Effect of externally applied Jidesheng anti-venom on skin and soft-tissue necrosis after Chinese cobra bite: a retrospective study

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Abstract

OBJECTIVE: To evaluate the effects of Jidesheng anti-venom used externally for skin and soft-tissue necrosis from Chinese cobra bite.

METHODS: A retrospective review was performed according to the clinical data recorded from January 2002 to December 2012. A total of 126 patients (116 females and 10 males) with skin and soft-tissue necrosis due to Chinese cobra bite were divided into two groups. The control group was treated externally with 40% glyceride magnesium sulfate (n=52), and the treatment group was given Jidesheng anti-venom externally (n=74). The data collected included maximum local necrotic area of skin and soft tissues, de-tumescence time, healing time, and skin-grafting rate.

RESULTS: There were no significant differences in gender, age, and disease condition between the control and treatment groups (P>0.05). No statistically significant difference was found in de-tumescence time between the two groups (P>0.05). The maximum local necrotic area of skin and soft tissues was (19.9±7.3) cm² in the treatment group, while it was (23.3±6.4) cm² in the control group. The healing time of the treatment group was shorter than that of the control group [(32.1±3.7) vs (34.4±4.5) days]. The skin-grafting rate in the treatment group was lower than that of the control group (10.81% vs 25.00%). There were statistically significant differences in maximum local necrotic area of skin and soft tissues, healing time, and skin-grafting rate between the control and treatment groups (all P<0.05).

CONCLUSION: External application of Jidesheng anti-venom may help to promote wound healing and reduce the skin-grafting rate in cases of skin and soft-tissue necrosis due to Chinese cobra bite.

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Key words: Snake bites; Necrosis; Antivenins; External application; Retrospective studies

INTRODUCTION

The Chinese cobra (Naja atra) is part of the Elapidae family. It is one of the ten most venomous snakes in China, and is mainly distributed in the area to the south of the Yangtze River. The illness caused by Chinese cobra bite is acute and critical, and is commonly seen in emergency departments. The cobra’s venom is a mixed poison that induces cytotoxicity, which can quickly necrotize skin and soft tissues. Necrosis is the most common complication following Chinese cobra bite.
bites. Since anti-cobra venom serum has been used in clinic, the mortality rate of cobra bites has greatly reduced. At present, however, few methods can effectively treat skin and soft-tissue necrosis due to Chinese cobra bite. Therefore, we carried out a retrospective study to evaluate the effects of external Jidesheng anti-venom on skin and soft-tissue necrosis caused by Chinese cobra bite.

**MATERIALS AND METHODS**

This retrospective study was approved by the Ethics Committee of Guangxi Medical University, and was performed according to the clinical data recorded from January 2002 to December 2012. The criteria for inclusion in the treatment group were: (a) The patient was diagnosed as having a Chinese cobra bite, with the snake caught and/or a picture taken as evidence; (b) the patient had necrotic skin and soft tissues; and (c) the patient received routine treatment. Patients who had other kinds of snakebites, had necrosis caused by other factors, failed to complete the routine treatment, or were allergic to Jidesheng anti-venom were excluded. All 126 patients received routine treatment, which included: (a) anti-cobra venom injection 50 IU/kg (Shanghai Serum Biological Technology Co., Ltd., Shanghai, China); (b) local block therapy with 5% lidocaine hydrochloride injection 5 mL (Shanghai Chao-hui Pharmaceutical Industry Co., Ltd., Shanghai, China) and chymotrypsin injection 4000 IU (The first Chemical Industry Co., Ltd., Shanghai, China); (c) oral administration of Jidesheng anti-venom tablets, 10 tablets each time, three times a day, for 3 days (Essence Pharmaceutical Group Co., Ltd., Nantong, China); and (d) anti-infection management. In addition, external medicine application was essential to the local necrotic area, with the dressing changed daily. In total, 52 patients in the control group received routine treatment, which included: (a) anti-cobra venom injection 50 IU/kg (Shanghai Serum Biological Technology Co., Ltd., Shanghai, China); (b) external application of 40% glyceride magnesium sulfate (Hunan Erkang Pharmaceutical Group Co., Ltd., Liuyang, China); (c) local application of 40% glyceride magnesium sulfate (Beijing Yanjing Pharmaceutical Co., Ltd., Beijing, China), and 100 mL glyceride (Hunan Erkang Pharmaceutical Group Co., Ltd., Liuyang, China); (d) anti-infection management. In addition, external medicine application was essential to the local necrotic area, with the dressing changed daily. Of the 52 patients in the control group, 49 were male and 3 were female; the average age was 40 ± 11 years. Of the 74 patients in the treatment group, 67 were male and 7 were female; the average age was 40 ± 10 years. There were no significant differences in gender, age, and skin-grafting rate between the two groups (Table 1, 2).

**Data collection**

- **Disease condition**: Grade I: local swelling confined to 1 segment of the bitten limb; minor pain and general signs (vomiting, headache, abdominal or chest pain). Grade II: local swelling meted 2 segments of the bitten limb; moderate pain and general signs. Grade III: extension of swelling beyond 2 segments; persistent and resistant pain to analgesics; severe general signs. Grade IV: swelling spreading to the trunk; disseminated intravascular coagulation; hypotension or coma.

**Comparison of general data**

There were no significant differences in gender, age, and disease condition between the control and treatment groups (P > 0.05) (Table 1, 2).

**Comparison of maximum local necrotic area, de-tumescence time, and healing time between the control and treatment groups**

No statistically significant difference was found in de-tumescence time between the control and treatment groups (P > 0.05). The maximum local necrotic area of skin and soft tissues was (19.9 ± 7.3) cm² in the treatment group, while it was (23.3 ± 6.4) cm² in the control.
group. The healing time of the treatment group was shorter than that of the control group [(32.1 ± 3.7) vs (34.4±4.5) days]. There were statistically significant differences in maximum local necrotic area of skin and soft tissues and healing time between the control and treatment groups (both P<0.05) (Table 3).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control group</th>
<th>Treatment group</th>
<th>t (x²)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>52</td>
<td>74</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Maximum local necrotic area (cm²)</td>
<td>23.3±6.4</td>
<td>19.9±7.3</td>
<td>2.670</td>
<td>0.009</td>
</tr>
<tr>
<td>De-tumescence time (d)</td>
<td>10.6±1.6</td>
<td>10.1±1.4</td>
<td>1.894</td>
<td>0.061</td>
</tr>
<tr>
<td>Healing time (d)</td>
<td>34.4±4.5</td>
<td>32.1±3.7</td>
<td>3.20</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Notes: patients in control group received routine treatment. Patients in the treatment group received routine treatment and an external application of Jidesheng anti-venom.

Comparison of skin-grafting rate between the control and treatment groups

The skin-grafting rate was 10.8% in the treatment group, which was significantly lower than the control group at 25.0% (P<0.05) (Table 4).

<table>
<thead>
<tr>
<th>Skin-grafting rate</th>
<th>Control group (n=52)</th>
<th>Treatment group (n=74)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin grafting</td>
<td>13 (25.0)</td>
<td>8 (10.8)</td>
<td></td>
</tr>
<tr>
<td>No skin grafting</td>
<td>39 (75.0)</td>
<td>66 (89.2)</td>
<td></td>
</tr>
</tbody>
</table>

Notes: patients in control group received routine treatment. Patients in the treatment group received routine treatment and an external application of Jidesheng anti-venom. \( \chi^2 = 4.211, P=0.040 \).

DISCUSSION

The Chinese cobra has a complex venom mainly consisting of neurotoxins, circulatory toxins, and cytotoxins. Neurotoxins can lead to nerve-muscle block, skeletal muscle paralysis, and severe respiratory paralysis. Circulatory toxins may cause heart damage, giving rise to a drop in blood pressure, weakened pulse, shock, and even death. The most common clinical cobra bite symptoms of skin and soft-tissue swelling and necrosis are attributed to the cytotoxins. Many clinical reports indicate that the cytotoxic reaction induced by the Chinese cobra bite is extreme.

There are many actions of the toxic proteins of Chinese cobra venom responsible for pain, swelling, and necrosis. Protein hydrolysis can dissolve vessel walls, cause local tissue necrosis, hemorrhaging, and even deep tissue ulceration. Phospholipase A\(_2\), mainly as a result of indirect hemolysis, \(^{11,12}\) can decompose lecithin into lyssolecithin, resulting in hemolysis, increased capil-
The main ingredients of Jidesheng anti-venom are Gan-chan (Succys Bufo), Dijincao (Herba Euphorbiae Humifusa), Chonglou (Rhizoma Paridis Chonglou) and Wugong (Scolopendra). Gan-chan (Succys Bufo), can secrete a type of bradykinin antagonizing peptide, which may inhibit the secretion of bradykinin to relieve pain, acute inflammation, edema, and hypotension. The flavone glycosides isolated from Dijincao (Herba Euphorbiae Humifusa) can regulate cellular immunity and delay apoptosis. Chonglou (Rhizoma Paridis Chonglou) is a folk medicinal plant in Asia traditionally used for the alleviation of pain and elimination of poisoning. It has the function of enhancing immunity, and decreasing toxicity and anti-apoptosis. Research has found that Wugong (Scolopendra) can promote blood circulation and remove blood stasis. In brief, each ingredient in Jidesheng anti-venom may exert antipyretic, antidotal, antiphlogistic, and analgesic effects.

The results from the present study demonstrate that external application of Jidesheng anti-venom may help to promote wound healing and reduce skin-grafting rate for skin and soft-tissue necrosis following the Chinese cobra bite.

REFERENCES
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