Review Article

Efficacy and safety of integration of traditional and Western medicine for the treatment of spontaneous bacterial peritonitis in liver cirrhosis: a systematic review

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Abstract: Integration of traditional and Western medicine (ITWM) has been widely used in China for the treatment of many diseases. ITWM may be a promising alternative for the treatment of spontaneous bacterial peritonitis (SBP). A systematic review was performed to evaluate the efficacy and safety of ITWM for the treatment of SBP in liver cirrhosis. PubMed, China National Knowledge Infrastructure, Wanfang, and VIP databases were searched electronically from inception to July 2016 to collect all randomized controlled trials (RCTs) about ITWM for the treatment of SBP in cirrhotic patients. A total of 42 RCTs were included. Rhubarb, Red Paeony Root, and Danshen Root were the three most commonly used traditional Chinese medicine (TCM) drugs; the third-generation cephalosporins were the most commonly used antibiotics. All included studies reported the effectiveness rate (ITWM group: 58.33–96.00%; control group: 32.20–93.75%); 41 studies showed a higher effectiveness rate in the ITWM group; and 38 studies found a significant difference. All included studies reported the cure rate (ITWM group: 9.00–95.00%; control group: 3.00–77.00%); 41 studies showed a higher cure rate in the ITWM group; and 10 studies found a significant difference. Four studies reported the mortality (ITWM group: 5.10–18.33%; control group: 7.69–52.78%) and showed a lower mortality in the ITWM group; and two studies found a significant difference. Six studies reported the adverse events (ITWM group: 0.00–13.33%; control group: 0.00–59.52%); five studies showed a lower rate of adverse events in the ITWM group; and four studies found a significant difference. ITWM might be effective and safe for the treatment of SBP. Further well-designed high-quality studies are needed to confirm the effectiveness and safety of ITWM for the treatment of SBP.

Keywords: Spontaneous bacterial peritonitis (SBP); liver cirrhosis; integration of traditional and Western medicine (ITWM); traditional Chinese medicine (TCM); treatment

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Background

Liver cirrhosis is the end stage of liver diseases with a high morbidity and mortality (1). Ascites is the most common complication of liver cirrhosis. Nearly 60% of patients diagnosed with liver cirrhosis will develop ascites within 10 years (2). Spontaneous bacterial peritonitis (SBP) is a common bacterial infection in cirrhotic patients with ascites. The morbidity and in-hospital mortality of SBP in patients with ascites is 7–30% and 10–50% (3-5).

Several guidelines unanimously recommend third-generation cephalosporins for the treatment of SBP (6-8). However, antibiotic resistance is increasing year by year in SBP patients (9-11). The effectiveness of antibiotics alone for the treatment of SBP is unsatisfactory.

Traditional Chinese medicine (TCM) refers to the drugs and compounds used under the guidance of the TCM theory. Integration of traditional and Western medicine (ITWM) refers to the combination of TCM with Western medicine, which has a great potential for the treatment of many diseases in China (12-14). More and more studies have focused on the ITWM for the treatment of SBP in China.

The aim of this study was to systematically evaluate the efficacy and safety of ITWM for the treatment of SBP.

Materials and methods

Eligibility and exclusion criteria

Eligibility criteria: randomized controlled trials (RCTs) about ITWM for the treatment of SBP in patients with cirrhosis. ITWM group should be patients who received TCM drugs combined with Western medicine drugs. Control group should be patients who received Western medicine drugs alone. Exclusion criteria: (I) incomplete data; (II) reviews; (III) case reports; (IV) duplicate publications; (V) commentaries; (VI) non-RCTs; and (VII) ITWM in the prevention of SBP. No limits on publication status or language.

Literature search

PubMed, China National Knowledge Infrastructure, Wanfang, and VIP databases were searched electronically from inception to July 2016 to collect all RCTs about ITWM for the treatment of SBP in patients with liver cirrhosis. All databases were searched using key words: TCM, SBP, and ITWM.

Data extraction

Data were extracted as follows: title, author's information, year of publication, study design, method of intervention, effectiveness of treatment, and adverse event.

Effectiveness rate was defined as the proportion of patients in whom SBP-related symptoms and/or laboratory data improved after treatment.

Cure rate was defined as the proportion of patients in whom SBP-related symptoms disappeared and laboratory data normalized after treatment.

Ineffectiveness rate was defined as the proportion of patients without any response to treatment.

Quality of studies

Jadad quality score was used to assess the quality of studies (*Table S1*) (15).

Randomization: studies using the method of randomization appropriately were graded as 2 points; studies without any description about the method of randomization were graded as 1 point; studies using the method of randomization inappropriately were graded as 0 point.

Double blinding: studies using and describing the double blinding method appropriately were graded as 2 points; studies in which the use of double blinding was just mentioned but the detailed method was lacking were graded as 1 point; studies in which the double blinding method was not used or the method of double blinding was inappropriate were graded as 0 point.

Withdraws and dropouts: studies in which both withdraws and dropouts were described were graded as 1 point; studies in which withdraws and dropouts were not described were graded as 0 point.

Results

Basic information

A total 628 studies were identified. Finally, 42 RCTs including 3,227 SBP patients were enrolled into this study (*Figure 1*). Information of the included studies is depicted in the *Table S2*. The distributions of included studies according to the region of China are described in the *Figure S1*.

Medications

Components of TCM-drugs

The most commonly used TCM drugs were demonstrated

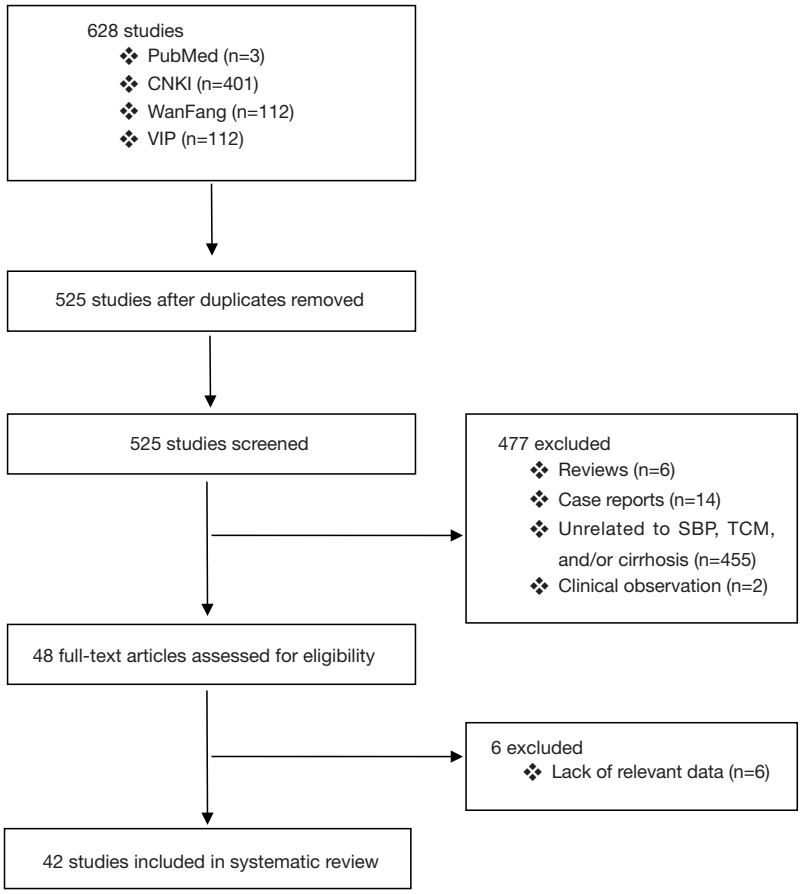

Figure 1 Flow diagram.

in *Figure 2*. Overall, 77 kinds of TCM drugs were used, including Rhubarb (N=24), Red Peony Root (N=20), Danshen Root (N=16), Baical Skullcap Root (N=14), Dahurian Patrinia Herb (N=11), Honeysuckle Flower (N=11), Golden Thread (N=10), Mongolian Dandelion Herb (N=10), Spreading Hedyotis Herb (N=8), Chinese Angelica (N=8), Largehead Atractylodes Rhizome (N=7), Indian Buead (N=7), Safflower (N=7), Officinal Magnolia Bark (N=7), Cape Jasmine Fruit (N=7), Weeping Forsythiae Capsule (N=6), Oriental Waterplantain Rhizome (N=6), Liquoric Root (N=5), Areca Peel (N=4), Sargent Gloryvine (N=4), Radix Astragali (N=4), Lightyellow Sophora Root (N=4), Virgate Wormwood Herb (N=4), Bitter Orange (N=4), Green Tangerine Peel (N=4), Agaric (N=4), Plantain Seed (N=3), Pilose Asiabell Root (N=3), Giant Knotweed Rhizome (N=3), Ginseng (N=3), Peach Seed (N=3), Heartleaf Houttuynia Herb (N=3), Indigowoad Root (N=2), Turtle Shell (N=2), Tangerine Peel (N=2), Myrrh (N=2), Frankincense (N=2), Common Yam Rhizome (N=2), Yanhusuo (N=2), Coix Seed (N=2), Turmeric Root-tuber (N=2), Hiraute Shiny Bugleweed Herb (N=2), Medicinal Indianmulberry Root (N=1), White Hyacinth Bean (N=1), Chinese Pulsatilla Root (N=1), Barbed Skullcap Herb (N=1), Pinellia Tuber (N=1), Areca Seed (N=1), Borneol (N=1), Chinese Thorowax Root (N=1), Halloysit (N=1), Rice Bean (N=1), Common Andrographis Herb (N=1), Indigowoad Leaf (N=1), Zedoary (N=1), Turmeric (N=1), Platycodon Root (N=1), Semen Nelumbinis (N=1), Beautiful Sweetgum Fruit (N=1), European Verbena (N=1), Parslane Herb (N=1), Dwarf Lilyturf Tuber (N=1), Mirabilite (N=1), Oyster Shell (N=1), Bezoar (N=1), Goat Horn (N=1), Common Clubmoss Herb (N=1), Garden Balsam Stem (N=1), Ground Beeltle (N=1), Cowherb Seed (N=1), Bear Gall Powder (N=1), Figwort Root (N=1), Dragon's Blood (N=1), Motherwort Herb (N=1), Epimedium Herb (N=1), Pearl Powder (N=1), and Common Anemarrhena

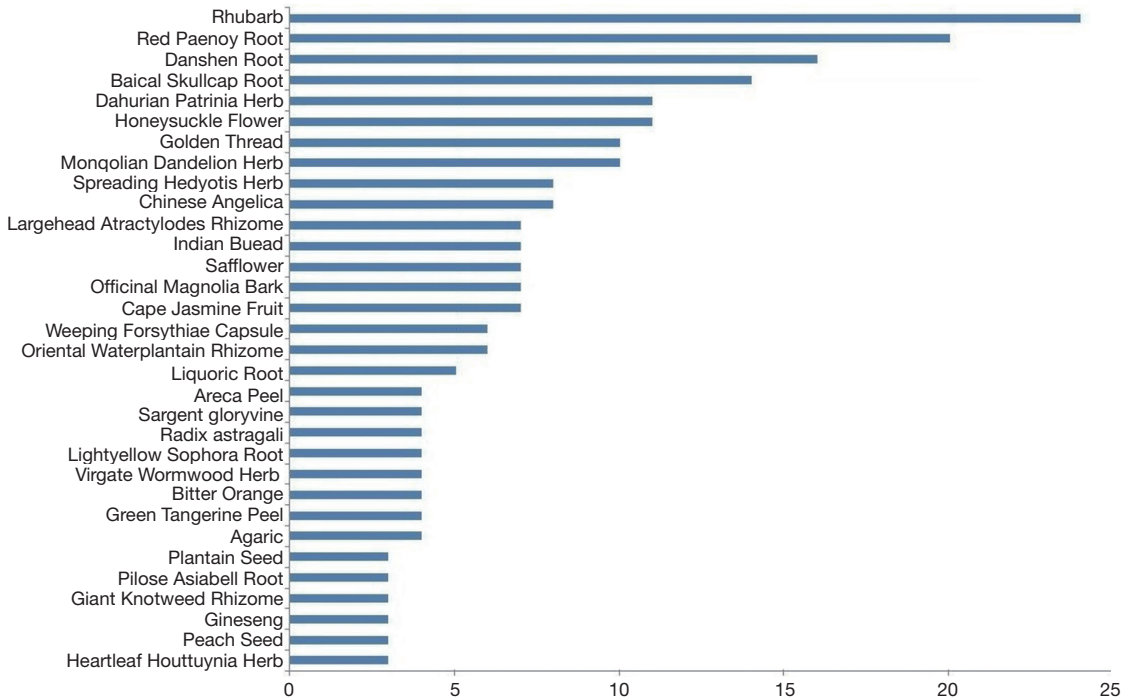

Figure 2 The most commonly used TCM drugs for the treatment of SBP.

Rhizome (N=1).

There were 12 categories of TCM drugs, including formula for heat-clearing and toxicity-relieving (N=20), formula for blood circulation promoting (N=13), formula for energy-restoring (N=12), formula for water-disinhibiting damp-percolating (N=8), desiccating formula (N=4), carminative formula (N=4), astringent formula (N=3), superficies-resolving formula (N=2), formula for purgation (N=2), formula for rheumatism (N=2), formula for expectorants, antitussives and dyspnea-relieving (N=2), and formula for resuscitation (N=1).

Western medicine drugs

The third-generation cephalosporins, including cefoperazone and ceftriaxone, were the most commonly used Western medicine drugs for the treatment of SBP (71.43%, 30/42).

Form of TCM drugs

Of all included studies, 38.10% (16/42) used the TCM decoction (16-31), 28.57% (12/42) used the Chinese patent medicine (32-43), 21.43% (9/42) used the TCM enema (44-51), 9.52% (4/42) used the TCM umbilicus compression (52-55), and 2.38% (1/42) used the TCM peritoneal lavage (56).

Of all included studies, 4.76% (2/42) used the single-TCM drug (27,57), 30.95% (13/42) used the TCM compounds that have been proven by the China Food and Drug Administration (CFDA) (22,32-43), 16.67% (7/42) used the classical TCM compounds (16-19,25,31,54), and 47.62% (20/42) used the self-made TCM compounds (20,21,23,24,26,28-30,44-53,55,56).

Effectiveness rate

All included studies reported the effectiveness rate. The effectiveness rate was 58.33–96.00% and 32.20–93.75% in ITWM and control groups, respectively (*Figure 3*). Of all included studies, 97.62% (41/42) reported a higher effectiveness rate in ITWM group; and 92.69% (38/41) of them found a significant difference.

Cure rate

All included studies reported the cure rate. The cure rate was 9.00–95.00% and 3.00–77.00% in ITWM and control groups, respectively (*Figure 4*). Of all included studies, 97.62% (41/42) reported a higher cure rate in ITWM group and 24.39% (10/41) of them found a significant difference.

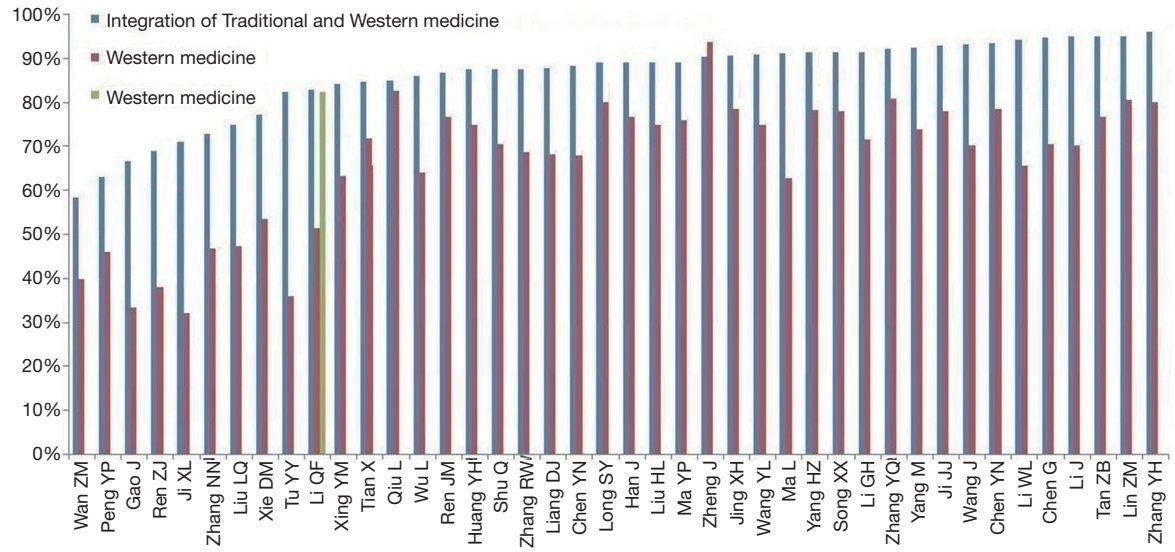

Figure 3 The effectiveness rate. In the study by Li *et al.* (16), the red bar refers to the control group that used Norfloxacin, the green bar refers to the control group that used Cefazolin.

In-hospital mortality

Four studies reported the in-hospital mortality. The in-hospital mortality was 5.10–18.33% and 7.69–52.78% in ITWM and control groups, respectively (*Figure 5*). All of the four included studies reported a lower in-hospital mortality in ITWM group; and 50% (2/4) of them found a significant difference.

Adverse events

Six studies reported the adverse events, including abdominal pain, diarrhea, vomiting, headache, and rash. The rate of adverse events was 0.00–13.33% and 0.00–59.52% in ITWM and control groups, respectively (*Figure 6*). Five of them (83.33%, 5/6) reported a lower rate of adverse events in ITWM group; and 80% (4/5) of them found a significant difference.

Study quality

Of all included studies, 30.95% (13/42) didn't describe any method of randomization; 64.29% (27/42) used the randomization but didn't describe any method of randomization; and 4.76% (2/42) used the random number table (*Table S1*). No studies used the double-blind method. No studies reported the withdrawal/dropout rates.

Discussion

TCM drugs have been used for the treatment of many diseases for over 2,000 years in China and Eastern Asian countries (58). TCM theory is based on the ancient Chinese philosophy, aiming to correct the maladjustments, restore the self-regulatory ability, and remove the harms (59). Due to the language barrier, studies that reported the effectiveness of ITWM for the treatment of SBP are rarely noticed in the Western world. As far as we concern, no review explored the ITWM for the treatment of SBP. Our systematic review found the following: 92.69% (38/41) and 24.39% (10/41) of included studies reported a significantly higher effectiveness and cure rate in ITWM group, respectively; 50% (2/4) showed a significantly lower in-hospital mortality in ITWM group; and 66.67% (4/6) showed a significantly lower proportion of adverse events in ITWM group. Thus, ITWM should be a promising treatment for SBP. Additional benefits of ITWM might be attributed to the inhibition of inflammation, improvement of immunity, regulation of intestinal microflora, improvement of antibiotics bioavailability, and inhibition of drug resistance. However, the accurate mechanisms remained unclear.

Our study also showed that Rhubarb was the most commonly used TCM drug, followed by Red Paeony Root and Danshen root. First, Rhubarb was

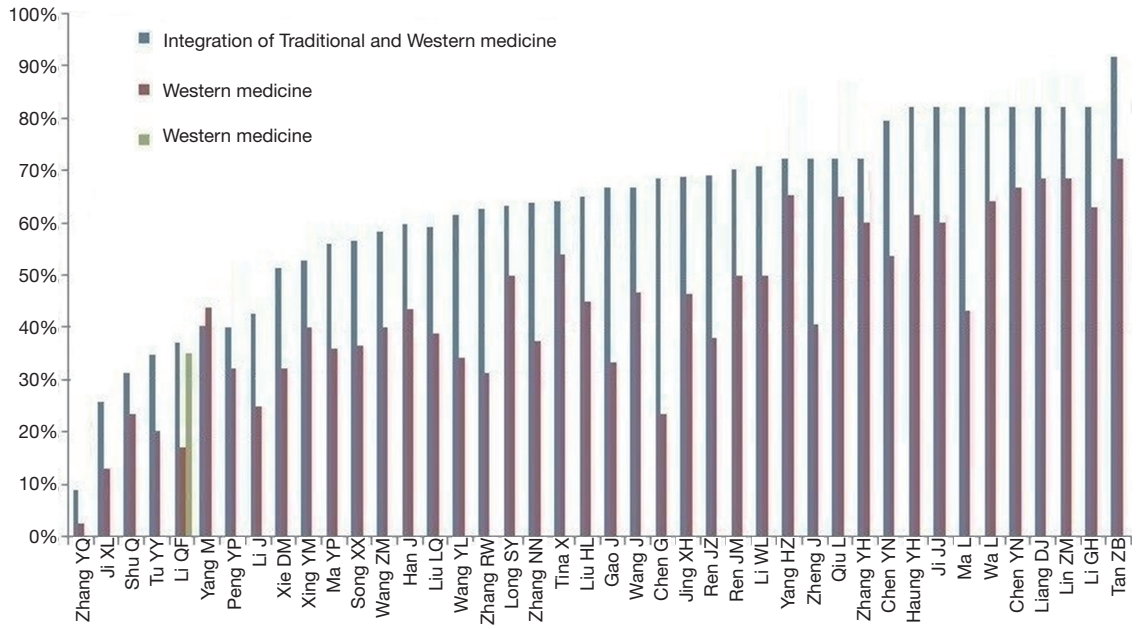

Figure 4 The cure rate. In the study by Li *et al.* (16), the red bar refers to the control group that used Norfloxacin, the green bar refers to the control group that used Cefazolin.

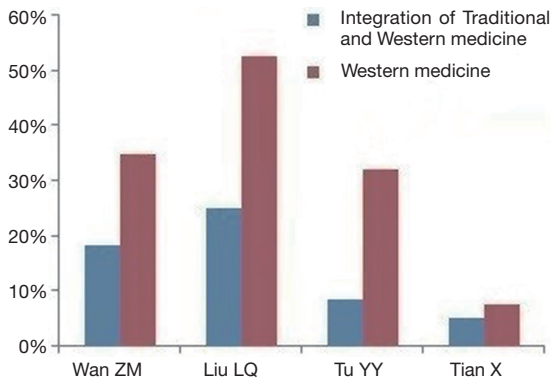

Figure 5 The in-hospital mortality.

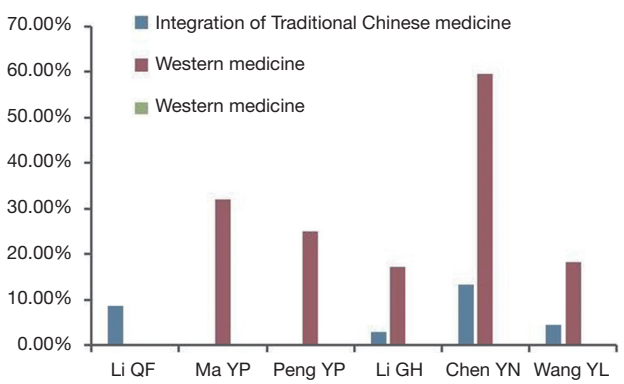

Figure 6 The rate of adverse events. In the study by Li *et al.* (16), the red bar refers to the control group that used Norfloxacin, the green bar refers to the control group that used Cefazolin.

used in 57.14% (24/42) of studies, which has a role in defecation-accelerating, heat-clearing, blood-cooling, toxin-relieving, blood stasis-dredging, dampness-dredging, and jaundice-resolving according to the TCM theory. Modern pharmacological studies conclude that Rhubarb can protect the digestive tract mucosa and promote the gastrointestinal peristalsis (60). Second, Red Paeony Root was used in 83.33% (20/42) of studies. The dry root of Paeonia Lactiflora Pallas has a role in heat-clearing, blood-cooling, toxin-relieving, and blood stasis-dredging according to the TCM theory. Third, Danshen root was used in 38.10% (16/42) of studies, which has a role in blood circulation-promoting, blood stasis-dredging, and blood-nourishing according to the TCM theory. Anti-inflammatory functions of Red Paeony Root and Danshen Root have been proved (61,62). Additionally, both Red Paeony Root and Danshen Root are the main components of Xuebijing injection, which is the ethanol extract derived from Chuanxiong, Red Paeony Root, Danshen Root, and Honghua. It is the most commonly used

Chinese herb compound in all included studies, well-known by its anti-inflammatory function (63). Seven (16.67%) studies used Xuebijing injection for the treatment of SBP.

There are many different forms of TCM drugs, including decoction, enema, sticking, and compound injection. Decoction is the most commonly used form of TCM drugs. It has some advantages: (I) the composition of a decoction can be modified according to the patient's condition; (II) water is the main carrier to promote the absorption of TCM drugs; and (III) TCM decoction is widely used in China and becomes more and more popular worldwide. However, it also has some disadvantages: (I) TCM decoction is a complex composition that is composed by different TCM drugs. However, the interaction among TCM drugs after boiling and taking remains unclear; (II) the process of preparing a TCM decoction is complex; (III) the quality of TCM drugs after decocted is variable; and (IV) TCM compounds are highly individualized, the indications for modifying the TCM drugs or compounds are unclear.

Safety of ITWM treatment should be carefully evaluated. However, adverse events related to ITWM treatment were generally lacking. Non-specific adverse events (including abdominal pain, diarrhea, vomiting, headache, and rash) were only reported in six studies. No study described the risk factors, management, and outcome of adverse events. Thus, in future studies, there is a need for more detailed reporting on this matter. Additionally, some TCM drugs, such as Medicinal Indian Mulberry Root and Yanhusuo, have the potential of inducing liver and/or renal injury (64,65). Thus, they might be cautiously used in patients with liver and/or renal diseases. Notably, our systematic review demonstrated neither liver nor kidney toxicity of Medicinal Indian Mulberry Root and Yanhusuo.

We found that 30.95% of studies used the CFDA-proved TCM compounds, 16.67% of studies used the classical TCM compounds, and 47.62% of studies used the self-made TCM compounds. The CFDA-proved TCM compounds can be identified on the CFDA official website (http://www.sda.gov.cn/WS01/CL0001/). The classical TCM compounds can be identified from the classic books of TCM and are recognized by many TCM practitioners. The self-made TCM compounds are invented by some TCM practitioners based on their own clinical experiences. Certainly, the quality of the self-made TCM compounds may be uncertain. Only two studies (27,57) used the single-TCM drug (Rhubarb and Heartleaf Houttuynia Herb).

Some limitations should be pointed out. First, the ITWM treatment strategy and patients' conditions are different among studies, which cause different rates of effectiveness, cure, and adverse events among studies. Thus, the data was not pooled due to these huge heterogeneities among studies. Second, a uniform definition of "therapeutic effectiveness" was lacking, which might contribute to the heterogeneity. For example, in Zhang's paper, the definition of "effectiveness" was broad and easy to achieve, but the definition of "cure" was strict (36). This may lead to a higher effectiveness rate and a lower cure rate. Third, the quality of included studies was relatively poor. The quality of TCM RCTs performed in China has been questioned (66). Almost all TCM RCTs claimed a superiority of TCM treatment, but only few of them were of high-quality. Some methodological components of the RCTs were incompletely reported. Wang *et al.* (67) identified a total of 7,422 RCTs published between 1999 and 2004. Surprisingly, only 17.9% (1,329/7,422) of them were truly randomized. Forth, the risk control of TCM drugs was unavailable (68). Fifth, there are few TCM specialized hospitals in Western countries. Thus, the TCM RCTs were hardly performed in Western countries. It is also hard to extrapolate our conclusions to Western countries. Sixth, only 11 out of the 42 trials used albumin for the SBP treatment. Indeed, the lack of albumin administration in most of the trials included is a reason of concern, because it impairs the subjects' outcome and makes difficult to compare the results.

In conclusion, ITWM might be effective and safe for the treatment of SBP. However, the quality of studies on ITWM for the treatment of SBP should be improved in future. Further well-randomized, double-blind, and placebo-controlled studies with a strict and uniform definition of effectiveness (i.e., partial response) and cure (i.e., complete response) are needed to explore the benefit/risk of a specific TCM drug or compound (i.e., Rhubarb or Xuebijing injection) for the treatment of SBP.

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Footnote

Conflicts of Interest: The authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/amj.2017.08.10). Dr. Qi serves as an Editor-in-Chief of *AME Medical Journal*. Andrea Mancuso serves as an unpaid editorial board member of *AME Medical Journal* from Mar 2017 to Mar 2019. Fernando Gomes Romeiro serves as an unpaid editorial board member of *AME Medical*

Journal from Apr 2017 to Apr 2019. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 The Jadad scores of all studies enrolled

Author	Jadad scores
Li QF	1
Chen YN	1
Chen YN	1
Ren ZJ	1
Long SY	1
Yang HZ	0
Huang YH	0
Xie DM	1
Li J	1
Li WL	1
Qiu L	0
Ren JM	1
Liang DJ	0
Lin ZM	0
Chen G	1
Wan ZM	1
Gao J	1
Liu LQ	1
Tu YY	0
Wu L	0
Han J	1
Tian X	1
Xing YM	1
Ji XL	1
Liu HL	1
Jing XH	1
Ma YP	1
Li GH	0
Yang M	1
Peng YP	0
Ji JJ	0
Zhang YH	0
Song XX	1
Tan ZB	1
Zhang YQ	1
Wang J	1
Shu Q	1
Zheng J	0
Zhang RW	2
Wang YL	1
Ma L	0
Zhang NN	2

Table S2 Basic information of the included studies

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
LI QF (16) [1995][#]	ITWM treatment					
	Taking TCM decoction: DaChengQi Decoction add or subtract TCM drugs with the clinical symptoms, 1-time/day, for 7 days	35	82.9	37.14	17.1	NA
	Antibiotics: Norfloxacin 0.6 g, 3-time/day, taken orally for 10 days					
	Western medicine treatment					
	Norfloxacin 0.6 g, 3-time/day, taken orally for 10 days	35	51.4	17.14	48.6	NA
	Cefazolin 2.0 g, 2-time/day, for 10 days	34	82.4	35.29	17.6	NA
Chen YN (17) [1997][#]	ITWM treatment					
	Taking TCM decoction: SanHuangXiaoDu Decoction: Spreading Hedyotis Herb 60 g, Baical Skullcap Root, Golden Thread, Rhubarb, Cape Jasmine Fruit 12 g, respectively; Honeysuckle Flower, Mongolian Dandelion Herb, Weeping Forsythiae Capsule 30 g, respectively; Oriental Waterplantain Rhizome, Red Paeony Root, Bitter Orange 15 g, respectively; Dahurian Patrinia Herb, Sargent gloryvine 20 g, respectively. 1-time/day, add or subtract TCM drugs with the clinical symptoms, 150 mL, 3-time/day, taken orally	34	88.24	79.41	11.76	NA
	Antibiotics: Ceftriaxone 4.0 g, 1-time/day, Norfloxacin 0.6 g, 1-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Ceftriaxone 1.0–2.0 g, 1-time/day, Norfloxacin 0.6 g, 1-time/day. Combined with the treatment of liver-protection, albumin supplements and diuretics	28	67.86	53.57	32.14	NA
Chen YN (18) [1999][#]	ITWM treatment					
	Taking TCM decoction: San Huang Xiao Du Decoction: Spreading Hedyotis Herb 60 g, Baical Skullcap Root, Golden Thread, Rhubarb, Cape Jasmine Fruit 12 g, respectively; Honeysuckle Flower, Mongolian Dandelion Herb, Weeping Forsythiae Capsule 30 g, respectively; Oriental Waterplantain Rhizome, Red Paeony Root, Bitter Orange 15 g, respectively; Dahurian Patrinia Herb, Sargent gloryvine 20 g, respectively. 150 mL, 3-time/day, taken orally	45	93.33	86.67	6.67	NA
	Antibiotics: Ceftriaxone 1.0–2.0 g, 1-time/day, Norfloxacin 0.6 g 1-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements					
	Course of treatment: 7 days					
	Western medicine treatment					
	Ceftriaxone 1.0–2.0 g, 1-time/day, Norfloxacin 0.6 g, 1-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements	42	78.57	66.67	21.43	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Ren ZJ (19) [2005][#]	ITWM treatment					
	Taking TCM decoction: QingWenJieDu Decoction: Baical Skullcap Root 15 g, Honeysuckle Flower 25 g, Mongolian Dandelion Herb 25 g, Cape Jasmine Fruit 15 g, Radix Astragali 30 g, Pilose Asiabell Root 15 g, Largehead Atractylodes Rhizome 15 g, Rhubarb 15 g, Officinal Magnolia Bark 15 g, Danshen Root 20 g, add or subtract TCM drugs with the clinical symptoms, 300 mL, 2-time/day	42	69.05	69.05	30.95	NA
	Antibiotics: Cefotaxime 2 g, 1-time/8 h. Combined the treatment of liver-protection, symptomatic treatment					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Cefotaxime 2 g, 1-time/8 h. Combined the treatment of liver-protection, symptomatic treatment	42	38.1	38.1	61.9	NA
Long SY (20) [2006][+]	ITWM treatment					
	Taking TCM decoction: HuaYuLiShui Decoction: Virgate Wormwood Herb 15 g, Indian Buead 15 g, Agaric 15 g, Largehead Atractylodes Rhizome 15 g, Mongolian Dandelion Herb 15 g, European Verbena 30 g, Spreading Hedyotis Herb 30 g, Giant Knotweed Rhizome 10 g, Zedoary 10 g, Ground Beeltle 10 g, Danshen Root 10 g, Peach Seed 10 g, Bitter Orange 10 g, Pilose Asiabell Root 10 g, Liquoric Root 6 g, add or subtract TCM drugs with the clinical symptoms, 150 mL, 2-time/day	30	90	63.33	10	NA
	Antibiotics: Ceftriaxone 1 g, 2-time/day. Combined with the treatment of peritoneal lavage					
	Course of treatment: 60 days					
	Western medicine treatment					
	Ceftriaxone 1 g, 2-time/day. Combined with the treatment of peritoneal lavage	30	80	50	20	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Yang HZ (21) [2006]+	ITWM treatment					
	Taking TCM decoction: QingXiaXiaoBu Decoction: (I) First step: DaChengQi Decoction: Rhubarb 20–30 g, Mirabilite 9–15 g, Weeping Forsythiae Capsule 30 g, Heartleaf Houttuynia Herb 30 g, Virgate Wormwood Herb 30 g, Cape Jasmine Fruit 24 g, Agaric 24 g, Dahurian Patrinia Herb 30 g. Usage: all herbal boiling into decoction, 1–2 time/day, maintains the times of defecation at 2–3 time/day, add or subtract TCM drugs with the clinical symptoms. Course of treatment: 1 week. (II) Second step: increase the dosage of Turmeric Root-tuber, Red Paeony Root: Rhubarb 6–9 g, Mirabilite 6–12 g, Turtle Shell 15 g, Virgate Wormwood Herb 20 g, Turmeric Root-tuber 30 g, Danshen Root 15 g, Red Paeony Root 30 g, Largehead Atractylodes Rhizome 12 g, Liquoric Root 9 g. Usage: 1-time/day. Combined with ChuanXiongQin injectioin 40–80 mg into glucose injection, 1-time/day, add or subtract TCM drugs with the clinical symptoms. Course of treatment: 1 week	46	91.3	76.09	8.7	NA
	Antibiotics: Cefoperazone 2 g, 2-time/day					
	Course of treatment: 2 weeks					
	Western medicine treatment					
	Cefoperazone 2 g, 2-time/day. Combined with diuretics, treatment of liver-protection and paracentesis	46	78.3	65.22	21.7	NA
Huang YH (22) [2008]*	ITWM treatment					
	Taking TCM decoction: ZhongManFenXiao Wan: Baical Skullcap Root 10 g, Golden Thread 5 g, Common Anemarrhena Rhizome 10 g, Officinal Magnolia Bark 10 g, Bitter Orange 10 g, Pinellia Tuber 10 g, Tangerine Peel 10 g, Indian Buead 15 g, Agaric 15 g, Oriental Waterplantain Rhizome 15 g, Pilose Asiabell Root 15 g, Largehead Atractylodes Rhizome 10 g, Turmeric 10 g, Liquoric Root 5 g, add or subtract TCM drugs with the clinical symptoms, 150 mL, 2-time/day	40	87.5	82.5	12.5	NA
	Western medicine treatment					
	Cefotaxime 2 g, 2–3 time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements	40	75	65	25	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Xie DM (23) [2009]+	ITWM treatment					
	Taking TCM decoction: JieDuLiShui Decoction: Rhubarb, Golden Thread, Sargent gloryvine, Agaric, Hiraute Shiny Bugleweed Herb, Areca Peel, Areca Seed, 1-time/day	35	77.14	51.43	22.86	NA
	Antibiotics: a compound that consist of third-generation cephalosporins, broad-spectrum penicillins and β-lactamase inhibitor and Quinolones					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	A compound that consist of third-generation cephalosporins, broad-spectrum penicillins and β-lactamase inhibitor and Quinolones	28	53.57	32.14	46.43	NA
Li J (24) [2010]+	ITWM treatment					
	Taking TCM decoction: Radix Astragali 30 g, Hiraute Shiny Bugleweed Herb 15 g, Plantain Seed 15 g, Areca Peel 30 g, Beautiful Sweetgum Fruit 15 g, Cowherb Seed 30 g, Danshen Root 30 g, Dahurian Patrinia Herb 30 g, Turmeric Root-tuber 10 g, Safflower 10 g, Figwort Root 30 g, Indian Buead 30 g, Common Yam Rhizome 30 g	40	95	42.5	5	NA
	Antibiotics chosen according to drug sensitivity profile					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Antibiotics chosen according to drug sensitivity profile	40	70	25	30	NA
Li WL (25) [2012]#	ITWM treatment					
	Taking TCM decoction: JiaWeiDangGuiShaoYao San: Chinese Angelica 9 g, Red Paeony Root 25 g, Indian Buead12 g, Largehead Atractylodes Rhizome 12 g, Oriental Waterplantain Rhizome 24 g, Coix Seed 30 g, Dahurian Patrinia Herb 15 g, Dwarf Lilyturf Tuber 12 g, Officinal Magnolia Bark 9 g, Areca Peel 15 g, Plantain Seed 30 g, Rice Bean 30 g, 2-time/day	34	94.12	70.59	5.88	NA
	Antibiotics: Ceftriaxone 3.0 g, 1-time/day. Combined with the treatment of liver-protection, diuretics and symptomatic treatment					
	Course of treatment: 7 days					
	Western medicine treatment					
	Ceftriaxone 3.0 g, 1-time/day. Combined with the treatment of liver-protection, diuretics and symptomatic treatment	32	65.63	50	34.37	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Qiu L (26) [2012]+	ITWM treatment					
	Taking TCM decoction: HuoXueYiQi Decoction: Radix Astragali, Indian Buead, Virgate Wormwood Herb 20 g, respectively; Motherwort Herb, Areca Peel, Turtle Shell 15 g, respectively; Tangerine Peel, Red Paeony Root, Oriental Waterplantain Rhizome, Rhubarb, Largehead Atractylodes Rhizome 10 g, respectively. Add or subtract TCM drugs with the clinical symptoms	40	85	77.5	15	NA
	Antibiotics chosen according to drug sensitivity profile					
	Course of treatment: 2 weeks					
	Western medicine treatment					
	Antibiotics chosen according to drug sensitivity profile and combined with the treatment of liver-protection, diuretics, albumin supplements and maintenance of fluid and electrolyte balance	40	82.5	65	17.5	NA
Ren JM (27) [2013]Δ	ITWM treatment					
	Taking TCM decoction: Rhubarb 30 g, 200 mL boiling for 20 min, 100 mL, 2-time/day	30	70	70	30	NA
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Treatment of liver-protection, diuretics, albumin supplements, blood transfusion, anti-inflammatory and maintenance of fluid and electrolyte balance plus symptomatic treatment	30	70	50	30	NA
Liang DJ (28) [2013]+	ITWM treatment					
	Taking TCM decoction: Self-made TCM Decoction, Rhubarb 10 g, Green Tangerine Peel 10 g, Red Paeony Root 10 g, Ginseng 10 g, Officinal Magnolia Bark 10 g, 200 mL, 2-time/day	41	87.8	87.8	12.2	NA
	Antibiotics: Ofloxacin 100 mg, taken orally, 3-time/day					
	Western medicine treatment					
	Ofloxacin 100 mg, taken orally, 3-time/day	41	68.3	68.3	31.7	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Lin ZM (29) [2013][+]	ITWM treatment					
	Taking TCM decoction: Self-made Decoction: Ginseng 10 g, Officinal Magnolia Bark 10 g, Rhubarb 10 g, Green Tangerine Peel 10 g, Red Paeony Root 10 g, 200 mL taken orally, 2-time/day	41	95.1	87.8	4.9	NA
	Antibiotics: Quinolones or third-generation cephalosporins. Combined with treatment of liver-protection, diuretics and maintenance of fluid and electrolyte balance					
	Course of treatment: 20 days					
	Western medicine treatment					
	Quinolones or third-generation cephalosporins. Combined with treatment of liver-protection, diuretics and maintenance of fluid and electrolyte balance	41	80.5	68.29	19.5	NA
Chen G (30) [2015][+]	ITWM treatment					
	Taking TCM decoction: WenYangJieDu Decoction: Medicinal Indianmulberry Root 30 g, Epimedium Herb 15 g, Radix Astragali 20 g, Danshen Root 15 g, Rhubarb 5 g, Indian Buead 15 g, Baical Skullcap Root 10 g, Dahurian Patrinia Herb 10 g, Liquoric Root 5 g, 100 mL, 3-time/day	19	94.73	68.42	5.27	NA
	Antibiotics: Cefoperazone 2 g, 2-time/day					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	According the results of drug sensitivity choose antibiotics, or Cefoperazone 2 g, 2-time/day and diuretics after paracentesis	17	70.59	23.53	29.41	NA
Wan ZM (31) [2015][#]	ITWM treatment					
	Taking TCM decoction: FuFangChaiShaoChengQi Decoction: Chinese Thorowax Root 12 g, Baical Skullcap Root 10 g, Green Tangerine Peel 12 g, Officinal Magnolia Bark 10 g, Rhubarb 10 g, Sargent gloryvine 30 g, Dahurian Patrinia Herb 30 g	60	58.33	58.33	41.67	18.33
	Antibiotics: Cefotaxime 2.0 g, 3-time/day					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Cefotaxime 2.0 g, 3-time/day, combined with treatment of liver-protection, symptomatic treatment and intestinal flora balance rebuilding	60	40	40	60	35

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Gao J (44) [1996]+	ITWM treatment					
	TCM enema: Rhubarb 12 g, Baical Skullcap Root 15 g, Golden Thread 10 g, Danshen Root 30 g, Red Paeony Root 30 g, 100 mL, TCM enema, 1-time/night	24	66.7	66.7	33.3	NA
	Antibiotics: Ampicillin 3.0 g, 2-time/day, or Ceftazidime 1.0 g, 2-time/day, associated with the treatment of liver-protection and symptomatic treatment					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Ampicillin 3.0 g, 2-time/day, or Ceftazidime 1.0 g, 2-time/day, associated with the treatment of liver-protection and symptomatic treatment	18	33.3	33.3	66.7	NA
Liu LQ (45) [1998]+	ITWM treatment					
	TCM enema: Honeysuckle Flower, Mongolian Dandelion Herb, Indigowoad Leaf, Heartleaf Houttuynia Herb, Chinese Angelica, Danshen Root, Frankincense, Myrrh 15 g, respectively. 200 mL, retention enemas for 2 h, 1-time/day	36	75	61.11	25	25
	Antibiotics: Amikacin, Ampicillin, Ampicillin, third-generation cephalosporins					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Amikacin, Ampicillin, third-generation cephalosporins, associated with paracentesis and symptomatic treatment	36	47.2	38.89	52.78	52.78
Tu YY (46) [2006]+	ITWM treatment					
	TCM enema: Rhubarb, Honeysuckle Flower, Mongolian Dandelion Herb 30 g, respectively. 100 mL, retention enemas for 0.5 h, 1-time/day	23	82.6	34.78	17.4	8.7
	Antibiotics: Cefotaxime 2.0 g, 2-time/day associated with the treatment of liver-protection, symptomatic treatment, diuretics					
	Course of treatment: 2 weeks					
	Western medicine treatment					
	Cefotaxime 2.0 g, 2-time/day. Combined with the treatment of liver-protection, symptomatic treatment and diuretics	25	36	20	64	32

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Wu L (56) [2006]+	ITWM treatment					
	Peritoneal lavage using IMS100A-Colonic irrigation machine. The peritoneal lavage consisted of a douche including: sodium chloride 50.4g, calcium chloride 3.2g, magnesium chloride 1.6g, lactate 50g, glucose 250g, combined with 1000ml distilled water. After the peritoneal lavage, a preparation enema included Rhubarb, Red Paeony Root, Virgate Wormwood Herb, Cape Jasmine Fruit, Giant Knotweed Rhizome	64	85.9	85.9	14.1	NA
	Course of treatment: 12 weeks					
	Western medicine treatment					
	Treatment of liver-protection, cholagogue, diuretics, hemostasis and anti-inflammatory.	50	64	64	36	NA
Han J (52) [2007]+	ITWM treatment					
	TCM compression on umbilicus: QiReHuaYu San: Red Paeony Root 30 g, Honeysuckle Flower 30 g, Dahurian Patrinia Herb 30 g, Yanhusuo 15 g, Lightyellow Sophora Root 30 g, Rhubarb 12 g, Spreading Hedyotis Herb 30 g, Peach Seed 20 g. Mixing batter use honey, compression on umbilicus for 8 h	30	90	60	10	NA
	Antibiotics: Cefoperazone 2.0 g, 2-time/day					
	Course of treatment: 20 days					
	Western medicine treatment					
	Cefoperazone 2.0 g, 2-time/day	30	76.6	43.33	23.4	NA
Tian X (53) [2008]+	ITWM treatment					
	TCM compression on umbilicus: Rhubarb 10 g, Oriental Waterplantain Rhizome 20 g, Plantain Seed 20 g, add or subtract TCM drugs with the clinical symptoms	39	84.62	64.1	15.38	5.13
	Antibiotics: Cefoperazone 2.0 g, Mezlocillin 2.5 g, 2-time/day					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Cefoperazone 2.0 g, Mezlocillin 2.5 g, 2-time/day	39	71.79	53.85	28.21	7.69

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Xing YM (47) [2009]+	ITWM treatment					
	TCM enema: Golden Thread 9 g, Baical Skullcap Root 6 g, Cape Jasmine Fruit 9 g, Mongolian Dandelion Herb 30 g, Barbed Skullcap Herb 15 g, Spreading Hedyotis Herb 30 g, Red Paeony Root 12 g, Danshen Root 20 g, Rhubarb 9 g, add or subtract TCM drugs with the clinical symptoms.100–150 mL, retention enemas half an hour, 2-time/day	38	84.2	52.63	15.8	NA
	Course of treatment: 2 weeks					
	Western medicine treatment					
	According the results of drug sensitivity choose antibiotics, or Cefotaxime 2 g. Combined with treatment of liver-protection, blood transfusion, albumin supplements and diuretics	30	63.3	40	36.7	NA
Ji XL (48) [2009]+	ITWM treatment					
	TCM enema: Rhubarb 20 g, Indigowoad Root 30 g, Lightyellow Sophora Root 20 g, Red Paeony Root 20 g, Halloysit 15 g. Combined with Lactulose 30 g, Bacillus Licheniformis 0.6 g, 100 mL, TCM enema, 1-time/day. Combined with Western medicine treatment: treatment of liver-protection, diuretics, paracentesis, immune-modulatory and microbiological agents	31	70.9	25.81	29.1	NA
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Combined with treatment of liver-protection, diuretics, paracentesis, and immune-modulatory, microbiological agents	31	32.2	12.9	67.8	NA
Liu HL (49) [2009]+	ITWM treatment					
	TCM enema: Honeysuckle Flower 30 g, Rhubarb 20 g, Mongolian Dandelion Herb 60 g, Giant Knotweed Rhizome 20 g, Oyster Shell 30 g, Spreading Hedyotis Herb 50 g, Danshen Root 30 g, Parslane Herb 30 g, Dahurian Patrinia Herb 20 g, Golden Thread 10 g, 200–300 mL, retention enemas for 4 h	40	90	65	10	NA
	Antibiotics: Ceftazidime 3.0 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and symptomatic treatment					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Ceftazidime 3.0 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and symptomatic treatment	40	75	45	25	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Jing XH (50) [2010][+]	ITWM treatment					
	TCM enema: Rhubarb 10 g, Baical Skullcap Root 10 g, Dahurian Patrinia Herb 30 g, Mongolian Dandelion Herb 30 g, 1-time/day. Combined with XueBiJing injection 60 mL, 1-time/day	32	90.6	68.75	9.4	NA
	Antibiotics: Ceftazidime 2 g, 1-time/day					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Ceftazidime 2 g, 1-time/day	28	78.6	46.43	21.4	NA
Ma YP (51) [2013][+]	ITWM treatment					
	TCM enema: JieDuGuanChangYe: Rhubarb 30 g, Honeysuckle Flower, Chinese Pulsatilla Root, Mongolian Dandelion Herb, Danshen Root, Red Paeony Root 20 g, respectively; Green Tangerine Peel, Officinal Magnolia Bark 10 g, respectively. 200 mL, 2-time/day, 30 minutes each time	50	90	56	10	NA
	Antibiotics: Ceftriaxone or Cefoperazone, 2-time/day. Combined with anti-inflammatory, treatment of liver-protection, blood transfusion, albumin supplements					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Ceftriaxone or Cefoperazone, 2-time/day. Combined with anti-inflammatory, treatment of liver-protection, blood transfusion, albumin supplements	50	76	36	24	NA
Li GH (54) [2014][#]	ITWM treatment					
	TCM compression on umbilicus: SiHuangMiShuiGao: Golden Thread, Baical Skullcap Root, Rhubarb, Borneol, Frankincense, Dragon's Blood, Myrrh 10 g, respectively; Lightyellow Sophora Root 20 g, Common Clubmoss Herb 15 g, Garden Balsam Stem 20 g, mixing batter use honey, compressing on umbilicus	35	91.43	88.57	8.57	NA
	Antibiotics: Quinolones or third-generation cephalosporins. Combined with diuretics, treatment of liver-protection, maintain fluid and electrolyte balance					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Quinolones or third-generation cephalosporins. Combined with diuretics, treatment of liver-protection and maintenance of fluid and electrolyte balance	35	71.43	62.86	28.57	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Yang M (55) [2015]+	ITWM treatment					
	TCM compression on umbilicus: QiReHuaYu San: Dahurian Patrinia Herb 30 g, Peach Seed 20 g, Rhubarb 12 g, Honeysuckle Flower 30 g, Lightyellow Sophora Root 30 g, Spreading Hedyotis Herb 30 g, Yanhusuo 15 g, Red Paeony Root 30 g. Mixing batter use honey	65	92.3	40	7.7	NA
	Antibiotics: Cefoperazone 2.0g, 2-time/day					
	Course of treatment: 1 month					
	Western medicine treatment					
	Antibiotics: Cefoperazone 2.0 g, 2-time/day	48	73.8	43.75	26.2	NA
Peng YP (57) [2015]Δ	ITWM treatment					
	TCM enema: Heartleaf Houttuynia Herb 30 g, 100 mL TCM enema 1-time/day	30	63	40	37	NA
	Antibiotics: Cefuroxime 1.5 g, 1-time/day					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Levofloxacin 0.4 g, and Cefuroxime 1.5 g, 1-time/day	28	46	32.14	54	NA
Ji JJ (32) [1999]*	ITWM treatment					
	Chinese patent medicine: ShuangHuangLian injection 3.6–4.8 g into 5% Glucose injection 250 mL.	42	93	83.33	7	NA
	Antibiotics: Piperacillin 4 g, 2-time/day. Ofloxacin 0.2 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Piperacillin 4 g, 2-time/day. Ofloxacin 0.2 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements	40	78	60	22	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Zhang YH (33) [2002]*	ITWM treatment					
	Chinese patent medicine: ShuangHuangLian injection 3.6–4.8 g into 5% glucose injection 250 mL	22	96	81.82	4	NA
	Antibiotics: Piperacillin 4 g, 2-time/day. Ofloxacin 0.2 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Piperacillin 4 g, 2-time/day. Ofloxacin 0.2 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and albumin supplements	20	80	60	20	NA
Song XX (34) [2008]*	ITWM treatment					
	Chinese patent medicine: QingKaiLing injection, 1,000 mg 1-time/day	46	56.52	56.52	43.48	NA
	Antibiotics: Cefoperazone or Cefotaxime 2.0 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and symptomatic treatment					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Antibiotics: Cefoperazone or Cefotaxime 2.0 g, 2-time/day. Combined with the treatment of liver-protection, diuretics and symptomatic treatment	41	36.59	36.59	63.41	NA
Tan ZB (35) [2008]*	ITWM treatment					
	Chinese patent medicine: TanReQing injection: 20 mL into 5% 250 mL Glucose injection, 1-time/day	40	95	95	5	NA
	Antibiotics: Cefotaxime 2 g, 1-time/8 h					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Cefotaxime 2 g, 1-time/8 h. Combined with the treatment of liver-protection, diuretics and albumin supplements	30	76.67	76.67	23.33	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Zhang YQ (36) [2010]*	ITWM treatment					
	Chinese patent medicine: XueBiJing injection: 50 mL into 100 mL normal saline, 1-time/12 h	90	92.22	8.89	7.78	NA
	Antibiotics: Ceftriaxone 2 g, 1-time/day					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Ceftriaxone 2 g, 1-time/day. Combined with the treatment of liver-protection, diuretics and correction of ionic disorders	78	80.77	2.56	19.23	NA
Wang J (37) [2010]*	ITWM treatment					
	Chinese patent medicine: XueBiJing injection: 50 mL into 100 mL normal saline, 2-time/day	30	93.3	66.67	6.7	NA
	Antibiotics: Ceftriaxone 2 g, 1-time/day					
	Course of treatment: 7 days					
	Western medicine treatment					
	Ceftriaxone 2 g, 1-time/day	30	70	46.67	30	NA
Shu Q (38) [2011]*	ITWM treatment					
	Chinese patent medicine: XueBiJing injection: 50 mL into 100 mL normal saline, 1-time/day	32	87.5	31.25	12.5	NA
	Antibiotics: the third-generation cephalosporins					
	Course of treatment: 14 days					
	Western medicine treatment					
	Third-generation cephalosporins. Combined with the treatment of liver-protection and symptomatic treatment	34	70.6	23.53	29.4	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Zheng J (39) [2012]*	ITWM treatment					
	Chinese patent medicine: XueBiJing injection: 50 mL into 100 mL normal saline, 1-time/12 h	31	90.32	77.42	9.68	NA
	Antibiotics: mainly depend on Levofloxacin and the third-generation cephalosporins					
	Course of treatment: 14 days					
	Western medicine treatment					
	Mainly depend on Levofloxacin and the third-generation cephalosporins. Combined with the treatment of liver-protection, diuretics and albumin supplements	32	93.75	40.62	6.25	NA
Zhang RW (40) [2014]*	ITWM treatment					
	Chinese patent medicine: Xuebijing injection: 50 mL into 100 mL normal saline, 2-time/day	32	87.5	62.5	12.5	NA
	Antibiotics: Ceftazidime 2 g, 1-time/day					
	Course of treatment: 28 days					
	Western medicine treatment					
	Ceftazidime 2 g, 1-time/day. Combined with conventional treatment including liver-protection and diuretics	32	68.75	31.25	31.25	NA
Wang YL (41) [2015]*	ITWM treatment					
	Chinese patent medicine: XueBiJing injection: 50 mL into 100 mL normal saline, 1-time/day.	44	90.91	61.36	9.09	NA
	Antibiotics: Imipenem cilastatin 0.5 g, 3-time/day; paracentesis ≤2,000 mL/day. Combined with Imipenem cilastatin 0.5 g inject into abdomen					
	Course of treatment: 7 days					
	Western medicine treatment					
	Imipenem cilastatin 0.5 g, 3-time/day; paracentesis ≤2,000 mL/day. Combined with Imipenem cilastatin 0.5 g inject into abdomen	44	75	34.09	25	NA

Table S2 *(continued)*

Table S2 *(continued)*

First author [year]	Strategy of the treatment	No. patients	Effectiveness rate (%)	Cure rate (%)	Ineffectiveness rate (%)	Mortality (%)
Ma L (42) [1999]*	ITWM treatment					
	Chinese patent medicine: ChuanHuNing injection peritoneal lavage: 3,000 mL, inject ChuanHuNing injection into abdomen, 40 mL + 2% Metronidazole 1,000 mL	57	91.23	84.21	8.77	NA
	Antibiotics: Ceftriaxone 4.0 g peritoneal lavage					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Metronidazole lavage and Metronidazole, Ceftriaxone inject into abdomen. Combined with conventional liver-protection, diuretics and correct electrolyte turbulence	51	62.75	43.14	37.25	NA
Zhang NN (43) [2015]*	ITWM treatment					
	Chinese patent medicine: ShenLingBaiZhu granule: White Hyacinth Bean, Largehead Atractylodes Rhizome, Indian Buead, Liquoric Root, Platycodon Root, Semen Nelumbinis, Ginseng, Common Yam Rhizome, Coix Seed, 3-time/day	33	72.73	63.64	27.27	NA
	Antibiotics: Cefoperazone 3 g, 2-time/day. Combined with conventional liver-protection, diuretics and treatment to improve circulation					
	The time of the treatment depended on the patient's condition					
	Western medicine treatment					
	Cefoperazone 3 g, 2-time/day. Combined with conventional liver-protection, diuretics and treatment to improve circulation	32	46.88	37.5	53.12	NA

$^{\Delta}$, study that used single-TCM drug; *, study that used TCM compound that have been proven by the China Food and Drug Administration; $^{\#}$, study that used the classical TCM compound; $^{+}$, study that used the self-made TCM compound. ITWM, integration of traditional and Western medicine; TCM, traditional Chinese medicine; NA, not available.

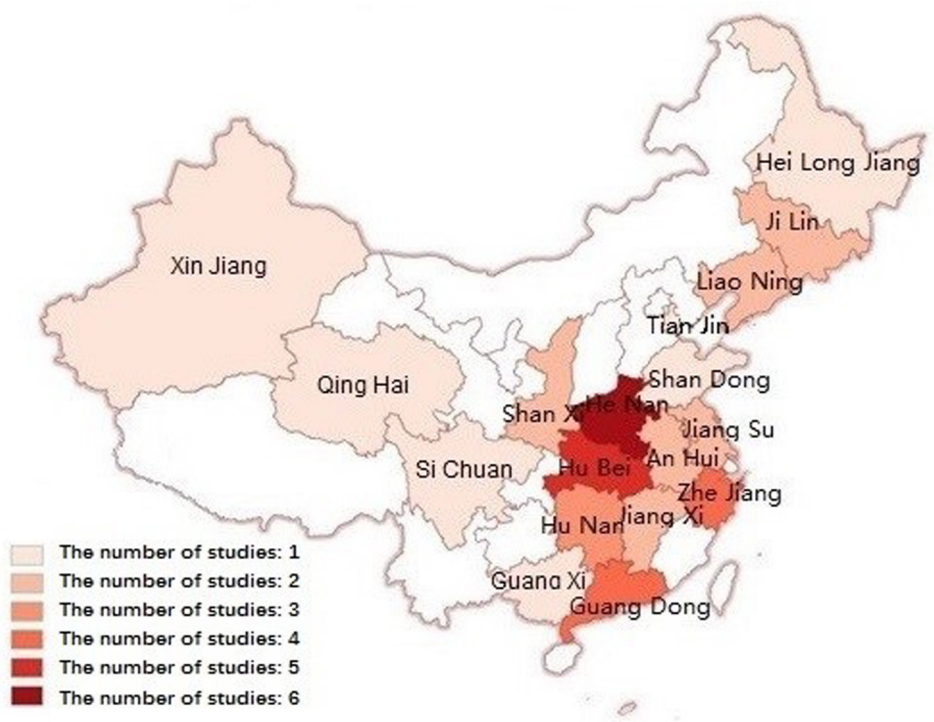

Figure S1 The distributions of studies regarding ITWM for the treatment of SBP according to the regions in China.