



ORIGINAL ARTICLE

Need for Registration and Reporting of Acupuncture Trials in Parkinson's Disease in Korea

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Objective Many people dealing with Parkinson's disease (PD) turn to complementary and alternative medicine when searching for a cure or relief from symptoms. Acupuncture is widely used in the Korean PD population to alleviate symptoms and in hopes of curing the illness. However, acupuncture use for PD patients has only recently begun to be studied scientifically and is still considered an unproven treatment for PD. Therefore, there is an urgent need for acupuncture to be studied, validated and used for PD. Thus, our study's aim is to examine how many acupuncture studies in PD are registered and reported in Korea.

Methods The registries Clinicaltrials.gov and the Clinical Research Information Service (CRIS) and the search engine PubMed were searched to find relevant human clinical studies involving acupuncture therapy in PD patients. We examined the registration of trials, the posting and publication of results, and whether published articles were registered.

Results In Clinicaltrials.gov, one completed trial was found with published results. In CRIS, one completed trial was found with published results. A total of 6 publications were found in our study: 2 articles were registered, but only 1 had the registered trial number listed in the article.

Conclusion Acupuncture is popular among the PD population in Korea regardless of its unproven safety and efficacy. Despite the pressing need for clinical trials, the number of studies listed in the registries was small, and only a few publications were registered. More effort and rigor are needed to validate the efficacy and safety of acupuncture for PD.

Key Words Acupuncture; Parkinson's disease; Korea; registration; reporting.

Research in the field of acupuncture is steadily increasing, particularly in the field of neurodegenerative disorders. Parkinson's disease (PD) is the second most common neurodegenerative disorder, affecting millions of people worldwide, and currently, no cure is available.^{1,2} With the debilitating motor and neurological manifestations involved and limited options to treat or cure them, patients are allured by what complementary and alternative medicine (CAM) treatments such as acupuncture

can offer.

Acupuncture is one of the most widely used CAM treatment methods in South Korea.³ This was also seen in a study by Kim et al.⁴ where acupuncture was found to be a commonly used form (62.8%) of CAM in patients with PD in Korea. Acupuncture has been practiced for a long time in Asian countries such as South Korea. However, this traditional form of medicine has only recently begun to be studied scientifically from an evidence-based

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medicine perspective. Particularly in South Korea, where the government coverage and regulation of such practices allow people to easily access some of these treatments, it is important to examine the efficacy and safety of its practice. As was discussed in a previous article, side effects are not systematically reported in CAM.⁵ At times, the results of acupuncture can also be dangerous, as was shown in a worrisome incident when an acupuncture needle was removed from one of the lungs of a former South Korean president.⁶

To aid in developing oriental medical science and research, two large organizations, the Korean Oriental Medical Association that was organized in 1952 and the Korea Institute of Oriental Medicine, initiated in 1994 by National Act 4,758, were established.⁷⁻⁹ The Civil Medical Treatment Law in 1951 established a dual system of medical treatment consisting of allopathic and oriental medicine. Thus, the practice of oriental medicine is recognized as a form of medicine by law in Korea. As a result, the Korean national medical insurance system covers the cost of treatments that include oriental medical diagnosis, acupuncture, moxibustion, and 56 different kinds of medicines based on herbal extracts. With the freedom of choice between electing conventional “Western” medicine and CAM, it is important to have accurate data that support the effectiveness and safety of practice in both forms of medicine.

Therefore, there is an urgent need for acupuncture to be studied and the results to become publicly available. In addition, we assessed whether publications regarding acupuncture therapy in PD were registered to examine possible publication bias. Accordingly, we examined the current situation regarding the registration of trials and publications of study results from South Korea involving acupuncture in PD.

MATERIALS & METHODS

Criteria for reviewable studies

Studies of patients with PD were included. Interventions were the use of acupuncture involving the use of electric current and stimulation, needles, or bee venom, while trials utilizing moxibustion were excluded. Analysis and classification were performed on the following: registration of trials, posting and publication of trial results, and whether published

articles were registered.

Search strategy

The following electronic databases were searched: Clinicaltrials.gov, Clinical Research Information Service (CRIS), and Pubmed. Only human clinical trials were included. There were no limitations on trials or articles in terms of start date, completion date or publication date.

Study selection and data extraction

Clinicaltrials.gov

Using the advanced search option in Clinicaltrials.gov, Interventional Studies was set for the Study Type filter. “Parkinson Disease” was searched in the “Condition/Disease” option under Targeted Search. Acupuncture was searched in “Other Terms.” For Korean studies, the “Locations” filter was set to Republic of Korea. To see whether all completed trials did or did not have published result articles, the registration numbers of trials were individually searched on all National Center for Biotechnology Information (NCBI) databases. Any relevant articles were examined manually and matched with trials accordingly.

CRIS

Using the advanced search option on the CRIS website, Interventional Studies was set as the Study Type filter. Acupuncture was searched in the “Scientific Title” search bar. “Parkinson Disease” was searched in the “Condition(s)/Problem(s)” search bar. Since CRIS is a Korean government-run website for Korean studies, no additional filter was set for Korean trials. To see whether all completed trials did or did not have published result articles, the registration numbers of trials were individually searched on all NCBI databases. Any relevant articles were examined manually and matched with trials accordingly.

PubMed

Using the Medical Subject Headings (MeSH) database, “Parkinson Disease” was searched. Additional words added via the PubMed Search Builder were “Korea” and “Acupuncture.” The results were filtered to include only clinical trials. After filtering through all relevant articles, each article was examined by hand, and data were extracted. The reference lists for

the resulting articles were also manually searched, and relevant articles per our methods were included.

RESULTS

Overall, 2 completed trials were found, one from Clinicaltrials.gov (NCT01970813) and the other from CRIS (KCT0001122). Neither had results posted on the databases. Only the completed trial from CRIS had a results article listed on the database.¹⁰ However, it was later found that the trial from Clinicaltrials.gov had published results as well.¹¹ A total of 6 publications were found in our study.¹⁰⁻¹⁵ One of the publications was an additional results publication found by searching all NCBI databases using the registration number for the completed CRIS trial.¹⁵ Thus, two of the published articles were related to the completed CRIS trial.^{10,15} One article was matched to the completed Clinicaltrials.gov trial using the Institutional Review Board (IRB) number.¹¹ One of the 6 articles included the registered trial number within the article.¹⁵

Clinicaltrials.gov

As of July 3, 2017, a total of 1 interventional registered trial (NCT01970813) was identified using our methods. This trial was completed without posted results or listed publication. The search on all NCBI databases using the study's trial registration number yielded no results. A results article was later found during the per methods PubMed search that matched this trial's IRB number,¹¹ but no matching trial registration number was found. However, the trial was registered as a randomized double-blind study with parallel assignment, but the article mentions it as an open-label self-controlled trial (Table 1).

CRIS

As of July 3, 2017, a total of 1 interventional registered trial (KCT0001122) was identified using our methods. The trial was completed without posted results but had a results article under "Study Results and Publication."¹⁰ However, upon examining the article, a matching registration number could not be found. An additional article was found after manually searching through all NCBI databases using the registration number.¹⁵ This additional article listed a registration number that matched that of the completed trial. The study completion date for the trial was not listed on the CRIS website; however, it was last updated May 30, 2014 (Table 2).

PubMed

As of July 3, 2017, a total of 6 articles were found using our methods.¹⁰⁻¹⁵ Three were found through the initial search using the MeSH and the PubMed Search Builder.¹¹⁻¹³ One of these articles was matched to the completed trial (NCT01970813) on Clinicaltrials.gov using the IRB number.¹¹ Two additional articles^{10,14} were found in the reference lists of two^{11,13} of the three articles found in the initial search. The last article¹⁵ was the one found after manually searching through all NCBI databases using the completed CRIS trial's registration number (KCT0001122) and was the only article that included registered trial information. Upon searching the reference list of one article,¹¹ a paper was found that matched that listed as a publication on the CRIS database for the completed trial found in the CRIS search (Table 3).¹⁰

DISCUSSION

Even with the popularity of acupuncture in Korea, there were only 2 clinically relevant trials and 6

Table 1. Clinicaltrials.gov summary

Status	Registration #	Completion date	Results posted	Published article	Article PMID	Article had registered trial info	Published date
Completed	NCT01970813	Nov 2014	N	Y	26230989	N	Oct 2015

N: no, Y: yes, PMID: PubMed Unique Identifier.

Table 2. CRIS study summary

Status	Registration #	Completion date	Results posted	Published article	Article PMID	Article had registered trial info	Published date
Completed	KCT0001122	N/A	N	Y	22943145	N	Sep 2012
Found Article With Trial # on NCBI					25220656	Y	Sep 2014

CRIS: Clinical Research Information Service, PMID: PubMed Unique Identifier, N/A: not applicable, N: no, Y: yes, NCBI: National Center for Biotechnology Information.

Table 3. PubMed summary

PMID	Published date	Registered trial info available in article	Registered trial has article listed	Registered trial number	Comments
26230989	Oct 2015	N	N	NCT01970813	Matched to clinicaltrials.gov completed trial via IRB #
22632852	Sep 2012	N	N	N/A	N/A
19533753	Sep 2009	N	N	N/A	N/A
N/A	Aug 2007	N	N	N/A	J Kor Acup Moxi Article/found in # 3's reference list
Articles linked from CRIS search					
25220656	Sep 2014	Y	N	KCT0001122	Found using registration #
22943145	Sep 2012	N	Y	KCT0001122	Listed on CRIS under "study results and publications"

PMID: PubMed Unique Identifier, N/A: not applicable, N: no, Y: yes, IRB: Institutional Review Board, CRIS: Clinical Research Information Service.

articles on this topic found in the databases. Therefore, it is difficult to assess the efficacy of this treatment modality for PD. Our study has shown the need for further research before any evidence-based conclusions can be made to support acupuncture use for treating PD. Other studies have shown inconclusive evidence to support the effectiveness of such treatment modalities in other neurological disorders.¹⁶⁻¹⁹

Discrepancies between trials and published articles were also found. The completed Clinicaltrials.gov trial (NCT01970813) was registered as a randomized double-blind study with parallel assignment, but the matching article¹¹ describes it as an open-label self-controlled trial. Because of this discrepancy in fundamental study design, it should not be considered as the results of the trial listed in the registry. There were also discrepancies in study design and intervention between the CRIS registered trial (KCT0001122) and the articles.^{10,15} The registered trial includes clinical parameters such as Unified Parkinson's Disease Rating Scale as one of the primary outcomes, which is not mentioned in the articles. This partial reporting of primary parameters may be considered selective reporting.

Acupuncture has a long history in Korea, being used for a variety of neurologic symptoms and disorders. Despite its traditional usage, there have not been many studies that have provided evidence of clinical effectiveness and safety. Many current studies have been deemed to be of poor methodological quality and potentially biased.¹⁶⁻²¹ In fact, one of these studies specifically reviewed the efficacy and safety of acupuncture trials in PD patients.²¹ The details in the usage of these treatments have a long history of being passed down from generation to gener-

ation in a "teacher-disciple" system and have the tendency to be kept secret.²² Since the establishment of university programs and regulation, the teacher-disciple system has lessened. However, the deeply rooted culture makes it especially hard to conduct studies on acupuncture.

Presently, the Oriental Medicine Bureau of the Ministry of Health & Welfare (MOHW) is involved in policy planning, oriental medical systems research, and the administration of oriental medicine. Through licensing, the Bureau also emphasizes quality control in manufacturing and distribution of oriental medicines. An oriental medical policy advisory council was also established in the MOHW. With many people utilizing this form of medicine, it is important for healthcare practitioners and patients to have open access to information regarding trials. With the new guidelines and policies in place, more studies are being registered.^{23,24} While trials are not required by law to be registered in Korea, MOHW requires MOHW trials to be registered to a public registry before enrollment. Thus, it is very likely that trials are still not being registered and results are not being reported. Studies have also shown the potential for reporting bias in acupuncture trials and publications.²⁵ Furthermore, assessment of registration information for acupuncture trials has reinforced the need for methodological design improvements.^{26,27}

There are some limitations to our study. Our study analyzed registered trials, so it might not have included all possible relevant trials. Although words encompassing broad relevant areas were used to maximize inclusiveness, some studies related to PD and acupuncture could have been missed. Furthermore, there were 8 acupuncture trials (5 completed, 1 active but not recruiting, 2 recruiting) in PD patients world-

wide from Clinicaltrials.gov. However, we only examined studies conducted in Korea because we wanted to examine the status in Korea. For this purpose, we also searched the search engine CRIS, which is in Korea. There is a possibility that studies registered in other databases were not included, as we used only two (even though they are deemed to be the most utilized) registries for our searches. PubMed was the only search engine for publication that was searched because it is the most popular engine used by the general public. In fact, we searched the Web of Science after completion of this study but found no additional relevant publications. Lastly, our study was designed not to examine whether acupuncture has any evidence but to show the need for more registered and reported studies to designate its status as evidence-based medicine.

Conflicts of Interest

The authors have no financial conflicts of interest.

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