

## PROSPERO International prospective register of systematic reviews

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### Chinese herbal medicines for aspirin resistance: a systematic review for randomized controlled trials

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#### Review question(s)

To evaluate the efficacy and safety of traditional chinese medicine used for therapy of AR

#### Searches

English database: MEDLINE (OVID SP), EMBASE (OVID SP), Cochrane Central Register of Controlled Trials (CENTRAL).

Chinese database: the Chinese BioMedical Database(CBMDisc),CMCI, Chinese National Knowledge Infrastructure Database(CNKI), VIP information database, and Wanfang Data Information Site

#### Types of study to be included

We included randomized controlled trials (RTC) published home and abroad concerned with using TCM to treat AR, with no restrictions on particular treatment, whether carry out blinding or allocation concealment, publication status. Language is restricted to Chinese and English. But quasi-randomised trials carried out according to their date of birth, the date to which the patients were sent to the hospital, ID number,their hospital record number, will be excluded.

#### Condition or domain being studied

Aspirin resistance has been a prominent clinical problem in recent years. Cardiovascular diseases cannot be effectively prevented and controlled if AR exists, repeatedly attacking and increasing the mortality, have induced some social burdens. Now Western medicine is still at the stage of discovery on treating this problem and it lacks specific treatment. While traditional Chinese medicine is also carrying out clinical research on AR, and some related scholars have done a systematic assessment on the clinical research done before 2012 about how TCM interfere AR. But they did not get certain conclusions due to the bad quality of the inclusive clinical research. It has been two years since the old systematic review, when some new clinical researches about it have been reported. We aim to do a new systematic review by accumulating the existed evidence so as to evaluate and observe the efficacy and safety of TCM on interfering AR, providing new treatment for antiplatelet-aggregation, which makes important sense.

#### Participants/ population

We will include participants of any age or sex who were diagnosed with AR.

Diagnostic criteria:

1. 10 $\mu$ mol/L adenosine diphosphate (ADP)-induced platelet aggregation rate =70%
2. 0.5mmol/L arachidonic acid(AA)-induced platelet aggregation rate=20%.

It can be diagnosed as AR if it meets both 1 and 2. The diagnostic criterion of aspirin semi-resistance (ASR) is meeting one of the two conditions above.

Exclusion criteria: aspirin allergy; cerebral hemorrhage or bleeding tendency; active gastric ulcer and gastrointestinal bleeding patient; liver damage; all kinds of blood disease; abnormal platelet count; aspirin allergy; Pregnancy or

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breast-feeding women; using drugs effecting platelet aggregation during the last 1 month of observation period.

### **Intervention(s), exposure(s)**

The Chinese herbal medicine(CHM) interventions included single herbs, extracts from any single herb, Chinese patent drug (for example oral liquid, capsule, tablet, pill, powder, or injection), or traditional Chinese prescriptions prescribed by TCM doctors.

Therapy in the treatment groups: any treatments using CHM monotherapy or adjunct therapy for AR was included regardless of the dose, formulations and frequency of CHM.

The treatment course was at least 2 weeks in these trials included.

### **Comparator(s)/ control**

Interventions of the control groups: aspirin (regardless of the dose), placebo , no intervention, or other conventional antiplatelet drug treatment. The treatment course was at least 2 weeks in these trials included.

### **Outcome(s)**

#### **Primary outcomes**

The variation of the platelet aggregation rate induced by AA/ADP, TXB2 and 6-KETO-PGF1a.

We will measure the outcome in the beginning and at the end of the treatment course.

#### **Secondary outcomes**

Clinical efficacy and safety.

Standard of the clinical efficacy:

1. AR becomes ASR or aspirin sensitive after the treatment;
2. ASR becomes aspirin sensitive after the treatment;
3. the decreased value of platelet aggregation rate is more than 10% and platelet active value is normal.

### **Risk of bias (quality) assessment**

We will evaluate included studies for risk of bias using a tool for assessing risk of bias of RTC introduced in the Cochrane Handbook for Systematic Reviews of Interventions (V.5.1.0). In particular, we studied the following six domains:

1. random sequence generation
2. Allocation concealment
3. blinding of participants, personnel and outcome assessors;
4. completeness of outcome data, including baseline measured before intervention, effects parameter after intervention, dropouts and withdrawals (whether the losses visit rate is under 10%), excluded data, whether or not they explained the reason of losses to follow-up, whether or not ITT Analysis is carried out in people lost to follow-up;
5. selective outcome reporting: Whether or not safety problems (e.g. adverse events such as death) and negative results are reported
6. other sources of bias: early termination of trials, imbalance baseline?

For each included article, make judgment of “yes” (low risk of bias), “no” (high risk of bias) or “unclear” (indicating unknown or unclear risk of bias) about the above mentioned six domains.

### **Strategy for data synthesis**

We planned to carry out the meta-analyses in Revman software. We will use a fixed-effect model for meta-analysis if there is no statistical heterogeneity between primary and secondary outcomes measures ( $P > 0.1$ , I-squared = 50%); If we had identified clinical homogeneity but statistical heterogeneity ( $P < 0.1$ , I-squared > 50%), the random-effects model would have been used.

Heterogeneity will be assessed using both the Chi-squared test and the I-squared statistic. We will consider an I-squared value greater than 50% to be indicative of substantial heterogeneity. We will conduct sensitivity analyses based on study quality, if necessary. Funnel plots will be generated to detecting publication bias if more than ten trials are identified.

### **Analysis of subgroups or subsets**

If the necessary data are available, subgroup analyses will be done for different outcome measures.

### **Contact details for further information**

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### **Conflicts of interest**

None known

### **Country**

China

### **Subject index terms status**

Subject indexing assigned by CRD

### **Subject index terms**

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**Stage of review**

Ongoing

**Date of registration in PROSPERO**

01 May 2015

**Date of publication of this revision**

04 August 2015

**Stage of review at time of this submission**

Preliminary searches

**Started**

**Completed**

Yes

Yes

Piloting of the study selection process

Yes

Yes

Formal screening of search results against eligibility criteria

Yes

No

Data extraction

No

No

Risk of bias (quality) assessment

No

No

Data analysis

No

No

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