

BRIEF COMMUNICATION

Safety of i.v. administration of redback spider antivenom

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Key words

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Abstract

It is unclear what the risk of allergic reactions is with appropriately given dilute i.v. redback spider antivenom (RBSAV). Ninety-five i.v. administrations of RBSAV referred from January 2001 to November 2006 were reviewed. All patients had local pain, 72% radiating pain, 57% diaphoresis and 39% systemic effects. Four patients (4%) had immediate systemic hypersensitivity reactions: none were severe, one was moderate and three mild. In 32 patients followed up for 2 weeks, three (10%) developed serum sickness. RBSAV given i.v. had a low reaction rate.

Redback spider antivenom (RBSAV) has been available for almost 50 years¹ and is the most commonly used antivenom in Australia.^{2,3} It was initially recommended to be used by the i.m. route,¹ but over the last decade, there has been increasing i.v. use because of reports of failure of i.m. antivenom.⁴ The use of i.v. antivenom is more consistent with the international experience⁵ and pharmacokinetic studies in humans and animals.^{6,7}

The most common cited reason for avoiding i.v. administration has been the apparent higher rate of allergic reactions.^{8,9} In a retrospective study of the administration of RBSAV in over 2000 cases, there were 11 cases defined as 'anaphylactic' reactions.⁹ Five of the 11 were following i.v. administration, but in only 44 cases was i.v. antivenom given. This was compared with six anaphylactic reactions in 2073 following i.m. antivenom administration. In all five cases, i.v. antivenom was given as an undiluted bolus, which is well known to cause a high rate of early complement-mediated reactions.¹⁰ However, the study does not provide any information on the use of diluted i.v.

antivenom given as an infusion. Therefore, it remains unclear what the risk of allergic reactions is with appropriately given i.v. RBSAV. This study aimed to estimate the incidence of adverse effects following the administration of i.v. RBSAV. This was undertaken by reviewing a cohort of cases collected by the author.

The study was approved by the Human Research Ethics Committee of Northern Territory Department of Health and Community Services and Menzies School of Health Research. All cases referred to the author from January 2001 to November 2006 were reviewed. The author maintained records of all cases of i.v. RBSAV administration because the use of RBSAV by the i.v. route is not recommended by the manufacturer and a clinical audit, i.v. use was deemed important. The following information was recorded and reviewed: patient details (age and sex), clinical effects (local pain, radiating pain, diaphoresis and systemic effects), antivenom treatment (number of vials used i.v. or any i.m. administration) and evidence of adverse reactions (early and delayed). The findings were entered into a Microsoft Excel database for analysis. In a subgroup of patients, details of follow up after 1–2 weeks were available to investigate delayed reactions. All statistical analysis was carried out using GRAPHPAD INSTAT (version 3.02 for Windows 95, GraphPad Software, San Diego, CA, USA).

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Table 1 Four cases with immediate systemic hypersensitivity reactions

Age/sex	Reaction to i.m. antivenom	Clinical features	Grading	Treatment of reaction	Recommended antivenom
37/M	No	Generalized erythema, itchiness and swelling	Mild	Promethazine, hydrocortisone	Yes
51/M	Yes	Generalized erythema, itchiness and facial swelling	Mild	Promethazine, hydrocortisone, adrenaline infusion	No
47/F	No	Dry cough, difficulty swallowing, uvular and soft palate oedema	Moderate	Promethazine, hydrocortisone, i.m. adrenaline	Yes
33/F	No	Generalized erythema and itchiness	Mild	Promethazine, hydrocortisone, i.m. adrenaline	Yes

Clinical data

Ninety-five patients were referred to the author over the 6-year period, excluding patients recruited to an ongoing controlled trial. The median patient age was 38 years (interquartile range (IQR): 20–48). Sixty (63%) were men, and 13 were children (<16 years). All patients had local pain, 68 (72%) had radiating pain, 54 (57%) had diaphoresis and 37 (39%) had systemic effects. Forty-two patients received at least one vial of RBSAV by the i.m. route before i.v. antivenom. The median dose of i.v. RBSAV was two vials (interquartile range: 1–2; range: 1–12).

Four patients had immediate systemic hypersensitivity reactions after commencement of i.v. antivenom. No patient had a severe reaction, one had a moderate reaction and three had mild reaction according to the grading system of Brown (Table 1)¹¹ Follow up for 1–2 weeks was only possible in 32 patients, three of which developed symptoms consistent with serum sickness (10%).

Discussion

A review of MEDLINE (1966 to October 2006) and Pre-MEDLINE using the following terms – ‘redback’, ‘spider’, ‘latrodectism’, ‘antivenom’ and ‘Latrodectus’ – only identified one study with information on more than two administrations of i.v. antivenom. The study by Ellis *et al.* enrolled 18 patients who were given i.v. RBSAV. None of these had immediate hypersensitivity reactions, and one developed serum sickness.¹² There were four other reports of i.v. RBSAV use with no adverse reactions.^{13–15}

This review suggests that reactions to i.v. administration of RBSAV are uncommon and occur in less than 5% of cases with no severe reactions causing hypotension, bronchospasm or coma. Serum sickness occurred in 10% of cases but was based on a small sample of cases because of the difficulty in following up patients for 2 weeks by phone.

The rate of immediate hypersensitivity reactions was less than previous reports of undiluted antivenom admin-

istration.⁹ However, it was higher than the 0.5% reaction rate with i.m. antivenom administration reported in the same study.⁹ In three of the four cases, antivenom was continued at a slower rate without any further reactions, supporting the rate of administration being a significant factor in reactions occurring.

One issue that is rarely discussed with i.m. antivenom is the problem that once it is given, it is impossible to prevent ongoing absorption. Although this is unlikely to be a problem with the majority of cases where anaphylaxis is not mediated by IgE, it will be a significant problem in persons who have previously been given antivenom and may have developed IgE-mediated hypersensitivity. In the case of i.v. administration, the infusion can be stopped when such a reaction occurs.

This study supports i.v. antivenom being relatively safe with a low reaction rate. This will allow clinicians to better balance the risk of using i.v. antivenom against its benefits. However, further research is required to determine whether i.v. antivenom is as effective or more effective than i.m. antivenom so that it can be recommended for routine management of redback spider envenoming.

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