

Japanese Acupuncture - Current Research

Japanese Traditional Medicine Text (11) – Acupuncture and Moxibustion Therapy for Rheumatoid Arthritis and Connective Tissue Diseases

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A. Introduction

Chronic inflammatory diseases as represented by rheumatoid arthritis (RA) have conventionally been considered indications of acupuncture and moxibustion therapy. According to a national basic health survey, approximately 80% of RA patients make regular visits to a masseur, acupuncture clinic or judo therapy clinic in addition to a medical institution. Even in today's society where clinical practice guidelines are centered on pharmacological treatment, patients with diverse complaints make visits to such abovementioned clinics seeking acupuncture and moxibustion therapy. This section will thus discuss the roles and possibilities of acupuncture and moxibustion therapy by introducing summaries of references, and particularly clinical studies, on the effectiveness and present status of acupuncture and moxibustion therapy with regard to rheumatoid arthritis and connective tissue diseases.

1. Collecting references

The Igaku Chuo Zasshi web database of the Japan Medical Abstracts Society (1983-2009) was used to collect all relevant Japanese references, excluding conference minutes. Western references were collected using PubMed and specifying "randomized controlled trial" and "clinical trial" as the research design. The search terms that were used included the following: acupuncture, moxibustion, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), polymyositis (PM), dermatomyositis (DM), systemic sclerosis (SSc), mixed connective tissue disease (MCTD), Behçet's disease (BD), vasculitis syndrome, Still's disease, Sjogren's syndrome (SjS), ankylosing spondylitis

(AS), antiphospholipid antibody syndrome, and Felty's syndrome. Osteoarthritis and fibromyalgia were excluded from the definition of connective tissue diseases. The results were then analyzed with regard to four items: (1) Conditions of subject-patients (disease activity and functional disorders), (2) method of acupuncture and moxibustion therapy, (3) evaluation method, and (4) effects.

2. Results

The search through the Igaku Chuo Zasshi database yielded the following results: 54 references on RA, 5 on SjS, 3 on SSc, 2 on SLE, 2 on BD, 2 on PM/DM, 1 on AS, one on MCTD and one on premature RA. RA accounted for more than 80% of all connective tissue diseases. The search of overseas references in MEDLINE yielded the following results: 42 references on RAs, 3 on AS, 3 on SSc, 2 on SjS, 2 on SLE, and 1 on BD. Again, many results tended to be acquired for RA. Based on these results, RA and other connective tissue diseases will be discussed separately below.

B. Present Status of Acupuncture and Moxibustion Therapy for RA

1. Case reports and accumulation of cases in Japan

● RA Conditions (disease activity and functional disorders)

Only 32 among the 54 references contained information about RA conditions. Of these 32, 30 deal with cases showing relatively stable disease activity, and 29 deal with cases in which patients are able to take care of themselves even while experiencing pain from a class 2 or 3 functional disorder. This shows that acupuncture and moxibustion therapy is mostly performed when RA activity and the patient's overall condition are relatively stable, and that the therapy tends to be applied to mild rather than severe cases of functional disorder.

● **Methods of acupuncture and moxibustion therapy**

The methods of treating RA by acupuncture and moxibustion therapy included the following: application of acupuncture and moxibustion to tenderness and induration of the affected joint or the whole body (13 references); modern medical treatment (emphasis on modern physiology, pathology, and anatomical science) (12 references); classic treatment (emphasis on proof of meridians) (8 references); traditional Chinese medicine treatment (emphasis on traditional causes and proof) (5 references); moxibustion only (4 references); ryodoraku medicine (3 references); the Nagano method (2 references); and others (5 references). In these ways, the results showed that RA is treated by a wide variety of schools, as there are no acupuncture points or treatment method specific to RA, and revealed the uniqueness of acupuncture and moxibustion therapy.

● **Evaluation method**

Effectiveness was measured by the following evaluation methods (with some overlapping): visual analogue scale (VAS) (22 references); the practitioner's own method of evaluation (11 references); rheumatoid activity index and improvement criteria of the American College of Rheumatology (ACR Core Data Set) (7 references); Arthritis Impact Measurement Scales version 2 (AIMS-2) (RA QOL assessment method) (6 references); face scale (4 references); pain scale (4 references); and no evaluation conducted (1 reference). Conventionally, evaluations by patients themselves, such as by using VAS, were the mainstream, but in recent years, a number of references has appeared that utilize the ACR Core Data Set, which serves as a global "gold standard" by also including blood and biochemical blood examination data, and RA QOL assessments.

● **Effects**

As to the effects based on the above-mentioned evaluation methods, the largest number of references referred to pain relief (42 references),

followed by mitigation of functional disorder (26 references), improvement of QOL (9 references), improvement of general conditions (1 reference), the value of acupuncture and moxibustion therapy as complementary medicine (1 reference), and the effectiveness of acupuncture and moxibustion therapy in combination with pharmacological treatment (1 reference). The main effects of acupuncture and moxibustion therapy for RA mostly tend toward the relief of joint pains and mitigation of functional disorder, including improvement of ADL.

As shown above, clinical reports on RA cases in Japan can be summarized as follows. (a) Subjects are patients whose RA activity or functional disorder is relatively stable. (b) There are diverse methods (concepts) of acupuncture and moxibustion therapy, but their goal is pain relief and functional improvement. (c) There is no specific acupuncture point for RA. (d) Immediate and cumulative effects are recognized, based on evaluations by patients. (e) Some of the known effects are pain relief, functional improvement and QOL improvement. (f) There is no mention of the corrective effects on autoimmune abnormalities or anti-inflammatory actions.

These clinical reports also pose the following issues. (a) Many do not provide information on the medical condition (extent of disease activity or functional disorder) of RA patients. (b) No observations are made regarding the effects of drugs even if they are administered in combination. (c) RA symptoms come and go, but only three references provide information of cases in which acupuncture and moxibustion therapy was continued for more than a year, where the same situation would normally warrant a long-term follow-up of more than a year in other treatment areas. (d) Pain relief and functional improvement were acknowledged from the results of this study, but pain relief alone cannot be said to control the bone destruction action unique to RA. (e) No shared understanding has been achieved on what type of indicator should be used if

anti-inflammatory actions and corrective effects on autoimmune abnormalities were to be presented in a clinical study.

2. Comparative tests in Japan and overseas (Table 16) 1-3)

Comparative tests by PubMed show that many reports recognize the effectiveness of diverse acupuncture and moxibustion treatment methods, ranging from electric acupuncture and ear acupuncture to moxibustion and systemic therapy, compared to using drugs alone or sham treatment (sham acupuncture). Furthermore, they acknowledge the effects of pain relief, functional improvement and QOL improvement, using such evaluation methods as VAS, ROM, blood tests and the ACR Core Data Set.

The “randomized comparative test of facilities that provide acupuncture and moxibustion therapy for rheumatoid arthritis,” which was conducted by this writer over a period of three years with funding from the Health Labor Sciences Research Grant, also recognized that the combination of pharmacological treatment with acupuncture and moxibustion therapy led to an improvement of pain and ADL and increased the QOL of rheumatoid patients compared to pharmacological treatment alone⁴⁾. Thus, it is thought that by properly assessing the conditions (degree of RA activity and functional disorder) of RA patients and administering treatment that is appropriate to each stage of the disease, acupuncture and moxibustion therapy could adequately address the diverse symptoms of RA.

At the same time, however, there are differences in opinion regarding the evaluation of RA reviews. Reports that evaluate the use of acupuncture and moxibustion therapy for RA as ineffective or undeterminable gave problems in research design or number of cases as their reason for not being able to make a judgment. Those that evaluate it as effective say that it is more effective than sham treatment, that effectiveness is increased in combination with pharmacological treatment and other such treatments, and that long-term treatment is effective.

C. Present Status of Acupuncture and Moxibustion Therapy on Collective Tissue Diseases Other than RA

1. Case reports and accumulation of cases in Japan

There are few reports compared to those on RA, indicating that acupuncture and moxibustion therapy is not frequently applied to collective tissue diseases in reality. However, reports that do exist acknowledge the improvement of pain, Raynaud’s phenomenon and functional disorder when current treatment is combined with acupuncture and moxibustion therapy against disease-specific symptoms. They utilize thermography and a blood flow meter to evaluate Raynaud’s phenomenon in SSc, SLE and MCTD, use saliva production as an indicator for dry symptoms in SjS, and examine immunological tests and changes in antinuclear antibodies for SSc, SLE and BD.

Table 16: Evaluation of RA reviews

Ineffective/Undeterminable	- Ernst E: Rheumatol, 2006(2) - Casimiro L: Cochrane Database Syst Rev, 2005(4) - Berman BM: Rheum Dis CLin North Am, 2004(1)	-> - It is difficult to judge, due to problems in research design and number of cases.
Effective	- Soeken KL: Clin J Pain, 2004(1) - Gaus W: Arzneimittel Forsch Hung, 1995(1) - Zijlstra FJ: Mediators Inflamm, 2003(2) - Linde K: BMC Complement Altern Med, 2001(3)	-> - It is more effective than Sham treatment. - Effectiveness is increased in combination with pharmacological treatment and other such treatments. - Long-term treatment is effective.

The above suggests that the mitigation of symptoms specific to connective tissue diseases could be expected to improve QOL. However, as with reports on RA, there are no reports that mention the corrective effects on autoimmune abnormalities or anti-inflammatory actions, and acupuncture and moxibustion therapy is regarded merely as a type of symptomatic treatment.

2. Comparative tests (Table 17)⁶⁾

As with RA, reports show that acupuncture and moxibustion therapy is effective compared to sham treatment, or more effective when used in combination with pharmacological treatment than such treatment administered alone, or in combination with exercise therapy. They thus indicate that mitigating symptoms specific to connective tissue diseases could improve QOL. However, compared to RA, there are few papers on respective diseases, and the accumulation of EBM is sought in the future.

acupuncture and moxibustion therapy. However, its effects can be roughly classified into four categories—(1) mitigation of joint pain and other such pain; (2) functional improvement, including improvement of the range of joint motion and ADL; and (3) maintenance of favorable general conditions through improvement of stiff shoulders, lower back pain, and poor circulation. This suggests the possibility of acupuncture and moxibustion therapy contributing to QOL improvement among patients of RA and connective tissue diseases⁶⁾.

However, many reports lack any specific mention of conditions, such as the degree of disease activity or functional disorder, or of evaluation methods. Therefore, it is hereafter necessary to establish a research design by assessing patients' conditions and examining the expected effects of combining existing pharmacological treatments with acupuncture and moxibustion therapy using a standard evaluation method. It is thought that cooperation with medical institutions and joint

Table 17 Reports on connective tissue diseases other than RA

	Author	Patients	Treatment/site	Evaluation	Effect
Ankylosing spondylitis	Jia J, et al: J Tradit Chin Med, 2006	30	Moxibustion RCT	CRP, ESR VAS Chopart	More effective than control
	Bai WJ, et al: Zhongguo Zhen Jiu, 2006	60	Acupuncture RCT	VAS Exercise therapy	Effective when combined with exercise therapy
Systemic scleroderma	Maeda M: J Dermatol Sci, 1998	11	Electric acupuncture CCT	Endothelin 1	Vasodilating action is observed
Systemic lupus erythematosus	Kung YY: Am J Chin Med, 2006	24	Moxibustion RCT meridian, san yin jiao	Immunological tests	More effective than control
Behçet's disease	Yu P, et al: J Tradit Chin Med, 2003	46	Acupuncture RCT	Antinuclear antibody	More effective than control

D. Effects and Possibilities of Acupuncture and Moxibustion Therapy on RA and Connective Tissue Diseases

As RA and connective tissue diseases are a large group of diseases, it is hardly possible to make a sweeping generalization of the effects of

studies with medical specialists are indispensable toward this end.

Additionally, most RCT and review reports contain information on comparisons with placebos and results of examinations of effects when used in combination with pharmacological treatment. While

a small number of papers show the effectiveness of acupuncture and moxibustion in relieving pain, improving functional disorders and maintaining favorable general conditions for QOL improvement, there were also papers that claim no significant difference, and there were systematic reviews that make many critical comments about research design, evaluation and other such methodologies. At present, there are few clinical reports about anti-inflammatory actions and corrective effects on autoimmune abnormalities (Table 18).

the theory of cytokine (TNF α , IL-10, INF) control by the interaction of neuropeptides and β -endorphins.

The majority of animal experiments looks at acute effects obtained from one stimulus, so it is necessary to hereafter examine the effect of sustainable stimuli on the immune system, but they suggest the possibility that pain relief and functional improvement, which are clinical effects on inflammatory diseases, are results of the anti-inflammatory actions of acupuncture and

Table 18 Current state and possibilities of acupuncture and moxibustion for connective tissue diseases

Treatment	(1) Stimulus site	<ul style="list-style-type: none"> • Meridians must be selected in accordance with the symptoms of each disease
	(2) Piercing depth	<ul style="list-style-type: none"> • Unknown
	(3) Treatment frequency	<ul style="list-style-type: none"> • Frequency cannot be determined, but the longer the treatment period, the more manifest the effect becomes.
	(4) Treatment method	<ul style="list-style-type: none"> • Greater effects can be expected in combination with a drug. • Long-term treatment tends to produce greater effects. • There is the possibility that moxibustion is effective.
Future issues	<ul style="list-style-type: none"> • Establishment of a research design that also takes into consideration anti-inflammatory actions and corrective effects on immunological abnormalities • Examination of outcomes that take into consideration such conditions as disease activity and functional disorders 	

Meanwhile, in basic studies based on animal experiments (Table 19), some reports were found that suggest anti-inflammatory actions. The mechanism is explained by a number of theories, including the theory that acupuncture and moxibustion (mainly moxibustion) stimulus on adjuvant arthritis controls arthritis through a T-cell and neutrophil-mediated immunological mechanism; the theory of immune function regulation by neuropeptides such as α -melanocyte stimulating hormones that are secreted by the pituitary gland; the theory of indirect immunosuppression via sympathetic nerves; and

moxibustion stimulus.

Based on the results of basic research also in clinical disciplines, future reports are awaited that deal with how to evaluate and intervene with chronic inflammatory autoimmune diseases, which are a condition of connective tissue diseases.

As discussed above, acupuncture and moxibustion therapy may be effective against pain and functional disorders of RA and connective tissue diseases, but as there is lack of strong evidence, it is necessary to conduct evidence-based clinical research that also includes an examination of its anti-inflammatory actions in the future.

Table 19 Basic research on acupuncture and moxibustion stimuli

Reports of basic studies that suggest anti-inflammatory effects		
Matsukuma et al J Jpn Soc Balneol Climatol Phys Med, 2005 (3)	Rat with adjuvant arthritis Moxibustion on stomach meridians (9 times in 4 weeks)	The increase of T cells (CD4 ⁺ T) was controlled. The number of neutrophils decreased. Anti-inflammatory effects were observed.
Fang JQ, et al. In Vivo, 1998 (12)	Rat with arthritis Moxibustion on stomach meridians (15 times in 30 days)	The increase of anti-type II collagen antibodies was controlled. Anti-inflammatory actions were observed.
REVIEW Azumaya et al. Zensin Journal, 2006 (5)	Examination of 94 references It is a fact that acupuncture and moxibustion stimulus directly and indirectly affects immunological parameters of the immune system, but universality and reproducibility are issues to be addressed in the future.	

- Control of inflammatory cytokines by neuropeptides such as α -melanocyte stimulating hormones
- Immune cell adjustment by increased production of glucocorticoid by the adrenal gland
- Indirect immune function regulation by somatic reflection of the immune system via sympathetic nerves
- Control of cytokines (TNF- α , IL-10, INF) by the interaction of neuropeptides and β -endorphins

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