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Predictors of *Bothrops jararaca* venom allergy in snake handlers and snake venom handlers ☆

Carlos R. de Medeiros[a,c,*], Kátia C. Barbaro[b], Marcela S. Lira[b], Francisco O.S. França[a], Vera L. Zaher[d], Cristina M. Kokron[c], Jorge Kalil[c], Fábio F.M. Castro[c]

[a]*Instituto Butatan, Hospital Vital Brazil, Av. Vital Brazil 1500, 05503-900 São Paulo, SP, Brazil*
[b]*Laboratório de Imunopatologia, Instituto Butantan, Av. Vital Brazil 1500, 05503-900 São Paulo, SP, Brazil*
[c]*Disciplina de Imunologia Clínica e Alergia, Departamento de Clínica Médica, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil*
[d]*Laboratório de Investigação Médica (LIM-01), Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil*

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Abstract

Since allergic sensitization to snake venom has been reported, anaphylactic reactions to snake venom might be an underestimated factor contributing to fatal snakebites, independently from the toxicity of the venom itself. However, little information is available on the determinants of such reaction. Hence, we studied a group of workers exposed to *Bothrops jararaca* venom (BJV), in order to clarify the factors related with snake venom allergy. The aim of this work was to investigate the prevalence and predictors of venom allergy among workers exposed to BJV and to confirm the involvement of IgE-mediated mechanisms in this condition. Workers exposed to BJV were assessed for venom allergy using questionnaires and immunological tests. The presence of BJV sensitization was determined through quantification of specific IgE. Allergens were studied using the Western blots and inhibition assays. Of the 67 workers evaluated, 7 (10.4%) presented specific IgE antibodies to BJV. Of those, 6 presented typical symptoms of an IgE-mediated allergic reaction when exposed to BJV. Venom sensitization was associated with length of employment ($P = 0.042$), high levels of total IgE ($P = 0.034$), atopy ($P = 0.051$), and specific tasks, primarily the handling of dried venom ($P = 0.014$). Our observations suggest that exposure to BJV can result in allergic sensitization in snake handlers through IgE-mediated mechanisms. The prevalence rate of this condition appears to be high among these workers, and the handling of dried venom, total IgE level above 100 kU/L, length of employment, and probably history of atopy were predictors of its occurrence.

Keywords: *Bothrops jararaca*; Snake handler; Snake venom; Allergy; Immunoglobulin E.

☆ *Ethical statement*: All participating subjects gave written informed consent. The study protocol was approved by the Ethics in Research Committee of the *Hospital das Cl!nicas*, University of São Paulo School of Medicine, São Paulo, Brazil (Protocol No. 1039/03).

*Corresponding author. Instituto Butantan, Hospital Vital Brasil, Av. Vital Brazil, 1500, 05503-900 São Paulo, SP, Brazil. Tel./fax: +55 11 37267962.
E-mail address: carlosrmedeiros@butantan.gov.br (C.R. de Medeiros).

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1. Introduction

Every year, 5 million envenoming by snakebites occur worldwide (Chippaux, 1998), with tens of thousands of deaths, particularly in tropical and subtropical countries, where they represent an important public health hazard (Gutiérrez et al., 2006). The morbidity and mortality from snakebites is secondary to direct systemic toxicity from the venom. However, since allergic sensitization to snake venom has been reported, anaphylactic reactions to snake venom might be an underestimated factor that may contribute to fatal snakebites in those endemic regions, independently from the toxicity of the venom itself (Parrish and Pollard, 1959; Schmutz and Stahel, 1985).

On the other hand, sporadic cases were reported in the medical literature describing allergic reactions to snake venom after recurrent exposure through bites (Lounsberry, 1934; Parrish and Pollard, 1959; Hogan and Dire, 1990; Ryan and Caravati, 1994; Alonso et al., 1995) and, presumably, through repeated inhalation of (or dermal/mucosal contact with) the venom (Stanic, 1956; Parrish and Pollard, 1959; Mendes et al., 1960; Ellis and Smith, 1965; Kelly and Patterson, 1973; Wadee et al., 1987; Brooks and Graeme, 2004; Prescott and Potter, 2005), mainly among amateur and professional snake handlers.

To date, there have not been published studies evaluating the factors contributing to this condition in specific exposure settings, or on the patterns involved in the observed immunological responses. Hence, we studied a group of workers exposed to *Bothrops jararaca* venom (BJV), in order to clarify the factors related with snake venom allergy. We focused on this species because snakes of the genus *Bothrops* are responsible for the vast majority of snakebites in South America, with the species *B. jararaca* being associated with most human envenomations in the Southeastern region of Brazil (França et al., 2003).

The specific aim of this study was to evaluate the prevalence and predictors of allergy among workers exposed to BJV, and to confirm the involvement of IgE-mediated mechanisms in this condition.

2. Methods

2.1. Study design and population

A cross-sectional study of 70 adult laboratory workers, scientists, technicians, and trainees, all employees of the Biology Museum, the Herpetology Laboratory, and the Production and Technological Development Division of the Butantan Institute, was carried out in November of 2005. Of the 70 subjects initially selected, 3 were excluded from analysis for being unable to participate due to their work obligations. Therefore, the study sample consisted of 67 subjects.

All of the subjects in the study sample had been exposed to snake venom or to the snakes themselves, most of which were of the genus *Bothrops*. All participating subjects gave written informed consent. The study protocol was approved by the Ethics in Research Committee of the *Hospital das Clínicas*, University of São Paulo School of Medicine, São Paulo, Brazil (Protocol No. 1039/03).

2.2. Questionnaire

All 67 subjects completed a physician-administered questionnaire containing questions regarding their personal history of allergy, snakes bites, and contact (oral or ocular) with snake venom, as well as their work history (length of employment and specific work tasks) and work-related symptoms.

Subjects were considered positive for a history of allergy if reporting any of the following symptoms: chest tightness; running nose/sneezing; itchy/watery eyes; and itchy skin due to common allergens such as dust, domestic animal dander or airborne fungi. Subjects were considered to have work-related allergic symptoms if they responded affirmatively to the question, "Do you have allergy during working hours, i.e. after contact with a specific snake or snake venom at work?"

The job of snake handler entails specific tasks, including snake cage cleaning, snake feeding, snake venom extraction, the handling of snake venom (liquid/dried), snake room cleaning, snake embalming, the capture/installation of snakes, snake-pit cleaning, and snake dissection. Estimates of the exposure times to snakes or snake venom were derived from the following questions: "How many days per week do you perform [the specific task]?"; and "For how many years have you been performing [the specific task]?" The frequency of exposure to each specific task was reported as a continuous variable, in days per year. To assess the influence of each task at different frequency levels, an exposure time index was calculated by multiplying the years of exposure by the frequency of exposure to each specific task.