

Research article

**Effect of Auriculotherapy on Multiple Sclerosis Related Pain: A Double Blind
Randomized Clinical Control Trial Parallel Design**

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ABSTRACT

Background and objectives: Multiple sclerosis (MS) is an autoimmune and a demyelinating disease. Pain is a relatively common finding in MS patients and Treatment is largely pharmacologic, but patients have often found the medications to have unwanted side effects. The purpose of this study is to evaluate the efficacy of auriculotherapy for pain associated with MS.

Materials and Methods: This was randomized, double-blind, placebo-controlled trial, parallel design with 128 MS patient, and two groups. MS patients were randomized to receive auriculotherapy and sham therapy, for 10 sessions. Pain was assessed before, after and a month after intervention by McGill questionnaire (VAS, PPI and PRI).

Results: The results showed that mean pain intensity (VAS) decreased in auriculotherapy group after and a month after intervention (6.14 to 2.08 and 2.66). PPI index was 51.2% uncomfortable pain before auriculotherapy then decreased to 27.6 % after intervention. PRI index was 2.81 before intervention and decreased to 0.89 and 1.14 after intervention and one month later. The results indicated that pain was significantly decreased in Auriculotherapy group after (P<0.05) and a month after intervention (P<0.05).

Conclusions: Auriculotherapy is an effective method to reduce MS-related pain. Using this safe and effective method is recommended for MS patients.

Keywords: multiple sclerosis, auriculotherapy, pain, clinical trial

INTRODUCTION:

Multiple sclerosis (MS) is an autoimmune and a demyelinating disease in which the insulating covers of nerve cells are damaged.(1,2) MS is characterized by axonal degeneration, chronic inflammation, and loss of the myelin sheath surrounding nerve fibers in the brain and spinal cord.(2) The cause of MS is still unknown and not clear. (3, 4) This damage disrupts the ability of the nervous system to communicate, resulting in a

range of signs and symptoms, including physical, mental, and sometimes psychiatric problems, (5) which usually diagnosed based on them and results of supporting medical tests.(6)

Multiple sclerosis (MS) is one of the world's most common neurological disorders and in many countries it is the leading cause of non-traumatic disability in young adults (typically begins between the ages of 20 and 40 years). (7, 8, 9) The

estimated number of people with MS have increased from 2.1 million in 2008 to 2.3 million in 2013.(7) More than 200 people are diagnosed with MS each week in the United States. (10) In this regards a systematic review and meta-analysis reported evidence suggested that the incidence of MS is increasing in females. (11, 12) Etemadifar wrote Iran has a medium-to-high prevalence rate of MS and the prevalence of MS significantly has increased during recent years. (13) Tolou-Ghamari (2015) showed that Isfahan is the highest in Iran MS ranking. (14)

MS patient can have almost any neurological symptom or sign. Fatigue, pain, and spasticity are three disruptive symptoms in people with MS. (15, 16) Pain is defined as an “unpleasant sensory experience associated with actual or potential tissue damage or described in terms of such damage”. (17) It is a sensory symptom directly related to the disruption of central nervous system myelin and is a relatively common finding in MS patients (53–57%). (18) According to Ashtari et al.(2016) prevalence of pain was 57.5% in MS patients in Isfahan and based on VAS, mean and standard deviation of pain severity were 5.5 (2.9).(19)

MS pain is multi factorial, occurring for both primary and secondary causes. (18) Painful tonic spasm (PTS) is an extreme form of spasticity seen in 1 in 10 people with MS. (20) According to Ashtari and her colleagues the most common types of MS pain belonged to cramp and contusion pain. (19)

Oral medications are the second line treatment of multiple sclerosis because of their complications. (21) Therefore, it is important to reduce these side effects and to prevent complications of MS drugs; non-pharmacological methods are recommended. As Karpatkin, Liu, and Tajik stated in their studied separately we can use complementary and alternative medicine such as acupuncture with the least symptoms to reduce some disease sideeffects. (24, 25, 18) Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, practices, and

products that are not presently considered to be part of conventional medicine.(26, 27) Their techniques are non-invasive(28) and acupuncture is commonly used for the treatment of pain. (33) Ear acupuncture is an effective method for treating acute and chronic diseases without producing side effects. (34) Auriculotherapy is a form of alternative medicine based on the idea that the ear is a microsystem which reflects the entire body, represented on the auricle, the outer portion of the ear.(35) This method is non-invasive stimulation of the ear and a signal send to the brain and organs to balance the physiological function of the body. (34, 36) Stimulation methods of the ear are needle stimulation, seed (Vaccaria), probes and fingers (acupressure ear), electrodes attached to needles and electrical stimulation directly over the ear or using a laser requirements. (37)

Studies' results of Asher (37) and Yeh(39) show the effectiveness of auriculotherapy in the pain relief and some body disorders. In the field of MS, some studies indicated the use of CAM as Karpatkin et al (2014) in his study titled "acupuncture and multiple sclerosis", wrote the use of acupuncture in the treatment of MS is one of the most common disease but few studies have examined its effectiveness. (18) For example Hao (2013) did acupuncture on a patient's head of an MS 60-year-old with a history of 20 years of disease. After ten sessions (weekly) he could walk without helping and he returned to work. (40)

As has been shown in some studies about auriculotherapy, this technique has been effective and in these studies, the side effects attributed to auriculotherapy have not mentioned. But of course, in many of these researches, design of study, sampling, sorting patients, intervention or placebo groups, randomization, are not scientific and appropriated methods need to apply correct analysis methods. MS Patients slowly lose their ability and most of them deal with symptoms such as pain. These signs affect significantly on their life. Also most of the patients are young people. Therefore conducting standard researchers on

patients and especially considering safe and low-risk method are necessary in order to decrease symptoms and side effects of disease. Since the survey about auriculotherapy and MS haven't included investigation standards and suitable design up to now, the researcher conducted the current study with the purpose of considering auriculotherapy efficacy on MS pain.

MATERIALS AND METHODS:

The main structure of this study was a double blind clinical trial, parallel design and two groups. Sampling was Simple Random Sampling and stratified randomization by Minimization. Because of many parameters in the study, such as sex, type of disease, the pattern of disease, drugs and disease duration, used Minimization.

The sample consisted of patients with MS who had been referred to the MS Clinic at the Kashani Hospital, and they had inclusion criteria. The estimated sample size to compare pain levels between two groups based on the highest variance was calculated 64 patients in each group.

Participants in this trial were 128 persons with MS who reported MS-related pain (e.g., neuropathic pain, pain related to muscle spasms, neuralgias) of at least moderate intensity (pain severity of 3 or greater on the numeric rating scale) despite optimal pharmacological management (Acetaminophen 325 mg/4h). (41) Acetaminophen was prepared for both groups by the researcher and the order intake was explained to them. Participants in the intervention and control groups remain until the end of the study in the same group. (See diagram)

Inclusion Criteria were MS disease and diagnosis confirmation, MS disease for at least a year, pain intensity score between 3 to 10 (according to McGill Questionnaire VAS), suffering from myalgia (muscle pain), lack of any advanced diseases, acute infectious diseases or cancer, Non-Pregnant, Iranian. Exclusion Criteria were unwillingness to continue the auriculotherapy,

unwillingness to complete questionnaires, Migration and Death. Data analysis software was SPSS 19.

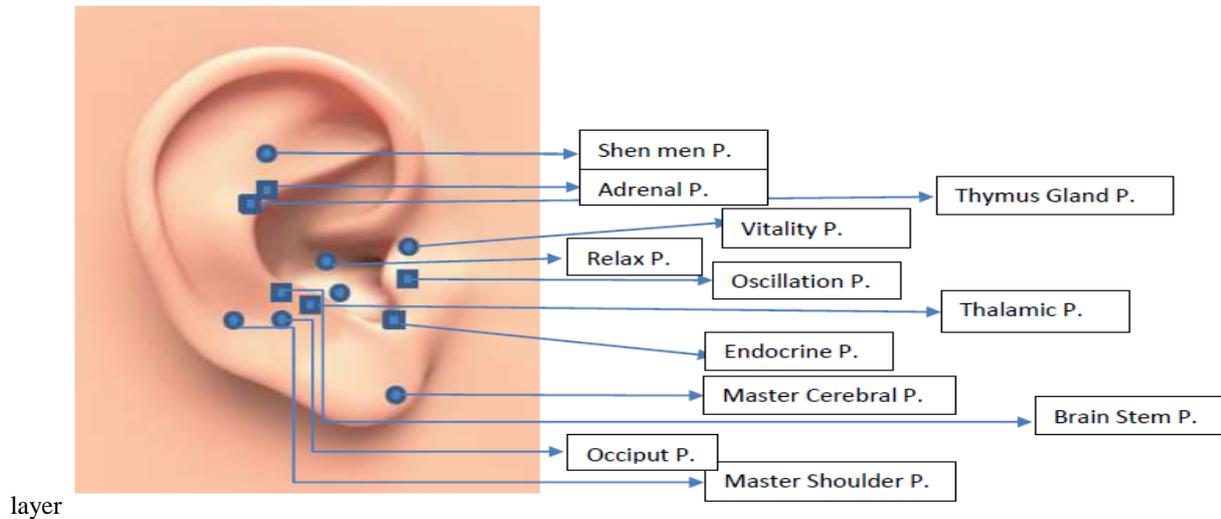
After getting written consent from subjects, and explanation of study objectives, the first to fifth part of data collection form completed and auriculotherapy intervention began. Auriculotherapy (stimulation of ear points by pointer Excel II) and medications by acetaminophen were conducted in the intervention group, but the control group took placebo auriculotherapy (no stimulation of ear points and pointer Excel II off, without pressure and vaccaria seed but just glue) and medications by Acetaminophen. The intervention was performed two times a week for ten sessions. After stimulation of the ear points, three vaccaria seeds were placed on the ear for three days. In the placebo group glue was left without any stimulation and vaccaria.

Data collection (May 2015 till July 2016) was conducted by the standard McGill questionnaire, which includes a ruler to measure visual analogue scale (VAS), present pain intensity (PPI), pain rating index (PRI), and was completed by person who was employed for questioning in three stages (before intervention, immediately after the end of intervention and one month after).

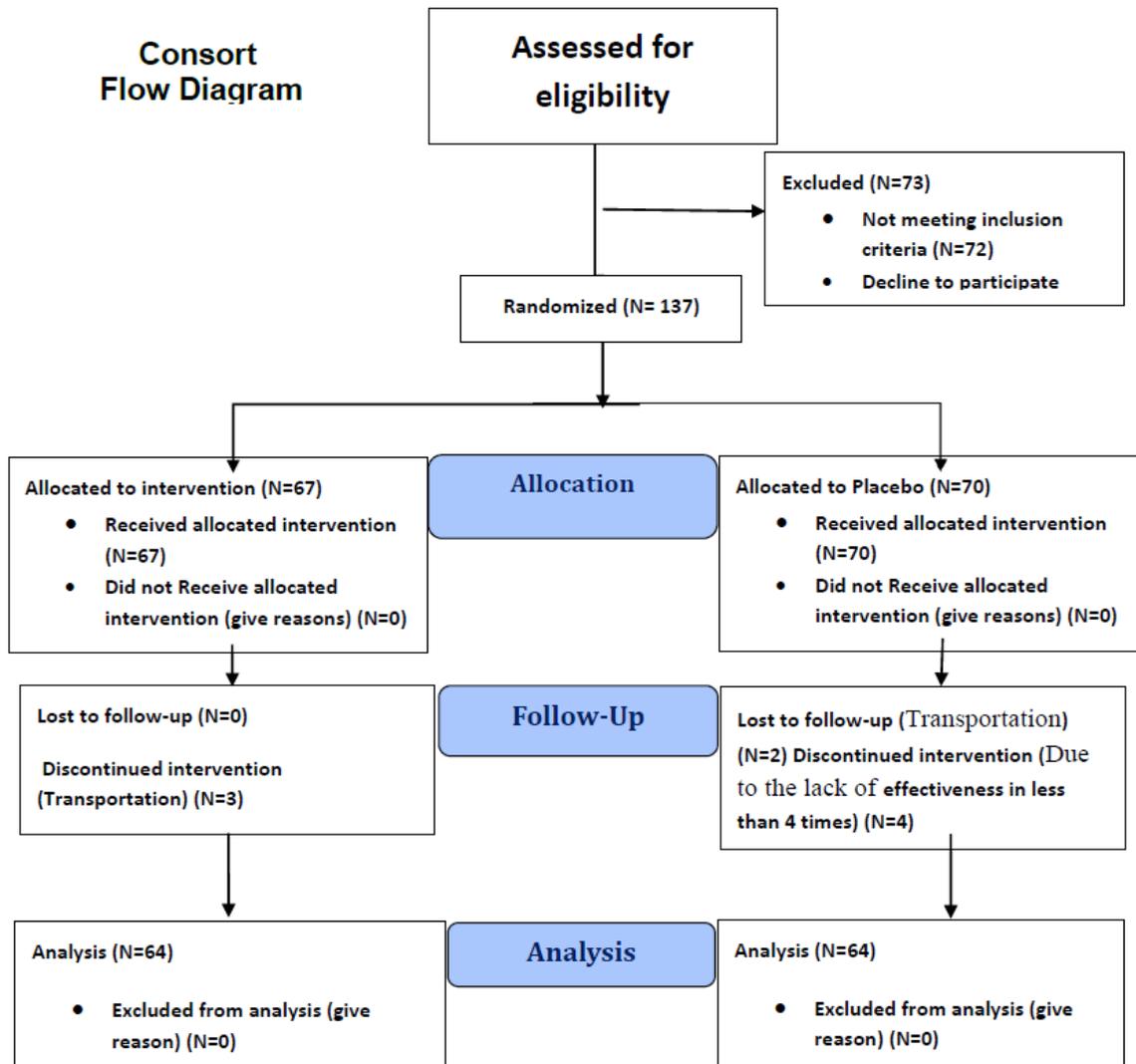
In each session, after using alcohol cotton to clean the outer ear and put the patient in the proper position (preferably supine), the ear points was stimulated for 15 seconds (34, 42). These points include: Shen men, Master Shoulder, Tranquilizer, Heart, Thymus, Posterior Hypothalamus, Endocrine, Adrenal, Vitality, Psychosomatic, Occiput, Brain and Brain Stem. (42) (See Figure 1) Questioning was done before and after the intervention, and then one month later after end of intervention.

Ethical considerations: This research project was approved by Isfahan University of Medical Sciences with the code 931119, date: 2014/January/8.

Figure 1: points for auriculotherapy in MS patients (circle= surface, Square= in the posterior layer



layer



RESULTS:

The results showed mean age was 35.86 ± 9.34 years in the intervention group and 36.17 ± 9.39 in the placebo group. There was no different between ages in two groups based on T-test ($P=0.70$). Most (77.3%) of the subjects were female while 22.7 % were male. 70.3% were married, 27.3% were alone, 1.6 % abandonment and 0.8% divorced. The subjects education were high school 28.9%,

T-test showed that duration of disease ($P=0.631$), EDSS ($P=0.747$) did not differ significantly in the two groups. Also the chisquare test showed that patients gender ($P=0.160$) and kind of MS disease ($P=0.146$) did not differ significantly in the two groups. (See Table 1)

Table 1: Frequency and compare some demographic and MS Disease Variables' in auriculotherapy and Placebo groups

Groups		Auriculotherapy N=64	Placebo N=64	P-value
Variable		M \pm SD/N (%)	M \pm SD/N (%)	
Sex	Male	7 (5.47%)	12 (9.37%)	P=0.160
	Female	57 (44.53%)	52 (40.62%)	
Age		35.86 \pm 9.34	36.17 \pm 9.39	P=0.851
Marriage	Married	44 (34.37%)	46 (35.94%)	P=0.381
	Alone	17 (13.28%)	18 (14.06%)	
	abandonment	2 (1.56%)	0 (0.0%)	
	divorced	1 (0.78%)	0 (0.0%)	
Education	High School	19 (14.84%)	18 (14.06%)	P=0.774
	diploma and associate degree	19 (14.84%)	28 (21.87%)	
	bachelor	24 (18.75%)	14 (10.94%)	
	master degree and higher	2 (1.56%)	4 (3.12%)	
Occupation	housewife	43 (33.59%)	33 (25.78%)	P=0.228
	employee	7 (5.47%)	7 (5.47%)	
	workers and farmers	1 (0.78%)	1 (0.78%)	
	Self-employed	5 (3.91%)	14 (10.94%)	
	Unemployed	8 (6.25%)	9 (7.03%)	
Setting Location	householder	17 (13.28%)	21 (16.41%)	P=0.468
	property rental	46 (35.94%)	42 (32.81%)	
	corporate home	1 (0.78%)	1 (0.78%)	
Duration		8.82 \pm 6.02	9.34 \pm 6.10	P=0.631
Kind of MS	RRMS	55 (42.97%)	60 (46.87%)	P=0.146
	PPMS	9 (7.03%)	4 (3.12%)	
EDSS		2.91 \pm 1.64	3.00 \pm 1.34	P=0.747

diploma and associate degree 36.7%, bachelor 29.7%, master degree and higher 4.7%. The subject's occupations were housewife 59.4%, employee 10.9%, workers and farmers 1.6%, Self-employed 14.8% and Unemployed 13.3%. The sample location is as follows: householder 68.8%, property rental 29.7% and corporate home 1.6%. Mean of MS duration was 8.82 ± 6.02 years in the intervention group and 9.34 ± 6.10 in the control group. Mean of EDSS was 2.95 ± 1.64 in the intervention group and 3.0 ± 1.34 in the control group. The kinds of MS disease were relapsing remitting (RRMS) 89.8% and primary progressive (PPMS) 10.2%.

The average pain (0-10) of VAS index in auriculotherapy group before intervention was 6.14 and in placebo group was 5.80. While the average pain after intervention was 2.08 and 5.25 and one month later was 2.98 and 5.62, respectively in two groups. ANOVA showed there was significant relationship between average score of pain intensity with VAS index before and immediately after the end of intervention ($P<0.05$) and one month after intervention ($P<0.05$) in auriculotherapy group. While there wasn't any significant differences among these three times in placebo group. ($P>0.05$) (See Table 2).

The findings on PPI index (pain score between 0-5 or from painless to terrible pain) indicated that the greatest amount of pain was reported 51.2 % before intervention in form of annoying pain and 23.6 % in form of mild pain. These pains have been

this test didn't specified significant difference in placebo group among these three times. (P>0.05) (See Table 2)

Table 2: Mean of severity of pain based on VAS, PPI, PRI and total pain in two groups in the different times

Variable	Groups	Auriculotherapy N=64		Placebo N=64		P- value Between Groups
		Mean	SD	Mean	SD	
VAS	Before intervention	6/1	1/9	5/8	2/1	P< 0.001
	After intervention	2/1	1/8	5/2	2/1	
	One month after intervention	2/9	2/7	5/6	2/3	
PPI	Before intervention	2/1	0/8	2/1	1/1	P< 0.001
	After intervention	0/8	1/1	2/1	1/01	
	One month after intervention	1/1	0/8	2/2	0/9	
PRI	Before intervention	2/8	1/5	3/3	1/9	P< 0.001
	After intervention	0/9	0/9	3/2	1/8	
	One month after intervention	1/1	0/9	3/5	2/1	
Total Pain	Before intervention	11/1	3/3	10/9	4/6	P< 0.001
	After intervention	3/7	2/8	10/5	4/3	
	One month after intervention	5/2	4/4	11/2	4/6	
P-value	Within Groups	P<0.001		P> 0.05		

decreased to 27.6 and 43.3 %, respectively after intervention. A month later, the annoying pain reached to 39.9 % and mild pain reached to 31.5%. Based on ANOVA in auriculotherapy group, there was significant difference between pain with PPI before and immediately after intervention (P<0.05) and a month after intervention (P<0.05). While this test didn't indicate significant difference in placebo group among these three times. (P>0.05) (See Table 2)

PRI was another index in which different types of pains in sensory dimension (11 types of pain) and emotional dimension (4 type of pain) were given from 0 to 3 scores (from no pain to severe pain). Based on assessing the index, tolerable pain with 26.6 % and moderate intensity (a score of 2), cramp pain with moderate intensity of 15.6 % (a score of 2), and high intensity of 12.5 (a score 3) indicated the greatest amount of pain. After intervention the amount of tolerable pain was 17.2 % and cramp pain was 0.12 % with moderate intensity and 6.2 % with high intensity. The results showed that these pains reached to 18.0 %, 12.5, and 9.4 % a month after intervention. ANOVA represented there was significant difference between PRI score in auriculotherapy group immediately after the end of intervention (P<0.001) and a month after (P<0.001). Whereas

Repeated measure ANOVA showed that the effect of time on pain intensity score based on the criteria of PRI, VAS and PPI as well as the total score was significant (P<0.001). The effect of the intervention (auriculotherapy) was significant (P<0.001). Also the interaction effect of the time and intervention was significant (P<0.001). It means that, pain scores were nearly identical between the two groups before the intervention but the mean pain scores in the two groups were different immediately after and one month after the intervention. (See Table 2)

In addition, the findings represented that auriculotherapy could decrease the MS pain through 10 sessions treatments on patients' ear with VAS, PPI, and PRI indexes. And its effect will remain until a month later.

The dose of acetaminophen of these two groups was assessed before and after intervention. The results specified that the consumption average of acetaminophen with 325 milligram dose in auriculotherapy and placebo groups respectively was 2.50±0.85 and 2.65±1.18 before intervention, 0.27±0.60 and 2.55±1.14 immediately after intervention, and 0.75±1.2 and 2.69±1.2 a month after. The ANOVA indicated that there was significant difference in

acetaminophen consumption between these two groups immediately after ($P < 0.001$) and a month after intervention ($P < 0.001$). Whereas there wasn't any significant difference in the consumption before intervention ($P = 0.289$). Independent t-test, moreover, demonstrated that although there was significant difference in auriculotherapy group for the average of acetaminophen tablets number before and after intervention ($P < 0.001$) and a month later ($P < 0.001$), this average indicated no significant difference in placebo group in the two times ($P > 0.05$).

Repeated measure ANOVA showed that the effect of time on consumer acetaminophen dose was significant ($P < 0.001$). The effect of intervention was also significant ($P < 0.001$). The interactive effect of the time and intervention was significant ($P < 0.001$). This means that the differences between the two groups were not identical at all times. Dose of acetaminophen consumption in the two groups were nearly identical before intervention, but the mean dose of acetaminophen are different in two groups immediately after and one month after the intervention.

DISCUSSION:

The study was conducted to determine auriculotherapy effect on the pain of the patients with MS. The analysis of statistical results showed that auriculotherapy decreases the pain, as total pain score average, which includes PPI, VAS and PRI indexes, indicated significant reduction in auriculotherapy in proportion to placebo group. Also according to considering separation of the indexes, there was a significant difference between pain intensity and VAS index in the two groups after intervention. These differences are indication of auriculotherapy effectiveness in pain relief with VAS index. Pain was "discomforting" in auriculotherapy group in PPI index before intervention. And the indexed were painless and mild pain after intervention and a month after. The findings indicated there was significant difference between pain intensity base on PPI index

immediately after and one month after intervention. Whereas impatient pain, cramp pain, and dull pain are comprised three common pains respectively in two groups, these pains had significant reduction in the auriculotherapy group after intervention. And there was significant reduction in PRI pain relief more than before intervention and it will continue a month after intervention.

The dose average or the number of acetaminophen in auriculotherapy group in three times had significant difference and showed the reduction of Acetaminophen consumption after intervention and one month after it in this group. But there wasn't any significant difference in the placebo group after consuming of the tablet. This finding is indication of pain relief and the effect of auriculotherapy technique on pain in MS patients.

The release of endorphins as neurotransmitters is a method in which auriculotherapy can affect pain relief. This release is exhilarating and domestic narcotic. Vas et al. conducted the study in two groups with the aim of assessing the auriculotherapy effect on 400 patients with chronic pain spine in Health Care Center in Andalusia randomly. The primary outcome was the change of pain intensity average (VAS) which was registered 3.32 for auriculotherapy and 8.19 for placebo group. And the difference was significant ($P < 0.05$). Researcher founded that auriculotherapy is a suitable technique (15). The results of this study are compatible with current study after controlling pain intensity as the primary outcome of this technique.

Vaz (2014) in his study of the *efficacy and safety of auriculopressure for primary care patients with chronic non-specific spinal pain* concluded that this technique follow with pain relief in short time and mid-term period and can increase patient life quality in mid-term period. He assessed patient satisfaction in high level (45). The results of this study are aligned with current study. Madsen during his meta-analysis research on 3025 patients who have not been blinded in three clinical trial researches proposed that there is

significant difference in acupuncture in comparison to placebo acupuncture. In addition there is significant difference between placebo acupuncture group and without acupuncture placebo group (46).

Rastegarzadeh et al. in their study of clinical trial research on birth pain of 80 nulliparous mothers (2015) found out that auriculotherapy technique affect the decreasing birth pain more in the intervention group with 40 mothers than control group. She mentioned to the Guerra et al study which was conducted with the aim of considering the effect of acupuncture on shoulder pain that clinical signs of patient has been decreased through Auriculotherapy.(44) Madsen and Rastegarzadeh realized that auriculotherapy is subsection of acupuncture and their findings cause to confirm our study in pain relief. Tajik et al. also studied MS patients which represented chronic pain relief and was aligned with our findings.

Karpatkyn (2014) and Chao (2014) studies also reported the durability of the auriculotherapy effect (47 & 18).

CONCLUSION: According to findings, it can be concluded that auriculotherapy as an easy and safe technique can decrease MS patients' pain. Therefore it is recommended the use of this technique in decreasing and controlling annoying pain in MS patients and the pains which are result from drugs consumption or without any relation to them.

Appreciate: The current article is part of doctoral thesis entitled Effect of Auriculotherapy on Multiple Sclerosis related pain: A double blind randomized clinical control trial parallel design that was conducted by supporting Isfahan University of Medical Sciences. This thesis would simply be impossible without the cooperation and assistance of the vice President of Research and Neuroscience Research Center of the University.

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