ASIA PACIFIC JOURNAL of MEDICAL TOXICOLOGY
APJMT 11;4 http://apjmt.mums.ac.ir December 2022

SHORT COMMUNICATION

Bee and wasp stings cause type I hypersensitivity reactions, Mechanism and Treatment.

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Abstract

Background: Humans are very susceptible to the poison of insects. Some animals can produce substances that cause allergic reactions in humans. In these conditions, the immune system responds through mechanisms that provoke a state of defense in the affected person to fight against the aggression. In many cases, this defense is very strong to the organism itself.
Methods: The topic: "hypersensitivity due to stings of insects (bees and wasps)" was reviewed by keywords of articles included in the Google Scholar, Web of Science, and PubMed databases. The articles were selected by their relevance. Recently published articles in peer-reviewed journals were included, conducting a detailed review of all contents.
Results: The review indicated that the hypersensitivity mechanisms produced by bee and wasp stings are mainly mediated by IgE's antibodies. In addition, the crucial importance of a rapid response to the first symptoms of hypersensitivity to prevent the venom severe symptoms leading to the patient´s death is emphasized.
Conclusions: The current knowledge of hypersensitivity reactions in individuals susceptible to bee and wasp stings was reviewed and summarized, revealing that IgE-mediated allergic reactions are the main mechanism. Adequate treatment after the inoculation of the poison is decisive in the patient´s recovery.

Keywords: Immune System, Hypersensitivity Reaction, Anaphylaxis, Bee Sting, Wasp Sting.

How to cite this article: Bee and wasp stings cause type I hypersensitivity reactions, Mechanism and Treatment. Serrano Sanchez T, Guirola Funtes J, Mastrapa Ochoa H, Batista Reyes Y, Jomarron Martinez Y, Pelaez Rodriguez R, Pedro Neto A. Asia Pac J Med Toxicol 2022; 11(4):163-165.

INTRODUCTION

Bees and wasps are widely and numerously distributed in cold and tropical climates; therefore, many humans can experience multiple stings during life. A few stings are enough to produce unwanted immune reactions in people, who are allergic to the venom of these insects [1,2].

Insect bite allergy is a topic, which is limitedly known and studied. The reaction due to the sting of wasps and bees can vary from a local reaction (involvement of that area exclusively) to anaphylaxis that could cause the death. When an insect bites, it is difficult to determine in many cases the specific insect it was, because a local reaction occurs in the area of the bite and the clinical manifestations (erythema, pruritus and edema) are usually similar [1;3].

According to the data described in the literature, bee and wasp stings can affect humans, producing mild reactions as well as hypersensitivity that endanger the patients' lives [1]. The immune responses are normally effective reducing the inoculated poison, in such a way that limits the produced damage. Nevertheless, a type 1 hypersensitivity response occurs in some individuals, which can be more severe in allergic subjects [4-6]. In this case, the organism responds in an exaggerated way, producing severe damage to the tissues invaded by the bee or wasp venom [4-6]. It is important to avoid the exposure to insect´s poison and when it happens the active surveillance of patients with a history of hypersensitivity reactions is necessary to prevent future severe episodes of anaphylaxis.

Despite the studies carried out, little is known about the immunological mechanisms responsible for hypersensitivity in individuals susceptible to bee and wasp stings. The objective of this study is to review and provide a comprehensive description of the mechanisms of hypersensitivity.

METHODS

We carried out a search strategy in reliable databases such as the Google Scholar, Web of Science, and PubMed databases. Specific search terms were used to explore the

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content such as "Immune System", "Hypersensitivity Reaction", "Anaphylaxis", "Insects", "Bee", and "Wasp". The selection criterion for the inclusion of articles were recency and relevance of the content regarding the production of hypersensitivity mechanisms and treatment. Articles that did not meet the inclusion criteria were discarded. The data related to the hypersensitivity mechanisms of susceptible individuals were unified into a representative scheme developed by the authors. On the other hand, an analysis of the therapeutic guidelines to follow in this medical emergency is presented.

RESULTS

Production mechanism of hypersensitivity for bee and wasp stings.

The type I hypersensitivity, also called IgE-mediated hypersensitivity, is produced by immunoglobulin E (IgE) class antibodies formed in response to a given antigen (allergen). In this type of hypersensitivity reaction, the antigen presentation to helper T cells initiates a cascade of immunological events that leads to the production of IgE antibodies. The re-exposure to antigen promotes degranulation of IgE-bound mastoid cells and basophils, releasing chemical mediators that cause various symptoms. Manifestations may be local, depending on the route of entry of the antigen. However, in severe cases, the systemic reaction leads to anaphylactic shock [1;3;7].

The insect venom (e.g., bee and wasp venom), can produce this type of hypersensitivity. When the individual is exposed to bee and wasp venom for the first time, a sensitization stage occurs, and the individual is asymptomatic. The insect venom is recognized by antigen-presenting cells. These cells process the antigens in their interior and migrate to the regional lymph nodes. There they present the poison binding in a class II major histocompatibility complex molecule to a naive T lymphocyte, inducing the differentiation of naive T cells into Th2 cells. This process also occurs in the respiratory and digestive mucosa of patients [8-11].

The release of interleukins (IL-4, IL-5, IL-13) produced by Th2 cells are responsible for plasma cells (B lymphocytes) that recognize the insects poison, making a change in the heavy chain isotype of the immunoglobulins they secrete and begin to produce IgE. The IgE secreted bind to mastoid cells and basophils through the FcεRI receptors. In the reaction or effector stage, mastoid cells and basophils bound with antigen-specific IgE antibodies will be ready to respond to re-exposure to wasp and bee venom [12;13]. (Fig 1). The presence of interleukin 4 (IL4) allows the activation of the STAT6 and GATA-3 transcription factors. They are the main regulators of lymphocyte differentiation towards a Th2 phenotype, increasing expression of interleukins 4, 5 and 13 genes (IL4, IL5 and IL13). In addition, IL5 plays an important role in the activation and chemotaxis of eosinophils, and IL13 stimulates bronchial mucosal hypersecretion [13-15].

The early phase reaction occurs in the first few minutes, producing a local or systemic reaction. Basophil and mastoid cells bound to the IgE antibody degranulate, releasing different mediators responsible for the symptoms reported by the patient. Mediators include histamine, prostaglandin, platelet activating factor, and leukotrienes (Table 1) [13;14].

The late phase reaction occurs 4–12 hours later, peaking at 6–9 hours. In this stage, the eosinophils (predominant) and other leukocytes migrate to the local tissue contaminated with bee or wasp venom [16-18]. This late response involves the recruitment of other effector cells and some factors such as chemokines, lipid mediators (leukotrienes and platelet-activating factor, PAF), and additional cytokines (IL-4 and IL-5), which perpetuate the TH2 response, contributing significantly to the immunopathology of an allergic response. This reaction usually causes symptoms in the nose, lungs, throat, sinuses, ears, lining of the stomach or in the skin [16, 18].

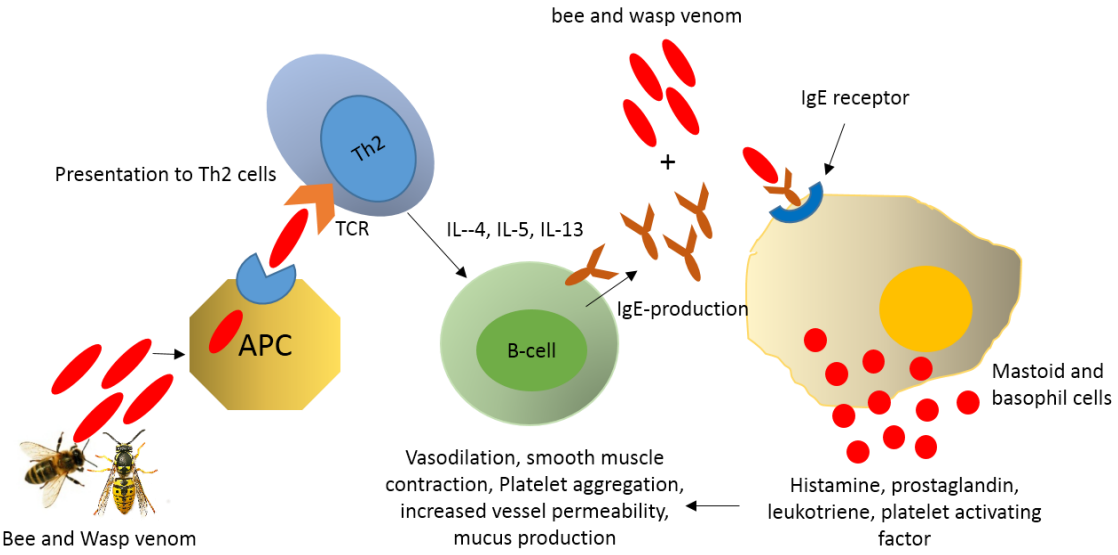

Fig 1. Hypersensitivity reaction to Bee and Wasp Venom. APC: Antigen Presenting Cells; Th2: T-helper cells 2; TCR: T cell receptor. (Source: author's own.)

Table 1. Releasing mediators of mastoid cell and basophil degranulation.

MEDIATOR	EFFECT
Histamine	Vasodilation, bronchial smooth muscle contraction, increased mucus secretion, and increased vessel permeability.
Prostaglandin	Pulmonary smooth muscle contraction
Platelet activating factor	Platelet aggregation, vasodilation
Leukotrienes	Bronchial smooth muscle contraction, increased vessel permeability, mucus production

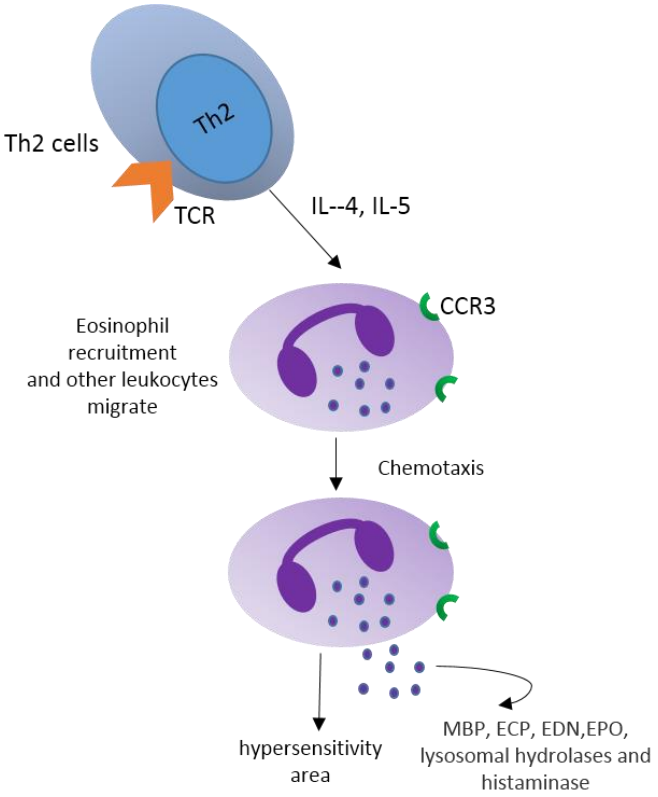

Fig 2. Eosinophil response. Th2: T-helper cells 2; TCR: T cell receptor; CCR3: Chemokine receptor 3; MBP: Major Basic Protein, ECP: Eosinophilic Cationic Protein; EDN: Eosinophil-Derived Neurotoxin; EPO: Eosinophil Peroxidase (Source: author's own).

Major mediators of eosinophils include: major basic protein, eosinophilic cationic protein, eosinophil-derived neurotoxin, eosinophil peroxidase and lysosomal hydrolases, and histaminase (Fig 2) [19;20].

Guideline to follow in the bee and wasp stings

The reaction to bee and wasp stings is different in each person. Most of the problems that require medical attention derive from the allergic reaction to the sting. There is variability in the immune response that predominates in the inflammatory process. Therefore, the disease can be present with a wide range of clinical manifestations (feeling of warmth, flushing, a red and itchy rash, feelings of light-headedness, shortness of breath, throat tightness, anxiety, pain/cramps, and/or vomiting and diarrhea). In severe cases, you may experience a drop in blood pressure that results in a loss of consciousness and shock. In most cases, complications respond well to medications when they are given in time. However, anaphylaxis is a medical emergency that requires immediate airway access with epinephrine administration if complications are develop. Immediate supportive treatment is the mainstay to reduce morbidity and mortality in such cases [21;22]. This aspect has also been considered in other human poisonings. [23-28].

Common treatment options are antihistamines and glucocorticoids to control the inflammatory response [29]. The drug can be administered intramuscularly, but in severe cases, such as an anaphylactic shock, the use of intravenous puncture will be necessary [30].

According to the data reported in the literature, the current therapy should include the molecules that are involved in the inflammatory process. The biological treatments developed will be aimed at directly blocking these molecules in the allergic pathway. This includes, for example, the use of monoclonal antibodies which increase the immediate response in these patients. [31-34].

CONCLUSION

Insect venom allergy is one of the most common causes of anaphylaxis in humans and it is a medical emergency, which will be more serious in allergic individuals. The production mechanism includes exaggerated IgE-mediated allergic reactions. The application of urgent treatment remains the safest alternative to stop the progression of tissue damage. New therapies are being implemented with the development of technology.

ACKNOWLEDGMENT

Thanks to my dearest Professor Jorge A. Bergado and PhD Margarita Baez for the review and corrections. We thank the authors, who were cited in this manuscript.

Conflict of interest: None to be declared.
Funding and support: None

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