

Venom immunotherapy and pregnancy

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Abstract

Introduction: The efficiency of venom immunotherapy (VIT) has been well documented by many studies. However, the most important for VIT is safety, particularly for a pregnant woman and a fetus.

Aim: To establish the influence of continuation of VIT on pregnant women and offspring.

Material and methods: The 6 women became pregnant during a specific immunotherapy. We retrospectively analyzed the influence of the immunotherapy on any complications for the pregnant women and their infants.

Results: Of the 6 patients who participated in this study, four had hyperemesis gravidarum, nausea, and heartburn, and two of them had gestational diabetes mellitus symptoms, typical of pregnancy. The observation indicated that VIT was safe for the pregnant women and their offspring.

Conclusions: The VIT is an appropriate therapeutic method for most patients with severe anaphylactic reactions after a hymenoptera sting. The observation indicated that VIT is safe for pregnant women and for their infants.

Key words: venom immunotherapy, pregnancy.

Introduction

The first description of an allergen-specific immunotherapy was published by Leonard Noon in 1911. The report showed that a subcutaneous injection of increasing doses of a grass pollen extract led to the tolerance of these pollens by sensitive patients [1]. Hymenoptera, including honeybee (*Apis mellifera*) and wasp (*Vespula germanica* and *Vespula vulgaris*) stings, usually can cause normal responses such as transient pain, itching, and swelling, but approximately 5% of the general population can develop severe, systemic, life-threatening reactions [2, 3].

Venom immunotherapy (VIT) was established in the 1970s. Venom immunotherapy protects against fatal anaphylaxis and prevents 90–95% of all reactions to stings. The recommended duration of the venom immunotherapy is 5 years, and this period is considered to be sufficient for allergic patients [4]. A special group of patients are women of childbearing age and pregnancy. According to the EAACI recommendations, the continuation of VIT is not a contra-indication during pregnancy [5].

Aim

This study examines the influence of VIT on any problems during pregnancy and the influence on offspring.

Material and methods

Six women with a history of a systemic reaction of grades III and IV according to Ring and Messmer [6] to a Vespidae (*Vespula germanica*, *Vespula vulgaris*) sting were included in the VIT and the study retrospectively. Only 1 patient was sensitized to airborne and cat allergens. Table 1 shows the characteristics of the tested group.

The blood for the examination was collected from ulnar veins into a test tube with lithium heparin of a final concentration of 10 U/ml using a closed Vacutainer system, and on a clot to a test tube without anticoagulants. The total IgE and asIgE were measured using enzyme immunoassay (EIA) Hycor TM kits (Hycor, United Kingdom). Additionally, in all examined patients the following were assessed: the level of serum tryptase by fluorescence enzyme immunoassay (FEIA) using ImmunoCAP tryptase kits on UNICAP 100. All tests were performed according to the producer's instructions.

The venom immunotherapy was performed with Venomenhal Wasp (Hal Allergy) (Table 2).

Results

In total, 6 patients with an average age of 31 to 17 years, were treated with wasp venom immunotherapy.

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The mean time to fertilization after VIT initiation was 26.5 ± 15.3 months.

Of the 6 pregnant women receiving VIT, 4 had hyperemesis gravidarum, nausea, and heartburn, and 2 of them had gestational diabetes mellitus symptoms, typical of pregnancy. All offspring were normal and in good condition. The mean birth weight was 3.68 ± 0.57 kg (Table 3).

Discussion

Allergy to insect stings and systemic anaphylactic reactions are most often IgE mediated [7]. Severe systemic anaphylaxis is a known cause of respiratory and cardiovascular symptoms and could lead to shock and cardiac arrest [8]. According to the Hymenoptera Venom Allergy (HVA) experts, adrenaline is the mainstay of therapy to halt the progression of anaphylaxis and to reverse potentially life-threatening, cardiopulmonary manifestations [9]. Anaphylaxis and maternal hypoxemia lead to placenta vasoconstriction and uterine contractions, and are a known cause of fetal abnormalities, premature labor and consequently maternal morbidity or even mortality [10]. The side effects of treatment with adrenaline also could be dangerous for pregnant women as well as for a fetus [11].

Table 1. Characteristics of the women ($n = 6$) who underwent VIT

Parameter	Characteristics
Age [years]	31.17 ± 3.97 (28–36)
BMI [kg/m^2]	24.02 ± 4.15 (21.2–30.4)
Grade of anaphylactic reaction	III – 2 patients IV – 4 patients
Other allergic sensitization (positive skin-prick test and symptoms)	Only 1 patient was sensitized to a tree, grass pollen, and cat allergens
IgE before VIT:	
Total	71 ± 53.67 KU/l
Wasp specific (asIgE)	1.75 ± 0.41 KU/l
Blood baseline tryptase	Mastocytosis was excluded, the tryptase levels were normal

Table 2. Protocol for venom immunotherapy. Rush method for initiation of the therapy [5]

Day 1: 0.1 μg , 1.0 μg , 2 μg , 4 μg , 8 μg , 10 μg , 20 μg 7 s.c. injections at 30 min intervals
Day 2: 40 μg , 60 μg , 80 μg and 100 μg fore s.c. injections at 30–60 min intervals
and continuation 100 μg s.c. monthly

Table 3. Pregnancy complications related to maternal and fetal birth status

VIT duration before fertilization [months]	Pregnancy complications	Fetal birth status
11	Heartburn	APGAR: 9 Gestational age at birth: 41 weeks Birth weight: 4.6 kg Cesarean delivery because of fetus weight and small maternal pelvis making vaginal birth impossible
16	Hyperemesis gravidarum	APGAR: 10 Gestational age at birth: 40 Birth weight: 3.56 kg Benign hip dysplasia
41	Cervical insufficiency	APGAR: 10 Gestational age at birth: 38 Birth weight: 3.3 kg
45	Gestational diabetes mellitus treated with diet	APGAR: 10 Gestational age at birth: 38 Birth weight: 3.08 kg
34	Gestational diabetes mellitus treated with diet and heartburn	APGAR: 10 Gestational age at birth: 40 Birth weight: 4.16 kg
12	Nausea	APGAR: 10 Gestational age at birth: 40 Birth weight: 3.4 kg

A specific venom immunotherapy is an important and recommended method of the curative treatment of patients with a high risk of a bad outcome [12]. Venom immunotherapy is effective and lessens the risk of a systemic reaction, prevents morbidity and mortality and improves the quality of life. The advised duration of VIT is 5 years. In the case of young women in the reproductive period, there is high probability of gestation [10, 13].

These studies confirm an earlier observation that VIT is safe for pregnant women. The data presented show that all the newborns were in a good condition. All babies were without congenital defects or fetal malformations and were born in a good condition. Except for one newborn who obtained nine APGAR points, all babies were given ten APGAR points.

The frequency of complications in mothers in our study did not demonstrate any apparent increase above that observed in pregnant women who did not receive VIT.

Conclusions

Pregnant women with a medical history of severe anaphylactic reactions after hymenoptera stings are at risk of potentially life-threatening reactions that result from insect re-stings. Self-injectable epinephrine, the current standard of treatment for anaphylaxis, also carries the risk of severe complications. Our studies have shown that VIT is safe for pregnant women and for infants.

Conflict of interest

The authors declare no conflict of interest.

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