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Original Article

Acupuncture and Cortisol Levels: a Systematic Review

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Objective: This study was undertaken to systematically assess and summarize the effects of acupuncture on cortisol secretion.
Materials and methods: We searched articles published up to May 2010 in six electronic databases (PubMed, Cochrane Library, KISS, KISTI, DBPIA, Kyobo Scholar). Randomized clinical trials (RCTs) which met all the inclusion criteria were reviewed. Eight RCTs were finally selected for this systematic review and assessed by three reviewers. The risk of bias was also estimated by using the Cochrane criteria.
Results: Six RCTs reported no distinct difference of cortisol levels between control and experimental groups. Two RCTs reported significant differences of cortisol levels between groups; one reported the acupuncture group with markedly higher concentrations of cortisol while the other reported the opposite result.
Conclusion: There are some difficulties in clearly identifying the effects of acupuncture on cortisol levels in this systematic review due to inconsistent results. Therefore, more rigorous trials with larger scales need to be conducted to clarify the effects of acupuncture on cortisol levels.

Key Words : Acupuncture, cortisol level, systematic review

Introduction

Acupuncture has been practiced for thousands of years, since long before there was any sound knowledge of anatomy, physiology or pathophysiology[1)]. It has been generally used in East Asian countries in the past, but is increasingly gaining popularity in Western countries nowadays.

Acupuncture treatment has been claimed to be effective at treating a wide range of conditions, including pain, musculoskeletal disorders, and several neurologic disorders[2)]. However, the underlying mechanisms of acupuncture have not been clearly demonstrated although many studies have tried to reveal these mechanisms. Recent studies suggest that acupuncture may affect the central and autonomic nervous systems[3-6)] and mental stress[7)]. There are some systematic reviews assessing the effect of acupuncture on some indicators of the autonomic nervous system such as heart rate variability (HRV)[8)], but there has been no systematic review examining the effect of acupuncture on the endocrine system.

Cortisol is a kind of hormone produced in the zona fasciculata of the adrenal cortex. Cortisol secretion is a key process in hypothalamic-pituitary-adrenal (HPA) axis activation[9)] and it facilitates the body's response to stress and regulates the immune system[10)]. Therefore, the aim of this systematic review was to summarize and assess the

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trials conducting experiments for the effects of acupuncture on cortisol secretion.

Methods

Data sources

We searched six electronic databases for all articles published up until May 2010. Included databases were four Korean electronic databases (KISS, KISTI, DBPIA, Kyobo Scholar), PubMed and The Cochrane Library. The terms for searching were "acupuncture AND cortisol" in PubMed and The Cochrane Library, and the Korean language terms for "침 AND 코티솔" in four Korean electronic databases. We manually searched the references of all articles for relevant articles.

Study selection

Only randomized clinical trials (RCTs) for human subjects were considered to be included. RCTs using needle acupuncture with electrical stimulation or auricular acupuncture were excluded. Articles written in Korean or English were considered to be included with language restriction. Articles of other languages were excluded. The trials which didn't assess cortisol level or were not related to acupuncture were also excluded. There was no restriction about the condition of subjects and the control group which was done by either sham acupuncture or conventional treatment.

Data extraction and assessment of risk of bias

The full text of selected articles was obtained and

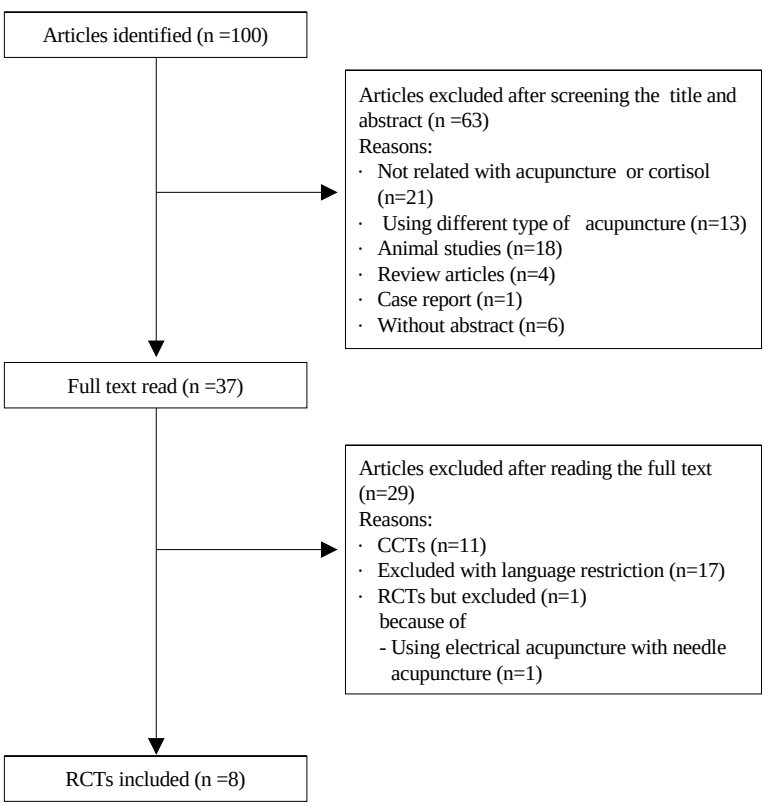

Fig. 1. Flowchart of process of selecting trials. RCT: randomized clinical trial; CCT: non-randomized clinical trial.

read in full by two independent reviewers (SHL, JWL). The relevant criteria for analyzing trials were defined by discussion among reviewers, then the two independent reviewers (SHL, JWL) extracted data from articles according to the criteria. The opinion of another reviewer (KTS) was considered, if needed. The extraction of data was based on the statement of author of each article or on outcome data reported in the article.

The risk of bias was assessed by six factors using the Cochrane criteria: sequence generation, allocation sequence concealment, blinding of participants, blinding of assessor, incomplete outcome data and selective outcome reporting[11]. The assessment was based on the statement of the author of each article. Two reviewers (SHL, JWL) estimated the risk of bias and the disagreements of opinion were resolved through discussion. The opinion of another reviewer (KTS) was also considered, if needed.

Results

Study description

The total number of articles searched through six electronic databases was 100, of which 92 were excluded and eight were RCTs which satisfied our inclusion criteria. The exclusion criteria for the 92 articles and selection process are described in Fig.1. Data extracted from eight RCTs were summarized in Table 1. Three RCTs were conducted in Germany[12-14], three in China[15-17], one in Belarus[18] and one in Japan[19]. Intradermal needle was used in one study[19], and the other studies used needle acupuncture. One study treated healthy subjects[14] and seven studies treated patients with other conditions: undergoing frozen-thawed embryo transfer (FET) treatment[15], with dysphonia[17], undergoing in vitro fertilization-embryo transfer (IVF-ET)[16], with irritable bowel syndrome[12], with chronic low back pain[13], undergoing operative procedures[18] and undergoing abdominal surgery[19]. Sham acupuncture treatment was conducted in six trials[12-17] and two trials compared acupuncture treatment with conventional treatment[18,19]. Three trials sampled cortisol from serum[15,16,18], two trials from saliva[12,17] and three from plasma[13,14]. Cortisol sampling times differed in each trial and are summarized in Table 1.

Risk of bias

The assessment of the risk of bias in each trial was summarized in Table 2. Four trials reported the specific methods of sequence generation[12,14-16], and allocation sequence concealment was described in four trials[14-16,19]. Five RCTs conducted participant blinding[12,14-16,19], of which three were considered to control blinding of participants with relevant methods[15,16,19] and one trial didn't blind the participants[13]. None of the eight RCTs stated the precise method of blinding assessors. Two RCTs reported incomplete outcome data because participants dropped out of trials[12,19]. There was no reported cortisol level in two trials[14,15].

Outcomes

Six articles reported no significant difference of cortisol levels between groups[13-18]. A difference of cortisol levels between groups was reported in two trials[12,19].

Among patients with irritable bowel syndrome (IBS), the cortisol level decreased more in the acupuncture-treated group than the sham-acupuncture-treated group[12]. It measured saliva cortisol level before and after treatment 4 times a day. Cortisol concentration in both two groups reduced, however, the gap of decline was more noticeable in the acupuncture treatment group.

The difference of cortisol levels in patients experiencing postoperative pain (after upper abdominal surgery and lower abdominal surgery) was

Table 1. Summary of RCTs Assessing Acupuncture and Cortisol Level

First author (Year) Origin	Design Subjects	Intervention	Source of Cortisol	Cortisol sampling time	Outcome (cortisol level)
So (2010) China	Parallel 226 female patients undergoing frozen-thawed embryo transfer(FET) treatment	(A) AC (25min immediately after FET, n=113) (B) SAC(non-penetration on acupuncture point, n=113)	serum	(1) Before treatment (2) After treatment	No differences between two groups
Kwong (2010) China	Parallel 18 female dysphonic speakers	(A) AC (30min session of acupuncture, n=9) (B) SAC(non-penetration on acupuncture point, n=9)	saliva	(1) 10 min before inserting acupuncture (2) Immediately before inserting acupuncture (3) 15 min after inserting acupuncture (4) Immediately after removing acupuncture (5) 10 min after removing acupuncture	No differences between two groups
So (2009) China	Parallel 370 female patients undergoing in vitro fertilization-embryo transfer(IVF-ET) treatment	(Two sessions) (A) AC(25min before and after ET, n=185) (B) SAC(non-penetration at acupuncture point, n=185)	serum	(1) Immediately before the first session (2) Immediately after the second session	No differences between two groups
Schneider (2007) Germany	Parallel 43 patients with irritable bowel syndrome	(Ten sessions) (A) AC(n, r, n=19) (B) SAC(non-penetration on acupuncture point, n=15)	saliva	(1) Immediately before ten sessions (2) Within 3 days after ten sessions	More decrease in AC group after 10 sessions
Harbach (2007) Germany	Cross-over 15 male patients with chronic low back pain	(Patients received five different treatments.) (A) Oral medication (with diclofenac, n=15) (B) AC (30 min, n=15) (C) SAC (minimal penetration on non-acupuncture point, n=15) (D) electro-acupuncture (4-10Hz, n=15) (E) electro-acupuncture at non-acupuncture points (4-10Hz, n=15)	plasma	(1) 15 min after puncture of the antecubital vein (2) 10 min after placement of the last acupuncture (3) 5 min after displacement	No differences between groups
Kou (2005) Germany	Cross-over 10 male healthy subjects	(Three sessions) (A) AC (30min, n=5) (B) SAC (penetration on non-acupuncture point, n=5)	plasma	(In first and third session) (1) 10 min before insertion (2) 15 min after insertion (3) 30 min after insertion (4) 10 min after removing	No differences between two groups
Pohodenko (2005) Belarus	Parallel 120 male patients undergoing operative procedures	(A) AC (with conventional anaesthesia, n=20) (B) AC (after conventional anaesthesia, n=100) (C) only chemical anaesthesia (n=30)	serum	(1) Before surgery (2) After incision (3) During surgical intervention (4) Immediately after surgery	A=B > C((1) and (2), minor differences) B > A=C((3) and (4), minor differences)
Kotani (2001) Japan	Parallel 191 patients undergoing abdominal surgery	(A) AC (intradermal needle, n=50 for upper abdominal surgery, n=39 for lower abdominal surgery) (B) not treated (n=48 for upper abdominal surgery, n=38 for lower abdominal surgery)	plasma	(1) Before induction of anesthesia (2) Immediately before surgery (3) 1 h after the beginning of surgery (4) On emergence from anesthesia in the recovery room (5) First postoperative day	A < B (during recovery and the subsequent day)

AC: acupuncture; SAC: sham-acupuncture; n.r.: not reported

reported in Kotani *et al.*[19] This trial compared the change of cortisol levels in acupuncture treatment and conventional treatment groups for upper abdominal surgery and lower abdominal surgery. Plasma cortisol was sampled 5 times: before induction of anesthesia, immediately before surgery, 1 hour after the beginning of surgery, on emergence from anesthesia in the recovery room and first postoperative day, and the difference was significant during recovery. Cortisol level in both groups (upper abdominal surgery and lower abdominal surgery) increased more in the acupuncture treatment group than conventional treatment group and both reduced on the postoperative day.

Discussion

From this systematic review, it is hard to conclude how acupuncture treatment affects cortisol secretion. Although two trials showed a difference of cortisol levels between two groups, since other trials reported no significant difference, any conclusion about the effect of acupuncture on cortisol secretion cannot be defined clearly. Therefore, we needed to consider some potential factors of bias in this systematic review by two aspects: one is the aspect of included trials and the other is the aspect of this review itself.

The aspect of included trials is as following:

First of all, the familiarity of patients with acupuncture treatment was not controlled at all. Acupuncture is the practice of inserting a needle or needles into certain points in the body for therapeutic purposes[20] and all trials recruited patients regardless of familiarity difference about acupuncture treatment. In this situation, patients' anxiety about sticking treatment of acupuncture might differ across the group and this state anxiety level could affect the secretion of cortisol[21] more significantly than acupuncture treatment affects do. Hence, it can be hypothesized that the anxiety level about acupuncture treatment concealed the effect of acupuncture on cortisol level.

Secondly, the suitability of acupuncture treatment should be suspected. The acupuncture treatment

Table 2. Results of Assessing the Risk of Bias

Author (Year)	Sequence generation	Allocation sequence concealment	Blinding of participants	Blinding of assessor	Incomplete outcome data	Selective outcome reporting
So (2010)	Y	Y	Y	Un	Y	N (no cortisol level reported)
Kwong (2010)	Un	N	N	N	Y	Y
So (2009)	Y	Y	Y	Un	Y	Y
Schneider (2007)	Y	N	Un	Un	N (17/34 did not deliver the salivary cortisol at appropriate time)	Y
Harbach (2007)	Un	N	N	Un	Y	Y
Kou (2005)	Y	Y	Un	Un	Y	N (no cortisol level reported)
Pohodenko (2005)	Un	N	N	N	Y	Y
Kotani (2001)	Un	Y	Y	Un	N (14/189 did not complete the trial. Reasons differ across group.)	Y

Y: appropriate; N: not reported or inappropriate; Un: unclear

Table 3. Summary of Acupuncture Treatment Administrated in Each Trial

First author (Year)	Experience of acupuncturist	De-qi	Body posture of patients	Acupuncture point
So (2010)	3 years	considered	n.r.	ST36, SP6, SP10, LI4
Kwong (2010)	more than 20 years	considered	supine	LI4, CV23, KI6, ST9, LU7
So (2009)	2 years	considered	n.r.	(Before embryo-transfer) PC6, SP8, LR3, GV20, ST39 (Afterembryo-transfer) ST36, SP6, SP10, LI4
Schneider (2007)	n.r.	considered	n.r.	LR3, ST36, SP6, CV12, ST21, ST25, HT7, GV20 (only in acupuncture group)
Harbach (2007)	n.r.	considered	n.r.	BL23, BL25, BL40, BL60 GV3, GV4, KI3
Kou (2005)	n.r.	considered	supine	ST36, LI11, SP10, GV14
Pohodenko (2005)	n.r.	considered	n.r.	LI4, LI10, LI11, SI3, SI14, SI15, ST2, ST10, ST26, ST36, BL11, BL62, TE20, GB1, GB20, GB21, GB22, GB26, GB38, LU7, SP6, HT1, HT5, HT7, KI6, KI15, PC6, GV4, GV12 GV14, CV22, CV23
Kotani (2001)	n.r.	n.r.	prone	(Upper abdominal group) T7-T10, T9-L3, BL18-BL24 (Lower abdominal group) T10-L1,T11-L5, BL20-BL26

n.r.: not reported

performed in each trial was summarized in Table 3. Five studies didn't reported the experience of the acupuncturist[12-14,18,19] and five trials didn't state the posture of patients when treated[12,13,15,16,18]. Also, sound evidence of the effect of real acupuncture compared with sham acupuncture was not reported in any trial. These trials used different types of sham acupuncture; none of them is accepted universally. Therefore, it can also be hypothesized that the suitability of acupuncture treatment conducted and the use of sham acupuncture treatment were not adequate for the trials.

Finally, some bias can be attributable to the relevant method of blinding. Although five trials mentioned they employed a double-blinded method[12,14-16,19], none of those trials reported the relevant process of blinding assessors. Lack of blinding of participants or healthcare providers could cause some bias in the results by affecting the actual outcomes of the participants in the trial[11]. It is also supposed that the inadequate method of blinding patients and observers may affect the outcome data of participants in trials.

Despite our attempt to reduce bias, there are some limitations in this systematic review. Articles in Chinese, Russian, Croatian and Italian were excluded before reading their full text because of language restriction. It is possible that this obstacle led us to insufficient data and finally some bias. Articles not appearing in the six electronic databases we browsed were also excluded. Moreover, selective publishing and reporting are other major causes of bias that must be considered[22,23]. To conclude, the limitations of this systematic review may have a chance to affect the whole results of this systematic review.

Conclusion

There are some difficulties in drawing clear conclusions about the effects of acupuncture on cortisol level in this systematic review. Therefore, more rigid and specific RCTs need to be conducted

to clarify the effects of acupuncture on cortisol secretion.

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