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Moxibustion for stroke: Systematic review, meta-analysis, and GRADE-based recommendations

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ABSTRACT

Introduction: Moxibustion is one of the most commonly used interventions in traditional medicine in East Asia, but only few published clinical practice guidelines mention this therapy. This study aimed to systematically review currently available literature and to provide evidence-based recommendations for moxibustion as an adjunctive therapy for stroke.

Methods: PubMed, EMBASE, Cochrane Library, China Knowledge Resource Integrated Database, and two Korean domestic databases were searched from their inception to 25 January 2017 to identify randomised controlled trials. The included trials assessed the effect of moxibustion for neurological deficit or activity of daily living (ADL) in patients with stroke. Meta-analysis from the post-treatment values of the outcome measures and review of all the reported adverse events were performed. The Grading of Recommendations Assessment, Development, and Evaluation Methodology (GRADE) was applied to convert the evidence from the quantitative analysis into recommendations for clinical practices.

Results: Among the 1121 articles searched from the databases, 45 were finally used for meta-analysis. According to currently available evidence, additional moxibustion may be considered to improve the neurological deficit and ADL of patients with stroke.

Conclusion: Moxibustion may be effective as an adjunctive treatment for patients with stroke. Therefore, we recommend to consider moxibustion as an optional intervention to improve neurological deficits and ADL in stroke patients. Further research is warranted to fully reflect the use of moxibustion in real-world clinical practice and include clinical trials with a better methodological quality.

1. Introduction

Moxibustion is one of the most commonly used interventions in traditional medicine in East Asia [1]. Moxibustion is a treatment that warms the acupuncture points of the body using ignited herbal materials, mainly mugwort-made moxa [2]. In recent years, modern types of moxibustion that produce heat using electricity or lasers have also been developed.

According to the theory of the traditional medicine in East Asia, the effect of moxibustion is induced by warming the acupoints and promoting the circulation of the *qi* and blood flow [3]. Recent studies have explained the mechanism of moxibustion as warm-hot (thermal) stimulative effect, radiation effect, or the biological activities of the ingredients of mugwort leaves and moxa smoke [3,4]. In addition, moxibustion is shown to activate the immune system [5] and improve blood circulation [6]. Even though several hypotheses have been suggested as mentioned earlier, the mechanism of this treatment has not yet been completely clarified [3].

Moxibustion has been used in a wide range of diseases traditionally and empirically [7]. The range of diseases targeted by recently published randomized controlled trials (RCTs) of moxibustion is various including neurological, respiratory, gastrointestinal diseases and so on [8]. Several systematic reviews presenting the result from pooling the data of these clinical trials have been published [7,9–19]. Two of the most popular published systematic reviews for clinical application of moxibustion are about correcting breech position [7] and treating knee osteoarthritis [9]. However, the effect of moxibustion on these indications is still controversial [10,11]. Recently, more systematic reviews

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have been published to evaluate the efficacy and safety of moxibustion for various clinical conditions including primary dysmenorrhea [12], chemotherapy-induced nausea and vomiting [13], diarrhea-predominant irritable bowel syndrome [14]. These studies suggested that moxibustion may be a promising intervention for these symptoms or diseases. Other systematic reviews to assess the effects of moxibustion on primary insomnia [15], primary osteoporosis [16], chronic wound [17], hypertension [18], and constipation [19] found no evidence that moxibustion is significantly superior to the control group.

Moxibustion has been frequently applied to stroke, in addition to the above-mentioned clinical conditions. Two systematic reviews are identified on the effectiveness and safety of moxibustion in stroke patients [20,21]. Lee et al. showed that moxibustion is beneficial for improving the motor function of patients with stroke compared with non-moxibustion; however, no difference was found between groups in the improvement of activity of daily living (ADL) [20]. Ma et al. found that moxibustion is significantly effective for patients with stroke and spastic hemiplegia [21]. However, they included only less than 10 Chinese RCTs that have registered patients with stroke who suffered from hemiplegia with spasticity, and this result cannot represent the whole picture of the role of moxibustion for stroke overall.

Several guidelines of traditional medicine for stroke have been published in East Asia. In China, a number of guidelines for ischemic stroke have been published since the 1990s, and they have covered a variety of interventions commonly used in traditional Chinese medicine, including moxibustion [22,23]. However, from the perspective of evidence-based medicine (EBM), these guidelines may not be fully equipped with the latest rigorous methodologies, such as the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [22–24]. In 2013, Hong Kong Hospital Authority initiated a project to develop evidence-based clinical guidelines of traditional Chinese medicine for three major diseases including ischemic stroke [24]. The authority has announced that it will deal with a variety of interventions of traditional Chinese medicine, including moxibustion, but the guideline for stroke is under development [24]. The guidelines that have already been published or are being developed in China and Hong Kong focus more on ischemic stroke than overall stroke.

A number of evidence-based clinical practice guidelines for stroke have been published worldwide, and many guidelines have referred to the intervention of traditional medicine such as acupuncture [25–29]. However, apart from few exceptional cases [28], most of them do not consider interventions other than acupuncture.

Compared to acupuncture, moxibustion has been relatively less studied. In contrast to acupuncture needles that pierce the skin, moxibustion treatment is not invasive. Thus, it may be one of the reasons moxibustion is more applicable in other cultures besides where the intervention originated. Despite of its popularity and potential scalability, evidence-based study on this topic is still lacking.

In South Korea, a research team for the development of a clinical practice guideline of Korean medicine for stroke was established in 2008 and developed a preliminary guideline and recommendations in 2010 [30]. This is the result of reviewing studies on the effect of Korean medicine for stroke published until 2010 and included commonly used interventions such as moxibustion. However, since then a large number of clinical studies have been published, and the guideline did not employ the rigorous methods such as GRADE [31]. The GRADE is a system that provides a transparent, comprehensive and structured process to rate the evidence level and develop recommendations [31].

Therefore, in this study, we aimed to systematically review related evidence including recently updated literature, as well as to provide evidence-based recommendations for moxibustion therapy for stroke based on a rigorous methodology of GRADE.

2. Methods

2.1. Setup of key questions

Three key questions were selected through discussion among authors and other experts who majored in cerebro/cardiovascular diseases in the colleges of Traditional Medicine in Korea.

Q1. Is moxibustion beneficial to improve neurological deficit in patients with stroke receiving conventional medical treatment?

Q2. Is moxibustion beneficial to improve the ADL in patients with stroke receiving conventional medical treatment?

Q3. Is moxibustion safe for patients with stroke receiving conventional medical treatment?

The target participants of the above three questions were patients with stroke receiving conventional medical treatment for stroke care and secondary prevention. Patients with stroke were defined as those diagnosed with stroke based on brain imaging or clinical judgement.

Intervention was defined as moxibustion. This study investigated the use of moxibustion as an adjunct therapy in patients with stroke receiving conventional medical treatment.

Comparison was defined as no moxibustion or sham moxibustion added to conventional medical treatment.

The outcome of the first key question was neurological deficit. The National Institute of Health Stroke Scale (NIHSS) was selected as an assessment tool to evaluate this outcome. The outcome measure for the second key question was determined using Barthel index (BI) or modified Barthel index (MBI). Higher score of both BI and MBI indicate better performance. Moreover, the overall score of the two scales are the same, and the domains are very similar. Therefore, in this study, MBI was regarded as BI for the meta-analysis and the results from the two measurement tools were mixed. To evaluate the safety of the moxibustion, the theme of the third key question, we investigated the reports of adverse events (AEs) from the included studies that have presented the values of the NIHSS or BI for the quantitative synthesis.

2.2. Systematic review and meta-analysis of relevant literature

Based on the evidence-based methodology, we systematically reviewed and meta-analysed related literature to derive recommendations for key questions.

2.2.1. Eligibility criteria for the study subjects

RCTs that have evaluated the effect of moxibustion as an adjunctive therapy for improvement of neurological deficit or ADL in patients with stroke receiving conventional medical treatment were selected. The inclusion criteria were as follows: (a) RCTs that evaluated the effects of moxibustion on patients with ischemic stroke, haemorrhagic stroke, or unspecified stroke (studies involving patients with ischemic stroke as well as patients with haemorrhagic stroke patients, or patients with unspecified type of stroke in the article) and (b) studies that provided the mean and standard deviation of NIHSS, BI or MBI measured after completion of planned treatment. The exclusion criteria were as follows: (a) studies without control group, (b) non-RCTs, (c) non-human clinical studies, (d) studies that investigated the combined effect of moxibustion and other therapies (e.g. moxibustion + acupuncture, moxibustion + herbal medicine, etc.) and (e) studies that did not provide numerical values of predetermined outcome measures

2.2.2. Search strategy

We selected PubMed, EMBASE, Cochrane Library, and China Knowledge Resource Integrated Database as main databases. Oriental Medicine Advanced Searching Integrated System and National Discovery for Science Library were also chosen as representative Korean domestic databases. Each database was searched for articles published from their inception to January 25, 2017. The language was limited to English, Chinese, and Korean. In addition to academic papers published