Protective effect of *Periplaneta americana* extract on intestinal mucosal barrier function in patients with sepsis

Hongwei Zhang, Liyou Wei, Zhenyu Zhang, Shuzheng Liu, Gang Zhao, Jing Zhang, Yanling Hu

**Abstract**

**OBJECTIVE:** To investigate the effect of the *Periplaneta americana* extract on the intestinal mucosal barrier and prognostic implications in patients with sepsis.

**METHODS:** Sixty and six patients with sepsis were assigned randomly to treatment group (32 cases) and control group (32 cases). The extract from *Periplaneta americana* plus conventional medication for sepsis was administered to the treatment group, while the control group only received conventional treatment. The gastrointestinal function scores and acute physiology and chronic health evaluation II (APACHE II) scores of all subjects were documented at baseline, at days 1, 3 and 7 after treatment respectively and their blood endotoxin was tested at the same time points as well. The incidence of death was recorded for both groups throughout the trial.

**RESULTS:** At days 3 and 7 after treatment, gastrointestinal function score, APACHE II, and endotoxin level in treatment group was better than that in control group and the difference between them was significant (both \( P < 0.05 \)). Although the incidence of death in treatment group was less than that in control group, the difference between the two groups was not significant (\( P > 0.05 \)).

**CONCLUSION:** The extract of *Periplaneta americana* had protective effect on intestinal mucosal barrier and could improve the condition and prognosis in patients with sepsis.

**INTRODUCTION**

Sepsis is one of the serious complications of trauma, burns, infections and major surgical operation in critically ill patients. It can induce multiple organ dysfunction syndrome (MODS) and acute MODS is a major cause of death in Intensive Care Unit (ICU).\(^1,2\) Its incidence is increasing year by year and average mortality rate was 28.6% and increased with age from 10% in children to 38.4% in those over 85 years.\(^3\) Gastrointestinal tract is the central organ of the stress response, due to bacterium, endotoxin translocation and intestinal immune function decline caused by intestinal barrier dysfunction, which is an important cause of MODS.\(^4,5\) In the early stage, administration of medications to protect intestinal mucosal barrier in patients with sepsis has great clinical significance. The extract of *Periplaneta americana* had a protective effect on gastric mucosa by increasing its blood flow, improving microcircula-
tion, and promoting gastric mucosal repair. Between January 2009 and December 2010, the treatment of sepsis with periplaneta americana extract was investigated in our hospitals. The study was approved by our hospital’s Ethic Committee and was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki. Subjects all signed an informed consent form prior to participating in the study.

METHODS

Subjects

A total of 64 patients, 42 males and 22 females, with sepsis admitted to our hospital’s ICU, were aged between 19 and 71. Thirty-four patients with injuries including 14 multiple injuries combined with shock, 6 open fractures, 8 chest or abdomen open injuries, 6 burns; 15 infection patients including 10 severe pneumonias, 3 empyemata, 2 liver abscesses; 15 postoperative patients. They were randomly assigned to treatment group and control group, 32 subjects for each group.

Inclusion and exclusion criteria

The diagnostic criteria of sepsis were recommended by the International Sepsis Conference in December 2001. Patients meeting the criteria were included without history of peptic ulcer or other gastrointestinal underlying diseases. Those with following conditions were excluded: intestinal paralysis due to anesthesia, hypokalemia, machinery and other causes, malignant hematologic diseases, rheumatic diseases, and acquired immune deficiency syndrome.

Interventions

The extract from periplaneta americana plus conventional medications for sepsis was administered to the treatment group, while the control group only received conventional treatment. The conventional treatment included blood and fluids transfusion, protective mechanical ventilation, analgesic, sedative, anti-inflammatory, and anti-infective medications, nutritional support, water and electrolyte balance maintaining, and so forth. The extract of periplaneta americana (kangfuxin solution, Hunan Nanke Lun Pharmaceutical Co., Ltd.) was administered by stomach tube, 10 mL/time, tid, starting from the day when diagnosis was confirmed and the treatment of the extract lasted for 7 days.

Outcome measurement

At the beginning of treatment and at days 1, 3, 7 after treatment, gastrointestinal function score and acute physiology and chronic health evaluation II (APACHE II) were recorded respectively and blood endotoxin was tested at the same time points. Incidence of death was record as well. Normal gastrointestinal function was scored 0, abdominal distension and decreased bowel sounds scored 1, high degree of abdominal bloating and intestinal sound almost absent scored 2, paralytic ileus and/or stress ulcer bleeding scored 3. Plasma endotoxin was tested with Limulus test etc were performed for the analysis. The descriptive data was expressed with mean ± standard deviation ( \( \bar{x} \pm s \)). \( P<0.05 \) was the significant level.

RESULTS

General information of the two groups

The gender ratios, age and primary disease of two groups were insignificantly different (\( P>0.05 \)). 5 death in treatment group, and 7 in control group. The incidence of death (15.63%) in treatment group was lower than that (21.88%) in control group. The difference was not significant (\( P>0.05 \)). See Table 1.

Comparisons of gastrointestinal function

Before treatment, the gastrointestinal function scores of the two groups were insignificantly different (\( P>0.05 \)). Three and seven days after treatment, Treatment groups’ gastrointestinal function score was compared with that of control group with Mann-Whitney test. The difference was significant (\( P<0.05 \)). See Table 2.

Comparisons of endotoxin

Before treatment, the blood endotoxin (EU/mL) in the

<table>
<thead>
<tr>
<th>Table 1 The basic features in two groups</th>
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<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Treatment</td>
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<tr>
<td>Treatment</td>
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Notes: Patients in control group received conventional treatment; the extract from periplaneta americana plus conventional medications for sepsis was administered to the treatment group.
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Table 2 Comparison of gastrointestinal function in two groups (cases)

<table>
<thead>
<tr>
<th>Group</th>
<th>Before treatment</th>
<th>1 days after treatment</th>
<th>3 days after treatment</th>
<th>7 days after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0/1/2/3 (score)</td>
<td>0/1/2/3 (score)</td>
<td>0/1/2/3 (score)</td>
<td>0/1/2/3 (score)</td>
</tr>
<tr>
<td>Control</td>
<td>3/6/11/12</td>
<td>4/6/10/10</td>
<td>3/5/9/10</td>
<td>5/5/7/8</td>
</tr>
<tr>
<td>Treatment</td>
<td>4/6/10/12</td>
<td>5/7/8/9</td>
<td>6/9/4</td>
<td>10/9/5/3</td>
</tr>
<tr>
<td>Z, P value</td>
<td>Z=0.184, P=0.854</td>
<td>Z=0.489, P=0.625</td>
<td>Z=2.080, P=0.038</td>
<td>Z=2.169, P=0.030</td>
</tr>
</tbody>
</table>

Notes: Patients in control group received conventional treatment; The extract from periplaneta americana plus conventional medications for sepsis was administered to the treatment group.

two groups were insignificantly different (P>0.05). On days 3, 7 after treatment, the difference of blood endotoxin between the T group and C group were statistically significant by t test (P<0.05, Figure 1).

DISCUSSION

Sepsis, defined as an infection accompanied by inflammation, is a serious condition caused by systemic inflammatory response. A rapid progression from sepsis to septic shock frequently occurs driven by inflammatory and anti-inflammatory responses to a pathogen, which makes the condition require immediate intervention.9 Intestinal tract is the body’s largest lymphoid organ. It has proved that the dysfunction of gut barrier plays an important role in

Figure 1 Comparison of endotoxin in two groups
Patients in control group received conventional treatment; The extract from periplaneta americana plus conventional medications for sepsis was administered to the treatment group.

Comparisons of APACHE II
Before treatment, the APACHE II scores in the two groups were insignificantly different (P>0.05). On days 3, 7 after treatment, the difference of APACHE II score between the T group and C group were statistically significant by t test (P<0.05, Figure 2).

Figure 2 Comparison of APACHE II in two groups
APACHE II: acute physiology and chronic health evaluation II. Patients in control group received conventional treatment; The extract from periplaneta americana plus conventional medications for sepsis was administered to the treatment group.

the development of sepsis.10,11 In patients with sepsis, the damage to their gastrointestinal barrier, and intestinal bacteria and toxins invasion of circulation system result in gut-derived infection. If the exacerbated inflammatory response is out of control, MODS eventually ensues and it significantly impacts on the patients’ prognosis.

The periplaneta americana extract is made with ethanol from American periplaneta dry worm. It contains peptides, polyols, epidermal growth factor, sticky sugar acid, amino acids, and other active substances. Studies showed that periplaneta americana extract could promote gastric mucosal synthesis of PGE2, increase vascular tone, reduce vascular permeability, reduce local congestion, protect the lysosomal membrane, avoid the cathepsin hydrolase release caused by lysosomal rupture, reduce the tissue decomposition, inhibit the release of inflammatory mediators and suppress neutrophils, monocytes and macrophages.12 The protective effect of periplaneta americana extract on intestinal mucosal barrier may be implemented through the mechanism. Endotoxin was released by gram-negative bacilli and
LPS was its main component. Monitoring endotoxin has practical significance on assessing intestinal mucosal barrier injury caused by sepsis. APACHE II score has been widely used to predict prognosis and mortality, especially in ICU.\textsuperscript{13,14} After 3 and 7 days treatment with periplaneta americana extract, endotoxin level and APACHE II score, gastrointestinal function score were better improved in treatment group than in control group. The findings of our study suggested that periplaneta americana extract had a protective effect on the intestinal mucosal barrier and could improve the condition and prognosis in patients with sepsis.

REFERENCES