

Original Article

A national survey examining recognition, demand for antivenom, and overall level of preparedness for redback spider bites in Japan

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Aim: Redback spiders are rapidly becoming a nationwide problem in Japan. The domestic production of antivenom for redback spider bites has been started because of extremely low supply. The purpose of this study was to investigate the ability of emergency physicians to recognize redback spider bites and to examine the demand for antivenom and identify the ideal choice for storage.

Methods: Questionnaires examining the ability to recognize redback spider bites, the demand for antivenom, and overall level of preparedness were sent to 271 emergency medical service centers in Japan in March 2015.

Results: Completed questionnaires were returned by 156 medical institutions (58%). Only 25% of the institutes correctly answered regarding the recognition of redback spider bites. A demand for the new, domestically produced antivenom was reported by 55% of the institutes. Antivenom demand was high and increased with the ability to recognize redback spider bites (0 correct answers, $n = 24$ [42.9%]; 1–2 answers, $n = 32$ [55.2%]; three answers, $n = 28$ [71.8%]; $P = 0.02$). The storage of antivenom within their prefectures or regions was the best option for initial supply planning. Approximately 90% of the emergency centers showed an ability to use the antivenom safely.

Conclusion: The recognition of redback spider bites was low; however, the demand for antivenom was high. The storage of antivenom within their own prefectures or regions was considered to be the best option for initial supply planning. Emergency medical service centers are also good candidates for storage and safe use of antivenom.

Key words: Anaphylaxis, antivenom, questionnaire, redback spiders, spider bites

INTRODUCTION

REDBACK SPIDERS (RBS) were first noticed in metropolitan Tokyo on September 25th, 2014, and they are rapidly becoming a nationwide problem in Japan.¹ However, physicians in Japan are unfamiliar with RBS bites as they rarely occur, resulting in limited clinical experience.² These spiders are very common in Australia and have recently spread to Southeast and West Asia.² We believe that there is a risk of them spreading to East Asia due to climate change and intensive interaction between people.

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The symptoms of RBS bites are usually mild and localized, such as localized pain and erythema.² However, these bites would often prove fatal until the development of antivenom, which is manufactured by the immunization of horses.³

Redback spider bites are treated with the specific RBS antivenom produced by the Commonwealth Serum Laboratories in Australia. However, it is currently considered to be an off-label drug in Japan, and therefore must be privately imported from Australia.² This issue has been further complicated by the suspension of RBS antivenom imports from Commonwealth Serum Laboratories in autumn 2013. The Japanese Ministry of Health, Labor, and Welfare launched a research group to evaluate the safety and efficacy of the antivenom, and to organize and maintain information on all RBS bites from April 2013.² This research group carefully

evaluated the option for domestic RBS antivenom production by themselves for this emergency. The first stage began in April 2014, and it is scheduled for completion by the end of March 2016.⁴

Considering the efficacy of the newly produced antivenom in clinical practice, appropriate supply planning to meet the demands of physicians is mandatory. For example, *Rhabdophis tigrinus* (Yamakagashi snake) bites or gas gangrene require an immediate administration of the antivenom to save the patient's life. However, inadequate supply planning has resulted in insufficient storage sites, which in turn leads to delays in the delivery of medication to patients.^{5–7}

The purpose of the present study was to investigate the ability of emergency physicians to recognize RBS bites and to examine the demand for antivenom and identify the optimum choice for storage.

METHODS

THIS cross-sectional, survey-based study was approved by the institutional review board of the Kagawa University Hospital (Kagawa, Japan) (Heisei 26-118).

I. Recognition for RBS bites

I-I: Do you think that RBS are lethal injuries?

1. Yes. 2. No. 3. N/A

I-II: Is the main symptom of RBS bites swelling and not pain as commonly induced by Mamushi bites?

1. Yes. 2. No. 3. N/A

I-III: Is the antivenom for RBS bites made from human serum?

1. Yes. 2. No. 3. N/A

II. Present Antivenom (imported from Australia) demands for RBS bites

II-I: What do you think of the use of antivenom to the patients with RBS bites?

1. Yes, with every cases. 2. Yes, but limited to severe cases. 3. No. 4. N/A

II-II: Do you use antivenoms from the area antivenoms are kept?

If antivenom is not kept at your institute, are you willing to transfer the patients for the use of antivenom and in which area?

1. Only own institute
2. Limited to same cities, towns and villages municipalities
3. Limited to same prefectures the largest administrative divisions units of Japan
4. their region (Hokkaido, Tohoku, Kanto,...etc.)

III. Newly domestically produced antivenom (will be made in 2016) demands

III-I: Does your institute wish to keep newly produced antivenom for RBS bites?

1. Yes. 2. No.

III-II: Why does your institute wish to keep newly produced antivenom for RBS bites?

1. To use for the patients positively. 2. To use limited to severe cases. 3. definite decision has made, but want to keep for the emergency 4. Others ()

IV. Preparedness for RBS bites

Does your institute have the ability to treat the patients with anaphylaxis?

1. Yes, including severe cases. 2. Yes, but only for mild cases. 3. No. 4. N/A.

Fig. 1. Questionnaire sent to 271 emergency medical service centers in Japan in March 2015 regarding recognition of redback spider (RBS) bites and supply of antivenom. N/A, not applicable.

Patients and setting

A questionnaire examining recognition skills, demand for antivenom, and overall preparedness for RBS bites in Japan was prepared and sent to 271 emergency medical service centers covering all areas of Japan in March 2015. The questionnaires were returned in May 2015, and their detailed contents are shown in Figure 1.

Correct answers for recognition of RBS bites in questionnaires

I-I: Do you think that RBS are lethal injuries? The answer is “No” because RBS bites are usually mild and localized. No fatal cases have been reported in Japan or in Australia since the development of the antivenom.²

I-II: Is the main symptom of RBS bites swelling and not pain as commonly induced by Mamushi bites? The answer is “No” because approximately 90% of patients develop local pain.²

I-III: Is the antivenom for RBS bites made from human serum? The answer is “No” because the antivenom is manufactured by the immunization of horses.²

Current antivenom supply

In autumn 2014, with great effort, the Ministry of Health, Labor, and Welfare research group obtained several vials of antivenom for emergency use. However, this quantity is insufficient to meet the demands of all major hospitals in Japan. Therefore, many emergency physicians working at currently surveyed institutes do not have access to antivenom in their own hospitals.

Primary data analysis

The χ^2 -test was used to examine the association between the demand of newly produced antivenom and the recognition of RBS bites

All statistical analyses were carried out using JMP version 11 (SAS, Cary, NC, USA), and two-tailed *P*-values ≤ 0.05 were considered statistically significant.

RESULTS

COMPLETED QUESTIONNAIRES WERE received from 156 medical institutions (58%).

I. Recognition of RBS bites

The questionnaire consisted of three basic questions. Thirty nine institutes (25%) answered them correctly, 59 institutes (38%) answered one or two questions correctly, and 58 institutes did not answer correctly at all (Fig. 2).

Number of correct answers to three questions

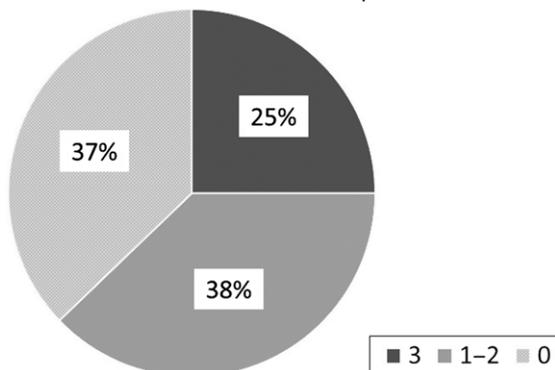


Fig. 2. Number of correct answers to three questions included on a questionnaire sent to 271 emergency medical service centers in Japan in March 2015 regarding the recognition of redback spider bites. Thirty nine institutes (25%) answered all correctly, 59 institutes (38%) answered one or two questions correctly, and 58 (37%) did not answer any correctly.

Table 1. Demand regarding storage area of redback spider antivenom in Japan. Emergency medical service centers were asked: If antivenom is not kept at your institute, are you willing to transfer the patients for the use of antivenom and in which area?

Area	No. of institutions	%
Within their own institutions	3	2.8
Within their own municipalities	19	17.9
Within their own prefectures	61	57.5
Within their own regions†	22	20.8

†Regions of Japan: Hokkaido, Tohoku, Kanto, Chubu, Kansai, Chugoku, Shikoku, and Kyusyu.

II. Present antivenom (imported from Australia) demand for RBS bites

Amongst all the surveyed institutes, 67% reported antivenom use for severe or all patients with RBS bites. Of these, 58% said that the use of antivenom would be positively considered if they were stored within their own prefectures, whereas 22 institutes (21%) reported that they would use it if it was stored within their own regions (Hokkaido, Tohoku, Kanto, Chubu, Kansai, Chugoku, Shikoku, and Kusyu-Okinawa) (Table 1).

III. Demand for new domestically produced antivenom (completion in 2016)

A total of 84 (55%) institutes showed demand for newly produced antivenom.

The association between this demand and ability to recognize RBS bites is shown in Figure 3. A significant difference was observed between the three groups with regard to demand for antivenom (0 correct answers, $n = 24$ [42.9%]; 1–2 correct answers, $n = 32$ [55.2%]; three correct answers, $n = 28$ [71.8%]; $P = 0.02$). Antivenom demand increased with increased ability to correctly recognize RBS bites.

IV. Preparedness for RBS bites

Sufficient level of preparedness against anaphylaxis was reported by 89.4% of the institutes (Table 2).

DISCUSSION

IN THE PRESENT study, only one-quarter of the institutes answered the question regarding the recognition of RBS bites correctly. Antivenom demands for RBS bites

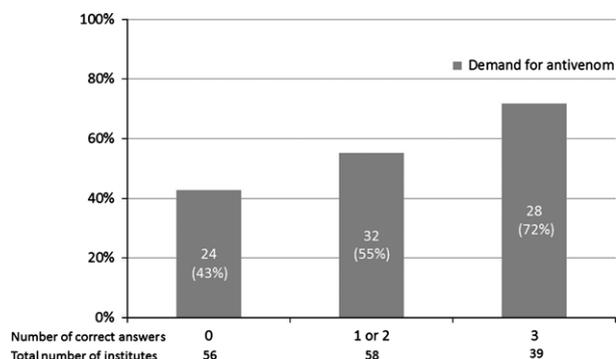


Fig. 3. Association between the rates of correct answers on a questionnaire sent to 271 Japanese emergency medical service centers regarding the recognition of redback spider (RBS) bites and demand for antivenom. The ability to recognize RBS bites was classified into three groups based on the number of correct answers to three questions (0 correct answers, 1–2 correct answers, and 3 correct answers). For example, 56 institutes answered none of the answers correctly; of these institutes, 43% expressed demand for antivenom. Antivenom demands increased with the increased ability to correctly recognize RBS bites.

Table 2. Preparedness against redback spider bite anaphylaxis in Japan. Japanese emergency medical service centers were asked: Does your institute have the ability to treat the patients with anaphylaxis?

	No. of institutions	%
Yes, including severe cases	136	89.4
Yes, but only for mild cases	5	3.3
No	4	2.6
N/A	7	4.6

N/A, not applicable.

were high and were seen to increase with the proportion of ability to correctly recognize RBS bites. Furthermore, the storage of antivenom within their own prefectures or regions was considered to be the best option for initial supply planning.

Although several antivenoms have been produced for emergency use,⁸ there are no studies that examine its efficacy in clinical practice. As a result, they have not been considered for functional use.

The most striking result of the current study was that only 25% of emergency medical service centers had basic knowledge about RBS bites. The 2014 dengue fever outbreak in Tokyo, Japan was promoted by climate change and intensive interaction between people, and we believe that these factors

may contribute to the outbreak of many other diseases, including RBS bites, in the future.⁹ Therefore, opportunities for learning more about RBS bites should be provided. In the present study, antivenom demands were elevated with the proportion of ability to correctly recognize RBS bites. Therefore, better understanding of these bites may result in higher demands for antivenom.

In a previous study focusing on the clinical characteristics of RBS bites in Japan, approximately one-third of the cases were seen to develop systemic symptoms.² In 2014, three patients with RBS bites developed systemic symptoms requiring the administration of antivenom. However, this was not carried out mainly because of inconveniences associated with its supply.¹⁰ The physicians were not willing to use antivenom to treat RBS bites as it would involve transfer of the patients to another hospital located closer to the prefecture.¹⁰ Therefore, it is important to carry out appropriate planning for the supply of antivenom. In the present study, most of the emergency physicians hoped to store the antivenom within their own prefectures or regions. Therefore, initial supply planning of newly produced antivenom should be based on these demands.

Antivenom is produced from the serum of immunized horses, and the level of preparedness for anaphylaxis should be considered when administering it. Premedication with an antihistamine and/or epinephrine should be carried out when the perceived benefits are greater than the risk of adverse effects.^{11,12} In the present study, approximately 90% of the emergency medical service centers were capable of using the antivenom safely. Therefore, these centers are ideal for antivenom storage.

The present study had several limitations that must be addressed. First, the response rate for the questionnaires was only 58%, and higher rates would provide better strength of evidence.

Second, the current survey was carried out only among emergency medical service centers. However, patients with RBS bites often visit outpatient services at local hospitals. Therefore, future studies should evaluate the opinion of dermatologists and primary care physicians also.

Finally, other treatment options, including the use of analgesics for the relief of localized pain, were not examined.

CONCLUSION

THE RECOGNITION OF RBS bites was low; however, the demand for antivenom was high. The storage of antivenom within their own prefectures or regions was considered to be the best option for initial supply planning. Emergency medical service centers are also good candidates for storage and safe use of antivenom.

CONFLICT OF INTEREST

NONE.

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