achieving clinically significant pain reduction. Oral NSAID treatment resulted in significantly better pain relief than homeopathy in the RCT comparing homeopathy with fenoprofen whereas this trial found no difference between homeopathy and placebo. The RCT comparing topical homeopathy with a topical NSAID showed pain reduction in both groups but no statistically significant difference.

The RCT of intra-articular treatment included in one systematic review\(^24\) showed improvement in both groups with no statistically significant difference between homeopathy and hyaluronic acid. The trial found the treatments to be therapeutically equivalent (defined as a difference of no more than 33% in the reduction in pain during active movement after 5 weeks treatment as measured using a visual analogue scale (VAS)) but the systematic review did not provide reassurance that the validity of that finding had been adequately appraised\(^24\). One review gave three of the RCTs a Jadad quality score of 3/5 and one RCT a score of 4/5\(^24\). The other review reported only a median score of 3/5 for the three RCTs that it included\(^23\). This scale is not ideal as it assesses reporting rather than how a trial was conducted and does not include allocation concealment, one of the most important sources of bias in RCTs.

A review of systematic reviews commissioned by the NHMRC found no other reviews of homeopathy for osteoarthritis published in English to January 2013\(^22\). A report of a comprehensive literature search for placebo and active treatment controlled RCTs of homeopathy found no subsequent RCTs published in English to early January 2012, but did identify three RCTs published in German in 2000 and 2002 that were not included in the systematic reviews summarised in this evidence note\(^13\). The English abstracts for these trials indicate that two are reports of the same study, and that both studies compared non-individualised oral homeopathy with NSAID treatment in patients with osteoarthritis of the knee in 121 and 80 patients, respectively.

**Safety**

None of three included systematic reviews of homeopathy for migraine reported on adverse outcomes\(^19\-21\).

One of the two included systematic reviews of homeopathy for osteoarthritis mentioned in its summary of the RCT of intra-articular homeopathy compared with intra-articular hyaluronic acid that fewer patients treated with the homeopathic preparation had adverse effects, but there was no statistically significant difference between the two groups in patient-assessed tolerance (VAS) at the end of the treatment period\(^24\). The same review noted that the RCT comparing oral homeopathy with paracetamol reported that homeopathic treatment had the advantage of fewer unwanted adverse effects, but later stated that the trial made no mention of adverse reactions from either treatment\(^24\).

A systematic review of adverse effects of any type of homeopathy for any condition documented in published case reports and case series, including effects reportedly caused by the substitution of conventional medicine with homeopathy, concluded that homeopathy can lead to adverse
effects with serious consequences\textsuperscript{28}. The review did not however provide sufficient reassurance that the evidence for causality as described in the studies reviewed was sufficiently robust to support the conclusion.

An earlier systematic review of the safety of homeopathic medicines pooled data from clinical trials published in English between 1970 and 1995 to obtain a mean risk of adverse effects of 9.4 for homeopathy and 6.17 for placebo (calculated as the proportion of patients taking homeopathy or placebo with at least one ‘adverse event’ giving a RR of 1.52 (CI not reported)\textsuperscript{29}). It is unclear if this was based on the 19 clinical trials identified that reported on adverse effects, or only the 12 that provided data for both homeopathy and placebo (no denominators were reported). Further, the overall mean values were apparently derived arithmetically, which is not a valid method for pooling data across studies. The review authors noted that the adverse effects reported which could be attributed to homeopathy were mild and transient and included aggravation of symptoms\textsuperscript{29}. Only two of the trials that reported on adverse effects described how the data were collected during the study, and an additional 36 clinical trials identified did not mention safety at all\textsuperscript{29}.

The authors also reviewed adverse effects reported in case reports and case series, and in homeopathic pathogenic trials (also called provings, which are studies designed to determine the effects of a homeopathic medicine by giving it to healthy volunteers and observing the symptoms)\textsuperscript{29}. Most case reports pertained to combination remedies, some judged by the review authors to be mislabelled as homeopathic products, and provided inadequate information to determine causality\textsuperscript{29}. The overall mean incidence of pathogenic effects in the included homeopathic pathogenic trials was 54.3% but each trial tested different medicines, which together with low methodological quality made it difficult to draw reliable conclusions\textsuperscript{29}.

As noted above, it has been suggested that some observed adverse effects of homeopathic remedies could be attributed to aggravations (acute and transient worsening of symptoms on starting treatment), which practitioners see as a good sign that the right treatment has been prescribed\textsuperscript{10}. A systematic review of placebo-controlled RCTs summarised the incidence of reported homeopathic aggravations, as distinct from adverse effects, as described by study authors\textsuperscript{30}. The review included one RCT in migraine in which 17/35 patients in the homeopathy group and 20/33 in the placebo group reported aggravation of symptoms; and one RCT in osteoarthritis of the knee and hip in which one patient in the oral homeopathy group and one in the placebo group dropped out because of symptoms aggravation\textsuperscript{30}. Overall, the review failed to show that homeopathic aggravations occurred more frequently in treatment groups than in placebo groups as reported in RCTs\textsuperscript{30}.

Cost effectiveness

No economic evaluations of homeopathy for migraine were identified.

A systematic review of economic evaluations included a cost-minimisation analysis published in German that appears to have been conducted alongside the aforementioned RCT that compared intra-articular injection of a non-individualised homeopathic preparation with hyaluronic acid for the treatment of osteoarthritis of the knee\textsuperscript{31}. The review states that the analysis was undertaken from a German societal perspective with a 12-month time horizon, but that the report provided insufficient details of the methodology used. The results as summarised in the review put the cost per successfully treated patient at US$2,084 for homeopathy and US$3,242 for hyaluronic acid (change from Deutsche Mark (DM) to Euro on 1 January 1999, 1 Euro=1.95583 DM); results adjusted for inflation rates from publication date (1996) to 2012\textsuperscript{31}. Treatment costs per successfully treated patient were 36% lower for homeopathy injections compared with hyaluronic acid. The study did not report indirect costs (work disability) or direct non-healthcare costs\textsuperscript{31}.

Conclusion

Published systematic reviews of homeopathy for migraine provide limited evidence on clinical effectiveness. The four available RCTs compared different homeopathic medicines with placebo in small numbers of patients. Only one of the four RCTs found homeopathy to be superior to placebo. No RCTs were identified that compared homeopathy with an active treatment control
group therefore the evidence reviewed cannot inform conclusions on the clinical effectiveness of homeopathy compared with standard treatment.

Published systematic reviews of homeopathy for osteoarthritis also provide limited evidence on clinical effectiveness. The four available RCTs compared different homeopathic medicines with different active control treatments variously administered orally, topically or by intra-articular injection in small numbers of patients. One RCT found no difference in pain outcomes between oral homeopathy and paracetamol; another found oral NSAID treatment superior to homeopathy and the latter no different to placebo. A topical homeopathy preparation gave similar pain relief as a topical NSAID in one trial; and in another, an intra-articular homeopathy preparation gave similar pain relief as hyaluronic acid injections.

Published systematic reviews of homeopathy for migraine and osteoarthritis contain very little or no information on safety. Secondary evidence on adverse effects of homeopathy in general highlights the lack of reporting of adverse effects in clinical trials, and the lack of attention to harmful effects in systematic reviews of clinical effectiveness. Systematic reviews to date indicate that published case reports provide insufficient evidence to support reliable conclusions about causality.

This rapid review did not identify any evidence on the cost effectiveness of homeopathy for migraine, and found only one cost-minimisation analysis of one homeopathic preparation for osteoarthritis that is not generalisable to the UK.

The secondary sources reviewed raise important questions about the methodological quality of the research evidence on homeopathy for migraine and osteoarthritis published to date. There is a need for higher quality primary and secondary research to inform decisions on the provision of homeopathy services for specific medical conditions, including those for migraine and osteoarthritis.

**Equality and diversity**

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The evidence note process has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org

**About evidence notes**

This evidence note will be considered for review 2 years post-publication, and at 2-yearly intervals thereafter. For further information about the evidence note process see http://www.healthcareimprovementscotland.org/our_work/clinical__cost_effectiveness/shtg/standard_operating_procedures.aspx

To propose a topic for an evidence note, email evidencenotes.HCIS@nhs.net

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network http://www.knowledge.scot.nhs.uk, or by contacting your local library and information service.
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• Professor Edzard Ernst, Emeritus Professor, University of Exeter, Independent topic reviewer
• Professor Gary MacFarlane, Professor of Epidemiology, University of Aberdeen, Topic advisor
• Dr Robert Mathie, Research Development Adviser, British Homeopathic Association, Independent topic reviewer
• Professor Alex McMahon, Director of Strategic Planning, Performance Reporting & Information, NHS Lothian, Independent topic reviewer
• Rachel Roberts on behalf of the Homeopathy Research Institute, Independent topic reviewer

Declarations of interest were sought from all peer reviewers. All contributions from peer reviewers were considered by the group. However the peer reviewers had no role in authorship or editorial control and the views expressed are those of Healthcare Improvement Scotland.

Healthcare Improvement Scotland development team

• Heather McIntosh, Lead Author/Health Services Researcher
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