

EVIDENCE-BASED INTEGRATIVE MEDICINE

Randomized Clinical Trials on Eastern-Western Integrative Medicine for Health Care in Korean Literature: A Systematic Review*

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ABSTRACT **Objective:** To summarize and critically evaluate the evidence for and against the effectiveness of Eastern-Western integrative medicine (EWIM) for health care compared to Eastern medicine (EM) or Western medicine (WM) alone. **Methods:** Systematic searches were conducted on five Korean medical databases. Manual searches were also conducted through nine major Korean medical journals. Prospective randomized clinical trials (RCTs) were included if EWIM was tested for any type of conditions compared to EM or WM. **Results:** There were one hundred forty-one possibly relevant studies were identified, and seven RCTs were included. The risk of bias was high in most studies. The EWIM methods were compared with EM or WM in patients with pain conditions in four studies. These studies showed favorable effects of EWIM on pain reduction in patients with shoulder pain and chronic headache compared with EM, while the other RCTs failed to do so in traffic injury patients. Two studies tested EWIM in patients with Bell's palsy compared with EM and found acute functional improvement. An RCT comparing EWIM with WM in patients with acne showed a significant difference. **Conclusion:** The results of our systematic review suggest that there is limited evidence for the superiority of EWIM over EM or WM in the treatment of pain and acute symptom improvement in patients with Bell's palsy. The evidence from our analysis was limited from the low number of RCTs included and the high risk of bias. Future RCTs appear to be warranted. **KEYWORDS** Eastern-Western integrative medicine, systematic review, randomized clinical trial, Korean literature

The medical system in Korea is regulated by the government and is comprised of two systems: one based on Western medicine (WM) and the other on Traditional Korean medicine (TKM) or Eastern medicine (EM). Only a TKM doctor may prescribe herbal formulas and practice acupuncture based on TKM theory. TKM is an integral part of the national medical insurance system. WM became part of the national insurance system on July 1, 1977, and TKM became part of this system on February 1, 1987^(1,2). This regulation has limited the collaborative treatment of EM and WM for patients. The meaning of integrative medicine in Korea may differ from China, the US or other countries. In Korea, the term, integrative medicine, is used more often to mean a collaborative medical service for one patient.

However, there have been several attempts to combine the two systems together to treat stroke, Bell's palsy, musculoskeletal disorders and pain conditions. Doctors' abilities to ensure a working collaboration are growing to offer high-quality medical service to their patients. However, neither EM nor WM are fully fit for this type of combined health care. This encourages both practitioners to promote Eastern-Western integrative medicine (EWIM). However, there is no evidence for whether EWIM is a better treatment

than EM or WM alone in improving medical service.

Several studies on the effectiveness of EWIM compared with EM or WM alone have been conducted. Most of these studies were led by TKM doctors. The results are contradictory, depending on the conditions and treatment methods. No systematic reviews have attempted to compare EWIM with EM or WM alone. The aim of this systematic review is to synthesize and critically appraise the evidence from randomized clinical trials (RCTs) regarding the effectiveness of EWIM compared with EM or WM alone.

METHODS

Data Sources

We searched five electronic Korean databases

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from inception through September 2010: Korean Studies Information, DBPIA, Korea Institute of Science and Technology Information, KERIS, and KoreaMed. The search terms used were "integrative", "integrative medicine", "Eastern-Western collaborative", "collaborative medicine", "Oriental-Western", "Eastern-Western", or Korean language terms related to Eastern-Western integrative medicine. In addition, we hand-searched nine Korean traditional oriental medical journals: Journal of Oriental Medicine, the Journal of Korean Acupuncture and Moxibustion Society, the Korean Journal of Meridian and Acupoint, the Journal of Oriental Rehabilitation Medicine, the Journal of the Korean Institute of Herbal Acupuncture, the Journal of Korean Chuna Manual Medicine, the Korean Journal of Oriental Physiology and Pathology, the Journal of Korean Oriental Internal Medicine, and the Journal of Sasang Constitutional Medicine (searched from their inception through September 2010).

Study Selection

We included prospective RCTs of any form of EWIM. There were no restrictions on population characteristics. The main outcome measure was the efficacy of EWIM when compared to EM or WM alone. Dissertations and abstracts were included. Hardcopies of all articles were obtained and read in full by two independent reviewers (TYC, BCS).

Data Extraction and Quality Assessment

Data were extracted systematically in a predefined standardized manner according to the condition, interventions, treatment duration, and main outcomes. Quality assessment was conducted using the Cochrane risk of bias criteria: sequence generation, allocation concealment, blinding, attrition bias, selective outcome reporting, and other risk of bias⁽³⁾. The point for evaluator blinding was only given if specified in the text. Discrepancies were resolved through discussion between two reviewers (MSL, BCS) and, if needed, by seeking the opinion of a third reviewer (JIK).

Data Synthesis

We originally intended to conduct a formal meta-analysis. However, the absence of data that was needed for possible pooling prevented us from doing so.

RESULTS

Study Description

Our searches identified 141 potentially relevant

articles, 134 of which were excluded. Seven RCTs met our inclusion criteria⁽⁴⁻¹⁰⁾. The key data are summarized in Table 1. Six RCTs compared EWIM with EM⁽⁴⁻⁹⁾, while two compared EWIM with WM^(5,10). The treated conditions were shoulder pain (two trials)^(4,5), chronic headache (one trial)⁽⁶⁾, traffic injury patients (one trial)⁽⁷⁾, Bell's palsy (two trials)^(8,9), and acne (one trial)⁽¹⁰⁾.

Assessment of Risk of Bias

The risk of bias of the trials was variable. Three of the RCTs had a low risk of bias in the domain of sequence generation methods^(4,5,7). Two RCTs had a low risk of bias in incomplete outcome measures and selection outcome reporting^(4,5). None of the reports described allocation concealment.

Outcomes

Four RCTs tested EWIM on pain conditions versus EM⁽⁴⁻⁷⁾. Two studies compared the effects of EWIM with EM or WM on shoulder pain^(4,5). EWIM reduced pain in both shoulders compared with the EM controls^(4,5) but failed to reduce shoulder pain compared with the WM control⁽⁵⁾. EWIM improves the range of motion compared with EM in patients with chronic shoulder pain⁽⁵⁾. The third RCT showed favorable effects of EWIM on pain reduction in patients with chronic headache compared with EM⁽⁶⁾, while the other RCT failed to reduce the pain or improve the functionality of traffic injury patients⁽⁷⁾.

Two trials assessed the effects of EWIM on functional improvement in patients with Bell's palsy compared with EM^(8,9). Both studies showed significant short-term improvement (after one or two weeks) compared with EM, while they failed to show favorable effects after three, four or five weeks.

One study tested EWIM versus WM in patients with acne and found that EWIM was superior to EM in surrogate parameters of acne⁽¹⁰⁾.

DISCUSSION

The most important finding of this systematic review is that there are very few rigorous trials comparing the effects of EWIM with EM or WM alone. Our systematic review provides evidence that EWIM is more effective than EM in the treatment of pain conditions and acute functional improvement in Bell's palsy. However, the total number of RCTs and the total sample size included in our analysis were too small to draw firm conclusions about the superiority of EWIM.

The risk of bias was high in most of the included

Table 1. Summary of Randomized Clinical Trials Using Eastern-Western Integrative Medicine in the Korean Literature

First author (year)	Design sample size condition	Intervention group (Regime)	Control group (Regime)	Treatment duration	Main outcomes	Intergroup differences	Adverse effect	Risk of bias*
Nam (2007) ⁽⁴⁾	3 parallel 60 women with chronic shoulder pain	(A): EWIM (Nerve block and injection, plus EM, n=20)	(B): EM (AT, n=20) (C): No treatment (n=20)	4 weeks (twice a week, 8 treatments)	(1) Pain (VAS) (2) Constant Shoulder Assessment (3) Shoulder Pain and Disability Index	(1) P=0.012 (2), (3) NS	n.r.	L,U,L, L,L,U
Nam (2006) ⁽⁵⁾	3 parallel 59 patients with frozen shoulder	(A): EWIM (EM plus WM, n=20)	(B): EM (AT, n=22) (C): WM (Nerve block and injection, n=17)	4 weeks (twice a week, 8 treatments)	(1) Global Symptom Improvement –Pain (VAS) (2) Range of motion	(1) A vs. B, P=0.001; A vs. C, NS (2) Abduction: A vs. B, P<0.01; A vs. C, NS; adduction: A vs. B, NS; A vs. C, NS; flexion: A vs. B, P<0.01; A vs. C, P=0.05; extension: A vs. B, NS; A vs. C, NS		L,U,U, L,L,U
Jung (2005) ⁽⁶⁾	2 parallel 92 patients with chronic headache	EWIM (Nerve block plus EM, n=49)	EM (AT, n=43)	8 weeks (twice a week, 16 treatments)	(1) Pain (VAS) (2) Pain (Brief pain inventory)	(1) P<0.05 (2) P<0.05	n.r.	U,U,U, U,U,U
Lee (2007) ⁽⁷⁾	2 parallel 61 traffic injury patients	EWIM [NSAIDs (oral+intramuscular injections), plus EM, n=32]	EM (AT, herbal medicine,herbal injection, physiotherapy and cupping, n=29)	2 weeks (once, daily)	(1) Pain (VAS) (2) Oswestry Disability Index (3) Neck Disability Index (4) Roland	(1)-(4) NS	n.r.	L,U,U, U,U,U
Kwon (2008) ⁽⁸⁾	2 parallel 30 patients with Bell's palsy	EWIM (oral steroids plus EM, n=15)	EM (AT, herbal medicine, and oriental physical therapy, n=15)	4 weeks (AT: 3times per week, oral steroid for 10 days)	Morris Disability Scale House-Brackmann Gross Grading System	NS, after 2,3, and 4 week except after 1 week (P=0.037)	n.r.	U,U,U, U,U,U
Park (2004) ⁽⁹⁾	2 parallel 50 patients with Bell's palsy	EWIM (oral steroid, plus EM, n=21)	EM (AT, Oriental physiotherapy and herbal medicine, n=20)	5 weeks (AT: twice a week, oral steroid daily for 7 days)	Yanangihara's Unweighted Grading System	P<0.05 after 1 and 2 week, NS after 3,4, and 5 week	n.r.	U,U,U, H,U,U
Xing (2009) ⁽¹⁰⁾	2 parallel 20 patients with acne	EWIM (WM plus herbal medicine, n=10)	WM (oral: antibiotics plus vitamin A; ointment: benzyl peroxide, n=10)	12 weeks (once per 2 weeks, 6 treatments)	(1) The number of papule and pustule (2) Inflammatory erythema level (3) Oil sebumeter level	(1) P<0.01 (2) P<0.05 (3) P<0.01	n.r.	U,U,U, U,U,U

Notes: AT: acupuncture; n.r.: not reported; NS: not significant; VAS: visual analogue scales; EWIM: Eastern-Western integrative medicine; EM: Eastern medicine; WM: Western medicine. *Risk of bias (sequence generation, allocation concealment, assessor blinding, incomplete outcome data, selective outcome reporting, and other sources of bias); L: low risk of bias; U: unclear risk of bias; H: high risk of bias

trials. Low-quality trials are more likely to overestimate the effect size⁽¹¹⁾. Most of the RCTs failed to employ patient or assessor blinding. None of the trials used allocation concealment. Trials with inadequate blinding or allocation concealment are likely to have exaggerated effects⁽¹²⁾. Most of the trials had small sample sizes, which reduced the possibility of drawing a meaningful conclusion. No power analysis was included.

One trial suggested positive effects on pain reduction in patients with frozen shoulders⁽⁵⁾. However, the differences in the baseline values of outcomes seemed to affect the significance of results between the groups. The baseline imbalances may lead to erroneous conclusions from the statistical analyses. Moreover, this study used an inappropriate statistical analysis. The effectiveness of EWIM has thus not been convincingly demonstrated.

We highlight some of the difficulties inherent in research on EWIM and offer some suggestions for future research. First, appropriate randomization was described in three trials^(4,5,7), and allocation concealment was not described in any of the RCT trials on EWIM published in the Korean literature. These RCTs are likely to show exaggerated treatment effects. Furthermore, most of the trials have neither adequate sample sizes nor sufficient statistical power, often resulting in negative findings (type II errors). Hence, a more rigorous methodology should be applied to future studies. Second, combining EM with WM may have some adverse reactions. None of the included RCTs assessed the adverse reactions of EWIM. Future studies should include adverse reactions as a key outcome measure.

The nonsignificant results in some trials can be interpreted in several ways. EWIM might be ineffective, the studies may have been inadequately designed, or the treatment may not have been optimally administered in the existing studies. For instance, the number of treatment sessions could have been too small to generate a significant effect, treatment could have been suboptimal, or the protocol applied in the EWIM group might not have been suitable for treating those conditions.

This systematic review has several limitations. Although we attempted to retrieve all relevant RCTs, we cannot be certain that our searches were all-inclusive. In fact, Korean databases may have incorrectly reported results, and there were several early papers missing from the search. Moreover, some acupuncture trials may have been published in journals not listed in any electronic database. The distorting effects arising from publication bias and location bias are well documented⁽¹³⁾. Further problems include the paucity and often suboptimal quality of the primary data.

Future trials testing the effectiveness of EWIM should adhere to rigorous trial designs that are suitable for research. Such trials should preferably be randomized and at least be assessor blinded, have adequate allocation concealment, have sample sizes based on appropriate sample size calculations, use validated outcome measures, and include a full description of the actual interventions being tested. They should also follow CONSORT procedures⁽¹⁴⁾.

In conclusion, the results of our systematic review suggest that there is limited evidence of EWIM's superiority to EM or WM alone in the treatments of pain

conditions, specifically shoulder pain, and the acute symptom management of Bell's palsy. The paucity of the RCTs included in our analysis, coupled with their small sample size and high risk of bias, prevents us from drawing firm conclusions about the effectiveness of EWIM. Future rigorous studies are required to confirm our limited findings.

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