

Original Article

## 금연에 대한 침술 병용 치료의 효과 및 안전성 : 체계적 검토를 위한 프로토콜

최인서<sup>1, #</sup>, 성원석<sup>2</sup>, 조민기<sup>1</sup>, 김정현<sup>3</sup>, 박연철<sup>3</sup>, 김은정<sup>2</sup>, 백용현<sup>3</sup>, 김근우<sup>4</sup>, 서병관<sup>3, \*</sup>

<sup>1</sup>경희대학교 한의과대학 <sup>2</sup>동국대학교 분당한방병원 침구과  
<sup>3</sup>강동 경희대학교 한방병원 침구과 <sup>4</sup>동국대학교 분당한방병원 한방신경정신과

### The effectiveness and safety of acupuncture combination treatment on smoking cessation: A protocol for systematic review

In Suh Choi<sup>1, #</sup>, Won-Suk Sung<sup>2</sup>, Min-gi Jo<sup>1</sup>, Jung-Hyun Kim<sup>3</sup>, Yeon-Cheol Park<sup>3</sup>,  
Eun-Jung Kim<sup>2</sup>, Yong-Hyeon Back<sup>3</sup>, Geun-Woo Kim<sup>4</sup>, Byung-Kwan Seo<sup>3, \*</sup>

<sup>1</sup>College of Korean Medicine, Kyung Hee University Graduate School

<sup>2</sup>Department of Acupuncture & Moxibustion, Dongguk University Bundang Oriental Hospital

<sup>3</sup>Department of Acupuncture and Moxibustion Medicine, Kyung Hee University Korean Medicine Hospital at Gangdong

<sup>4</sup>Department of Neuropsychiatry, Dongguk University Bundang Oriental Hospital

**Objectives:** Smoking had a long negative impact on public health. The ingredients of a cigarette are major risk factors for several diseases. Owing to the problems about economic and quality of life, we need to ensure smoking cessation (SC). There are several approaches for SC including pharmacological therapy, nicotine replacement therapy, education, and behavioral intervention. However, due to some limitations, other alternative approaches are gaining popularity. Acupuncture has been reported to have few side effects and be more effective than some conventional treatments in several articles. However, there are no systematic reviews on the comparison of acupuncture combination treatment with other conventional monotherapies.

**Methods:** Randomized controlled trials that used acupuncture as an adjunct treatment for SC will be searched and data will be summarized according to the predefined criteria. The primary outcome will be the abstinence rate, and secondary outcomes will be adverse events and biochemical indicators. We will use Review Manager to perform a meta-analysis, Cochrane Collaboration Risk of Bias tool for the risk of bias assessment, and the Grades of Recommendation, Assessment, Development and Evaluation approach to determine the quality of evidence. We will investigate the efficacy and safety of acupuncture combination treatment for SC with this study.

**Ethics and dissemination:** This study will provide reliable clinical evidence on additional effect of acupuncture on smoking cessation. We will publish our results in a peer-review journal.

**PROSPERO registration number:** CRD42022318639

**Keywords** : smoking cessation, acupuncture, adjunct treatment, systematic review, meta-analysis

\* Correspondence to : Byung-Kwan Seo, Department of Acupuncture and Moxibustion Medicine, Kyung Hee University Korean Medicine Hospital at Gangdong, 892, Dongnam-ro, Gangdong-gu, Seoul, 05278, Republic of Korea.

· Tel : +82-31-713-6622 · E-mail : seohbk@hanmail.net

# First author : In Suh Choi, College of Korean Medicine, Kyung Hee University Graduate School, Seoul, 02447, Republic of Korea.

· Tel : +82-31-713-6622 · E-mail : reme2020@naver.com

· Received : 29 May 2022 · Revised : 20 Jun 2022 · Accepted : 25 Jun 2022

## ARTICLE SUMMARY

### Strengths and limitations of this study

- This study will be the first systematic review to evaluate the effectiveness and safety of acupuncture combination treatment for smoking cessation.
- This study will assess more than 10 electronic databases without language limitation.
- We will use credible assessments including risk of bias and GRADE.
- Expected limitations include the possibility of the different quality and the lack of the related studies

## INTRODUCTION

Cigarette smoking is harmful to human health. Nicotine, carbon monoxide (CO), and tar are its main ingredients associated with adverse health effects<sup>1</sup>. Nicotine causes addiction and withdrawal symptoms during periods of abstinence<sup>1,2</sup>. CO increases the possibility of cardiovascular disease and is associated with low birth weight in infants<sup>1</sup>. Tar in tobacco smoke is a carcinogenic and mutagenic agent<sup>1</sup>. Therefore, smoking is a major risk factor for many chronic diseases, including cardiovascular and respiratory diseases and cancer<sup>3</sup>.

The World Health Organization has declared tobacco use a major public health concern globally, and there have been over 7 million deaths related directly related to some form of tobacco use<sup>4</sup>. The United States had approximately 40 million and over 50.6 million adult smokers in 2017 and 2019, respectively,

indicating an alarming increase in the number of smokers<sup>5</sup>. Regarding the economic burden, the United States reported 96.8 billion dollars as the annual productivity loss because of smoking<sup>6</sup>. In South Africa, the economic cost of smoking was 2.88 billion dollars, of which about ~1 billion dollars was the healthcare cost (including outpatient department visits and hospitalization)<sup>7</sup>. Given these data, it is important to ensure that the incidence of smoking reduces globally to improve public health and decrease economic losses.

There are several methods to help quit smoking: pharmacological therapies, such as varenicline, bupropion, and nicotine replacement therapy (NRT), education, behavioral intervention, and hypnosis<sup>3,5</sup>. Particularly, NRT is associated with a 50%-70% increased probability of smoking cessation (SC), at least in the short term<sup>8</sup>. However, 25%-43% of smokers using NRT develop adverse effects, such as skin irritation, gastrointestinal distress, vivid dreams, nausea, heart palpitations, mouth sores, insomnia, and coughing<sup>9</sup>.

Acupuncture for SC has been used in several countries since 1977<sup>5</sup>. Since psychological and behavioral interventions alone cannot easily control withdrawal symptoms, acupuncture helps effectively manage withdrawal symptoms by suppressing the craving for smoking and promotes the clearance of endogenous opioids<sup>5</sup>. In addition, acupuncture offers the advantages of simple operation, few adverse effects, and low cost<sup>3</sup>. Systematic reviews (SRs), including a Cochrane Review on acupuncture monotherapy for SC, comparing other

conventional treatments have been published<sup>3),9-11)</sup>.

Regarding acupuncture combined treatment, several studies reported that auricular therapy as an adjunct therapy in combination with acupuncture treatment achieved better effects on SC than acupuncture monotherapy<sup>12)</sup>, and NRT combined with auricular acupuncture was reported to be safer and more effective than NRT alone<sup>13)</sup>. However, to our knowledge, no SR has been reported on acupuncture used as an adjunct treatment.

Therefore, to our knowledge, this will be the first SR on the comparison of acupuncture combination treatment with other conventional monotherapies.

## MATERIALS AND METHODS

### Study design

This SR was designed according to the Preferred Reporting Items for Systemic reviews and Meta-Analyses Protocols (PRISMA-P) 2015 Statement<sup>14)</sup>.

### Study registration

The protocol was registered in PROSPERO (Registration number: CRD42022318639).

### Eligibility criteria

#### *Participants*

This SR will include participants who aspired to achieve SC. There are no limitations in terms of age or gender but patients who were diagnosed with other addictions will be excluded.

### *Types of interventions*

This SR will mainly include randomized controlled trials (RCTs) that used acupuncture as an adjunct therapy. We will ensure that the use of other treatments alongside acupuncture in the experimental group was consistent with the control group. Regarding acupuncture, studies comparing different stimulation, treatment durations, and acupuncture points will be excluded.

### *Type of comparators*

There is no limit on comparators. Conventional treatments for SC, including medication, NRT, and psychological therapy, will be eligible.

### *Type of studies*

Owing to there being insufficient RCTs on this topic, we will include not only RCTs that investigated the additional effect of acupuncture but also non-RCTs, such as observation studies and pilot studies. Uncontrolled clinical trials including case reports and SR will be excluded, and RCTs that did not provide the randomization method or conducted randomization incorrectly will be excluded as well. There will be no restrictions in terms of the language of publication or the journal.

### *Outcome measures*

Abstinence rate will be the primary outcome measure. Abstinence rates are measured by changes in cigarette consumption, cigarette withdrawal, symptom scores, or self-developed criteria. Adverse events and biochemical indicators will be secondary outcome measures.

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Reported on Page #
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2, 6
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	10
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	10
Sponsor	5b	Provide name for the review funder and/or sponsor	10
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	10
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4-5
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as 6-7 years considered, language, publication status) to be used as criteria for eligibility for the review	7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	7
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	7-8

Study records: Data management	11a Describe the mechanism(s) that will be used to manage records and data throughout the review	8
Selection process	11b State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	8
Data collection process	11c Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8
Data items	12 List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	8-9
Outcomes and prioritization	13 List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	14 Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9
Data synthesis	15a Describe criteria under which study data will be quantitatively synthesised	9
	15b If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	9
	15c Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	9
	15d If quantitative synthesis is not appropriate, describe the type of summary planned	9
Meta-bias(es)	16 Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	9
Confidence in cumulative evidence	17 Describe how the strength of the body of evidence will be assessed (such as GRADE)	9-

Table 1. Search strategy for the Pubmed

No.	Search terms
#1	tobacco cessation [MeSH Terms]
#2	smoking cessation [MeSH Terms]
#3	(tobacco OR cigarette OR Smoke OR nicotine) AND (quit OR stop OR cessation OR cease OR cut down)
#4	#1 OR #2 OR #3
#5	acupuncture
#6	acupoint
#7	dry needling
#8	#5 OR #6 OR #7
#9	#4 AND #8

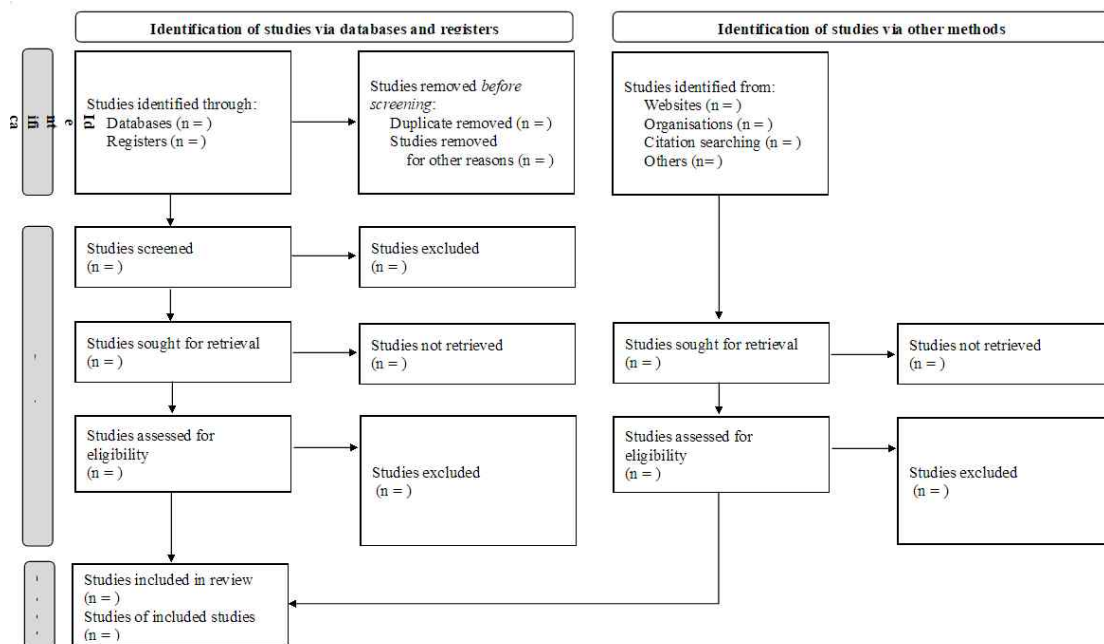
### Information sources and search strategy

The following electronic databases will be used for extracting literature: MEDLINE, EMBASE, Cochrane Library, China National Knowledge Infrastructure, CiNii, J-STAGE (Japanese database), KoreaMed, Korean Medical Database, Korean Studies Information Service System, National Digital Science Library, Korea Institute of Science and Technology Information, and Oriental Medicine Advanced Searching Integrated System. We will search for studies in these databases since databases' inception to August 2022 and use search terms related to SC (e.g., smoking and smoking cessation) and type of acupuncture (e.g., auricular, acupuncture, and acupressure). The search will be performed in accordance with the primary language associated with each database (Table 1). Regarding additional

research, we will perform a manual search of textbooks and sourced studies from the reference lists of retrieved articles. Further, we will attempt to contact the corresponding authors if any additional information is required.

### Study selection

Two researchers will screen and review the studies to determine eligibility for inclusion. During the screening procedure, the relevance of studies will be determined from their titles, abstracts, and full-texts (if possible). After excluding duplicates and irrelevant results, the remaining studies will be reviewed for eligibility by reading their full-texts (Figure 1). Disagreements will be resolved by discussion or mediation with a third reviewer.



**Figure 1. PRISMA flow diagram**

## Data management

Studies will be managed by using Endnote X20.

## Data extraction

Reviewers will extract the information on first author, publication year, patient characteristics, intervention in each group (process, treatment site, and period), outcome measures, results, and study quality. Disagreements will be resolved by either discussion or mediation. If necessary, the corresponding authors will be contacted to obtain missing data. If there is no response, we described this omission in the SR.

## Data synthesis and analysis

We will use Review Manager software (Version 5.3; Copenhagen; The Nordic Cochrane Center, The Cochrane

Collaboration, 2014) for the meta-analysis. The changes from the baseline to the completion of the intervention will be considered. In addition, the mean difference and 95% confidence intervals (CIs) in the same outcome measures and the standardized mean difference and 95% CI in different outcome measures will be calculated to estimate the effect.

Heterogeneity will be determined by Chi-squared and I-squared tests. The interpretation of heterogeneity will be as follows: I-squared: 0-40% unimportant heterogeneity; 30-60% moderate heterogeneity; 50-90% substantial heterogeneity; and 75-100% considerable heterogeneity.

If subgroup analysis is possible, it will be conducted based on the main intervention in the control group. If quantitative synthesis is

not possible, a narrative synthesis will be conducted using the available data. Funnel plots with more than 10 included studies will be applied to assess the publication bias. The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach will be used to determine the quality of evidence<sup>15</sup>.

### Risk of bias assessment

Reviewers will assess the risk of bias independently using the Cochrane Collaboration Risk of Bias tool, which comprises seven domains (sequence generation, allocation concealment, blinding of participants and investigators, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other biases)<sup>16</sup>. Disagreements will be resolved by either discussion or mediation mentioned above.

### ETHICS AND DISSEMINATION

Smoking is one of the most common social problems that lower the quality of life. Although previous treatments have helped achieve SC, there is a need for alternative treatment options. Acupuncture has the potential to serve this purpose, and several studies have been published on the use of acupuncture to achieve SC. However, there is no SR on this to suggest clinical evidence. We hope that our review can help health policymakers, clinical practitioners, patients, and researchers.

### ACKNOWLEDGEMENT

This research was funded by the Traditional Korean Medicine R&D program funded by the Ministry of Health and Welfare through the Korean Health Industry Development Institute (KHIDI) (grant No. HF21C0192). Funder only provided the financial support and did not involve in this article including the review, editing, or the submission for publication.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### REFERENCES

- 1) Calafat AM, Polzin GM, Saylor J, Richter P, Ashley DL, Watson CH. Determination of tar, nicotine, and carbon monoxide yields in the mainstream smoke of selected international cigarettes. *Tob Control*, 2004;13(1):45-51.
- 2) Herman M, Tarran R. E-cigarettes, nicotine, the lung and the brain: multi-level cascading pathophysiology. *J Physiol*, 2020;598(22):5063-71.
- 3) Wang JH, van Haselen R, Wang M, et al. Acupuncture for smoking cessation: A systematic review and meta-analysis of 24 randomized controlled trials. *Tobacco Induced Diseases*, 2019;17:48.
- 4) Dai R, Zhang J, Zhang H, Zhao N, Song F, Fan J. Effect of acupuncture and auricular acupressure on smoking cessation: Protocol of a systematic review and Bayesian network meta-analysis.



- Medicine*, 2020;99(22):e20295.
- 5) Zhang YY, Yu ZY, Lan HD et al. Non-traditional acupuncture therapies for smoking cessation: a systematic review of randomized controlled trials. *European Journal of Integrative Medicine*, 2021;10:101390.
  - 6) Adhikari B, Kahende J, Malarcher A, Pechacek T, Tong V. Smoking-Attributable Mortality, Years of Potential Life Lost, and Productivity Losses. *Oncology Times*, 2009;31(2):40-3
  - 7) Boachie MK, Rossouw L, Ross H. The economic cost of smoking in South Africa, 2016. *Nicotine Tob Res*.2021;23(2):286-93.
  - 8) Zvolensky MJ, Paulus DJ, Garey L, et al. Anxiety Sensitivity and Nicotine Replacement Therapy Side Effects: Examining the Role of Emotion Dysregulation Among Treatment-Seeking Smokers. *J stud Alcohol Drugs*, 2017;78(6):877-83.
  - 9) Dai R, Cao Y, Zhang H, et al. Comparison between Acupuncture and Nicotine Replacement Therapies for Smoking Cessation based on Randomized Controlled Trials: A Systematic Review and Bayesian Network Meta-analysis. *Evid Based Complement Alternat Med*, 2021;2021:9997516.
  - 10) Cheng HM, Chung YC, Chen HH, Chang YH, Yeh ML. Systematic review and meta-analysis of the effects of acupoint stimulation on smoking cessation. *Am J Chin Med*, 2012;40(3):429-42.
  - 11) Chai X, Yang JS, Liu Z, et al. Effect of the different smoking cessation regimens with acupuncture on smoking withdrawal and their influence factors; a multi-center randomized controlled trial. *Zhongguo Zhen Jiu*, 2019;39:1255-61.
  - 12) Hyun S, Huh H, Kang NG. Effectiveness of auricular acupuncture combined with nicotine replacement therapy for smoking cessation. *Tobacco Induced Diseases*, 2018;16:40.
  - 13) White AR, Rampes H, Liu JP, Stead LF, Campbell J. Acupuncture and related interventions for smoking cessation. *Cochrane Database Syst Rev*, 2014;2014(1):CD000009.
  - 14) Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*, 2015;4(1):1.
  - 15) Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations, *BMJ*.2008;336:924-6.
  - 16) Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev*, 2019;10:ED000142.