Research Trends of Acupuncture-Related Therapy on Microbiome in Musculoskeletal Disorders

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In this review, we searched for clinical and experimental studies related to acupuncture-related therapy (ART) on the microbiome in musculoskeletal disorders (MSDs) through the electronic databases of MEDLINE via PubMed, EMBASE, and Oriental Medicine Advanced Searching Integrated System up to May 2023, without language restriction, and after the selection/exclusion process, the study design, target disease, intervention details, treatment period, outcomes, and study results were extracted. A total of 8 articles were selected. Two randomized controlled trials and 6 animal studies evaluated knee osteoarthritis, rheumatoid arthritis, spinal cord injury, ankylosing spondylitis, and osteoporosis. ART, including electroacupuncture, thread-embedding acupuncture, and moxibustion, affected microbiome modulation in MSDs. The results reveal that ART could be a potential treatment for regulating the microbiome in MSDs. However, further high-quality studies are needed.

Keywords: Acupuncture; Microbiome; Musculoskeletal disorders; Research trends

INTRODUCTION

Musculoskeletal disorders (MSDs), medical conditions that can affect the muscles, bones, joints, ligaments, tendons, nerves, and other connective tissues, are one of the most common causes of physical disability and morbidity. The global burden of MSDs, including osteoarthritis (OA), rheumatoid arthritis (RA), and lower back pain, on the healthcare system and individuals has increased significantly [1,2]. MSDs are multifactorial diseases with aging and genetic and environmental components. A recent study reported that intestinal microbiota and its derived metabolites are associated with the initiation and progression of various MSDs, including osteoporosis, OA, and RA [3].

The microbiome is defined as the collection of all microorganisms and their genomes residing in a given environment including the human body [4]. With the development of next-generation sequencing technologies and advanced computational tools, accumulating evidence shows that the microbiome may play a crucial role directly or indirectly in the pathogenesis of various diseases [5]. The interaction between the host and the microbiome is disturbed in Crohn's disease [6]. A study also reported on the interaction between high salt intake causing hypertension and the gut–immune axis and the potential role of the gut microbiome [7]. In addition, several studies have demonstrated that the gut microbiome acts on MSDs by modulating gut permeability, hormonal secretion, immune response, and so on [8].

Acupuncture, the most popular traditional Korean medicine modality, has been effectively and safely used for treating various diseases including MSDs. Some studies have shown that acupuncture not only improves clinical symptoms but also changes the intestinal microflora in various diseases, including poststroke depression [9], cancer-related fatigue [10], irritable bowel syndrome [11], and Crohn's disease [12]. However, no review has reported the effect of acupuncture on the microbiome in MSDs.

Therefore, this study aimed to review the clinical and animal model literature related to acupuncture therapy on microbiome in MSDs and analyze the research trends for further study.

MATERIALS AND METHODS

1. Databases and search methods

A literature search was conducted using the databases of MEDLINE via PubMed, EMBASE, and Oriental Medi-cine Advanced Searching Integrated System (OASIS) up to May 2023. The search terms combined multiple free texts including Medical Subject Headings terms related to microbiome and acupuncture with Boolean operators. The search strategies were also adjusted for each database as appropriate. Language restriction was not implemented.

2. Inclusion and exclusion

This review included both human and animal model studies that have evaluated the effect of acupuncture on the microbiome in MSDs. In clinical literature, the study design was limited to randomized controlled trials. Interventions included all kinds of acupuncture-related therapy (ART), nonpharmacological Korean medicine treatments such as moxibustion, thread-embedding acupuncture, manual acupuncture, and electroacupuncture (EA).

Review papers were excluded; however, in the case of acupuncture review papers on the microbiome, the list of the included studies was reviewed to see if the literature on MSDs was included. Two researchers (JHK and HJY) independently performed the selection of the searched studies for eligibility. After screening the title and abstract to remove obviously irrelevant studies, the full text was examined to confirm the eligibility criteria.

3. Data extraction

Full texts of the selected studies were reviewed, and the author, publication year, study design, disease type, interventions on the treatment and control groups, and microbiome results were extracted according to a predetermined extraction form.

RESULTS

1. Study search results

A total of 490 studies were retrieved from PubMed (n = 144), EMBASE (n = 319), and OASIS (n = 27). After removing duplicates, 303 papers were reviewed after eligibility, and 8 were finally selected for review (Fig. 1).

2. Characteristics of the included studies

By publication year, 1 study was published in 2020, 5 in 2021, and 2 in 2022 among the 8 studies. In addition, 2 articles were human studies, and 6 were animal studies. The characteristics of the included studies and microbiome modulation results are shown in Tables 1 [13,14] and 2 [15-20].

3. Classification by disease type

Among the 8 articles included in this review that evaluated MSDs, 3 studies focused on knee OA (KOA), 2 on spinal cord injury, 1 on RA, 1 on ankylosing spondylitis (AS), and 1 on osteoporosis (Tables 1 and 2).

4. Classification by intervention

Of the 8 studies, 3 studies used EA, 1 used acupoint catgut embedding, and 4 used moxibustion. In 2 clinical trials, EA was performed at ST35, EX-LE5, LR8, GB33 and an ashi point in KOA patients, and moxibustion was applied from DU 14 to DU 2 of governor vessel in AS patients.

5. Modulation on microbiome in human studies

In a randomized controlled trial [13] in which EA was performed on patients with KOA, *Blautia*, *Streptococcus*, and *[Eubacterium]_hallii_group* were significantly in-creased; however, *Bacteroides* and *Agathobacter* were decreased in the KOA group compared with the healthy control group. After 8 weeks of EA, the abundance of KOA-related pathogenic bacteria including *[Eubacterium]_hallii_group* and *Streptococcus* significantly decreased, and the abundance of beneficial bacteria such as *Agathobacter* and *Lachnoclostridium* significantly increased.

Another study [14] investigated the effectiveness of moxibustion on clinical outcomes and the gut microbiome modulation in patients with AS. After moxibustion, various clinical outcomes including bath AS disease activity index and bath AS function index were significantly improved in the AS patients. Furthermore, the abundances of *Bacteroides* and *Prevotella* decreased while those of *Lactobacillus* increased in the gut microbiome.
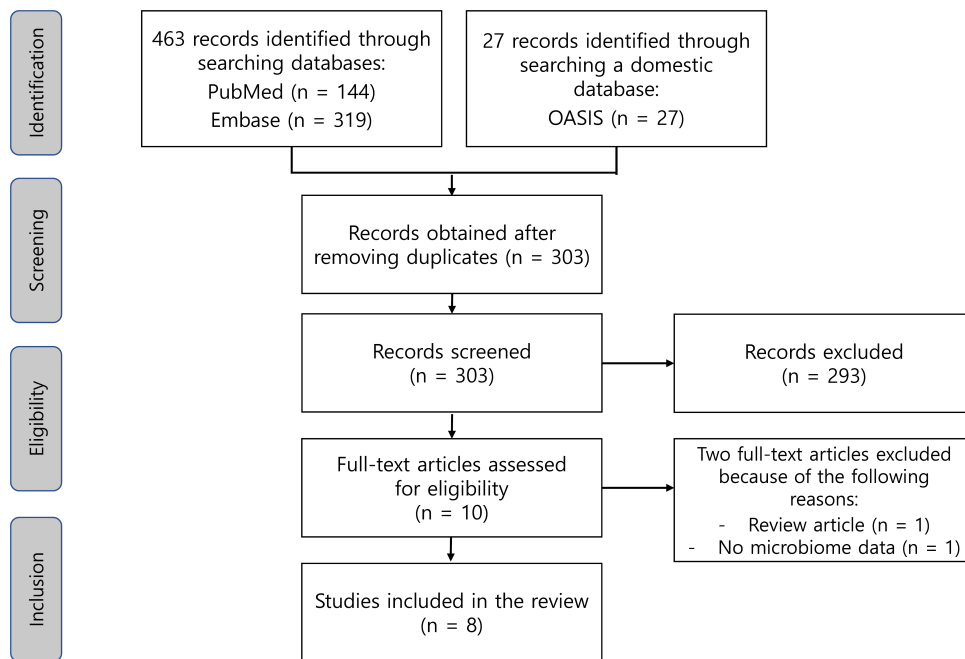

Fig. 1. Flowchart of the study selection process according to PRISMA. OASIS, Oriental Medicine Advanced Searching Integrated System; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Table 1. Characteristics of the included human studies

Study	Study design	Disease	Groups (n)	Intervention duration (wk)	Clinical outcomes	Modulation on microbiome
Wang et al. [13] (2021)	RCT	KOA	EA (30), sham EA (30), healthy (30)	8	WOMAC, NRS, response rate	The abundances of *Bacteroides*, *Agathobacter* increased/*Streptococcus* decreased.
Sun et al. [14] (2021)	RCT	AS	MT (9), healthy (9)	4	BASDAI, BASFI, VAS	The abundances of *Bacteroides*, *Prevotella* decreased/*Lactobacillus* increased.

AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; EA, electroacupuncture; KOA, knee osteoarthritis; MT, moxibustion; NRS, Numerical Rating Scale; RCT, randomized controlled trial; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. Characteristics of the included animal studies

Study	Model	Disease	Intervention type	Intervention duration (wk)	Modulation on microbiome
Xie et al. [15] (2020)	High-fat diet-induced obese rats	KOA	EA	2	Ratio of *Bacteroidetes/Firmicutes* increased. Recovery of the relative abundance of *Clostridium*, *Akkermansia*, *Butyricimonas*, and *Lactococcus* promoted.
Zhu et al. [16] (2021)	Adjuvant arthritis rats	RA	MT	3	Relative abundance of uncategorized *Clostridium*, *Lactobacillus*, and uncategorized *Prevotella* decreased, whereas that of uncategorized *Spironella* increased.
Cheng et al. [17] (2022)	SCI rats	SCI	EA	2	Phylum *Proteobacteria*, class *Clostridia*, order *Bacteroidales*, and genus *Dorea* was reshaped.
Jia et al. [18] (2022)	MIA-induced KOA rats	KOA	MT	2/4/6	The abundances of *Eubacterium coprostanoligenes* and *Ruminococcaceae* UCG-014 increased, whereas that of the *Lachnospiraceae* NK4A136 decreased.
Zhang et al. [19] (2022)	SCI mice	SCI	MT	4	Relative abundance of *Lactobacillales* and *Bifidobacteriales* increased, whereas that of *Clostridiales* decreased.
Shi et al. [20] (2021)	Ovariectomized osteoporotic rats	Osteoporosis	ACE	12	The abundance of *Lactobacillales* (*lactobacillaceae* and *lactobacillus*), *bacillales*, and *Streptococcus* increased.

ACE, acupoint catgut embedding; EA, electroacupuncture; KOA, knee osteoarthritis; MIA, monosodium iodoacetate; MT, moxibustion; RA, rheumatoid arthritis; SCI, spinal cord injury.

DISCUSSION

In recent years, the field of microbiome research is growing rapidly and is becoming a theme of great scientific interest in MSDs [21]. In this review, studies on changing the microbiome after ART in MSDs were selected and analyzed. Among MSDs, acupuncture can effectively regulate the microbiome. KOA is the most frequently studied disease, and the included studies [13,15, 18] showed that EA and moxibustion modulated the structure of the gut microbiome, including *Bacteroides*, *Agathobacter*, *Clostridium*, and *Streptococcus*. Patients with KOA have shown microbial dysbiosis compared with healthy individuals. After EA, the abundance of pathogenic bacteria including *[Eubacterium]_hallii_group* and *Streptococcus* was significantly decreased, whereas the abundance of beneficial bacteria such as *Agathobacter* and *Lachnoclostridium* was significantly increased [13]. The experimental study using KOA rats showed that microbial diversity was lower in diet-induced obesity rats (DIO-KOA) group than in control group, while 2 weeks of EA increased the microbial diversity and altered the structure of the fecal community in DIO-KOA rats. Furthermore, in the DIO-KOA group, the relative abundances of *Akkermansia*, *Clostridium*, *Lactococcus*, and *Butyricimonas* increased, whereas those of *Lactobacillus*, *Streptococcus*, *Ruminococcus*, *Coprococcus*, *Roseburia*, and *Treponema* decreased. After 2 weeks of EA in the DIO-

KOA group, the relative abundance of *Akkermansia*, *Clostridium*, *Lactococcus*, and *Butyricimonas* was recovered, whereas that of *Lactobacillus* increased [15]. Moxibustion applied at ST35 and ST36 in monosodium iodoacetate-induced KOA rats also increased the abundances of *Eubacterium coprostanoligenes* group and *Ruminococcaceae* UCG-014, while decreased that of *Lachnospiraceae* NK4A136 group. Moreover, the 4-week moxibustion was more effective than the 2-week treatment [18].

In addition to KOA, this review showed the effect of ART on the microbiome modulation in various MSDs such as AS, RA and spinal cord injury. However, more studies are needed to draw definite conclusions.

CONCLUSION

Based on 8 studies published up to May 2023, ART including EA, thread-embedding acupuncture, and moxibustion could be potential treatments for regulating the microbiome in MSDs. However, given the insufficient number and quality of studies, well-designed and high-quality research is necessary.

CONFLICTS OF INTEREST

The author has no conflicts of interest to declare.

ETHICAL STATEMENT

This research did not involve any human or animal experiment.

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