Acupuncture for discomfort in patients during gastroscopy: a systematic review protocol

<table>
<thead>
<tr>
<th>Journal:</th>
<th>BMJ Open</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID:</td>
<td>bmjopen-2014-005735</td>
</tr>
<tr>
<td>Article Type:</td>
<td>Protocol</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>20-May-2014</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>WANG, Weiming; Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Department of acupuncture; Beijing University of Chinese Medicine, school of graduate; ZHANG, Tao; Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Department of acupuncture; PENG, Weina; Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Department of acupuncture; WU, Jiani; Guang’anmen Hospital, China Academy of Chinese Sciences, Department of acupuncture; LIU, Zhishun; Guang’anmen hospital, China Academy of Chinese Medical Sciences, Department of acupuncture</td>
</tr>
<tr>
<td>Primary Subject Heading:</td>
<td>Complementary medicine</td>
</tr>
<tr>
<td>Secondary Subject Heading:</td>
<td>Gastroenterology and hepatology, Medical publishing and peer review, Evidence based practice</td>
</tr>
<tr>
<td>Keywords:</td>
<td>COMPLEMENTARY MEDICINE, Endoscopy &lt; GASTROENTEROLOGY, Protocols &amp; guidelines &lt; HEALTH SERVICES ADMINISTRATION &amp; MANAGEMENT</td>
</tr>
</tbody>
</table>
Acupuncture for discomfort in patients during gastroscopy: a systematic review protocol

Weiming Wang¹,²†, Tao Zhang³†, Weina Peng¹, Jiani Wu¹, Zhishun Liu¹*  
¹ Department of acupuncture, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing (100053), China.  
² School of graduate, Beijing University of Chinese Medicine, Beijing (100029), China  
³ Department of acupuncture, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing (100010), China

†Weiming Wang and Tao Zhang contributed equally to this protocol.  
*Correspondence to: Professor Zhishun Liu; Tel: 86-10-88001124; E-mail:liuzhishun@aliyun.com

Key words: acupuncture, gastroscopy, system review, protocol  
Word count: 3669
Abstract

Introduction: The systematic review aims to assess the effect and safety of acupuncture for discomfort in patients during gastroscopy.

Methods and analysis: Randomized controlled trials will be searched electronically in several databases including PubMed, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Database and China National Knowledge Infrastructure (CNKI) from their founding date to April, 2014. We will also try to gain literatures by hand searching. The selection of studies, extraction of data and assessment of studies quality will be conducted by two researchers independently. Meta-analysis will be performed by the use of RevMan 5.2 statistical software. Data will be combined with random effect model. The results will be presented as risk ratio for dichotomous date and standardized mean difference for continuous data.

Dissemination: The systematic review will evaluate the current evidence of acupuncture therapy for discomfort in patients during gastroscopy. The findings will be disseminated through peer-reviewed publication or conference presentations.

Protocol registration: PROSPERO CRD42014008966.

Key words: acupuncture, gastroscopy, systematic review, protocol.

Strength and limitations of this study

- To the best of the authors’ knowledge, there is only one systematic review related to acupuncture and gastrointestinal endoscopy which was published in 2004 without any update till now. Our review will be the latest one to assess the effect and safety of acupuncture for the discomfort in patient during gastroscopy.
- The studies selection, data extraction and quality assessment will be performed independently by two researchers.
- The results of the systematic review will give gastroscopists more ways to help patients relieve discomfort during gastroscopy.
- It is difficult to pool data with varies kinds of manipulations and outcomes. Thus...
subgroup analysis will be proceeded to solve the problem.

Introduction

Gastroscopy is an important method of gastrointestinal endoscopy in the diagnosis and treatment for digestive system diseases. It has been the most commonly performed endoscopic procedures with an incidence of about 8.6 per 1000 of population in the Trent region of England since 1990s.\(^1\)\(^2\) The amount of patients accepted gastroscopy reached 0.2 million in Shanghai of China in 2001.\(^3\) Recent research indicated that the average number of gastrointestinal endoscopes in 169 endoscopy units of China (all of the units possess gastroscopy) gained three times in the nearly 12 years, from 2.3 in 2001 to 9.3 in 2013 per unit. Along with the aging population, work pressure and dietary changes, it is believed that the number of patients receiving gastroscopy is increasing continuously.\(^4\) During gastroscopy, gag reflex or the distention of gastric wall may be induced, which would cause throat discomfort, nausea, retching or even emesis.\(^5\)\(^6\) Moreover, it could evoke anxiety, increase heart rate, lower blood oxygen and change blood pressure.\(^7\)\(^-\)\(^9\) Pharyngeal anesthesia (e.g. lidocaine) and conscious sedation (e.g. diazepam, midazolam or propofol) are effective to minimize discomfort during gastroscopy.\(^10\)\(^-\)\(^13\) They could make the gastroscopy procedure smooth to some extent. However, it might cause retch in the anesthesia induction.\(^5\) Furthermore, conscious sedation may associate with some potential risks such as the inhibition of respiratory and cardiovascular system, hypotension, or even coma.\(^7\)\(^14\)\(^15\) Besides, its financial burden is much heavier. Those are also the reasons that unsedated gastrointestinal endoscopy (including gastroscopy) has been widely applied for many years and is still the major procedure selected by patients in China\(^16\) and other developing countries.

Acupuncture, with a history of more than 2000 years, plays an important role in complementary and alternative medicine. A number of clinical trials have been conducted to assess the effect of acupuncture therapy for discomfort during gastroscopy.\(^17\)\(^18\) In the pre-retrieval of 8 electronic databases, we have found more than 51 studies of acupuncture for this health issue. Meanwhile, recent study has suggested acupuncture as an alternative way to increase tolerance and reduce
discomfort during gastroscopy. Furthermore, there is only one published systematic review referring to “acupuncture” and “gastrointestinal endoscope” so far. The review was published in 2004 and assessed the effect of traditional manual acupuncture and electroacupuncture for gastrointestinal endoscopy. 6 randomized controlled trials (RCTs) published from 1978 to 2003 were included and analyzed in the review. To our knowledge, acupuncture is originated and widely used in China. But Chinese periodical databases were not searched in that review. In addition, 3 of the 6 included RCTs were acupuncture for colonoscopy. Thus, we could not draw a definite conclusion on this health issue from that review. However, with a more superior search strategy and more included databases, our systematic review may obtain a more convincing conclusion.

Therefore, we raised two questions: 1) is acupuncture effective for the discomfort during gastroscopy? 2) is acupuncture safe for reducing discomfort during gastroscopy? In order to find the answers, we will conduct a systematic review of acupuncture therapy for discomfort in patients during gastroscopy. In this article, we present the protocol of the systematic review.

METHODS AND ANALYSIS
Criteria for considering studies for this review
Types of studies
All of the clinical RCTs of acupuncture for discomfort in patients with gastroscopy will all be included in the review. While randomized crossover studies and quasi-RCTs will be excluded. Because of the particularity of acupuncture manipulation, it is difficult to blind the acupuncturists. Blinding will not be strictly limited in the inclusion criteria. But it will be evaluated as an item in the risk of bias assessment.

Types of participants
Participants who accepted gastroscopy will be included without the limitation of age. For those participants who accepted colonoscopy, or suffered from chronic pharyngolaryngitis, severe digestive system diseases, persistent hiccups, severe nausea and retching, proven tumors in upper digestive tract, and uncontrolled...
cardiopulmonary disease will be excluded.

Types of interventions

Any kind of acupuncture used in experimental group will be included, such as manual acupuncture, electroacupuncture, fire needling, warm needling, pyonex, scalp acupuncture, auricular acupuncture, and intradermal needling etc., without the limitation of the treatment length and frequency. The control group with no intervention, sham acupuncture, placebo control and drugs therapy (such as lubricant, anesthesia and sedative) will be included. Acupuncture combined with other therapy could also be included if the combined therapy is same in both groups. The combined interventions contain drugs, but exclude complementary and alternative therapy such as relax therapy, music therapy, etc. In order to assess the efficacy of acupuncture therapy, we intend to compare acupuncture treatment with either no intervention or sham acupuncture. To assess the effectiveness of acupuncture therapies, we plan to compare them with conventional positive intervention consisting of lubricant, pharyngeal anesthesia or (and) sedative.

Types of outcome assessments

The primary outcome measures are the proportion of patients with discomfort calculated from questionnaire and the degree of discomfort assessed by visual analogue scale (VAS). If condition permits, the proportion of various symptoms of throat discomfort, nausea, salivation, retch, vomit or hiccup will be assessed respectively. The secondary outcomes consist of the proportion of patients satisfying with the whole process, the proportion of patients opting for the same procedure if required, and the proportion of patients with gastroscope proceeding smoothly. If the included trails permit, the doses of anesthesia or sedative, the operation time of gastroscopy examination and the revival time of patients after gastroscopy will also be evaluated. Moreover, the incidence of adverse events will be assessed as safety outcome.

Search methods for identification of studies

Electronic searches

We will electronically search the following database regardless of the publication
status: PubMed, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Database and China National Knowledge Infrastructure (CNKI) from their founding date to April, 2014. The search strategy has been worked out after a discussion among all reviewers according to the guidance of the Cochrane handbook. The key words include “gastroscopy”, “gastroscope”, “endoscopy” or “endoscopy” combining with “acupuncture”, “manual acupuncture”, “electroacupuncture”, “fire needling”, “warm needling”, “pyonex”, “scalp acupuncture”, “auricular acupuncture”, “intradermal needling”. The search words used in Chinese databases have the same meaning as the English version.

Other sources

Potentially eligible studies will also be searched through the following ways.

- The reference list of the previously published reviews related to both endoscopy and acupuncture for potentially eligible studies;
- Conference abstracts that may have on-going or unpublished trials in relation to both gastroscopy and acupuncture. The data could be collected by contacting the author if applicable.

Data collection and analysis

Selection of studies

Prior to the selection of the studies, all reviewers will undergo a training to ensure a basic understanding of the background and purpose of the review. Meanwhile, reviewers will reach a consensus on screening and the later procedure. After electronic searches, the records will be moved to a database set up by endnote software (version X6). Records searched from other sources will also be moved to the same database. Then, two reviewers (Weiming Wang and Tao Zhang) will independently obtain the included studies as the following steps: firstly, remove the duplicates (the same study published in different languages, or studies sharing the same title and abstract both in a journal and a conference proceedings, or different articles reported the same trial in different aspects); secondly, exclude studies in
which participants accepted acupuncture treatment during colonoscopy, or participants receiving acupuncture injection or other excluded intervention according to the criteria; thirdly, remove the studies which were not designed as randomized controlled trials, and trials in which no data can be extracted; fourthly, exclude the trials in which participants under the age of 18 were recruited. The details of the study selection are shown in a PRISMA flow chart (figure 1). During this procedure, any disagreement between the reviewers will be discussed and judged by a third author (Zhishun Liu).

Data extraction and management

Before data extraction, all of the reviewers will take part in a discussion and make a unified data extraction form. The following factors will be contained in the data extraction form: 1) general information (including reference ID, author, time of publication, journal, location of performance, etc.); 2) characteristics of participants; 3) randomization; 4) method of allocation concealment; 5) blinding; 6) interventions (including name of the intervention, length of treatment, type of control, etc.); 7) outcome measures (including primary and secondary outcomes); 8) results; 9) adverse events; 10) conflict of interest; 11) other information (such as the machine type of gastroscope, etc.). The applicability of the form will be tested by extracting information from 3 or more studies. After testing, Weiming Wang and Tao Zhang will independently extract the data from the included studies and fill in the form. The result of extraction will be checked in the end. Any disagreement between the reviewers will be discussed and judged by a third author (Zhishun Liu). Zhishun Liu will also check the final data afterwards to make sure no error left.

Assessment of risk of bias in included studies

Two reviewers (Weiming Wang and Tao Zhang) will evaluate the methodological quality of the included trials independently, with the use of Cochrane collaboration’s tool for risk of bias assessment. The tool consists of six domains of a trial, such as sequence generation, allocation concealment, blinding, etc. The assessments will be categorized into 3 levels of bias: low risk, high risk, and unclear risk.

Measures of treatment effect
For the dichotomous outcomes, data will be analyzed by using risk ratio (RR) with 95% Confidence Intervals (CI). For continuous outcomes, a standard mean difference (SMD) with 95% CI will be used.

Unit of analysis issues

Because the gastroscopy procedure is a transient process, and the acupuncture is often used before or/and during the gastroscopy, the outcomes will usually be measured as soon as the end of process. So we will mainly focus on the instant effect of acupuncture therapy. For the cross-over trials, the first phase of the trial will be analyzed.

Dealing with missing data

If data required for the data extraction form is missing, we will try to contact with the first or corresponding authors of the literatures by telephone or email to get related information. If missing data is unobtainable, complete case analysis for continuous outcomes and dichotomous outcomes will be firstly finished by using the methods of Ebrahim et al. and AKL et al. Then we will conduct a sensitivity analysis.

Assessment of heterogeneity

We will perform a heterogeneity test using the Higgins $I^2$ test prior to the meta-analysis, in order to find out if the inconsistencies exist within the included trials. We set a cut-off point of 50% for the $I^2$ statistics. We consider that there will be significant heterogeneity among trials when an $I^2$ value exceeds 50%. In that case meta-analysis will not be suggested.

Assessment of reporting biases

If 10 or more trials are included in a meta-analysis, we will generate funnel plots to assess the reporting biases. The plots will be assessed visually and by using Egger’s test.

Data synthesis

Data synthesis will be performed by the use of RevMan V.5.2 software from Cochrane collaboration. For dichotomous data, if no heterogeneity could be found, we will combine RR of each study and compute 95%CI with fixed effect model. And if
significant heterogeneity is detected, the random effect model will be used. For continuous data, we will combine standard mean difference (SMD) of each study and calculate the 95%CI according to the outcome measurement. Meanwhile, either the fixed or random effect model will be used on the basis of the result of heterogeneity test.

Subgroup analysis

Subgroup analysis will be conducted according to different interventions, controls and outcome measures. If the included trials permit, we will also perform subgroup analysis based on the participants’ age and different diseases.

Sensitivity analysis

We will carry out a sensitivity analysis to get rid of the impact of lower quality studies if the heterogeneity remains after sub-group analysis and input data verification. The meta-analysis will be reformed by excluding the studies with lower quality. The result will be compared and discussed according to the pooled effect size.

Ethics and dissemination

This systematic review is free from ethical approval because all the data what we will use are not involved in individual data and privacy. The results of this review will provide a general view and evidence of acupuncture therapy for discomfort in patients during gastroscopy. The findings will be disseminated through peer-reviewed publication or conference presentations.

DISCUSSION

During gastroscopy, throat discomfort, nausea, retching and vomiting are the most common complications. Take vomiting for example. Its neural center located at the reticular formation of brain stem, next to the other vegetative nerve center such as the respiratory center, vasomotor center etc. Chemoreceptor trigger zone (CTZ) exists at the area postrema of vomiting center, which transmits neurotransmitters to the center. The neurotransmitters mainly include dopamine, 5-hydroxytryptamine (5-HT), substance P, etc. The vomiting center will be excited by the physical stimulation of gastroscope, increase of neurotransmitters at CTZ and psychological factors. In addition, psychological factors such as anxiety or depression may raise the
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

content of blood 5-HT and aggravate the vomiting symptom. Researches indicated
that acupuncture may adjust the function of vegetative nerve, regulate the
gastrointestinal tract function, protect gastric mucosa, and have anti-anxiety function
which might reduce the content of blood 5-HT. Thus acupuncture may reduce the
vomiting symptom during gastroscope. Similar mechanism could be found for the
other complications. Acupuncture could take effect from both anatomical and
physiopathologic factors.

In this paper, we present a systematic review protocol of acupuncture for
discomfort in patients during gastroscopy. With a history of more than 2000 years,
acupuncture therapy plays an important part in complementary and alternative
medicine. Although clinical researches showed acupuncture could reduce the
discomfort generated by gastroscopy, there is no such high-quality synthesis as
evidence for the health problem to the best of our knowledge. Thus, this systematic
review will give analysis of current clinical evidence on the effect and safety of
acupuncture for the discomfort during gastroscopy. The result may benefit the patients
who accept gastroscopy with minimum discomfort.

Since the improvement of discomfort, which is the primary outcome of the
systematic review, varies from general description of the whole body to specifically
discomfort symptoms across different studies. It may be a difficult problem for the
reviewers to pool the various data together. Therefore subgroup analysis will come in
handy. After a discussion among all the reviewers, we decided to handle the problem
as follows: subgroups will be divided according to the description of discomfort.
Studies generally described the discomfort of the whole body will be categorized and
analyzed as one group. Studies specifically describing the same symptoms will be
classified and analyzed as another. Moreover, because of the language barrier,
Japanese and Korean medical databases will not be involved. Some of the relevant
researches might be missed.

Authors' contributions

Weiming Wang and Zhishun Liu contributed to the conception of the study. The
manuscript of the protocol was drafted by Weiming Wang and Tao Zhang, and was revised by Jiani Wu and Weina Peng. The search strategy was developed by all authors and run by Weiming Wang and Tao Zhang, who will also independently screen the potential studies, extract data of included studies, assess the risk of bias and finish data synthesis. Zhishun Liu will arbitrate the disagreements and ensure that no errors entry during the study. All authors approved for the publication of the protocol.

**Funding statement**

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests**

No competing interests exist.

**REFERENCES**


258-62.


Figure 1: Flow diagram of the trials selection process.
# Acupuncture for discomfort in patients during gastroscopy: A systematic review protocol

<table>
<thead>
<tr>
<th>Journal:</th>
<th><em>BMJ Open</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID:</td>
<td>bmjopen-2014-005735.R1</td>
</tr>
<tr>
<td>Article Type:</td>
<td>Protocol</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>17-Aug-2014</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>WANG, Weiming; Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Department of acupuncture; Beijing University of Chinese Medicine, school of graduate&lt;br&gt;Zhang, Tao; Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Department of acupuncture&lt;br&gt;PENG, Weina; Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Department of acupuncture&lt;br&gt;WU, Jiani; Guang’anmen Hospital, China Academy of Chinese Sciences, Department of acupuncture&lt;br&gt;LIU, Zhishun; Guang’anmen hospital, China Academy of Chinese Medical Sciences, Department of acupuncture</td>
</tr>
<tr>
<td>Primary Subject Heading:</td>
<td>Complementary medicine</td>
</tr>
<tr>
<td>Secondary Subject Heading:</td>
<td>Gastroenterology and hepatology, Medical publishing and peer review, Evidence based practice</td>
</tr>
<tr>
<td>Keywords:</td>
<td>COMPLEMENTARY MEDICINE, GASTROENTEROLOGY, Protocols &amp; guidelines&lt;br&gt;&lt; HEALTH SERVICES ADMINISTRATION &amp; MANAGEMENT</td>
</tr>
</tbody>
</table>
Acupuncture for discomfort in patients during gastroscopy:
A systematic review protocol

Weiming Wang¹,²†, Tao Zhang³†, Weina Peng¹, Jiani Wu¹, Zhishun Liu¹*

¹ Department of Acupuncture, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing (100053), China
² School of Graduates, Beijing University of Chinese Medicine, Beijing (100029), China
³ Department of Acupuncture, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing (100010), China

†Weiming Wang and Tao Zhang contributed equally to this study.

*Corresponding author: Professor Zhishun Liu; Tel: 86-10-88001124; Email: liuzhishun@aliyun.com

Key words
Acupuncture; gastroscopy; systematic review; protocol.

Word count: 2,886
ABSTRACT

Introduction This systematic review aims to assess the effectiveness and safety of acupuncture for discomfort in patients during gastroscopy.

Methods and analysis Randomized controlled trials will be searched electronically in several databases including OVID MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Database, and China National Knowledge Infrastructure (CNKI) from their respective founding dates to April 30, 2014. We will also try to find literature by manually searching conference abstracts and reference lists. The study selection, extraction of data, and assessment of study quality will be conducted independently by two researchers. Meta-analysis will be performed using RevMan 5.2 statistical software. Data will be combined with either the fixed or random effect model based on a heterogeneity test. The results will be presented as a risk ratio for dichotomous data and standardized mean difference for continuous data.

Dissemination This systematic review will evaluate the current evidence of acupuncture therapy for discomfort in patients during gastroscopy. The findings will be disseminated through peer-reviewed publication or conference presentations.

Protocol registration: PROSPERO CRD42014008966.
Strength and limitations of this study

- To the best of the authors’ knowledge, there is only one systematic review related to acupuncture and gastrointestinal endoscopy, which was published in 2004 without any update until now. Our review will assess the effectiveness and safety of acupuncture for discomfort in patients during gastroscopy.

- The study selection, data extraction, and quality assessment will be performed independently by two researchers. This will help ensure all relevant studies are included and not excluded for personal reasons.

- Japanese and Korean medical databases will not be included in our searches because of the language barrier. Hence, some relevant studies might be missed.

- The results of the systematic review may give gastroscopists more ways to help relieve patient discomfort during gastroscopy.

- Subgroup analysis will be used as the reports to be reviewed use varying methods of acupuncture and varying measures of outcome, potentially making data analysis difficult.
INTRODUCTION

Gastroscopy is an important method of gastrointestinal endoscopy in the diagnosis and treatment of digestive system diseases. It has been the most commonly performed endoscopic procedure, with an incidence of about 8.6 per 1000 of the population in the Trent region of the UK since the 1990s. The number of patients receiving gastroscopy reached 0.2 million in Shanghai, China in 2001. The average number of gastrointestinal endoscopes performed in 169 endoscopy units in China (all of the units possess gastroscopy) increased threefold in nearly 12 years, from 2.3 per unit in 2001 to 9.3 per unit in 2013. It is believed that the number of patients receiving gastroscopy is continuously increasing because of the aging population, work pressure, and dietary changes.

During gastroscopy, gag reflex or distention of the gastric wall may be induced, which causes throat discomfort, nausea, retching, or even emesis. Moreover, gastroscopy can evoke anxiety, increase heart rate, lower blood oxygen, and change blood pressure. Pharyngeal anesthesia (e.g. using lidocaine) and conscious sedation (e.g. using diazepam, midazolam, or propofol) are effective in minimizing discomfort during gastroscopy. However, the use of these drugs increases the associated cost of the procedure, and may cause retching during anesthesia induction. Furthermore, potential risks of conscious sedation include respiratory and cardiovascular inhibition, hypotension, or even coma. For these reasons, unsedated gastrointestinal endoscopy (including gastroscopy) has been widely applied for many years and is still the major procedure selected by patients in China and other developing countries.

Acupuncture has a history of more than 2000 years, and plays an important role in complementary and alternative medicine. Recent study has suggested acupuncture as a way to increase tolerance and reduce discomfort during gastroscopy, with a number of clinical trials being conducted to assess the effectiveness of acupuncture.
therapy for discomfort during gastroscopy.\textsuperscript{18,19} In the pre-retrieval of eight electronic databases, we have found more than 51 studies of acupuncture during gastroscopy.

There is so far only one published systematic review referring to “acupuncture” and “gastrointestinal endoscope”.\textsuperscript{20} The 2004 review assessed the effect of traditional manual acupuncture and electroacupuncture for gastrointestinal endoscopy. Six randomized controlled trials (RCTs) published from 1978 to 2003 were included and analyzed in the review. However, no significant result was concluded as more high-quality RCTs with adequate sample size were needed. Although acupuncture originated from and is widely used in China, Chinese periodical databases were not searched in that review. In addition, three of the six included RCTs were acupuncture for colonoscopy. Thus, no definite conclusions on the effectiveness of acupuncture during gastroscopy could be drawn from that review. However, with a more superior search strategy and more included databases, we hope that our systematic review will obtain a more convincing conclusion.

Our systematic review aims to determine whether acupuncture is effective in reducing discomfort during gastroscopy, and also whether acupuncture is safe for reducing discomfort during gastroscopy. In this article, we present the protocol of our proposed systematic review.

METHODS AND ANALYSIS

Criteria for inclusion of studies in this review

\textit{Types of studies}

All clinical RCTs of acupuncture for discomfort in patients with gastroscopy will be included in the review, while randomized crossover studies and quasi-RCTs will be excluded. Because of the particularity of acupuncture manipulation, it is difficult to blind the acupuncturists. Therefore, blinding will not be part of the inclusion criteria,
although it will be evaluated as an item in the risk of bias assessment.

Types of participants

Participants who underwent gastroscopy will be included, with no age limitation. Excluded participants will be those who have had a colonoscopy, and those who have suffered from chronic pharyngolaryngitis, severe digestive system diseases, persistent hiccups, severe nausea and retching, proven tumors in the upper digestive tract, or uncontrolled cardiopulmonary disease.

Types of interventions

Any method of acupuncture usage will be included, such as manual acupuncture, electroacupuncture, fire needling, warm needling, pyonex, scalp acupuncture, auricular acupuncture, and intradermal needling, without limitations on the treatment length and frequency. The control groups with no intervention, sham acupuncture, placebo control, and drug therapy (such as lubricant use, pharyngeal anesthesia, and sedation) will be included. Acupuncture combined with another therapy will also be included if the combined therapy is the same in both groups. The combined interventions include drugs, but exclude complementary and alternative therapy such as relaxation and music therapy. To assess the efficacy of acupuncture therapy, we intend to compare acupuncture treatment with either no intervention or sham acupuncture. To assess the effectiveness of acupuncture therapies, we plan to compare them with conventional positive intervention consisting of lubricant use, pharyngeal anesthesia, and/or sedation.

Types of outcome assessments

The primary outcome measurement is the proportion of patients with discomfort as assessed via completed questionnaire or visual analog scale (VAS). If the patient’s condition permits, the proportion of throat discomfort, nausea, salivation, retching, emesis, or hiccuppings will be assessed. The secondary outcomes consist of the proportion of patients satisfied with the whole process, and the proportion of patients
who would opt for the same procedure again if required. If the included trials permit, the doses of anesthesia or sedatives, the operation time of gastroscopy examination, and the revival time of patients after gastroscopy will also be evaluated. The incidence of adverse events will be assessed as a safety outcome.

**Search methods for identification of studies**

**Electronic searches**

We will electronically search the following databases from their founding date to April 30, 2014, regardless of the publication status: OVID MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Database, and China National Knowledge Infrastructure (CNKI). The search strategy has been decided upon after a discussion among all reviewers according to the guidance of the Cochrane handbook. The key words include “gastroscopy”, “gastroscope”, “endoscopy” or “endoscope” combined with “acupuncture”, “manual acupuncture”, “electroacupuncture”, “fire needling”, “warm needling”, “pyonex”, “scalp acupuncture”, “auricular acupuncture”, or “intradermal needling”. The search strategy for OVID MEDLINE is shown in Table 1. The search words used in Chinese databases have the same meaning as those used in the English databases.

**Other sources**

Potentially eligible studies will also be found through searching:

- The reference list of previously published reviews related to both endoscopy and acupuncture;
- Conference abstracts that may have ongoing or unpublished trials in relation to both gastroscopy and acupuncture. The data could be collected by contacting the author if applicable.

**Data collection and analysis**
Selection of studies

We plan to conduct this systematic review between February 28, 2014 and November 30, 2014. Prior to the selection of the studies, all reviewers will undergo training to ensure a basic understanding of the background and purpose of the review. Reviewers will then reach a consensus on screening and later procedures. After electronic searching, the records will be moved to a database set up by EndNote software (version X6). Records found through other sources will also be moved to the same database. Two reviewers (Weiming Wang and Tao Zhang) will then independently determine the included studies using the following steps: first, remove duplicates (the same study published in different languages, or studies sharing the same title and abstract both in a journal and conference proceedings, or different articles reporting the same trial in different aspects); second, exclude studies in which participants accepted acupuncture treatment during colonoscopy, or studies in which participants received acupoint injections or other excluded interventions according to the exclusion criteria described above; third, remove studies that were not designed as randomized controlled trials, and trials in which no data can be extracted. The details of the study selection procedure are shown in a PRISMA flow chart (Figure 1). During this procedure, any disagreement between the reviewers will be discussed and judged by a third author (Zhishun Liu).

Data extraction and management

Before data extraction, all of the reviewers will jointly discuss and create a unified data extraction form. The following factors will be contained in the data extraction form:

1) General information including reference ID, author, time of publication, journal, and location of performance.

2) Characteristics of participants.

3) Randomization.

4) Method of allocation concealment.

5) Blinding.
6) Interventions including the name of the intervention, length of treatment, and type of control.

7) Outcome measures including primary and secondary outcomes.

8) Results.

9) Adverse events.

10) Conflicts of interest.

11) Other information such as the type of gastroscope.

The applicability of the form created will be tested by extracting information from three or more studies. After testing, Weiming Wang and Tao Zhang will independently extract the data from the included studies and fill in the form. The final results of extraction will be checked, with any disagreement between the reviewers discussed and judged by a third author (Zhishun Liu). Zhishun Liu will also check the final data to make sure there are no errors.

**Assessment of risk of bias in included studies**

Two reviewers (Weiming Wang and Tao Zhang) will evaluate the methodological quality of the included trials independently, with the use of the Cochrane Collaboration’s tool for risk of bias assessment. The tool consists of six domains of a trial, such as sequence generation, allocation concealment, and blinding. The assessments will be categorized into three levels of bias: low risk, high risk, and unclear risk.

**Measures of treatment effect**

For dichotomous outcomes, data will be analyzed using a risk ratio (RR) with 95% confidence intervals (CI). For continuous outcomes, a standard mean difference (SMD) with 95% CI will be used.

**Unit of analysis issues**

Because the gastroscopic procedure is a transient process, and the acupuncture is often applied before and/or during the gastroscopy, the outcomes will usually be
measured once the intervention is complete. Therefore, we will mainly focus on the
instant effect of acupuncture therapy.

Dealing with missing data
If data required for the data extraction form are missing, we will try to contact the first
or corresponding authors of the studies by telephone or email to obtain the
information. If missing data are unobtainable, complete case analysis for continuous
outcomes and dichotomous outcomes will be finished using the methods of Ebrahim
et al.\textsuperscript{22} and Akl et al.,\textsuperscript{23} with a sensitivity analysis then conducted.

Assessment of heterogeneity
We will perform the Higgins $I^2$ test for heterogeneity prior to the meta-analysis, to
find out if inconsistencies exist within the included trials. We have set a cutoff point
of 50\% for the $I^2$ statistics, as we consider that there will be significant heterogeneity
among trials when an $I^2$ value exceeds 50\%. If this is the case, meta-analysis will not
be suggested.

Assessment of reporting biases
If 10 or more trials are included in a meta-analysis, we will generate funnel plots to
assess the reporting biases. The plots will be assessed visually and by using Egger’s
test.

Data synthesis
Data synthesis will be performed using RevMan V.5.2 software from the Cochrane
Collaboration. For dichotomous data, if no heterogeneity can be found, we will
combine the RR of each study and compute 95\% CI with the fixed effect model. If
significant heterogeneity is detected, the random effect model will be used. For
continuous data, we will combine the SMD of each study and calculate the 95\% CI
according to the outcome measurement.
Subgroup analysis

Subgroup analysis will be conducted according to different interventions, controls, and outcome measures. If the included trials permit, we will also perform subgroup analysis based on the participants’ age and different diseases.

Sensitivity analysis

We will carry out a sensitivity analysis to remove the impact of lower-quality studies if heterogeneity remains after subgroup analysis and input data verification. The meta-analysis will be repeated and studies of lower quality will be excluded. The result will be compared and discussed according to the pooled effect size.

Ethics and dissemination

This systematic review does not require formal ethical approval because the data we will use are not involved in individual data and privacy. The results of this review will provide a general overview and evidence of the effectiveness and safety of acupuncture therapy for discomfort in patients during gastroscopy. The findings will be disseminated through peer-reviewed publications or conference presentations.

DISCUSSION

The most common complications during gastroscopy are throat discomfort, nausea, retching, and vomiting. The neural center for vomiting is located at the reticular formation of the brain stem, next to other vegetative nerve centers such as the respiratory center and vasomotor center. The Chemoreceptor Trigger Zone (CTZ) exists at the area postrema of the vomiting center, which transmits neurotransmitters to the center. These neurotransmitters include dopamine, 5-hydroxytryptamine (5-HT), and substance P. The vomiting center is excited by the physical stimulation of the gastroscope, increase of neurotransmitters at CTZ, and psychological factors. In
addition, psychological factors such as anxiety or depression may raise the concentration of blood 5-HT and aggravate vomiting symptoms. Research indicates that acupuncture may adjust the function of vegetative nerves, regulate gastrointestinal tract function, protect gastric mucosa, and have an anti-anxiety function that might reduce the concentration of blood 5-HT. Thus acupuncture may reduce the side effect of vomiting during gastroscopy. Similar mechanisms could be found for the other side effects. Acupuncture could have an effect on both anatomical and physiopathological factors.

In this paper, we present a protocol for a systematic review of acupuncture for discomfort in patients during gastroscopy. With a history of more than 2000 years, acupuncture therapy plays an important part in complementary and alternative medicine. Although clinical research has shown that acupuncture could reduce the discomfort generated by gastroscopy, to the best of our knowledge there is currently no high-quality review of these separate studies. Thus, this systematic review will analyze current clinical evidence on the effectiveness and safety of acupuncture for discomfort during gastroscopy. The results may benefit patients who undergo gastroscopy by minimizing their associated discomfort.

As stated previously, the primary outcome of our systematic review is the removal of discomfort. The measurement of this outcome varies across different studies from a general description of the whole body to specific discomfort symptoms. Therefore, it may be difficult for the reviewers to pool the various data together, making subgroup analysis necessary. After a discussion among all the reviewers, we decided to divide subgroups according to the description of discomfort. Studies generally describing the discomfort of the whole body will be categorized and analyzed as one group, while studies describing specific symptoms will be classified and analyzed as another group. Moreover, Japanese and Korean medical databases will not be included in our searches because of the language barrier. Hence, some relevant studies might be missed.
Authors' contributions

Weiming Wang and Zhishun Liu contributed to the conception of the study. The manuscript of the protocol was drafted by Weiming Wang and Tao Zhang, and was revised by Jiani Wu and Weina Peng. The search strategy was developed by all authors and run by Weiming Wang and Tao Zhang, who will also independently screen the potential studies, extract data of included studies, assess the risk of bias and finish data synthesis. Zhishun Liu will arbitrate the disagreements and ensure that no errors occur during the study. All authors have approved the publication of the protocol.

Funding statement

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Competing interests

No competing interests exist.
REFERENCES


Table 1. Search strategy used in OVID MEDLINE database

<table>
<thead>
<tr>
<th>Number</th>
<th>Search terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>randomized controlled trial.pt.</td>
</tr>
<tr>
<td>2</td>
<td>controlled clinical trial.pt.</td>
</tr>
<tr>
<td>3</td>
<td>randomized.ab.</td>
</tr>
<tr>
<td>4</td>
<td>randomised.ab.</td>
</tr>
<tr>
<td>5</td>
<td>placebo.ab.</td>
</tr>
<tr>
<td>6</td>
<td>randomly.ab.</td>
</tr>
<tr>
<td>7</td>
<td>trial.ab.</td>
</tr>
<tr>
<td>8</td>
<td>groups.ab.</td>
</tr>
<tr>
<td>9</td>
<td>or 1-8</td>
</tr>
<tr>
<td>10</td>
<td>exp gastroscopy/</td>
</tr>
<tr>
<td>11</td>
<td>gastroscopy. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>12</td>
<td>gastroscope. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>13</td>
<td>endoscopy. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>14</td>
<td>endoscope ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>15</td>
<td>or 10-14</td>
</tr>
<tr>
<td>16</td>
<td>exp acupuncture therapy, or acupuncture</td>
</tr>
<tr>
<td>17</td>
<td>acupuncture. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>18</td>
<td>manual acupuncture. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>19</td>
<td>electroacupuncture. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>20</td>
<td>fire needling. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>21</td>
<td>warm needling, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>22</td>
<td>pyonex, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>23</td>
<td>scalp acupuncture, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>24</td>
<td>auricular acupuncture, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>25</td>
<td>intradermal needling, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>26</td>
<td>or 16-25</td>
</tr>
<tr>
<td>27</td>
<td>9 and 15 and 26</td>
</tr>
</tbody>
</table>

This search strategy will be modified as required for other electronic databases.
Acupuncture for discomfort in patients during gastroscopy: a systematic review protocol

Weiming Wang¹,²†, Tao Zhang³†, Weina Peng¹, Jiani Wu¹, Zhishun Liu¹*

¹ Department of Acupuncture, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing (100053), China.
² School of Graduate, Beijing University of Chinese Medicine, Beijing (100029), China
³ Department of Acupuncture, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing (100010), China

*Corresponding author: Professor Zhishun Liu; Tel: 86-10-88001124; E-mail: liuzhishun@aliyun.com

Key words: Acupuncture; gastroscopy; systematic review; protocol.


Key words: Acupuncture, gastroscopy, systematic review, protocol.

Word count: 2,886
ABSTRACT

Abstract

Introduction: This systematic review aims to assess the effectiveness and safety of acupuncture for discomfort in patients during gastroscopy.

Methods and analysis: Randomized controlled trials will be searched electronically in several databases including OVID MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Database and China National Knowledge Infrastructure (CNKI) from their respective founding dates to April 30, 2014. We will also try to gain-find literature by manually searching conference abstracts and reference lists. The study selection of study, extraction of data, and assessment of study quality will be conducted independently by two researchers independently. Meta-analysis will be performed using the use of RevMan 5.2 statistical software. Data will be combined with either the fixed or random effect model based on the basis of the result of heterogeneity test. The results will be presented as a risk ratio for dichotomous data and standardized mean difference for continuous data.

Dissemination: This systematic review will evaluate the current evidence of acupuncture therapy for discomfort in patients during gastroscopy. The findings will be disseminated through peer-reviewed publication or conference presentations.

Protocol registration: PROSPERO CRD42014008966.

Key words: Acupuncture, gastroscopy, systematic review, protocol.

Strength and limitations of this study

To the best of the authors’ knowledge, there is only one systematic review related to acupuncture and gastrointestinal endoscopy, which was published in 2004 without any update until now. Our review will be the latest one to assess the effectiveness and safety of acupuncture for the discomfort in patients during
gastroscopy.

- The study selection, data extraction, and quality assessment will be performed independently by two researchers. This will help ensure all relevant studies are included and not excluded for personal reasons.
- Japanese and Korean medical databases will not be included in our searches because of the language barrier. Hence, some relevant studies might be missed.
- The results of the systematic review may give gastroscopists more ways to help patients relieve patient discomfort during gastroscopy.
- Subgroup analysis will be used as the reports to be reviewed use varying methods of kinds of acupuncture method and varying measures of outcome, potentially measures may making bringing difficulty for data analysis. Thus subgroup analysis will be used to address the problem.

INTRODUCTION

Gastroscopy is an important method of gastrointestinal endoscopy in the diagnosis and treatment of digestive system diseases. It has been the most commonly performed endoscopic procedure, with an incidence of about 8.6 per 1000 of the population in the Trent region of England the UK since the 1990s.1,2 The number of patients receiving accepted gastroscopy reached 0.2 million in Shanghai of China in 2001.3,4 Recent research indicated that the average number of gastrointestinal endoscopes performed in 169 endoscopy units in China (all of the units possess gastroscopy) increased threefold times in the nearly 12 years, from 2.3 per unit in 2001 to 9.3 per unit in 2013 per unit. It is believed that the number of patients receiving gastroscopy is continuously increasing because of the aging population, work pressure, and dietary changes, it is believed that the number of patients receiving gastroscopy is increasing continuously.4

During gastroscopy, gag reflex or the distention of the gastric wall may be induced,
which would cause throat discomfort, nausea, retching, or even emesis.\textsuperscript{5,6} Moreover, gastroscopy can not only evoke anxiety, increase heart rate, lower blood oxygen, and change blood pressure.\textsuperscript{7-9} Pharyngeal anesthesia (e.g. using lidocaine) and conscious sedation (e.g. using diazepam, midazolam, or propofol) are effective in minimizing discomfort during gastroscopy.\textsuperscript{10-13} They could make the gastroscopy procedure smooth to some extent. However, the use of these drugs increases the associated cost of the procedure, and may cause retching during the anesthesia induction.\textsuperscript{5}

Furthermore, potential risks of conscious sedation include potential risks such as the inhibition of respiratory and cardiovascular inhibition system, hypotension, or even coma.\textsuperscript{7-14,15} Besides, its financial burden is much heavier. For these reasons, unsedated gastrointestinal endoscopy (including gastroscopy) has been widely applied for many years and is still the major procedure selected by patients in China\textsuperscript{16} and other developing countries.

Acupuncture has a history of more than 2000 years, and plays an important role in complementary and alternative medicine. Recent study has suggested acupuncture as a way to increase tolerance and reduce discomfort during gastroscopy,\textsuperscript{17} with a number of clinical trials being conducted to assess the effectiveness of acupuncture therapy for discomfort during gastroscopy.\textsuperscript{12-15} In the pre-retrieval of eight electronic databases, we have found more than 51 studies of acupuncture during gastroscopy for this health issue. Meanwhile, recent study has suggested acupuncture as an alternative way to increase tolerance and reduce discomfort during gastroscopy.\textsuperscript{15}

Furthermore, there is only one published systematic review referring to “acupuncture” and “gastrointestinal endoscope” so far.\textsuperscript{20} The 2004 review was published in 2004 and assessed the effect of traditional manual acupuncture and electroacupuncture for gastrointestinal endoscopy. Six randomized controlled trials (RCTs) published from 1978 to 2003 were included and analyzed in the review. However, no significant result was concluded as more high-quality RCTs with
adequate sample size were needed. Although To our knowledge, acupuncture is originated from and is widely used in China. But Chinese periodical databases were not searched in that review. In addition, three of the six included RCTs were acupuncture for colonoscopy. Thus, no we could not draw a definite conclusions on the effectiveness of acupuncture during gastroscopy could be drawn this health issue from that review. However, with a more superior search strategy and more included databases, we hope that our systematic review will may obtain a more convincing conclusion.

Therefore, we raised two questions systematic review aims to determine : whether is acupuncture is effective in for reducing the discomfort during gastroscopy2, and also whether is acupuncture is safe for reducing discomfort during gastroscopy. In order to find the answers, we will conduct a systematic review of acupuncture therapy for discomfort in patients during gastroscopy. In this article, we present the protocol of our the proposed systematic review.

METHODS AND ANALYSIS

Criteria for inclusion of considering studies in this review

Types of studies

All of the clinical RCTs of acupuncture for discomfort in patients with gastroscopy will all be included in the review. While randomized crossover studies and quasi-RCTs will be excluded. Because of the particularity of acupuncture manipulation, it is difficult to blind the acupuncturists. Therefore, blinding will not be strictly part limited of in the inclusion criteria although. But it will be evaluated as an item in the risk of bias assessment.

Types of participants
Participants who underwent accepted gastroscopy will be included, without no age the limitation of age. Excluded will be those who have had accepted colonoscopy, and those who have suffered from chronic pharyngolaryngitis, severe digestive system diseases, persistent hiccups, severe nausea and retching, proven tumors in the upper digestive tract, or uncontrolled cardiopulmonary disease will be excluded.

**Types of interventions**

Any kind of acupuncture usage used in experimental group will be included, such as manual acupuncture, electroacupuncture, fire needling, warm needling, pyonex, scalp acupuncture, auricular acupuncture, and intradermal needling and so on, without the limitations of the treatment length and frequency. The control groups with no intervention, sham acupuncture, placebo control, and drugs therapy (such as lubricant use, pharyngeal anesthesia, and sedation) will be included. Acupuncture combined with another therapy will also be included if the combined therapy is the same in both groups. The combined interventions include drugs, but exclude complementary and alternative therapy such as relaxation therapy and music therapy, and so on. In order to assess the efficacy of acupuncture therapy, we intend to compare acupuncture treatment with either no intervention or sham acupuncture. To assess the effectiveness of acupuncture therapies, we plan to compare them with conventional positive intervention consisting of lubricant use, pharyngeal anesthesia, and sedation.

**Types of outcome assessments**

The primary outcome measurement is the proportion of patients with discomfort as assessed from completed questionnaire or visual analogue scale (VAS). If the patient's condition permits, the proportion of various symptoms of throat discomfort, nausea, salivation, retching, emesis, vomit or hiccupping will be assessed respectively. The secondary outcomes consist of the proportion of patients satisfied with the whole process, and the proportion of patients who would opt for acupuncture.
for the same procedure again if required. If the included trials permit, the doses of anesthesia or sedatives, the operation time of gastroscopy examination, and the revival time of patients after gastroscopy will also be evaluated. Moreover, the incidence of adverse events will be assessed as a safety outcome.

**Search methods for identification of studies**

**Electronic searches**

We will electronically search the following databases from their founding date to April 30, 2014, regardless of the publication status: OVID MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese Medical Current Content (CMCC), Chinese Scientific Journal Database (VIP database), Wan-Fang Database, and China National Knowledge Infrastructure (CNKI) from their founding date to 2014. The search strategy has been worked out decided upon after a discussion among all reviewers according to the guidance of the Cochrane handbook. The key words include “gastroscopy”, “gastroscope”, “endoscopy” or “endoscopy”, combining with “acupuncture”, “manual acupuncture”, “electroacupuncture”, “fire needling”, “warm needling”, “pyonex”, “scalp acupuncture”, “auricular acupuncture”, or “intradermal needling”. The search strategy for OVID MEDLINE is shown in Table 1. The search words used in Chinese databases have the same meaning as those used in the English databases version.

**Other sources**

Potentially eligible studies will also be found searched-through searching the following ways:

- The reference list of the previously published reviews related to both endoscopy and acupuncture for potentially eligible studies;
- Conference abstracts that may have on-going or unpublished trials in relation to both gastroscopy and acupuncture. The data could be collected by contacting the
author if applicable.

Data collection and analysis

Selection of studies

We planned to conduct this systematic review between February 28, 2014 and November 30, 2014. Prior to the selection of the studies, all reviewers will undergo a training to ensure a basic understanding of the background and purpose of the review. Meanwhile, reviewers will then reach a consensus on screening and the later procedures. After electronic searching, the records will be moved to a database set up by EndNote software (version X6). Records found through from other sources will also be moved to the same database. Then, two reviewers (Weiming Wang and Tao Zhang) will then independently determine the included studies using the following steps: firstly, remove the duplicates (the same study published in different languages, or studies sharing the same title and abstract both in a journal and conference proceedings, or different articles reporting the same trial in different aspects); secondly, exclude studies in which participants accepted acupuncture treatment during colonoscopy, or studies in which participants receiving acupoint injections or other excluded interventions according to the exclusion criteria described above; thirdly, remove the studies which were not designed as randomized controlled trials, and trials in which no data can be extracted; fourthly, exclude the trials in which participants were under the age of 18 were recruited. The details of the study selection procedure are shown in a PRISMA flow chart (Figure 1). During this procedure, any disagreement between the reviewers will be discussed and judged by a third author (Zhishun Liu).

Data extraction and management

Before data extraction, all of the reviewers will take part in a jointly discussion and create a unified data extraction form. The following factors will be contained in the data extraction form:
1) **General information** (including reference ID, author, time of publication, journal, and location of performance, and so on);

2) **Characteristics** of participants;

3) **Randomization**;

4) **Method** of allocation concealment;

5) **Blinding**;

6) **Interventions** (including the name of the intervention, length of treatment, and type of control, and so on);

7) **Outcome measures** (including primary and secondary outcomes);

8) **Results**;

9) **Adverse events**;

10) **Conflicts of interest**;

11) **Other information** (such as the machine type of gastroscope, and so on).

The applicability of the form created will be tested by extracting information from three or more studies. After testing, Weiming Wang and Tao Zhang will independently extract the data from the included studies and fill in the form. The final results of extraction will be checked in the end, with any disagreement between the reviewers will be discussed and judged by a third author (Zhishun Liu). Zhishun Liu will also check the final data afterwards to make sure there are no errors left.

**Assessment of risk of bias in included studies**

Two reviewers (Weiming Wang and Tao Zhang) will evaluate the methodological quality of the included trials independently, with the use of the Cochrane Collaboration’s tool for risk of bias assessment. The tool consists of six domains of a trial, such as sequence generation, allocation concealment, and blinding, and so on. The assessments will be categorized into three levels of bias: low risk, high risk, and unclear risk.

**Measures of treatment effect**

For dichotomous outcomes, data will be analyzed by using a risk ratio (RR).
with 95% confidence intervals (CI). For continuous outcomes, a standard mean difference (SMD) with 95% CI will be used.

**Unit of analysis issues**

Because the gastroscopy procedure is a transient process, and the acupuncture is often applied before or and/or during the gastroscopy, the outcomes will usually be measured once the intervention is complete. Therefore, we will mainly focus on the instant effect of acupuncture therapy.

**Dealing with missing data**

If data required for the data extraction form is are missing, we will try to contact the first or corresponding authors of the studies by telephone or email to obtain the related information. If missing data is are unobtainable, complete case analysis for continuous outcomes and dichotomous outcomes will be firstly finished by using the methods of Ebrahim et al.\(^22\) and Akl et al.\(^23\), with then we will conduct a sensitivity analysis then conducted.

**Assessment of heterogeneity**

We will perform a heterogeneity test using the Higgins I\(^2\) test for heterogeneity prior to the meta-analysis, in order to find out if the inconsistencies exist within the included trials. We have set a cut-off point of 50% for the I\(^2\) statistics, as we consider that there will be significant heterogeneity among trials when an I\(^2\) value exceeds 50%. If this is the case, meta-analysis will not be suggested.

**Assessment of reporting biases**

If 10 or more trials are included in a meta-analysis, we will generate funnel plots to assess the reporting biases. The plots will be assessed visually and by using Egger’s test.

**Data synthesis**
Data synthesis will be performed by the use of RevMan V.5.2 software from the Cochrane Collaboration. For dichotomous data, if no heterogeneity can be found, we will combine the RR of each study and compute 95% CI with the fixed effect model. If significant heterogeneity is detected, the random effect model will be used. For continuous data, we will combine the standard mean difference (SMD) of each study and calculate 95% CI according to the outcome measurement. Meanwhile, either the fixed or random effect model will be used on the basis of the result of heterogeneity test.

**Subgroup analysis**

Subgroup analysis will be conducted according to different interventions, controls, and outcome measures. If the included trials permit, we will also perform subgroup analysis based on the participants’ age and different diseases.

**Sensitivity analysis**

We will carry out a sensitivity analysis to remove the impact of lower-quality studies if the heterogeneity remains after sub-group analysis and input data verification. The meta-analysis will be repeated and studies of lower quality will be excluded. The result will be compared and discussed according to the pooled effect size.

**Ethics and dissemination**

This systematic review does not require formal ethical approval because all the data we will use are not involved in individual data and privacy. The results of this review will provide a general overview and evidence of the effectiveness and safety of acupuncture therapy for discomfort in patients during gastroscopy. The findings will be disseminated through peer-reviewed publications or conference presentations.
DISCUSSION

The most common complications during gastroscopy are throat discomfort, nausea, retching, and vomiting. The neural center for vomiting is located at the reticular formation of the brain stem, next to the other vegetative nerve centers such as the respiratory center and vasomotor center and so on etc. The Chemoreceptor Trigger Zone (CTZ) exists at the area postrema of the vomiting center, which transmits neurotransmitters to the center. These neurotransmitters mainly include dopamine, 5-hydroxytryptamine (5-HT), and substance P and so on etc. The vomiting center is will be excited by the physical stimulation of the gastroscope, increase of neurotransmitters at CTZ, and psychological factors. In addition, psychological factors such as anxiety or depression may raise the concentration of blood 5-HT and aggravate the vomiting symptoms. Researches indicated that acupuncture may adjust the function of vegetative nerves, regulate the gastrointestinal tract function, protect gastric mucosa, and have an anti-anxiety function which that might reduce the concentration of blood 5-HT. Thus acupuncture may reduce the side effect of vomiting symptoms during gastroscopy. Similar mechanisms could be found for the other side effect complications. Acupuncture could have an take effect on from both anatomical and physiopathological factors.

In this paper, we present a protocol for a systematic review protocol of acupuncture for discomfort in patients during gastroscopy. With a history of more than 2000 years, acupuncture therapy plays an important part in complementary and alternative medicine. Although clinical research has shown acupuncture could reduce the discomfort generated by gastroscopy, to the best of our knowledge there is currently no such high-quality review synthesis of these separate studies as evidence for the health problem to the best of our knowledge. Thus, this systematic review will analyze give analysis of current clinical evidence on the effectiveness and safety of acupuncture for the discomfort during gastroscopy. The results may benefit...
patients who undergo gastroscopy by minimizing their associated with minimum discomfort.

As stated previously, the primary outcome of our systematic review is Since the improvement removal of discomfort, The measurement of this outcome—which is the primary outcome of the systematic review—varies across different studies from a general description of the whole body to specifically discomfort symptoms across different studies. Therefore, it may be a difficult problem for the reviewers to pool the various data together, making subgroup analysis necessary will come in handy. After a discussion among all the reviewers, we decided to divide handle the problem as follows: subgroups will be divided according to the description of discomfort. Studies generally describing the discomfort of the whole body will be categorized and analyzed as one group, while studies specifically describing specific—the same symptoms will be classified and analyzed as another group. Moreover, because of the language barrier, Japanese and Korean medical databases will not be included in our searches because of the language barrier involved. Hence, Some of the relevant studies researches might be missed.

Authors' contributions

Weiming Wang and Zhishun Liu contributed to the conception of the study. The manuscript of the protocol was drafted by Weiming Wang and Tao Zhang, and was revised by Jiani Wu and Weina Peng. The search strategy was developed by all authors and run by Weiming Wang and Tao Zhang, who will also independently screen the potential studies, extract data of included studies, assess the risk of bias and finish data synthesis. Zhishun Liu will arbitrate the disagreements and ensure that no errors occur during the study. All authors have approved for the publication of the protocol.

Funding statement

This research received no specific grant from any funding agency in the public,
commercial, or not-for-profit sectors.

Competing interests

No competing interests exist.
REFERENCES


Figure 1. Flow diagram of the study trials selection process.
Table 1. Search strategy used in OVID MEDLINE database

<table>
<thead>
<tr>
<th>Number</th>
<th>Search terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>randomized controlled trial.pt.</td>
</tr>
<tr>
<td>2</td>
<td>controlled clinical trial.pt.</td>
</tr>
<tr>
<td>3</td>
<td>randomized.ab.</td>
</tr>
<tr>
<td>4</td>
<td>randomised.ab.</td>
</tr>
<tr>
<td>5</td>
<td>placebo.ab.</td>
</tr>
<tr>
<td>6</td>
<td>randomly.ab.</td>
</tr>
<tr>
<td>7</td>
<td>trial.ab.</td>
</tr>
<tr>
<td>8</td>
<td>groups.ab.</td>
</tr>
<tr>
<td>9</td>
<td>or 1-8</td>
</tr>
<tr>
<td>10</td>
<td>exp gastroscopy/</td>
</tr>
<tr>
<td>11</td>
<td>gastroscopy. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>12</td>
<td>gastroscope. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>13</td>
<td>endoscopy. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>14</td>
<td>endoscope ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>15</td>
<td>or 10-14</td>
</tr>
<tr>
<td>16</td>
<td>exp acupuncture therapy, or acupuncture</td>
</tr>
<tr>
<td>17</td>
<td>acupuncture. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>18</td>
<td>manual acupuncture. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>19</td>
<td>electroacupuncture. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>20</td>
<td>fire needling. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>21</td>
<td>warm needling. ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>22</td>
<td>pynex, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>23</td>
<td>scalp acupuncture, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>24</td>
<td>auricular acupuncture, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>25</td>
<td>intradermal needleling, ti, ab. {Including Related Terms}</td>
</tr>
<tr>
<td>26</td>
<td>or 16-25</td>
</tr>
<tr>
<td>27</td>
<td>9 and 15 and 26</td>
</tr>
</tbody>
</table>

This search strategy will be modified as required to suitable for other electronic databases.
Figure 1. Flow diagram of the study selection process.
Acupuncture for discomfort in patients during gastroscopy: a systematic review protocol

Weiming Wang, Tao Zhang, Weina Peng, Jiani Wu and Zhishun Liu

*BMJ Open* 2014 4:
doi: 10.1136/bmjopen-2014-005735

Updated information and services can be found at:
http://bmjopen.bmj.com/content/4/9/e005735

These include:

**References**
This article cites 23 articles, 1 of which you can access for free at:
http://bmjopen.bmj.com/content/4/9/e005735#BIBL

**Open Access**
This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
- Complementary medicine (85)
- Evidence based practice (363)
- Gastroenterology and hepatology (122)
- Medical publishing and peer review (40)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/