



The effect of Chinese herbal medicine on hemorrhagic shock: A systematic review and meta-analysis



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ABSTRACT

Background: Chinese herbal medicine (CHM) has been widely used in the treatment of hemorrhagic shock (HS) in China. Many controlled trials have been undertaken to investigate its efficacy.

Objective: To evaluate the effectiveness and safety of CHM for Hemorrhagic Shock patients.

Methods: We screening the Web of ScienceDirect database, PubMed, the Cochrane Library, EMBASE, China Biomedical Database web (CBM), China National Knowledge Infrastructure (CNKI) and WanFang database (WF), from inception to January 2015. All the randomized controlled trials (RCTs) that compared CHM plus conventional therapy with conventional therapy alone for HS patients were included. Meta-analysis on included studies was performed using fixed-effects model with RevMan 5.2. Risk ratio (RR) or mean difference (MD) with a 95% confidence interval (CI) was used as effect measure. STATA 12.0 was used for publication bias.

Results: Fifteen RCTs involving 1076 participants were included in the meta-analysis. CHM combined with conventional therapy was tested to be more effective in reduce mortality (RR=0.24, 95%CI:0.13–0.46, $P<0.0001$), reduce the incidence of MODS (RR=0.47, 95%CI: 0.34–0.66, $P<0.00001$), symptomatic improvement: increase blood pressure (BP) (MD=8.83, 95%CI:6.82–10.84, $P<0.00001$), regulate heart rate (MD=−7.6, 95%CI:−9.17 to −6.02, $P<0.00001$), increase urine volume (MD=7.26, 95%CI:5.00–9.53, $P<0.00001$), compared with conventional therapy alone. No serious adverse events were reported.

Conclusions: CHM combined with conventional therapy seems to be more effective on HS patients. However, the analysis results should be interpreted with caution due to the low methodological quality of the included trials. Future, the rigorously designed, high methodological quality, multicenter and large-scale trials are needed to confirm these conclusions.

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Contents

1. Introduction.....	79
2. Methods.....	79
2.1. Search strategy.....	79
2.2. Criteria for considering studies for this review.....	79
2.2.1. Types of studies.....	79
2.2.2. Types of participants.....	79
2.2.3. Types of interventions.....	80
2.2.4. Types of outcome measures.....	80
2.3. Data extraction.....	80
2.4. Data analysis.....	80
3. Results.....	80
3.1. Search result.....	80
3.2. Study characteristics.....	83

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3.3.	Risk of bias in included studies	83
3.4.	The effectiveness of interventions	83
3.4.1.	Mortality	83
3.4.2.	The incidence of MODS	83
3.4.3.	Mean arterial pressure (MAP)	83
3.4.4.	Heart rate	83
3.4.5.	Urine volume	83
3.4.6.	Publication bias	83
3.4.7.	Adverse effects	83
4.	Discussion	83
4.1.	Limitation	87
5.	Conclusion	87
	Funding	87
	Author's contribution	87
	Conflicts of interest	88
	References	88

1. Introduction

Trauma is the leading cause of death among people aged 15–44 y, with more than 5 million injury-related deaths every year in the world. And the deaths caused by traumatic is still increasing year by year. By 2020, deaths from traumatic injury may increase to 8 million on a global scale, with one-third resulting from Hemorrhagic Shock (HS).^{1,2} Mortality is directly linked to massive blood loss or occurs indirectly due to secondary multiple organ failure(MOF).³ Immediately after injury, the volume of blood loss is a main determinant of outcome. If the blood loss greater than 25–30% of total blood volume within a short time, that exceeded the compensatory mechanisms of body, then the cardiac output and mean arterial pressure(MAP) decreased, and eventually led to shock. Once the blood loss greater than 45–50% of total blood volume, that could be rapidly lead to death.⁴ In later stages, posttraumatic hemorrhagic shock, initiated by massive tissue injury and ischemia/reperfusion, primes the innate immune system and trigger systemic inflammatory response syndrome (SIRS).⁵ When hemorrhagic shock occurs, the blood of intestinal was first discarded to supply center organs of human body, such as cerebrum, heart and lung.^{6,7} Intestinal ischemia will lead to intestinal barrier damaged, then translocation of bacterial and endotoxin from the lumen into blood circulation caused intestinal endotoxemia (IETM), and trigger SIRS.^{8,9} This process ultimately results multiple organ dysfunction syndrome (MODS), which is the leading cause of death among those patients who die in the intensive care unit.¹⁰

Currently, therapy should be guided by the rate of bleeding and changes in hemodynamic parameters, such as blood pressure, heart rate, cardiac output, central venous pressure, pulmonary artery wedge pressure, mixed venous saturation, or metabolic markers (lactate, base deficit).¹¹ Treatment strategy is to stop the source of hemorrhage first, then rapid and aggressive fluid resuscitation should be conducted to restore blood pressure and tissue perfusion prior to blood transfusion.¹² However, after initial survival period, there is still great risk of death comes from multi-organ failure(MOF) in later hospital course.¹³ We have to consider prophylaxis and treatment intestinal endotoxemia (IETM) when therapy of HS patients, that is important for reduce the incidence of MODS and mortality.

Hemorrhagic shock belongs to the category of “JueTuo syndrome” in traditional chinese medicine (TCM). “JueTuo syndrome” is mainly characterized pale complexion, cold limbs, profuse perspiration, decrease in urine output, dysphoria or lethargic, rapid and weak pulse, which is approximately consistent with the clinical manifestation of HS.¹⁴ TCM theory recognizes HS as deficiency pattern, which is mainly caused by massive hemorrhage, qi exhaus-

tion because of massive hemorrhage, disharmony of yin and yang, then Yin and yang movements not smoothly.¹⁵

In China, CHM has been wildly used as adjuvant therapy on HS. Recently years, a number of RCT studies have demonstrated that CHM has positive effects as complementary therapy for HS, such as improve the effect of fluid resuscitation, improving microcirculation, reducing mortality and the incidence of MODS.^{16–18} However, there has been no systematic review to assess the effectiveness and safety of CHM combine with conventional therapy on HS. Therefore, this review aims to systematically evaluate the effects and safety of CHM as an adjuvant treatment for treating HS.

2. Methods

2.1. Search strategy

A comprehensive search was conducted in seven databases—PubMed, EMBASE, Cochrane Library, ScienceDirect, CBM, CNKI database, and Wan Fang database. The bibliographic databases were searched from respective inceptions to January 2015. We used the following keywords treated as title/abstract for the literature search: “hemorrhagic shock” or “hemorrhagic traumatic shock” and “traditional Chinese medicine” or “Chinese herbal injection” or “integrative medicine” or “herbal” or “herbs-botanical drugs” and examined the reference lists of the obtained articles. The search was restricted to studies in humans. No restrictions were imposed on publication language. We contacted authors of original studies for additional data when necessary.

2.2. Criteria for considering studies for this review

2.2.1. Types of studies

Randomized controlled trials (RCTs) of CHM combined with conventional Western treatment versus conventional Western treatment only for HS patients. Case studies, case series, qualitative studies and uncontrolled trials were excluded. No language restrictions were imposed.

2.2.2. Types of participants

All of the participants suffered from hemorrhagic shock caused by trauma, esophageal varices, hepatorrhaxis and pepticulcer. Hemorrhagic shock cases diagnosed by generally accepted criteria (World Health Organization diagnostic guidelines⁴ or by the Chinese Ministry of Health's guidelines were included).¹⁹ Hemorrhagic shock cases complicated with other illnesses such as severe cardiovascular disease or cancer were excluded. We did not intend to make any restrictions on age, gender and race.

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