

Pharmacopuncture for Cervicogenic Dizziness

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Key Words

acupoint injection, cervicogenic dizziness, dizziness, pharmacopuncture, review

Abstract

Objectives: Pharmacopuncture is a treatment that medicinal fluid including herbal extract is injected in body under qi/flavor theory and meridian theories. There are a number of studies investigating the efficacy of pharmacopuncture for cervicogenic dizziness but its usage differs in each study. This study aimed to review previous studies of pharmacopuncture treatment for cervicogenic dizziness to navigate the direction of improvement.

Methods: Literature review was conducted on studies aimed at pharmacopuncture for cervicogenic dizziness. The randomized controlled studies which assessed the efficacy of pharmacopuncture on cervicogenic dizziness were selected. The studies were searched in PubMed, RISS, OASIS and CNKI. After selecting eligible studies, the authors read the articles and summarized the points those are necessary in pharmacopuncture treatment for cervicogenic dizziness.

Results: Twenty seven studies and 2,709 participants were included. The diverse solutions were used and the most popular were *Salvia miltiorrhiza*, *Angelica gigas*, a compound in *Gastrodia elata*, *Panax notoginseng* saponins. Some studies investigated the efficacy of conventional medical compounds (lidocaine, vitamin B, dexamethasone) injected in acupoints. Adopting acupoints and combining with body acupuncture have shown the tendency to enhance the cure rate. Pharmacopuncture could improve the efficacy of conventional treatment for cervicogenic dizziness.

Conclusion: As the solution and injection method varies, principles of pharmacopuncture for dizziness should be investigated.

1. Introduction

20-30% of adults suffered dizziness in their lifetime [1]. As common symptom, there are diverse causes for dizziness. Main causes of dizziness comprise central origin, benign paroxysmal positional vertigo, hyperventilation syndrome, otic diseases (eg. Meniere's disease, vestibular neuritis), cardiovascular diseases, cerebrovascular diseases, medication, aging, etc [2, 3] and their symptoms vary widely such as vertigo, dis-

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equilibrium, presyncope, lightheadedness accordingly. Among these, cervicogenic dizziness is dizziness or vertigo deriving from a disturbance of the neck which can be owed to impingement of the vertebral arteries, whiplash, or degenerative disturbances of the cervical spine [4]. Evidence on the disease has not been developed much so far and physical therapy is mentioned to be preferred for cervicogenic dizziness in general.

Pharmacopuncture is a treatment that combines acupuncture and herbal medicine. Medicinal fluid including herb extract is inserted, inhaled or embedded into the points where acupuncture needle is usually applied (acupoints, meridian sinews, joints, body cavities, blood vessels, etc) to mediate vital function and treat diseases, based on qi/flavor theory and meridian theories [5]. In Korea, 98.6% of inpatients and 77.6% of outpatients in 12 Korean medicine hospitals and clinics received pharmacopuncture treatment [6]. In China, pharmacopuncture was studied by the terms of 'acupoint injection' or 'aqua acupuncture'. This method is used in wide spectra of diseases such as musculoskeletal disorders, neurological disorders and disorders of digestive system, circulatory system [7].

Administration route of pharmacopuncture includes injecting herb extract into acupoints, intravenously injecting herb extracts, injecting chemical compounds into acupoints, or needle-embedding. These routes and solution can be differed in accordance with symptoms or progress of diseases. Acupoints on different body regions were also applied to regulate targeted diseases. The medicinal material can be absorbed by human body rapidly and many resources can be used as component of pharmacopuncture. As dizziness has chronic progress and frequent relapse, pharmacopuncture can be used as new complementary tactic due to these features.

The studies on pharmacopuncture treatment for dizziness included diverse types of dizziness such as inner ear vertigo such as Meniere's disease [8-10], vertebral arteriosclerosis [8], hypertension [8, 9], vertebrobasilar arterial disease [8, 9], and anemia [8]. Interestingly, there were overwhelming number of observational studies and randomized controlled trials [11-37] regarding the efficacy of pharmacopuncture for cervicogenic dizziness compared with those for dizziness with other origin, considering its portion which accounts for 7.5% among diverse causes of dizziness [38]. There were a number of studies about pharmacopuncture on dizziness, especially cervicogenic dizziness, but overall review on specific treatment forms and methods were not discussed so far. In this regard, this study aimed to review previous researches on cervicogenic dizziness treatment with various forms of pharmacopuncture.

2. Methods

This article aimed to provide narrative review of pharmacopuncture treatment on dizziness as therapeutic option. To achieve this, the authors searched published literature comprehensively. Literature which was published by Au-

gust 2016 was searched on Pubmed, RISS (<http://www.riss.kr/>), Korean Traditional Knowledge Portal (<http://www.koreantk.com>), Oriental Medicine Advanced Searching Integrated System (OASIS), (<http://oasis.kiom.re.kr/>) and China National Knowledge Infrastructure (CNKI) (www.cnki.net). Eligible studies were randomized controlled trials that assessed the efficacy of pharmacopuncture on cervicogenic dizziness. Studies were excluded when the study did not include a control group or randomization was not performed. The eligible studies included the method of either injecting herb extract in acupoints and vein or injecting conventional medicine in acupoints, but catgut embedding method and needle embedding method were excluded. Combination of pharmacopuncture with other interventions were basically included but we excluded the cases which were difficult to discriminate the efficacy of pharmacopuncture from the other.

The authors reviewed the titles, abstracts, and article and irrelevant studies were excluded. After the authors read the full article of eligible studies, they summarized and discussed points which deserves consideration in pharmacopuncture treatment for cervicogenic dizziness.

3. Results and Discussion

Twenty seven studies were included and the number of participants was 2,709 (Figure 1). The included studies were all conducted in China. The solution, selected acupoints, and administration method were diverse and the details were summarized as below (Table 1).

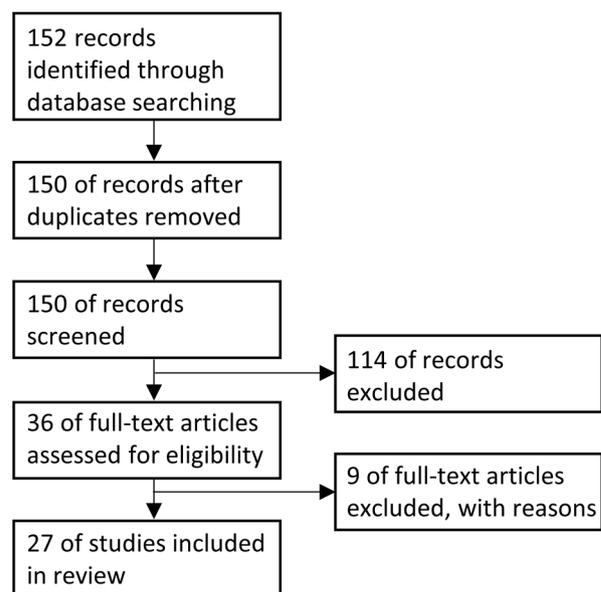


Figure 1 Flowchart of literature selection on review of pharmacopuncture for cervicogenic dizziness

Table 1 Characteristics of RCTs of pharmacopuncture for cervicogenic dizziness

First Author; pub. year	No. of participants; Age*	Duration of disease*	Intervention type	Injection route and acupoints	Treatment period	Type of control group	Outcome measure	Results	Adverse events
Cao, 2013 [11]	120; 18 ~ 70	1d ~ 10y	Angelica gigas extract, IA, qd	GB20, ST36, holographic acupoints on second metacarpal bones	11d ~ 17d	●Tuina, qd ●Herbal medicine, po, tid	Symptom improvement	T > C, P < 0.05	NR
Chang, 2015 [12]	116; 43.0	10.1m	●Anisodamine ●Cervical traction, qid ●Salvia miltiorrhiza, Carthamus tinctorius, IV ●Herbal medicine, po	Anisodamine: GB20 Salvia miltiorrhiza, Carthamus tinctorius: IV	10d	●Cervical traction, qid ●Salvia miltiorrhiza, Carthamus tinctorius, IV ●Herbal medicine, po	Symptom improvement	T > C, P < 0.05	NR
Huo, 2010 [13]	80; > 40	NR	●Ligustrazine, IA, qd ●Salvia miltiorrhiza, Dalbergia odorifera, betahistine, IV, qd	Ligustrazine: GB20 Salvia miltiorrhiza, Dalbergia odorifera: IV	22d	Salvia miltiorrhiza, Dalbergia odorifera, betahistine, IV, qd	Symptom improvement	T > C, P < 0.05	NR
Li, 2006 [14]	74; 32 ~ 69	1y ~ 21y	Salvia miltiorrhiza, Dalbergia odorifera, IA qd	GB20	24d	AT, qd	Symptom improvement	T > C, P < 0.05	NR
Liu, 2001 [15]	300; 27 ~ 58	1m ~ 12y	Salvia miltiorrhiza, Dalbergia odorifera, Angelica gigas extract, Panax notoginseng saponins, lidocaine, vitamin B ₁₂ , IA, q3d	GB20, BL10, GV16	15d	AT, GV16	Symptom improvement	T > C, P < 0.05	NR
Wang, 2009 [16]	48; 18 ~ 77	20d ~ 6y	●Carthamus tinctorius, lidocaine, vitamin B ₁₂ , tid	GV20, GB20, cervical paravertebral points	12d	●Cervical traction, bid ●Iontophoresis with herbal	Symptom improvement	T > C, P < 0.05	NR
Cao, 2005 [17]	35; 47.9	1d ~ 15y	Anisodamine, lidocaine, IA, qd	GB20	7d	Salvia miltiorrhiza, Dalbergia odorifera, IV, qd	(1) Symptom improvement (2) Relapse rate for the first year	(1) T > C, P < 0.05 (2) T > C, P < 0.05	NR
Weng, 2006 [18]	112; > 45	3m~10y	●Gastrodin, IA, q3d ●Flunarizine hydrochloride, po, qd	GB20	9d	Salvia miltiorrhiza, IV, qd	(1) Symptom improvement (2) Change of TCD flow velocity	(1) T > C, P < 0.05 (2) Vd: VA [left]: P < 0.05, VA [right]: P > 0.05, BA: P < 0.01	NR

First Author; pub. year	No. of participants; Age*	Duration of disease*	Intervention type	Injection route and acupoints	Treatment period	Type of control group	Outcome measure	Results	Adverse events
Zou, 2007 [19]	73; 35 ~ 70	1m~6y	Salvia miltiorrhiza, qod	GB20, BL10	20d	Salvia miltiorrhiza, IV	Symptom improvement	T > C, P < 0.01	NR
Ju, 2011 [20]	80; 57.5	11.7d	Lidocaine, vitamin B ₁₂ , vitamin B ₁ , dexamethasone, IA, qod	ST10, GB20, GV14, and cervical paravertebral point	10d	●Aspirin, po ●Panax notoginseng saponins, citicoline, IV, qd	Symptom improvement and change of TCD flow velocity	T > C, P < 0.05	NR
Yang, 2010 [21]	78; NR	NR	Angelica gigas extract, Ligusticum striatum extract and Carthamus tinctorius extract, IA, qd	GB20, cervical paravertebral points, GV16	14d	Salvia miltiorrhiza, Dalbergia odorifera, IV, qd	Symptom improvement and change of TCD flow velocity	T > C, P < 0.05	NR
Sun, 2001 [22]	242; 26 ~ 77	1d ~ 14y	Salvia miltiorrhiza, Dalbergia odorifera, IA qd	GV20, CV04, Jingyun acupoint, additional acupoints according to pattern differentiation	22d	●Salvia miltiorrhiza, Dalbergia odorifera, IV, qd ●Herbal medicine, po	Symptom improvement	T > C, P < 0.01	NR
Yang, 2006 [23]	68; 29 ~ 72	12d ~ 7m	Salvia miltiorrhiza, Dalbergia odorifera, IA, qod	GB20, cervical paravertebral points	27d	●Salvia miltiorrhiza, Dalbergia odorifera, IV, qd ●Flunarizine hydrochloride, po, qd	Symptom improvement	T > C, P < 0.05	NR
Wang, 2003 [24]	48; 28 ~ 67	3d ~ 5y	Salvia miltiorrhiza, Dalbergia odorifera, Angelica gigas extract, lidocaine, vitamin B ₁₂ , IA, qd	GB20, cervical paravertebral points	25d	●Salvia miltiorrhiza, Dalbergia odorifera, IV, qd ●Flunarizine hydrochloride, po, qd	Symptom improvement	T > C, P < 0.05	NR
Tang, 2011 [25]	60; 43 ~ 69	NR	●Gastrodin ●AT, qd	cervical paravertebral points	10d	Gastrodin, IV, qd	Scoring for dizziness	T > C, P < 0.05	NR
Wang, 2008 [26]	68; 42.0	3.2y	●Salvia miltiorrhiza, Dalbergia odorifera, IA, qd ●Physical therapy, cervical traction, manipulation, qd	GB20, BL10, cervical paravertebral points	22d	●Physical therapy, cervical traction, manipulation, qd	Symptom improvement	T > C, P < 0.05	NR
Xiao, 2016 [27]	114; 49.8	2m ~ 14y	●Gastrodin, IV, qd ●AT, qd	IV	20d	●Group1: AT, qd ●Group2: Gastrodin, IV, qd	Scoring for symptoms and function rehabilitation of cervical vertigo	●Group1: T > C, P > 0.05 ●Group2: T > C, P < 0.05	NR
Tan, 2013 [28]	70; 43.2	5d ~ 8y	Panax notoginseng saponins, IV, qd	IV	14d	AT, qd	Symptom improvement	T < C, P < 0.05	NR
Long, 2004 [29]	92; 36 ~ 70	2m ~ 10y	●Panax notoginseng saponins, Angelica gigas extract, Carthamus tinctorius extract, IA, qod	GB20	30d	●Salvia miltiorrhiza, IV, qd ●Nimodipine, tid	(1) Symptom improvement (2) Scoring for symptoms	(1) T > C, P < 0.05 (2) T > C, P < 0.01	NR

First Author; pub. year	No. of participants; Age*	Duration of disease*	Intervention type	Injection route and acupoints	Treatment period	Type of control group	Outcome measure	Results	Adverse events
			•AT, qd				and function rehabilitation of cervical vertigo		
Zhang, 2011 [30]	75; 30 ~ 78	2h ~ 20y	Salvia miltiorrhiza, Dalbergia odorifera, qd	IV	10d	AT, qd~bid	Symptom improvement	T < C, P < 0.01	NR
Zhu, 2012 [31]	120; 37 ~ 74	NR	Ginkgo biloba, qd	IV	28d	AT, qd	(1) Dizziness symptom score (2) Symptom improvement	(1) T < C, P < 0.05 (2) T < C, P < 0.05	NR
Li, 2006 [32]	108; 50 ~ 75	6m ~ 12y	Puerarin, qd	IV	15d	AT, qd	Symptom improvement	P < 0.01	NR
Li, 1998 [33]	140; 38 ~ 67	12d ~ 5y	•Scopolamine, vitamin B ₆ , IA, qd •AT, qd	cervical paravertebral points	10d	•Herbal medicine •Tuina, cervical traction, physiotherapy	Symptom improvement	T > C, P < 0.05	NR
Jin, 2014 [34]	82; 37 ~ 74	NR	•Ligustrazine, qd •Symptomatic treatment	IV	14d	•Cinepazide maleate, qd •Symptomatic treatment	(1) Remission time of dizziness, tinnitus and balance disorder (2) Symptom improvement and change of TCD flow velocity	(1) T < C, P < 0.05 (2) T < C, P < 0.05	NR
Yi, 2012 [35]	98; 35 ~ 74	NR	Ligustrazine, qd	IV	14d	Cinepazide maleate, qd	Symptom improvement and change of TCD flow velocity	T < C, P < 0.05	NR
He, 2013 [36]	128; 57 ~ 78	NR	Ligustrazine, qd	IV	NR	Cinepazide maleate, qd	Symptom improvement	T < C, P < 0.05	NR
Yang, 2015 [37]	80; 25 ~ 72	5m ~ 13y	•Angelica gigas extract, Ligusticum striatum extract and Carthamus tinctorius extract, IA, qd •AT, qod	Ashi points, cervical paravertebral points, ST36, GB20 and BL23	21d	AT, qod	Symptom improvement	T > C, P < 0.05	NR

* The values are presented as range or average.

Abbreviations: publication, pub.; number, no.; control group, C; Treatment group, T; day, d; month, m; year, y; everyday, qd; every other day, qod; every third day, q3d; twice a day, bid; three times a day, tid; four times a day, qid; acupuncture, AT; systolic velocity, Vs; diastolic velocity, Vd; vertebral artery, VA; basilar artery, BA; intra-acupoint, IA; intravenously, IV; not reported, NR;

3.1. Types of pharmacopuncture solution used in cervicogenic dizziness

Single compound derived from medicinal plants or the extract of herbs were commonly used. *Salvia miltiorrhiza* was most frequently used either by mixture with *Dalbergia odorifera* (also known as compound *Salvia miltiorrhiza* injection) [13-15, 17, 21-24, 26, 30] or *Carthamus tinctorius* [12] or *Salvia miltiorrhiza* alone [18, 29]. *Angelica gigas* extract [11, 15, 24], *Gastrodin* (a compound in *Gastrodia elata*) [18, 25, 27] and *Panax notoginseng saponins* (also known as *Xuesaitong*) [15, 28, 29] were also studied in clinical trials. *Angelica gigas* extract was also used in combination with *Ligusticum striatum* extract and *Carthamus tinctorius* extract (also known as compound *Angelica* injection) [21, 37] or only with *Carthamus tinctorius* [29]. Besides, the effect of injecting *Anisodamine* (a compound of *Anisodus tanguticus*) [12, 17], *Ligustrazine* (a compound of *Ligusticum striatum*) [13, 34-36], *Carthamus tinctorius* [16], *Scopolamine* (alkaloid component of *Semen Hyoscyami*) [33], *Ginkgo biloba* [31] and *Puerarin* (a compound of *Pueraria lobata*) [32] was also studied for cervicogenic dizziness. Injecting compound *Angelica* injection in Ashi points, cervical paravertebral points, ST36, GB20 and BL23 combined with body acupuncture significantly improved symptom compared with body acupuncture alone (97.5% versus 80.0%, $P < 0.05$) [37].

Pharmacopuncture solution was usually applied solely to human body. In some studies they were used as mixture with other conventional medicine like lidocaine [15-17, 24], Vitamin B12 [15, 16, 24], betahistine [13]. Injecting combination of *Angelica gigas* extract, compound *Salvia miltiorrhiza*, *Panax notoginseng saponins*, lidocaine, and Vitamin B12 in GB20, BL10 and GV16 had significantly better efficacy compared with body acupuncture group (symptom improvement 96.7% versus 80.0%, $X^2 = 3.96$, $P < 0.05$) [15]. Statistical difference was found in injecting *Carthamus tinctorius*, lidocaine, Vitamin B12 in GV20, GB20, cervical paravertebral points compared with cervical traction and iontophoresis with herbal *Angelica sinensis*, *Ligusticum striatum*, *Corydalis yanhusuo*, *Clematis chinensis*, *Gentiana macrophylla*, *Phryma leptostachya*, etc) (symptom improvement 96.4% versus 75.0%, $X^2 = 4.90$, $P < 0.05$) [16]. Compound *Salvia miltiorrhiza* injected in GB20 effectively improved symptom compared with acupuncture alone in cervical paravertebral points (95% versus 81%, $P < 0.05$) [14]. When pharmacopuncture solution was infused intravenously, it was diluted to intravenous fluids such as normal saline or 5% dextrose in water [12, 13, 17-19, 21-25, 27, 28, 30-32].

Conventional medicine (lidocaine [20], Vitamin B12 [20], Vitamin B1 [20], Vitamin B6 [33], dexamethasone [20]) was often injected in acupoints. Injecting lidocaine, Vitamin B12, Vitamin B1, dexamethasone in ST10, GB20, GV14, and cervical paravertebral points was superior to oral administration of aspirin and intravenous administration of *panax notoginseng saponins* and citicoline in the change of blood flow velocity monitored by transcranial Doppler ultrasonography ($P < 0.05$) [20].

3.2. Importance of adapting acupoints in pharmacopuncture

Researches studied efficacy of pharmacopuncture applied in acupoints. [11-26, 29, 33, 37]. Some studies especially revealed that injecting solution in acupoints is more effective than injecting the identical solution intravenously. Applying *Salvia miltiorrhiza* in GB20 and BL10 showed better efficacy than injecting *Salvia miltiorrhiza* intravenously (symptom improvement 95.0% versus 66.7%, $X^2 = 9.855$, $P < 0.01$) [19]. While control group adapted intravenous injection of compound *Salvia miltiorrhiza* and oral administration of herbal decoction, injecting compound *Salvia miltiorrhiza* in GV20, CV04 and Jingyun acupoint (0.8 cun lateral to the space between C5-6 spinous processes) showed significant difference (100.0% versus 86.2%, $P < 0.01$) and the efficacy was consistent in patients of different syndrome differentiations [22]. Injecting compound *Salvia miltiorrhiza* in GB20 and cervical paravertebral points showed better efficacy in comparison with intravenously injecting compound *Salvia miltiorrhiza* and orally taking flunarizine hydrochloride (symptom improvement 97.1% versus 76.5%, $X^2 = 4.61$, $P < 0.05$) [23]. These findings are well worth considering in terms of the importance of exploiting acupoints in pharmacopuncture.

Many researcher have selected GB20 the most for PA injection point in cervicogenic dizziness [11-21, 23, 24, 26, 29, 37]. GV20 was also popular acupoint for cervicogenic dizziness [8, 16, 22]. GB20 [8, 9, 39] and GV20 [8-10] were similarly frequently selected in pharmacopuncture treatment for dizziness of other causes. As for cervicogenic dizziness, the acupoints located on occipital region such as cervical paravertebral points [16, 20, 21, 23-26, 33, 37], BL10 [15, 19, 26] and GV16 [21] which are adjacent to GB20, were mainly used in cervicogenic dizziness. Among distal acupoints, ST36 was mostly used [8, 11, 37].

3.3. Pharmacopuncture as complement to conventional treatment for cervicogenic dizziness

Pharmacopuncture yielded synergetic effect when it is used with conventional treatment for cervicogenic dizziness. Injecting *Anisodamine* in GB20 yielded complementary effect when it was added to cervical traction, intravenous injection of *Salvia miltiorrhiza* and *Carthamus tinctorius* and oral administration of herbal medicine (98.3% versus 86.2%, $P < 0.05$) [12]. Adding compound *Salvia miltiorrhiza* in GB20 and BL10 enhanced the efficacy from the control group which simply received physical therapy, cervical traction, and manipulation (symptom improvement 94.1% versus 76.4%, $X^2 = 4.86$, $P < 0.05$) [26]. Injecting scopolamine and vitamin B6 in cervical paravertebral points yielded better efficacy compared with the control which received usual treatment comprising conventional medicine, herbal medicine, tuina, cervical traction and physiotherapy (symptom improvement 100% versus 89.2%, $U = 2.0143$, $P < 0.05$) [33].

3.4. Interaction with body acupuncture

Some studies have shown that combining body acupuncture with pharmacopuncture resulted in better efficacy on cervicogenic dizziness than treating with body acupuncture alone. Intravenous injection of Gastrodin with body acupuncture group was better than either body acupuncture group or Gastrodin injection group (symptom improvement 94.7% versus 86.8% versus 57.9%) and it showed significant difference compared with Gastrodin injection group ($P < 0.05$) but not with body acupuncture group ($P > 0.05$) [27]. Injecting compound Angelica in acupoints combined with body acupuncture showed better efficacy than body acupuncture alone (symptom improvement 97.5% versus 80.0%, $P < 0.05$) [37].

On the other hand, several studies reported that body acupuncture exceeded the efficacy of intravenous injection of pharmacopuncture. Body acupuncture showed better efficacy than daily intravenous injection of Panax notoginseng saponins (symptom improvement 91.4% versus 71.4%, $P < 0.05$) [28]. Penetrating across both GB20 with dry needle had better efficacy than intravenous administration of compound Salvia Miltiorrhiza (100.0% versus 46.7%, $P < 0.01$) [30]. Applying acupuncture on GB20, GV20, PC06, cervical paravertebral points and additional acupoints according to syndrome differentiation was more effective than intravenous injection of Ginkgo biloba (symptom improvement 93.3% versus 68.3%, $P < 0.05$) [31]. Applying acupuncture on GB20, GV21, GB21, GV14, GV13, LR03 and cervical paravertebral points was significantly better than injecting Puerarin [32]. Treatment group received head acupuncture on GB20, BL10, GB12, GV14 with injecting Panax notoginseng saponins, Angelica gigas extract and Carthamus tinctorius extract in GB20 while the control group had intravenous injection of Salvia miltiorrhiza extract and oral administration of Nimodipine. Both groups had significant change after the treatment and the former group have significant difference compared with the latter group [29].

4. Conclusion

Dizziness is a very common but debilitating symptom that often impedes patients from maintaining everyday lives. For this reason, new intervention for dizziness is important and its adjunctive use with other current treatments would improve the severity and duration of the symptom. Pharmacopuncture would make up for it and a great number of pharmacopuncture studies for cervicogenic dizziness indicates its possibility. Its vast studies might be partially related to traditional use of acupuncture on cerebrovascular diseases [40].

Throughout previous trials, diverse kinds of injecting solution were used. The same solutions were both injected on acupoints [11-24, 26, 29, 30, 33, 37] or injected intravenously [12, 13, 17-24, 27-31, 35]. These issues leave the necessity to establish the criteria for selecting the injection solution and their usage according to certain symptoms or features of dizziness. Several studies reported the effi-

cacy of needling in acupoints over intravenous injection of pharmacopuncture and acupoints on occipital region were distinctively used for cervicogenic dizziness. These results remind us the importance of adoption of acupoints and their selection. Principles or schematized plan of pharmacopuncture treatment depending on the type of dizziness should be investigated further.

Conflict of interest

The authors declare that there are no conflicts of interest.

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