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The Analysis of the Treatment of Rhabdomyolysis by Snake Bites

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Abstract

Objective: To explore the treatment measure of rhabdomyolysis caused by snake bites, and provide guidance for further prevention and control of snake bites. **Methods:** To retrospectively analyze the 841 cases of serpentine bites in our hospital from January 2006 to July 2017; 127 cases of patients with rhabdomyolysis syndrome were screened out, and their clinical manifestations, laboratory results, related treatment and prognosis were analyzed. **Results:** 127 cases patients were rhabdomyolysis out of 841 cases, 28 cases patients developed acute renal failure; treatment measures included local wound treatment, application of tetanus antitoxin, anti-snake venom serum, anti-infection, fluid "hydration" and diuretic, alkaline urine and hybrid renal replacement therapy. 112 cases were cured, improved conditions in 9 cases, 3 cases of death, 3 cases uncured. The improvement rate of is 95.26% after treatment. **Conclusion:** The rhabdomyolysis had a high incidence in snake bite patients, severe cases often developed acute renal failure. Serum myopsin and related biochemical blood tests could be used to diagnose rhabdomyolysis quickly. Combined treatment methods are the main measure to increase the cured rate and decrease the death rate.

Keywords

Snake Bite, Rhabdomyolysis, Acute Renal Failure, Combined Treatment

1. Introduction

At present, snake bites still have a high incidence in summer and autumn. Due to the complex composition of snake venom and its quick speed into the blood circulation, it could cause systemic poisoning symptoms after snake bites, and some patients had rhabdomyolysis syndrome (RM) due to a large number of myoglobin (Mb), creatine phosphokinases (CPK) and lactate dehydrogenase

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(LDH) into the peripheral blood released from striated muscle injury. Some patients even had acute renal failure because of MB filtered into the renal tubules directly resulted from damaged kidney tubules or renal tubules obstruction, leading to high mortality rate, thus needing to be treated as soon as possible. Therefore, we retrospectively analyzed 841 cases of snake bites patients in our hospital from January 2006 to July 2017 and screened out 127 cases with rhabdomyolysis syndrome. By analyzing its clinical manifestations, laboratory tests, related treatment and prognosis, we hope to provide guidance for further treatment of snake bites.

2. Materials and Methods

1) Basic information collecting To retrospectively analyze the 841 cases of serpentine bites in our hospital from January 2006 to July 2017 by medical records management system retrospective; 485 males and 356 females, aged from 2 to 85 years (mean age 49.15 ± 14.31); 127 patients with rhabdomyolysis syndrome, 74 males and 53 females, aged from 8 to 79 years (mean age 51.67 ± 11.43); with acute renal failure complications in 28 patients, aged from 23 to 79 years, (mean age 54.18 ± 10.75) (Table 1).

2) clinical criteria: The diagnostic criteria of rhabdomyolysis syndrome caused by snake bites: 1) history of snake bites; 2) the corresponding clinical manifestations of rhabdomyolysis (myalgia, muscle weakness, muscle damage, washed meat's water like urine, etc.); 3) creatine or myoglobin was at least 5 times higher than normal; 4) CPK and myoglobin increase after excluding other causes(drug effects, myocardial infarction, and other skeletal muscle diseases). The diagnostic criteria of acute renal failure: a) in keeping with the diagnostic criteria of rhabdomyolysis syndrome by snake bites; b) clinical manifestations with oliguria or anuria, edema; c) serum creatinine, urea nitrogen, uric acid more than normal reference value, or d) laboratory results showed high P^{+++}, high K^{+}, low Ca^{++} and metabolic acidosis. The evaluation criteria of prognosis: i) cured: when patients were discharged, the laboratory test results were normal, the symptoms completely disappeared, vital signs were stable, wound was without infection. ii) improved: after treatment, the test results were normal, systemic poisoning symptoms were significantly reduced, vital signs were stable, the wound situation was controled. iii) not cured: one of the following: the test results did not return to normal; vital signs were unstable; poisoning symptoms and signs per; wound infection is not completely controlled after treatment. iv) death: the

Table 1. Sociodemographic and clinical characteristics of the participants.

Index	male	female	aged	totle
Snake bite	485	356	49.15 ± 14.31	841
rhabdomyolysis syndrome	74	53	51.67 ± 11.43	127
acute renal failure	19	9	54.18 ± 10.75	28

patient died.

3) The laboratory tests: The blood CPK, LDH, Mb, blood routine, blood electrolytes (Na^+, K^+, Cl^-, P^{+++}, Ca^{++}, HCO_3^-), ALT, AST, AKP, BUN, Cr, UA, blood gas analysis on all patients.

4) Treatment:

a) Local wound treatment: all patients with local wound debridement, stretch the end of limbs near the heart, topical anti-snake tablets and so on.

b) comprehensive treatment: (1) intramuscular tetanus antitoxin; (2) applying anti-snake venom serum; (3) anti-infection; (4) oral anti-snake tablets; (5) hydration and diuretic: the total amount of fluid up to 2 - 3 L/d, improve blood volume, the patients with oliguria and anuria use diuretics; (6) alkaline urine: infusioning sodium bicarbonate and increasing the urine pH to 6.5 or more.

c) Heterozygous renal replacement therapy: the patients complicated with acute renal failure were mixed with renal replacement therapy, central venous catheter, blood flow 200 ml/min, dialysis fluid flow rate 100 - 300 m/min, using unfractionated heparin or low molecular weight heparin anticoagulation, treatment time 6 - 12 h, take a daily dialysis method.

5) Statistical analysis: The quantative data are described as the number of cases (n) and the percentage (%), and the metrological data is described as the mean± standard deviation ($\bar{x} \pm S$) in the normal distribution, and median and range in the skewed distribution. Comparison between groups using t test, $P < 0.05$, the difference was statistically significant.

3. Results

1) Course of the patient: the number of hospitalization days in 841 patients was skewed distribution, it was 1 - 32 days, an average of 3.85 days, the median was 3 days [3 (31)]; 127 cases patients of rhabdomyolysis syndrome, the days of hospitalization was skewed distribution, it was 3 - 32 days, an average of 5.23 days, the median of 5 days [5 (29)]; 28 cases patients of acute renal failure, the days of hospitalization was skewed distribution, it was 7 - 32 days, an average of 9.10 days, the median of 9 days [7 (25)].

2) Comparison of major biochemical indexes before and after treatment in 99 patients without acute renal failure The levels of CPK, LDH, Mb, BUN, Cr and UA after treatment were significantly lower than those of before treatment ($p < 0.01$) (Table 2).

3) Comparison of major biochemical indexes before and after treatment in 28 patients with acute renal failure: the levels of CPK, LDH, Mb, BUN, Cr and UA after treatment were significantly lower than those of before treatment ($p < 0.01$) (Table 3).

4. Clinical Outcome

112 cases was cured out of 127 cases with rhabdomyolysis syndrome, accounting for 88.18%, 9 cases improved, accounting for 7.08%, the total effective rate is

Table 2. Comparison of the blood level of Mb, CPK, LDH, BUN, Cr, UA before and after treatment on 99 patients (x ± S).

Index	Before treatment	After treatment	Normal level	p
Mb (μg/L)	654.8 ± 213.6	74.9 ± 46.2	13 - 45	$p < 0.01$
CPK (U/L)	13,427.6 ± 4723.3	467.5 ± 674.7	0 - 100	$p < 0.01$
LDH (U/L)	763.1 ± 324.7	186.3 ± 101.4	0 - 250	$p < 0.01$
BUN (mmol/L)	6.7 ± 3.2	6.3 ± 2.9	2.2 - 7.2	$p > 0.01$
Cr (μmol/L)	87.4 ± 23.6	81.7 ± 25.2	27 - 132	$p > 0.01$
UA (μmol/L)	234.6 ± 78.3	246.9 ± 72.6	119 - 146	$p > 0.01$

Note: Myoglobin (Mb), ccreatine phosphokinase (CPK), lactate dehydrogenase (LDH), Blood urea nitrogen (BUN), creatinine (Cr), uric acid (UA).

Table 3. Comparison of the blood level of Mb, CPK, LDH, BUN, Cr, UA before and after treatment on 28 patients (x ± S)

Index	Before treatment	After treatment	p
Mb (μg/L)	1758.4 ± 926.3	128.5 ± 37.4	$p < 0.01$
CPK (U/L)	54,368.7 ± 36,451.2	1976.5 ± 723.2	$p < 0.01$
LDH (U/L)	1584.3 ± 726.4	265.7 ± 143.2	$p < 0.01$
BUN (mmol/L)	24.3 ± 8.5	7.1 ± 2.7	$p < 0.01$
Cr (μmol/L)	320.2 ± 225.0	123.7 ± 93.5	$p < 0.01$
UA (μmol/L)	674.3 ± 128.5	356.4 ± 78.7	$p < 0.01$

95.26%, 3 patients died, due to respiratory failure, accounting for 2.37%, 3 cases left untreated, because the family demanded going back to local treatment, accounting for 2.37%.

5. Discussion

Snake bites still has a high incidence currently in China, more than 10 million people were bitten by snake per year, the mortality rate is 3% - 5%, and disability rate is 25% - 30% [1]. Because the most often victims are farmers, it brings a huge economic and psychological burden to the family and society. Snake bites has acute onset, rapid progression and more complications. Some patients were prone to develop rhabdomyolysis syndrome, even acute renal failure. If not being treated in time, it can easily lead to death. Therefore, we retrospectively analyzed 841 cases of snake bites in patients in our hospital from January 2006 to July 2017 and screened out 127 cases rhabdomyolysis syndrome patients, to analyze its clinical manifestations, laboratory tests, related treatment and prognosis, hoping to provide guidance for the further treatment of snake bites.

In 841 cases patients of snake bites, 127 cases developed rhabdomyolysis and the incidence was 15.1%, while 28 cases were combined with acute renal failure and the incidence was 3.3%, which is slightly lower than that reported in previous literature [2]. Because our hospital is located in Jianghan Plain, the snake is mainly agkistrodon because of the subtropical climate. The mechanisms of

rhabdomyolysis after snake bites include the following: 1) the direct effect of toxins, venom is mixed toxins containing neurotoxin, blood toxins and cytotoxins (commonly known as muscle toxins) [3]. The cytotoxic enzymes and their analogues, proteolytic enzymes and phospholipase A2 (PLA2) in the agkistrodon venom can cause cell lysis by directly damaging cell structure, especially the cell membrane [4]. After separation and purification of the muscle toxins, it has been found that skeletal muscle toxin has PLA2 activity [5] [6], and had more specific proteases and could hydrolyze peptide bonds, hydrolyze different proteins, damage vascular endothelial cells, release histamine and vasoactive substances, thus causing ischemia and hypoxia in skeletal muscle and leading to muscle dissolution. 2) skeletal muscle necrosis was caused by tissue swelling, due to the toxic effects of snake venom, resulting in limb tissue swelling, lymphatic and venous obstruction, increased venous pressure and capillary pressure increased. Continuous exudation, tissue causing swelling lead to muscle tissue compression, damage and lysis [7]. Rhabdomyolysis can last for 6 - 7 days after snake bites [8]; if not treated in time, it can easily develop renal failure, threatening the lives of patients. So it must be treated promptly and efficiently.

The first adverse effect of rhabdomyolysis caused by snake bites is the toxin action. So it is, of key important to reduce the absorption of toxins, which includes local wound treatment and then the application of anti-venom serum to neutralize the toxins in the blood. Then methods to accelerate the excretion of myoglobin including hydration, diuretic and alkalization, should be taken to keep the total urine at the level of 2 - 3 L/d, and pH at 6.5 or more. The third step is to reduce the swelling pressure. These measures include anti-infection, applying osmotic diuretics (mannitol, etc.). But it is currently controversial to increase local tissue swelling if stitching the end of limbs near the heart. So it should be careful. The fourth is to use hemodialysis if complicated acute renal failure occurs. In our hospital, we take a combined kidney replacement therapy. Through our treatment, 112 cases had been cured out of 127 rhabdomyolysis cases, accounting for 88.18%; 9 cases were improved, accounting for 7.08%, the total effective rate being 95.26%. 3 patients died, due to respiratory failure, accounting for 2.37%; uncured in 3 cases, for the reason that the family was automatically discharged, accounting for 2.37%. The mortality rate is low.

In short, the rhabdomyolysis caused by snake bites must be treated with combined measures as soon as possible, which can effectively increase the rate of rescue and reduce mortality.

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