Original Article

Characteristics of Sham/Placebo Acupuncture Controlled Trials for Headache

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국문초록

두통에 대한 Sham/Placebo 침술 대조군 연구의 특성에 대한 연구

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목적 : 두통의 침술효과에 대한 연구가 꾸준히 이루어지고 있다. 하지만 많은 연구들에서 서로 상충되는 결과를 내놓고 있다. 이에 저자는 대조군 집단 시술의 역할과 시험의 특성에 대해 연구하는 데 있어 몇 가지 유형의 두통, 특히 긴장성 두통(Tension-type headache, TTH)과 편두통에 대한 침술의 대조군 시험에서 나타나는 일관성 없는 발견 사항들의 원인이 무엇인지에 대해 밝히려고 하였다.

방법 : 두통의 침술효과에 대해 보고하고 있는 11개의 임의대조군 시험(Randomized controlled trials, RCTs)을 대상으로 하여 위약 침술과 방법론적 특성 범주 III과 IV를 중심으로 위약 시술 분석, 비교를 실시하였다.

결과 : 임상적 유효성과의 상관관계에 있어 범주 III과 IV 사이에는 유의한 차이가 없었다. 표본 크기 계산, 표본 전체 크기, 진짜 집단과 위약 집단에 속한 피험자의 수에는 긍정적 결과와 중립적 결과 사이에 유의한 차이가 없었다.

결론 : 두통의 임의대조군 시험에 대한 다양한 유형의 위약 대조군과 침술의 방법론적 특성이 임상적 효과를 예측해 주는지의 여부에 대해 추가 연구가 이루어져야 하겠다.

핵심단어 : 두통, 대조군시험, 거짓침

Ⅰ. Introduction

Tension-type headache (TTH) and migraine are major types of headache and the prevalence of migraine peaks during the most productive years of adulthood (age 25 to 55 years) in both sexes and the prevalence is higher in individuals of lower socioeconomic status in the United States[1]. The first-line treatment for these conditions is drug-therapy such as aspirin and ibuprofen. However, these medications are not able to produce complete relief and have been reported to be associated with adverse effects including gastrointestinal problems and drowsiness[2,3].

Acupuncture has been increasingly and widely used as an alternative for the treatment of headache and has been well tolerated by patients[4-6]. In parallel, there have also been an increasing number of randomized controlled trials (RCTs) on the efficacy of acupuncture for headache management with conflicting effectiveness[7-18].

However, findings from these studies were not conclusive due to a number of methodological issues that are yet to be adequately addressed. These include concerns about the appropriateness of sham or placebo control, inadequate sample size, intervention consideration, statistical analyses and others. Of these, the effective use of sham or placebo acupuncture for control groups has played a significant role with respect of interpreting the findings of these studies. Dincer and colleagues[19] have previously examined the types of sham and placebo acupuncture being used in RCTs in acupuncture. However, the quality of each of these types of sham or placebo acupuncture is yet to be determined.

This review aims to investigate whether there have been correlations between the types of sham/placebo control interventions employed and the reported effectiveness from these trials with an effort to partially address the potential contributing factors to the conflicting findings of acupuncture RCTs for TTH and migraine.

Ⅱ. Methods

1. Search strategies

Search was conducted to identify all RCTs include-ing major databases; Pubmed, Medline, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), from their inceptions to February 2006. Key words used for search were acupuncture, sham, placebo, headache, migraine, cephalgia, cephalalgia or combination of them. In addition, we searched the reference lists of review articles and hand-searching on departmental files. The Language of publications was English only.

2. Study inclusion/exclusion criteria

Only human RCTs using acupuncture needles with headache as a main clinical outcome measure were included. In case of cross-over design, only the first phase was included and pilot studies with various sample sizes were also included in this review. Trials of acupressure, laser acupuncture, acupuncture point injection, transcutaneous electrical nerve stimulation (TENS), ear acupuncture, hand acupuncture, and dry-needle technique were excluded. Studies that included other diseases except headache or migraine were withdrawn and headache caused by other diseases were excluded.

3. Data extraction

For each study, data concerning study design, experience of acupuncture of participants, medication, detailed description of acupuncture interventions (such as type, condition and duration), sham/placebo control interventions, and outcome measures of headache, quality of life (QoL) and effectiveness were extracted. The extraction process was facilitated by using a pre-defined, standardized template.

4. Categorisation of sham/placebo control interventions and findings

The 5 category structure of sham/placebo acupuncture control interventions classified by Dincer et al[19] was adapted. The following 2 out of 5 categories were included in this review : Category Ⅲ : non-acupuncture points, that is needling "outside" of acupuncture points; and Category Ⅳ : placebo needles using of devices which mimic acupuncture but where skin penetration does not occur. The findings of these studies were also recorded as per Dincer et al[19], that is, positive findings were defined as when acupuncture significantly more effective than the control; neutral as when there no significant difference between the acupuncture and the control; while negative as when acupuncture significantly less effective than the control. A p-value less than 0.05 was considered as significant.

5. Assessment of methodological quality

The quality of acupuncture trials was assessed using the checklist for Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA)[20]. Assessment of methodological quality was carried out using the Jadad's Scale[21]. During this process, we adapted the Jadad's scale for assessing the randomization procedures. For assessment of blinding, the credibility scales[14] for blinding procedures were employed with additions of the followings two questions : Was credibility test included in this study? If yes, was the blinding procedure successful?

To assess the trial quality, additional items were added to assess sample size, these are sample size-total, number of subjects in the real acupuncture group and the sham/placebo group, information concerning sample size calculation (yes/no), and statistical power calculation.

6. Statistical Analyses

Statistical analyses were performed using SPSS software (SPSS for Windows, release 13.0 ; SPSS Inc, Chicago, IL, USA). Mann-Whitney U test and Chi square test were performed to examine the group differences. Differences were considered significant at p<0.05.

Ⅲ. Results

1. Search results

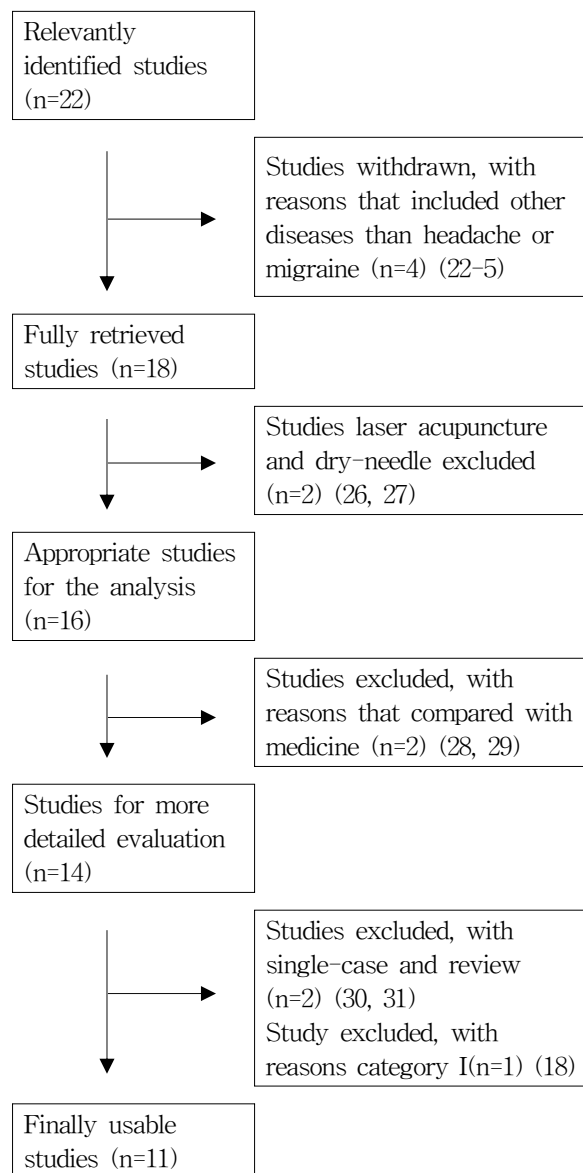A total of 22 publications were identified, of

Fig. 1. Flow diagram of this review

which 11 were excluded for the reasons given in Fig. 1. Studies that included other diseases than headache or migraine were excluded[22-25]. Trials of laser acupuncture, and dry-needle technique were excluded[26,27]. Studies that compared to medicine were withdrawn[28,29]. Two studies were also excluded because of single-case and review[30,31]. Based on Dincer et al[19] classification, 6 out of 11 trials belonged to Category III while the remaining 5 in Category IV and 1 in Category I (superficial needling of true points). For the comparison 1 trial of Category I was excluded[18]. Thus, 11 studies were included in this review[7-17], of which, 3 studies on migraine and 8 on TTH studies. Of the 11 studies, one was a pilot study[15] and one employed a cross-over design[7]. There were no studies including patients with different headache types in one study (Fig. 1).

2. Effectiveness regarding categories III and IV control interventions

Of the 11 trials included, three trials reported a positive finding, while the other 8 studies with neutral findings. All 5 studies in category IV reported neutral outcome findings. For those in

Table 1. Classification According to Effectiveness of Sham/placebo Acupuncture Control Interventions

First author	Disease	Experience of acupuncture	Medication	Randomization method	Jadad's score	Effecti-veness	Category*	Credibility test**
Hansen[7]	TTH†	Unknown	Not allowed	No	4	Positive	III	No
Karst. 2000[8]	TTH	Unknown	Allowed	No	3	Neutral	IV	Yes
Karst. 2001[9]	TTH	Unknown	Allowed	No	2	Neutral	IV	Yes
Linde K. 2005[10]	TTH	No experience during the last 12 months	Allowed	Telephone randomization	5	Neutral	III	Yes
Linde M. 2005[11]	Migraine	Unknown	Allowed	Lottery	4	Neutral	IV	No
Melchart[12]	TTH	No experience during the previous 12 months	Allowed	Telephone randomization	5	Neutral	III	Yes
Tavola[13]	TTH	Unknown	Allowed	No	4	Neutral	III	No
Vincent[14]	Migraine	Unknown	Allowed	No	3	Positive	III	Yes
White. 1996[15]	Migraine	Naïve	Allowed	Computer generated numbers	5	Neutral	IV	Yes
White. 2000[16]	TTH	Naïve	Allowed	Telephone randomization	5	Neutral	IV	Yes
Xue[17]	TTH	Unknown	Not allowed	Computer generated numbers	5	Positive	III	No

 * category III : non-acupuncture points (needling "outside" of acupuncture points).
   category IV : placebo needles (use of devices which mimic acupuncture but where skin penetration does not occur).
 ** : Credibility scales for blinding procedure tested and If tested, was it kept blinded?
 † : Tension-type headache .

category Ⅲ, 3 studies reported a positive finding while the other 3 neutral. However, there were no significant differences between categories Ⅲ and Ⅳ concerning correlation with effectiveness(p>0.05, Table 1).

3. Experience of acupuncture or medication

Of the 11 studies included in this review, 2 studies only included acupuncture naïve participants and the other 2studies on subjects with no acupuncture experience over the last 12 months. 7 studies did not report this. There was no association between positive/neutral outcome findings and previous experience of acupuncture or medication (p>0.05, Table 1).

4. Randomization method

Of the 8 studies with neutral findings, 5 included descriptions on randomization methodsuch as telephone randomization and computer generated numbers. In contrast, only 1 out of 3 studies with positive findings provided such information. There were no significant differences with regard to randomization method and other Jadad's scores between studies with positive and neutral findings (p>0.05, Table 1).

5. Modified credibility scale

There was 1 study from the group with positive findings and 6 out of 8studies from those with neutral findings reported on findings of the credibility scales. There were no differences in modified credibility scale between positive and neutral outcome findings (p>0.05, Table 1).

6. Sample size calculation

Only half of the studies with neutral findings and none of those with positive findings provided details about sample size calculation and power (80 to 90) of calculation. There were no significant differences between positive and neutral findings about sample size calculation. Concerning sample size-total, number of subjects in real group and sham/placebo group, there were no differences between positive and neutral outcome findings (p>0.05, Table 2).

7. Outcome measures

There were no clear differences between positive and neutral outcome findings regarding following headache outcome measures : headache (pain) intensity (including average pain, visual analogue scale (VAS)), headache duration, headache index

Table 2. Sample Size Calculation of Sham/placebo Acupuncture Control Interventions

First author	Sample size calculation (power)	sample size-total	No. of verum group	No. of sham (placebo) group
Hansen	No	25	13	12
Karst. 2000	No	39	21	18
Karst. 2001	Yes (90)	69	34	35
Linde K. 2005	Yes (80)	226	145	81
Linde M. 2005	No	31	15	13
Melchart	Yes (80)	195	132	63
Tavola	No	30	15	15
Vincent	No	32	16	16
White. 1996	No	10	5	5
White. 2000	Yes (80)	50	25	25
Xue	No	40	20	20

Table 3. Outcome Measures in This Reviewed Articles

First author	Outcome measures
Hansen	weeks(days) free of headache/ days with headache/ period index
Karst. 2000	pain intensity/ frequency/ pain threshold/ analgesic consumption days/ ADS(depression scale)/ clinical global impressions/ FQCI(Freiburg questionnaires of coping with illness)/ NHP(Nottingham Health Profile)/ ELQ(everyday life questionnaire)
Karst. 2001	pain intensity/ duration/ frequency/ analgesic consumption days/ ADS / clinical global impressions/ FQCI/ NHP/ ELQ/ LS(life quality scale)
Linde K. 2005	pain intensity/ days with headache/ migraine attacks/ accompanying symptoms/ symptom reduction/ activities impaired/ analgesic consumption days/ headache disability index/ SF-36(short form -36)/ ADS/ SES(assessing emotional aspects)
Linde M. 2005	pain intensity/ frequency/ days with headache
Melchart	pain intensity/ headache score/ days with headache/ hours with headache/ analgesic consumption days/ headache disability index/ SF-36/ ADS/ SES
Tavola	pain intensity/ duration/ headache index/ frequency/ analgesic consumption days
Vincent	pain intensity/ weeks(days) free of headache/ peak pain scores/ medication scores
White. 1996	pain intensity/ duration/ headache index/ weeks(days) free of headache/ analgesic consumption days
White. 2000	pain intensity/ duration/ days with headache/ SF-36/ General health questionnaire
Xue	pain intensity/ duration/ frequency/ pain threshold/ headache(pain) disability index/ sickness impact profile

Table 4. STRICTA Items in This Reviewed Articles

First author	Rationale for treatment	Responses elicited	Total numbers of needles inserted	Needle retention time (minutes)	Period of treatment	Frequency of treatment	Total number of acupuncture treatment
Hansen	Essentials of Chinese Acupuncture	Sensation of soreness, numbness or distension around the point	6	15	3w	twice a week	6
Karst. 2000	No	No	15	30	5w	twice a week	10
Karst. 2001	No	No	15	30	5w	twice a week	10
Linde K. 2005	Individually according to symptoms	De qi	10	30	8w	twice a week*2 then weekly	12
Linde M. 2005	No	De qi	12	30	12w	3 treatments a month	9
Melchart	Individually according to symptoms	De qi	10	30	8w	twice a week*2 then weekly	12

Tavola	Individual energy status	Manifested pain, torpor or swelling around the point	6-10	20	8w	weekly	8
Vincent	Vincent	No	8	15	6w	weekly	6
White. 1996	Individually either for tenderness or from list	De qi	6	0	6w	weekly	6
White. 2000	Individually either for tenderness and symptoms	De qi	8	0	6w	weekly	6
Xue	Patterns diagnosis	De qi	4	30	4w	twice a week	8

(=pain intensity x duration), headache score (=sum of intensity of days with headache), headache frequency, weeks (days) free of headache, days with headache, hours with headache, headache period index, migraine attacks, pain threshold, peak pain scores, accompanying symptoms, symptom reduction, activities impaired, analgesic consumption days, medication scores, QoL such as headache (pain) disability index, sickness impact profile, short form-36 (SF-36), general health questionnaire, depression scale, questionnaire for assessing emotional aspects, clinical global impressions, Freiburg questionnaires of coping with illness (FQCI), Nottingham Health Profile (NHP), everyday life questionnaire (ELQ), and life quality scale (LS) ($p > 0.05$, Table 3).

8. STRICTA items

For those reported neutral outcome findings, 3 out of 8 did not provide the rationale of treatment such as patterns diagnosis and individualized acupoints selection, while all studies with positive findings did so. However, there were no significant differences with respect of rationale of treatment between studies reported positive and neutral findings. There were also no differences concerning

needling responses elicited and other STRICTA items, such as total numbers of needles inserted, needle retention time (minutes), period of treatment, frequency of treatment, total number of acupuncture treatments, between positive and neutral effectiveness ($p > 0.05$, Table 4).

IV. Discussion

In controlled trials, appropriateness of the control interventions is very important especially in acupuncture studies. Many devices and procedures have been developed as sham/placebo controls[10,14,19,20,32-37]. However, none of these devices really mimic personal perceptions of acupuncture, so it is usually accepted that a 'real placebo' acupuncture has not been made until now[38]. Furthermore, the sham acupuncture cannot be regarded as a real placebo, thus it possibly leads to a relatively high effectiveness in the control interventions[28,38,39].

This study attempted to address one of the difficult issues in acupuncture research; that is, to search a factor determining a contradictory results in sham/placebo controlled trials. To the best of our knowledge, the current study is the first of its kind.

This review first demonstrated that the different types of sham/placebo control interventions used in RCTs in TTH and migraine could not predict the clinical effectiveness of the study. This is also supported by analyses of the quality of acupuncture interventions, trial design and credibility of acupuncture trials included in this systematic review.

The increasing adaptation of evidence-based medicine (EBM) in health policy development and clinical decision making requires acupuncture as a form of healthcare to meet stringent requirements of scientific scrutiny. This development imposes significant challenges to this relatively new form. To meet these challenges, RCTs in acupuncture are deemed to be essential and this "gold standard" study design has been adapted in trials of acupuncture for a number of clinical conditions particularly various types of pain. However, many reports have produced conflicting findings concerning the effects of acupuncture. In terms of evidence of acupuncture therapy on headache or migraine, its efficacy is lacking until now[7-18]. The small sample sizes and poor quality have contributed to the lack of conclusive evidence demonstrating the benefit of acupuncture for TTH and migraine. Many plausible explanations have been proposed including the critical evaluation of the approaches adapted for devising a credible control group intervention.

This review aimed to investigate potential correlations between the types of sham/placebo acupuncture used and the effectiveness of trials and to identify possible factors that might have contributed to the inconsistent effectiveness of headache so that it may offer useful insight of future design of trials on acupuncture for TTH and migraine. The first objective of this study is to reveal whether different types of sham/placebo control in acupuncture RCTs for headache predict clinical effectiveness or not. Even though 3 trials were positive, the majority of the remaining 8 were with neutral findings. However, there were no significant differences between category III and IV sham/placebo interventions with the findings. The second objective of this review is to investigate which factors

determine the conflicting effectiveness of acupuncture employed in RCTs for headache, such as TTH and migraine. Clinically, individuals with previous acupuncture experience tend to have clearer expectations of needling procedures and their body's response to these and thus it is inappropriate to include them in studies using a non-invasive sham/placebo intervention as a control[32]. Thus, previous experience of acupuncture is deemed to be an important factor that may influence effectiveness of acupuncture trials. Interestingly, comparison of studies that included subjects with or without previous experience of acupuncture showed no differences between positive and neutral outcome findings. Thus, it is obscure whether experience with acupuncture would be a factor that influences clinical effectiveness in trials for TTH and migraine.

For acupuncture RCTs, criticisms have been commonly laid on the inadequacy of reporting standardization of needling technique and sham/placebo interventions as well as diagnostic procedures. STRICTA guidelines were developed to improve the overall quality of reporting standards of acupuncture trials. This review compared the difference between real acupuncture and sham/placebo intervention concerning the needling procedures and whether or not traditional Chinese medicine (TCM) theory was incorporated into the trial design[10]. However, there were no significant differences between the two groups based on STRICTA items. The lack of differences between the real acupuncture and sham/placebo intervention in our study indicates that some aspects, including De qi, considered relevant for acupuncture practice might have not contributed to the inconsistent effectiveness of headache. This finding, to some extent, contradicts current evidence in the TCM literature[10].

It is desirable to measure treatment credibility directly, instead of indirectly, in both intervention groups in order to ascertain where differences in credibility could have affected the study's outcome measures[32]. To ensure quality of the study, ad-

equate sample size calculation and randomization procedure is important. A proper randomization procedure should be reported that it is well described in the published papers[40]. However, there were no correlations between positive and neutral outcome findings about above items. Like other reviews[41], this review also identified a number of other factors that might have contributed to the conflicting findings on acupuncture for TTH and migraine. These included some studies with poor study design such as inadequate follow-up, insufficient sample size, and poor reporting details.

Based on these findings, the hypotheses of correlations between different types of sham/placebo control procedures and effectiveness was rejected. In addition, even though there were no significant differences between the two groups in all items included in this review, due to the small number if trials that met the inclusion criteria, these findings need to be interpreted with caution particularly with respects to methodological quality of these trials. It is worth-mentioning that most studies included in this review had small numbers of subjects which limited the generalizability of the findings. With small sample sizes, false negative results may be produced. Besides sample sizes, the other important factor that may offer an explanation to the finding of the review is the appropriateness of the control interventions that may result in potent placebo effects[10]. Therefore, the issue about proper and effective application of placebo control remains as a methodological challenge[42]. Findings from this review might support the conclusion that poorer quality acupuncture RCTs tend to produce positive findings which were concluded by a recent review on systematic reviews of acupuncture published from 1996 to 2005[43].

V. Conclusions

Due to the general inadequacies of the studies such as the sample sizes and the small number of studies included in this review, no conclusion can be drawn whether different types of sham/placebo control and methodological qualities of acupuncture randomized controlled trials of headache predict clinical effectiveness or not. Larger trials that apply different control group interventions and incorporation of Chinese medicine theory in treatment planning should be conducted to further address the issue concerning the efficacy of acupuncture for pain management.

VI. References

1. Lipton RB, Bigal ME. Migraine : epidemiology, impact, and risk factors for progression. Headache. 2005 ; 45(Suppl 1) : S3-S13.
2. Le Jeunne C, Gomez JP, Pradalier A, Titus I Albareda F, Joffroy A, Liano H et al. Comparative efficacy and safety of calcium carbasalate plus metoclopramide versus ergotamine tartrate plus caffeine in the treatment of acute migraine attacks. Eur Neurol. 1999 ; 41(1) : 37-43.
3. Moore N. Forty years of ibuprofen use. Int J Clin Pract Suppl. 2003 ; 57(s135) : 28-31.
4. Acupuncture. NIH Consens Statement. 1997 ; 15(5) : 1-34.
5. Melchart D, Linde K, Fischer P, Berman B, White A, Vickers A, Allais G. Acupuncture for idiopathic headache. Cochrane Database Syst Rev. 2001 ; (1) : CD001218.
6. Elorriaga Claraco A, Hanna SE, Fargas-Babjak A. Reporting of clinical details in randomized controlled trials of acupuncture for the treatment of migraine/headaches and nausea/vomiting. J Altern Complement Med. 2003 ; 9(1) : 151-9.
7. Hansen PE, Hansen JH. Acupuncture treatment of chronic tension headache-a controlled crossover trial. Cephalalgia. 1985 ; 5(3) : 137-42.
8. Karst M, Rollnik JD, Fink M, Reinhard M, Piepenbrock S. Pressure pain threshold and

needle acupuncture in chronic tension-type headache-a double-blind placebo-controlled study. Pain. 2000 ; 88(2) : 199-203.

9. Karst M, Reinhard M, Thum P, Wiese B, Rollnik J, Fink M. Needle acupuncture in tension-type headache : a randomized, placebo-controlled study. Cephalalgia. 2001 ; 21(6) : 637-42.

10. Linde K, Streng A, Jurgens S, Hoppe A, Brinkhaus B, Witt C, et al. Acupuncture for patients with migraine : a randomized controlled trial. JAMA. 2005 ; 293(17) : 2118-25.

11. Linde M, Fjell A, Carlsson J, Dahlof C. Role of the needling per se in acupuncture as prophylaxis for menstrually related migraine : a randomized placebo-controlled study. Cephalalgia. 2005 ; 25(1) : 41-7.

12. Melchart D, Streng A, Hoppe A, Brinkhaus B, Witt C, Wagenpfeil S, et al. Acupuncture in patients with tension-type headache : randomised controlled trial. BMJ. 2005 ; 331(7513) : 376-82.

13. Tavola T, Gala C, Conte G, Invernizzi G. Traditional Chinese acupuncture in tension-type headache : A controlled study. Pain. 1992 ; 48(3) : 325-9.

14. Vincent CA. A controlled trial of the treatment of migraine by acupuncture. Clin J Pain. 1989 ; 5(4) : 305-12.

15. White AR, Eddleston C, Hardie R, Resch KL, Ernst E. A Pilot Study of Acupuncture for Tension Headache, Using a Novel placebo. Acupunct Med. 1996 ; 14(1) : 11-5.

16. White AR, Resch KL, Chan JC, Norris CD, Modi SK, Patel JN, et al. Acupuncture for episodic tension-type headache : a multicentre randomized controlled trial. Cephalalgia. 2000 ; 20(7) : 632-7.

17. Xue CC, Dong L, Polus B, English RA, Zheng Z, Da Costa C et al. Electroacupuncture for tension-type headache on distal acupoints only : a randomized, controlled, crossover trial. Headache. 2004 ; 44(4) : 333-41.

18. Pintov S, Lahat E, Alstein M, Vogel Z, Barg J. Acupuncture and the opioid system : implications in management of migraine. Pediatr Neurol. 1997 ; 17(2) : 129-33.

19. Dincer F, Linde K. Sham interventions in randomized clinical trials of acupuncture--a review. Complement Ther Med. 2003 ; 11(4) : 235-42.

20. MacPherson H, White A, Cummings M, Jobst K, Rose K, Niemtzow R. Standards for reporting interventions in controlled trials of acupuncture : the STRICTA recommendations. Complement Ther Med. 2001 ; 9(4) : 246-9.

21. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials : is blinding necessary? Control Clin Trials. 1996 ; 17(1) : 1-12.

22. He D, Hostmark AT, Veiersted KB, Medbo JI. Effect of intensive acupuncture on pain-related social and psychological variables for women with chronic neck and shoulder pain-an RCT with six month and three year follow up. Acupunct Med. 2005 ; 23(2) : 52-61.

23. Ng DK, Chow PY, Ming SP, Hong SH, Lau S, Tse D, et al. A double-blind, randomized, placebo-controlled trial of acupuncture for the treatment of childhood persistent allergic rhinitis. Pediatrics. 2004 ; 114(5) : 1242-7.

24. He D, Veiersted KB, Hostmark AT, Medbo JI. Effect of acupuncture treatment on chronic neck and shoulder pain in sedentary female workers : a 6-month and 3-year follow-up study. Pain. 2004 ; 109(3) : 299-307.

25. Engelhardt PF, Daha LK, Zils T, Simak R, Konig K, Pfluger H. Acupuncture in the treatment of psychogenic erectile dysfunction : first results of a prospective randomized placebo-controlled study. Int J Impot Res. 2003 ; 15(5) : 343-6.

26. Ebneshahidi NS, Heshmatipour M, Moghaddami A, Eghtesadi-Araghi P. The effects of laser acupuncture on chronic tension headache-a randomised controlled trial. Acupunct Med. 2005 ; 23(1) : 13-8.

27. Karakurum B, Karaalin O, Coskun O, Dora B, Ucler S, Inan L. The 'dry-needle technique' :

intramuscular stimulation in tension-type head-ache. Cephalalgia. 2001 ; 21(8) : 813-7.

28. Melchart D, Thormaehlen J, Hager S, Liao J, Linde K, Weidenhammer W. Acupuncture versus placebo versus sumatriptan for early treatment of migraine attacks : a randomized controlled trial. J Intern Med. 2003 ; 253(2) : 181-8.

29. Hesse J, Mogelvang B, Simonsen H. Acu-puncture versus metoprolol in migraine pro-phylaxis : a randomized trial of trigger point inactivation. J Intern Med. 1994 ; 235(5) : 451-6.

30. Vincent CA. The treatment of tension headache by acupuncture : a controlled single case design with time series analysis. J Psychosom Res. 1990 ; 34(5) : 553-61.

31. Gaus W, Hogel J. Studies on the efficacy of unconventional therapies. Problems and designs. Arzneimittelforschung. 1995 ; 45(1) : 88-92.

32. Sherman KJ, Hogeboom CJ, Cherkin DC, Deyo RA. Description and validation of a noninvasive placebo acupuncture procedure. J Altern Com-plement Med. 2002 ; 8(1) : 11-9.

33. Streitberger K, Kleinhenz J. Introducing a placebo needle into acupuncture research. Lan-cet. 1998 ; 352(9125) : 364-5.

34. Park J, White A, Stevinson C, Ernst E, James M. Validating a new non-penetrating sham acupuncture device : two randomised controlled trials. Acupunct Med. 2002 ; 20(4) : 168-74.

35. Goddard G, Shen Y, Steele B, Springer N. A controlled trial of placebo versus real acu-puncture. J Pain. 2005 ; 6(4) : 237-42.

36. Witt C, Brinkhaus B, Jena S, Linde K, Streng A, Wagenpfeil S, et al. Acupuncture in patients with osteoarthritis of the knee : a randomised trial. Lancet. 2005 ; 366(9480) : 136-43.

37. Xue CC, English R, Zhang JJ, Da Costa C, Li CG. Effect of acupuncture in the treatment of seasonal allergic rhinitis : a randomized con-trolled clinical trial. Am J Chin Med. 2002 ; 30(1) : 1-11.

38. Fink M, Gutenbrunner C, Rollnik J, Karst M. Credibility of a newly designed placebo needle for clinical trials in acupuncture research. Forsch Komplementarmed Klass Naturheilkd. 2001 ; 8(6) : 368-72.

39. Ernst E. Acupuncture research : where are the problems? Acupunct Med. 1994 ; 12(2) : 93-7.

40. Birch S. Clinical research on acupuncture. Part 2. Controlled clinical trials, an overview of their methods. J Altern Complement Med. 2004 ; 10(3) : 481-98.

41. Kaptchuk TJ. Acupuncture : theory, efficacy, and practice. Ann Intern Med. 2002 ; 136(11) : 374-83.

42. Kaptchuk TJ. The placebo effect in alternative medicine : can the performance of a healing ritual have clinical significance? Ann Intern Med. 2002 ; 136(11) : 817-25.

43. Lewith G, Berman B, Cummings M, Filshie J, Fisher P, White A. Systematic review of systematic reviews of acupuncture published 1996-2005. Clin Med 2006 ; 6(4) : 381-6.