

The Better Safety of Acupuncture as a Complementary Therapy for Sepsis

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Abstract: Objectives: Sepsis is a physiological, pathological, and biochemical syndrome caused by infection. The application of acupuncture as a complementary therapy for sepsis patients remains controversial. Our objective was to organize the relevant articles to assess the efficacy and safety of acupuncture as a complementary therapy for sepsis. Materials and methods: PubMed, the Cochrane Central Register of Controlled Trials, EMBASE, CNKI, Wan Fang Data, VIP database and TCM Literature Analysis and Database were searched for randomized studies that compared acupuncture as a complementary therapy with conventional treatment for sepsis patients. The odds ratios (ORs), with 95% CI, was calculated by using a corresponding effects model for continuous data, according to the value of I². Meta-analysis was performed by RevMan 5.3 software. Results: A total of eleven articles were included in our study. On comparing the clinical indexes, the acupuncture as a complementary therapy group was found to be better than the conventional treatment group in 28-day mortality [OR=0.61, 95%CI (0.36,1.04), P=0.07], APACHE II score at 7th day [MD=-3.36, 95%CI (-4.30, -2.41), P<0.00001], concentrations of procalcitonin (PCT) [MD=-2.23, 95%CI (-3.33, -1.13), P<0.0001] and TNF- α [MD=-14.86, 95%CI (-23.74, -5.97), P=0.001] at 7th day. However, there was no significant difference between the two groups about the CD8⁺ T cells count [MD=0.36, 95%CI (-1.57,2.29), P=0.71]. Conclusion: Based on the current evidence, acupuncture as a complementary therapy treatment had better clinical safety features than the conventional treatment. For those indicators with a small amount of data, a greater number of randomized, high-quality controlled trials should be conducted in order to verify the findings.

1. Introduction

Sepsis is a syndrome caused by infection, burns and so on. The incidence of sepsis is increasing, causes lots of deaths in hospitals. The problem is serious in the world.

Acupuncture, an important part of complementary therapy guide by the theory of traditional Chinese medicine. This method could inhibit the inflammatory and ignore the regulation of the immune system. Some studies have showed that acupuncture was beneficial for sepsis due to the anti-inflammation and its ability to regulate immunity ^[1, 2]. And this benefit may be related to the

fact that acupuncture can reduce inflammation and regulate immunity. This effect has been demonstrated in several clinical trials [3]. So far, however, there was still a lack of high-quality research on acupuncture for sepsis treatment. Thus, this study aimed to assess the effectiveness and safety of acupuncture as a complementary therapy for sepsis.

2. Methods

2.1 Study Registration

The present analysis was performed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [4]. If the protocol was modified, we extracted the information in the final report.

2.2 Criteria for Including Studies in the Review

2.2.1 Types of Studies

All the randomized controlled trials (RCTs) of acupuncture therapy for sepsis without any limitation of blinding or publication language were included, and we will also exclude cohort studies, case reports, and duplicate publications.

2.2.2 Types of Participants

Participants will be include who have been diagnosed with sepsis were included. There was no restriction on age, sex, or ethnicity of the enrolled subjects.

2.2.3 Types of Interventions

We included all RCTs which treatment group using acupuncture plus routine therapies and control group using routine therapies alone. Routine therapies included anti-infection, nutritional support, fluid management, mechanical ventilation, and other necessary therapies. The acupuncture treatment defined as needle at acupoints on the meridians, including manual acupuncture or electroacupuncture, excluding other acupuncture treatments such as ear acupuncture, scalp acupuncture, dry needling, acupressure.

2.2.4 Types of Outcomes

2.2.4.1

The primary outcomes

The primary outcomes included the mortality at 28 days and acute physiology and chronic health evaluation II (APACHE II) scores.

2.2.4.2. The Secondary Outcomes

The secondary outcomes included inflammatory index, immune index, such as the TNF- α counts, procalcitonin(PCT), the level of CD8⁺T cell subsets and adverse events or reactions.

2.3 Search Methods

2.3.1 Electronic Searches

We searched PubMed, the Cochrane Central Register of Controlled Trials, EMBASE, CNKI, Wan Fang Data, VIP database and TCM Literature Analysis and Retrieval Database with the keywords “acupuncture”, “electroacupuncture”, “sepsis” and “septic shock”. The initial time periods and languages of the articles were not limited, we just ruled the deadline to June 20, 2020.

2.4 Data Collection and Analysis

2.4.1 Selection of Studies

Two reviewers selected the studies independently. They checked the results with each other. When disagreements occurred, a third reviewer made the final decision. They read the full texts of all included studies if necessary.

2.4.2 Data Extraction and Management

The citations were screened independently by two authors, they extracted the data using a standardized data extraction form and any differences of opinion were resolved through discussion, if failed, by arbitration by the third reviewer.

2.4.3 Assessment of Heterogeneity

Data analysis and statistical methods Review Manager (version 5.3) was used to analyze the data. A risk ratio was used to calculate the dichotomous results, and the mean difference (MD) and standard mean difference were used to calculate both similar and differing evaluation indicator data of the dichotomous results. We used I^2 values to assess the heterogeneity among the articles. If $I^2 > 50$, we used the random-effect model; if $I^2 < 50$, the fixed-effect model was used.

2.4.4 Risk of Bias Assessment

In these incorporated studies, all studies were RCTs, and the methodological quality of each study was evaluated according to the Cochrane Collaboration’s tool. Only two RCTs were considered to be low risk, whereas the remainder were not considered to be of a better quality, due to an uncertainty bias. In these studies, the biases mainly existed in regard to allocation concealment, binding of participants and other biases

2.5 Outcomes of Meta-Analysis

2.5.1 28-Day Mortality after Treatment

Four reports provided data (n=261) on 28-day mortality. A fixed-effect model was used and there was no significant heterogeneity was found ($I^2=0\%$, $P=0.40$). The result was not different (two studies, 261 participants, OR: 0.61, 95% CI: 0.36, 1.04, $P=0.07$).

2.5.2 Apache Ii Score At 7th Day after Treatment

Six reports provided data (n=403) on APACHE II score at 7th day after treatment. A fixed-effect model was used and no significant heterogeneity was found ($I^2=0\%$, $P=0.98$). The acupuncture treatment group was lower (two studies, 403 participants, MD: -3.36, 95% CI: -4.30, -2.41, $P<0.01$).

2.5.3 Concentrations of Pct at 7th Day after Treatment

Seven reports provided data (n=427) on Concentrations of PCT at 7th day after treatment. A random-effect model was used, a higher degree of heterogeneity was found ($I^2=64\%$, $P=0.01$). The acupuncture treatment group was lower (two studies, 427 participants, MD: -2.23, 95% CI: -3.33, -1.13, $P<0.01$).

2.5.4 Concentrations of Tnf-A At 7th Day after Treatment

Four reports provided data (n=268) on Concentrations of TNF- α at 7th day after treatment. A random-effect model was used, a higher degree of heterogeneity was found ($I^2=78\%$, $P=0.003$). The acupuncture treatment group was lower (two studies, 268 participants, MD: -14.86, 95% CI: -23.74, -5.97, $P=0.001$).

2.5.5 The Level of Cd8^t Cell Subsets At 7th Day after Treatment

Four reports provided data (n=236) on the level of CD8⁺ T cell subsets at 7th day after treatment. A random-effect model was used, a higher degree of heterogeneity was found ($I^2=90\%$, $P<0.01$). The acupuncture treatment group was no lower than the routine therapies group (two studies, 236 participants, MD: 0.36, 95% CI: -1.57, 2.29, $P=0.71$).

3. Discussion

Sepsis is a severe life-threatening infection accompanied by organ dysfunction. Acupuncture is widely used for anti-inflammation can reduce the levels of serum PCT. It also can regulate immunity by reducing the ratio of CD8⁺ T cells and TNF- α level, which were the important indicator for inflammation. Both PCT and TNF- α at 7th day in the acupuncture treatment group was lower than that in the routine therapies group. Acupuncture is simple operation with the low cost, If acupuncture can be proved useful to sepsis, it could greatly improve the quality of patient's life.

In our analysis, we analyzed the evaluation indicators. On comparing the APACHE II score, both groups at the 7th day of treatment, the experimental group was better than the control group. There was no difference of 28-day mortality. It was also elucidated in a previous study that immune stimulation treatment improved prognosis of patients with sepsis with reversing immune suppression^[5]. And this study reflected that the acupuncture treatment has obvious clinical effect in patients with sepsis and its mechanism may be involved in immune stimulation, so as to improve low immune status and correct immune disorders in patients with sepsis.

Previous animal studies showed that the immune indexes of sham acupuncture group were not significant different compared with control group^[6,7]. Considering the compliance and stability of sham acupuncture, our study did not set up sham acupuncture group.

4. Conclusion

In conclusion, this analysis suggested that acupuncture treatment could decrease the decreased the APACHE II score, the levels of serum PCT and TNF- α , but has no effect on 28-day mortality, CD8⁺ T cells count and had a better clinical effectiveness in the treatment of sepsis patients. It was also elucidated in a previous study that immune stimulation treatment improved prognosis of patients with sepsis with reversing immune suppression.

The current quality and quantity of the experiments for this study are both still at a relatively low degree, more research is needed from other countries in order to avoid the possibility of race deviation.

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