



Review Article

Adverse Events of Thread Embedding Acupuncture for the Musculoskeletal Conditions and Diseases: A Narrative Review of Clinical Studies

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ABSTRACT

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This study aimed to analyze the status of adverse events (AEs) in the treatment of musculoskeletal conditions/diseases using thread embedding acupuncture (TEA). Five electronic databases were searched to retrieve data on clinical studies published in the last 5 years (2016 to 2021). Of the 151 studies retrieved, 22 studies analyzed AEs and were selected for this review. There were no AEs reported in 6 studies (27.3%); of the remaining 16 studies, 4 studies (18.2%) reported AEs that were not related to TEA. The most common AEs reported in the Chinese studies were redness of skin with/without swelling and tingling sensation, and in the Korean studies they were stiffness, a foreign body sensation, and bruising. The percentage of patients with AE experience was 5.1% in the Chinese studies and 19.9% in the Korean studies. The discrepancies between the findings in the Chinese and Korean studies may be attribute to differences in the diameter of needles, thread materials, TEA treatment procedure, and evaluation methods for AEs. Most of the reported AEs were of a mild status and did not last for a long time. However, further research on the clinical course after TEA treatment is needed.

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Introduction

Thread embedding acupuncture (TEA) is an acupuncture therapy used to treat various conditions/diseases by inserting medical threads into acupoints for continuous stimulation [1-6]. Various materials such as chromic catgut, polyglycolic acid, polydioxanone (PDO), and catgut are currently used for TEA. The safety of PDO has been demonstrated and it is widely used in the Republic of Korea [1]. In addition, polyglycolide-lactide (PGLA) thread, which has high biocompatibility, biodegradability, and biostability has recently been developed [7] and be used safely and effectively for TEA.

The World Health Organization defines an adverse event (AE) as “any response that is noxious, unintended, or undesired, which occurs at doses normally used in humans for prophylaxis, diagnosis, therapy of disease, or modification of physiological function.” According to the acupuncture moxibustion medicine textbooks used in Korean medicine education, symptoms such as local redness, swelling, pain, and warmth, which appear within 1 to 5 days after TEA, are considered normal reactions [1]; but they can be considered AEs according to the World Health Organization definition. Studies on Korean medicine/traditional Chinese medicine have been published since the 2000s; these have mainly focused on musculoskeletal conditions/diseases, ophthalmology/

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otorhinolaryngology, plastic surgery, and internal medicine. However, most of them were literature review studies, and were clinical studies where sufficient safety evaluation had not been carried out [8,9]. Although various studies have analyzed the research trends related to TEA in Korea, none have analyzed AEs.

In China, TEA has been recognized and developed as an independent form of therapy since the 1980s [10]. Clinical and literature review studies and basic research on various conditions/diseases have been conducted, and the scope of TEA application has continuously expanded through the accumulation of clinical experience. In addition, a study on the independent evaluation criteria for AEs was published to determine the safety of TEA [11]. Although there are studies which report the overall AEs of TEA or AEs related to obesity treatment for example, no studies have been reported on AEs related to the musculoskeletal conditions/disease in China. In this study, in order to investigate the status of AEs reported after TEA for musculoskeletal conditions/diseases, a review of randomized controlled trials (RCTs) on TEA published in domestic and foreign academic journals for the past 5 years (2016 to 2021) was performed.

Materials and Methods

Databases and search methods

Clinical studies on AEs of TEA for musculoskeletal conditions/diseases published from January 2016 to October 1, 2021 were searched. Domestic databases [the Korean Studies Information Service System (KISS), Oriental Medicine Advanced Searching Integrated System (OASIS), and the Research Information Sharing Service (RISS), and foreign databases (PubMed and the China Academic Journal (CAJ))] were used. Keywords “Maeseon,” “thread embedding,” “catgut embedding,” and “acupoint embedding” were used for the domestic literature search; and the same keywords (except for “Maeseon”) were used in the foreign databases.

Inclusion and exclusion criteria

The inclusion criteria: (1) studies related to musculoskeletal conditions/diseases based on the abstract and title; (2) clinical studies, including RCTs, observational studies, and retrospective studies; (3) clinical studies in which TEA was provided as an intervention in the experimental group or control group; (4) studies in which TEA and co-intervention (e.g., acupuncture, moxibustion, herbal medicine, oral medication) were provided to the treatment group; (5) studies in which AEs were analyzed. The exclusion criteria: (1) studies that were not original research; (3) duplicate studies; (4) studies where the full text was unavailable; (5) studies not related to musculoskeletal conditions/diseases; (6) theses; (7) protocol studies; (8) pilot studies; (9) systematic reviews; (10) laboratory research; (11) studies published in nonacademic journals; (12) studies that did not report AEs in the main text.

Study selection

One researcher retrieved candidate articles, and 2 researchers

selected eligible articles independently based on the inclusion and exclusion criteria. After the search, 4 studies were retrieved from KISS, 6 from OASIS, 9 from RISS, 17 from PubMed, and 105 from CAJ. Of the total 151 studies, 29 were duplicates, 4 were not related to musculoskeletal conditions/diseases, 10 were protocol studies, 6 were pilot studies, and 5 were systematic reviews, all of which were excluded. The texts of the remaining 97 studies were reviewed and 22 studies that reported AEs were selected and analyzed.

Data extraction and analysis

Study data including target conditions/disease, intervention description, and occurrence of AEs, was initially extracted by 1 researcher and cross-checked for details and AEs related to intervention by 2 researchers independently. Study characteristics were qualitatively illustrated. Numeric data were summarized as frequency or percentage where appropriate. The percentage of AEs were calculated by dividing the number of patients reporting AEs associated with TEA by the total number of patients treated with TEA.

Results

The overview of selected studies

A total of 151 clinical studies were retrieved from the literature search, and 122 studies were reviewed after excluding 29 duplicate studies. Of these 122 studies, there were protocol studies ($n = 10$), pilot studies ($n = 6$), systematic reviews ($n = 5$), and studies which had conditions/disease inconsistency ($n = 4$) which were excluded. The abstract, title, and full-text of the remaining 97 articles had a full-text review, and 22 studies which reported AEs as part of their protocol were selected, regardless of the occurrence of AEs. Of these 22 studies, 4 studies were conducted in Korea and the remaining 18 studies in China.

The musculoskeletal conditions/diseases in the included 22 clinical studies were lumbar disc herniation (5 studies, 22.7%) [12-16], cervical spondylotic radiculopathy (4 studies, 18.2%) [17-20], chronic low back pain (3 studies, 13.6%) [21-23], chronic neck pain (3 studies, 13.6%) [24-26], ankylosing spondylitis (2 studies, 9.1%) [27,28], rheumatoid arthritis (2 studies, 9.1%) [29,30], and other conditions/diseases (3 studies, 13.6% each) such as acute adhesive capsulitis [31], primary restless legs syndrome [32], and Duchenne muscular dystrophy [33]. There were 10 studies in which TEA was applied as a single intervention in the experimental group, and 11 studies in which TEA was used in a combined intervention, such as adjuvant or synergistic therapy. There were 6 studies (27.3%) which did not observe AEs, 4 studies (18.2%) reported AEs that were not related to TEA treatment, and the remaining 12 studies (54.5%) reported AEs associated with TEA treatment (Table 1).

Details of TEA treatment

The details of TEA conducted in the 12 studies which reported AEs related to TEA treatment are presented in Table 2. The type absorbable suture used was catgut or PGLA in the 18 studies from

Table 1. General Characteristics of Selected Clinical Studies.

Author y [reference]	Condition/disease	Intervention by group (N)	AE (associated with TEA)	Author y [reference]	Condition/disease	Intervention by group (N)	AE (associated with TEA)
Bao 2020 [12]	Lumbar disc herniation	EG: TEA (30) CG: EA (30)	N (N.A.)	Ma 2016 [30]	Rheumatoid arthritis	EG: TEA + WM (30) CG: WM (30)	Y (y)
Cheng 2018 [17]	Cervical spondylotic radiculopathy	EG: TEA (73) CG: AT (73)	N (N.A.)	Naerbuli 2020 [31]	Duchenne muscular dystrophy	EG: TEA + WM (25) CG: WM (25)	Y (N)
Du 2016 [29]	Rheumatoid arthritis	EG: TEA (45) CG: WM (42)	Y (y)	Sun 2016 [14]	Lumbar disc herniation	EG: TEA (60) CG: Sacral canal closure (60)	Y (N)
Gui 2017 [21]	Chronic lumbar muscle strain	EG: TEA (63) CG: AT + Moxa (63)	Y (y)	Sung 2020 [23]	Chronic low back pain	EG: TEA + AT (19) CG: AT (19)	Y (N)
He 2019 [18]	Cervical spondylotic radiculopathy	EG1: deep layer TEA (52) EG2: middle layer TEA (52) CG: sham TEA (51)	Y (y)	Wang 2016 [26]	Neck pain due to cervical spondylosis	EG1: TEA (35) EG2: AT + sham TEA (35) CG: AT (35):	Y (y)
Huang 2020 [22]	Chronic non-specific low back pain	EG: TEA + AT (46) CG: AT (46)	Y (y)	Yue 2018 [15]	Lumbar disc herniation	EG: warm needle Moxa + TEA + WM† (39) CG: WM* (39)	N (N.A.)
Jiang 2021 [31]	Acute adhesive capsulitis	EG: TEA + TDP (30) CG: AT + TDP (29)	Y (y)	Zhang 2019 [32]	Primary restless legs syndrome	EG1: TEA + WM + EDU (10) EG2: TEA (10) EG3: WM (10) CG: EDU (10)	N (N.A.)
Kim 2019 [24]	Chronic Non-specific neck pain	EG: TEA + usual care (51) CG: usual care (53)	Y (y)	Zhang 2021 [19]	Cervical Spondylotic radiculopathy	EG: TEA + nerve block (35) CG: nerve block (35)	Y (N)
Kim 2021 [25]	Chronic non-specific neck pain	EG: TEA (64) CG: ICT + Hot pack (64)	Y (y)	Zhang 2018 [16]	Lumbar disc herniation	EG: TEA (20) CG: EA + TDP (20)	N (N.A.)
Lim 2016 [13]	Lumbar disc herniation	EG: Combination treatment of Korean Medicine including TEA (10) CG: N.A. (retrospective study*)	Y (y)	Zhao 2019 [20]	Cervical spondylotic radiculopathy	EG: TEA (45) CG: AT (45)	N (N.A.)
Ma 2021 [27]	Ankylosing spondylitis	EG: TEA + HM (46) CG: WM (47)	Y (y)	Zhao 2021 [28]	Ankylosing spondylitis	EG: TEA + Moxa (53) CG: TEA (53)	Y (y)

* Except for this retrospective review, all other clinical studies are RCTs.

† Non-steroidal anti-inflammatory drugs and intravenous infusion of osteopeptide injection

AE, adverse event; AT, acupuncture treatment; CG, control group; EA, electroacupuncture; EDU, education; EG, experiment group; HM, herbal medicine; ICT, interferential current therapy; Moxa, moxibustion; N, no; N.A., not applicable; Y, yes; TDP, Tending Diancibo Pu; TEA, thread embedding acupuncture; WM, western medication.

China and PDO in the 4 studies from Korea. The suture size varied from a United States Pharmacopeia's classification size of 0 to 6-0 mm, and the guide needle had a diameter of 0.3-0.9 mm, and a length of 25-65 mm. The most common embedding points were acupoints or tender points around the symptom site (especially, EXB2 points in spinal conditions/diseases), and in 9 studies (75.0%), individualized embedding points were also used to enhance the

therapeutic effect through systemic action and synergy with other fixed points. The frequency of TEA treatment was once every 1 to 2 weeks, and a total of 2 to 4 sessions were conducted, except for studies including ankylosing spondylitis (12 sessions [17]) and rheumatoid arthritis (6 sessions [20]).

Analyses of AEs associated with TEA treatment

In the 9 studies conducted in China, the most common AEs reported were redness of skin with or without swelling, followed by a tingling sensation, and other AEs included itching, hematoma, soreness, induration, local bleeding, and a strong needling sensation. In 3 studies, the progress of the AE was not reported, and in 2 studies, ointment application [19], and bloodletting therapy with acupuncture [18] was performed at the symptomatic sites. There were 4 studies which reported that the AEs improved within 3 days without any treatment (Table 2).

The most common AEs in the Korean studies ($n = 3$) were stiffness, sensation of a foreign body, bruising, irritation, skin flare, pruritus, and pain exacerbation. One severe AE reported was a pneumothorax which was iatrogenic (due to the inexperience of the operator rather than TEA) but was resolved following hospitalization [15]. One AD was thread protrusion after the embedding therapy however, the participant had received an intense massage over the treated area [14].

The average rate of AEs in the studies using catgut or PGLA sutures was 5.1% (10.0% was the maximum rate). In the studies that reported the use of PDO sutures, the average rate of AEs was 19.9% (22.6% was the maximum rate), except for 1 study [2], in which all participants reported a transient foreign body sensation that disappeared within 48 hours.

Discussion

In this study, the AEs of TEA were reviewed for musculoskeletal conditions/diseases. Clinical studies published within the past 5 years which reported the safety and efficacy of TEA for musculoskeletal conditions/diseases were retrieved from national and international databases. Of the 22 selected studies, 12 (54.5%) reported AEs associated with TEA treatment. In the Chinese studies, the most common AEs were skin redness with/without swelling, followed by foreign body sensation, and itching, and in the Korean studies, stiffness, followed by foreign body sensation, and bruising were common. Most of the AEs recovered spontaneously without any treatment, and most events lasted less than 3 days. All AEs lasting more than 7 days were observed in studies conducted in Korea [24] and included stiffness and bruising, which also recovered without specific treatment. There was 1 serious AE, a pneumothorax, which was not due to the nature of TEA treatment, but was attributed to the inexperience of the operator; the pneumothorax resolved after appropriate inpatient treatment.

The differences between TEA and conventional manual acupuncture are that in TEA, the puncture is performed with a guide needle and there is continuous stimulation after the procedure due to the sutures embedded in the acupoints. Clinically, needle insertion causes greater pain during and after TEA compared with manual acupuncture, which may be due to the greater damage to soft tissues caused by the thicker needle used for TEA treatment. The studies included in this review also showed that the diameter of the TEA needles used in the Chinese studies ranged from 0.6-0.9 mm, and those used in the Korean studies ranged from 0.3-0.4 mm. In addition, various kinds of postoperative discomfort, such as

foreign body sensation, itchiness, and tingling sensation occurred. This is possibly due to the stimulation of the soft tissue and the nerve periphery by the embedded suture.

There were some differences in the types of AEs that occurred in the Chinese and Korean studies; Firstly, these were differences due to the needle type and treatment procedures used in each country. Based on the analysis of the studies in China, thicker needles were used to embed the thread and they were inserted perpendicular to the skin in most cases. In Korea, thinner needles were used and diagonal or horizontal insertions were performed more frequently. This difference in treatment procedure may be the reason for redness and bleeding being the most common symptoms reported in the Chinese studies, and stiffness being the most common AE in the Korean studies. Excluding 1 retrospective study [13], the proportion of patients reporting AEs associated with TEA in the Korean studies was 19.9% on average, which was higher than in the Chinese studies (5.1% on average). Secondly, differences in the types of AEs that occurred may be considered to be due to differences between the evaluation methods for AEs in the studies of the 2 countries. In a Korean retrospective study of patients with herniated lumbar discs [13], the rate of AEs was 100% because all patients experienced mild stiffness after the embedding therapy. Considering the RCT [24] where the proportion of patients who complained of AEs was 22.6%, multiple responses were collected for all AEs that occurred. In addition, the level of stimulation induced by the embedded threads in this RCT may have been too strong due to the large number of embedding points. Therefore, when designing TEA clinical trials, the proportion of individualized embedding points could be increased using the acupoint pool, which the practitioners chose according to the patient's symptoms, and reduce the number of fixed embedding points to obtain an appropriate level of stimulation. This strategy was confirmed by the proportion of patients who reported AEs, which was reduced from 22.6% to 17.2% [25].

Furthermore, the risk of under-reporting AEs in clinical studies cannot be excluded, and there is a concern that the intervention may be evaluated as safer than it actually is [34]. There is a possibility that AEs were underestimated not only in the studies included in this review but also in the 75 studies excluded from the study selection process, so caution is required in interpreting the analysis of this study.

Presently, the AE reporting system is inappropriate for reporting the details of AEs occurring post-TEA treatment [35-37]. This is because, in the case of TEA, treatment is not completed immediately after the procedure because the treatment effect is achieved through continuous stimulation induced by the embedded thread. Clinically, patients with chronic pain feel that the pain and discomfort caused by the insertion procedure is more bearable than their own conditions/disease [38]. Therefore, if the researcher guides the participant to report unbearable discomfort, the number of reports of AEs will be limited, whereas if the participant is instructed to state all AEs that occurred, the number of AEs reported may be higher. In future clinical research, all AEs should be collected and analyzed so that the clinical course post-TEA treatment can be studied, which will provide useful information on the expected course of AEs to both, the patient, and the

Table 2. Intervention and Adverse Events Associated with Thread Embedding Acupuncture.

Author y [reference]	Condition/disease	TEA treatment				Adverse event (number of occurrence); progress	‡AE
		Thread (USP)	Needle diameter (length)	Acupoint	Frequency (# of sessions)		
Du 2016 [29]	Rheumatoid arthritis	Catgut (0)	N.R.	* BL23, BL18, BL11, BL20 † LI4, TE3, SI3; TE4, LI4, TE5; LI11, LI10; LI15, TE14, LI14; SP10, ST34, EX-LE2; BL60, GB40, KI3; LR3, ST43	1x/2 wk (4)	× Redness & swelling (2); reduced after application of erythromycin ointment	4.4%
Gui 2017 [21]	Chronic lumbar muscle strain	Catgut (N.R.)	0.9 mm (N.R.)	* BL23, BL25, BL58, BL60 † Ashi-point	N.R.	× Local bleeding (N.R.); stopped after administration of dry cotton ball	Unknown
He 2019 [18]	Cervical spondylotic radiculopathy	PGLA (N.R.)	0.3 mm (40 mm)	* EX-B2 (C5, C6) † TE5, GB34, BL60, SI3, LI4, ST44, LR3, GB40	1x/wk (3)	× Tingling sensation (6); recovered without any treatment	5.7%
Huang 2020 [22]	Chronic non-specific low back pain	Catgut (N.R.)	N.R.	*† Sensitive tender points selected from EX-B2 (L1-5)	1x/2 wk (4)	× Mild back itching (1); disappeared without any treatment	2.2%
Jiang 2021 [31]	Acute adhesive capsulitis	Catgut (N.R.)	0.6 mm (N.R.)	* LI15, SI9, Jianqian, GB34, Zhongping † Local Ashi-point 1-2	1x/wk (2)	× Hematoma (1); N.R. × strong needling sensation (2); tolerable	10.0%
Kim 2019 [24]	Chronic non-specific neck pain	PDO (6-0)	29 gauge (25 or 38 mm)	* GB21, SI14, GB20, BL10, TE16, LI17 † EX-B2 (C2-T3), local Ashi-point 0-2	1x/wk (4)	× Stiffness (10), bruise (2), irritation (2), skin flare (1), pruritus (1); self-recovery × thread sticking out from skin (1); removed by a research clinician	22.6%
Kim 2021 [25]	Chronic non-specific neck pain	PDO (6-0)	29 gauge (30 or 40 mm)	*† 4-8 points per side from acupoints pool (SI12, SI14, BL10, BL11, BL12, TE15, TE16, LI17, GB20, GB21, EX-B2)	1x/wk (4)	× Stiffness (3), bruise (6), pain (2), edema (1), Pricking (1), irritation (1); self-recovery × pneumothorax (1); recovered after hospitalization	17.2%
Lim 2016 [13]	Lumbar disc herniation	PDO (5-0, 6-0)	27 gauge (30/40/60 mm) 29 gauge (40 mm)	* BL23, BL24, BL25, BL26 on both sides † acupoints from BL/GB meridian of affected leg	1x/wk (1-4)	× Mild sensation of foreign body (10), lower leg spasm (1), pain exacerbation (1); self-recovery	100%
Ma 2021 [27]	Ankylosing spondylitis	Aatgut (5-0)	N.R.	* EX-B2 (T1, T9, T11, L2, L4) † None	1x/wk (12)	× Skin rash (1); N.R.	2.2%
Ma 2016 [30]	Rheumatoid arthritis	Catgut (0)	0.9 mm (N.R.)	* ST36, BL23 † None	1x/15 d (6)	× Redness & swelling (3); recovered without any treatment	10.0%
Wang 2016 [26]	Neck pain due to cervical spondylosis	PGLA (2-0)	0.9 mm (N.R.)	* EX-B2 (C5-6, C6-7), GV14 † None	1x/wk (3)	× Soreness & pain (N.R.); N.R.	Unknown
Zhao 2021 [28]	Ankylosing spondylitis	Aatgut (2-0)	0.9 mm (65 mm)	* GV14, GV4, BL17, BL22, CV6, CV4 † 2-3 tender points from EX-B2	1x/2 wk (4)	× Induration (1); disappeared 1 wk after acupuncture and bloodletting therapy	0.9%

‡ Number of patient reporting AEs associated with thread embedding acupuncture / total number of patients treated with thread embedding acupuncture.

* Fixed points, † Individualized points

AE, adverse event; N.R., not reported; PDO, polydioxanone; PGLA, polyglycolide-lactide, TEA, thread embedding acupuncture; USP, United States Pharmacopoeia monographs.

practitioner. For example, Feng et al [39] reported the course of an AE over time, and Kim et al [24] and Kim et al [25] reported the duration of each AE.

The findings of this review showed that, since most of the AEs were mild, self-healing, and short-term, TEA treatment may be considered safe. However, considering that there is a high possibility of heterogeneity between studies in the collection system for AEs, and because the information on the progression of the AEs is insufficient, more in depth studies are required in the future. In addition, this study not only reported the target conditions/disease and study design of the clinical studies, but also reported the type and size of the thread, the thickness of the needle, the embedding points, and the treatment interval and frequency. However, the effect of each component of TEA treatment on AEs could not be determined, and this also warrants further research.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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Ethical Statement

This research did not involve any human or animal experiment.

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