

Short report

Kissing selectively decreases allergen-specific IgE production in atopic patients

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Abstract

Objective: Stress enhanced allergic skin wheal responses and allergen-specific IgE production. In contrast, mothers' kissing caused relaxation in infants, and kissing by lovers or spouses to atopic patients reduced allergic skin wheal responses. I studied the effect of kissing on production of allergen-specific IgE and cytokines in atopic patients. **Methods:** Twenty-four patients with mild atopic eczema and 24 patients with mild allergic rhinitis kissed with lovers or spouses freely for 30 min while listening to

soft music. Just before and immediately after kissing, blood mononuclear cells were separated cultured for allergen, and production of allergen-specific immunoglobulin and cytokine was measured. **Results:** Kissing selectively decreased allergen-specific IgE production with skewing cytokine pattern toward Th1 type. **Conclusion:** Kissing may alleviate allergic symptoms by decrease in allergen-specific IgE production.

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Keywords: Kissing; Atopic eczema; Allergic rhinitis; Japanese cedar pollen; Allergen-specific IgE production

Introduction

Increased stress in early childhood is associated with atopic immune profile [1]. In fact, stress enhanced allergic skin wheal responses and allergen-specific IgE production in atopic patients [2]. In contrast, I have reported that relaxation by laughter or listening to Mozart reduces allergic responses and decreases allergen-specific IgE production [3–5]. It has been reported that mothers' kissing causes relaxation in healthy infants [6]. Moreover, I have previously reported that kissing by lovers or spouses to atopic patients reduces allergic responses and skews cytokine pattern toward Th1 type [7]. These reports prompted me to study whether kissing could modulate production of allergen-specific IgE and cytokines in atopic patients.

Methods

Subjects

Twenty-four patients with mild atopic dermatitis (AD) (12 females and 12 males; mean age, 28 years; range, 22–34 years), who were allergic to Japanese cedar pollen (JCP), house dust mite (HDM), and latex, and 24 patients with mild allergic rhinitis (AR) (12 females and 12 males; mean age, 26 years; range, 21–32 years), who were allergic to JCP, were recruited after obtaining informed consent. All of the patients were outpatients at the Department of Allergy, Satou Hospital. All of them are Japanese, and they do not kiss habitually. Allergy to each allergen was confirmed by positive serum allergen-specific IgE levels (mean $\pm$ S.E.M.) as follows: JCP-specific IgE, 57.1 ± 3.2 IU/ml in AD patients and 70.3 ± 4.1 IU/ml in AR patients; HDM-specific IgE, 72.5 ± 4.5 IU/ml in AD patients; latex-specific IgE 36.9 ± 1.4 IU/ml in AD patients. All of the AD patients were treated with application of mixtures of pinetar (Yoshida Pharmaceuticals, Tokyo, Japan) and zinc ointments, but without oral medication [5].

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Table 1
Effect of kissing on JCP-specific immunoglobulin and cytokine

Effect of kissing on JCP-specific immunoglobulin and cytokine								
	Ig and cytokine production							
	AD				AR			
	Control study		Kissing study		Control study		Kissing study	
	Before	After	Before	After	Before	After	Before	After
(A) JCP-specific immunoglobulin (ng/ml)								
IgE	2.3 (0.2)	2.5 (0.2)	2.6 (0.2)	1.1 (0.1)*	4.9 (0.4)	4.7 (0.5)	4.5 (0.5)	2.9 (0.3)*
IgG ₄	1.9 (0.2)	2.2 (0.2)	2.0 (0.2)	1.7 (0.2)	6.2 (0.6)	6.4 (0.6)	6.9 (0.8)	6.6 (0.7)
IgA ₁	1.6 (0.1)	1.9 (0.1)	1.4 (0.2)	1.6 (0.1)	3.5 (0.3)	3.8 (0.4)	3.2 (0.3)	3.5 (0.4)
(B) Cytokine (pg/ml)								
IFN-γ	152 (9)	135 (8)	143 (9)	286 (11)**	346 (25)	309 (21)	358 (26)	457 (35)**
IL-12	157 (10)	148 (9)	144 (9)	207 (9)**	268 (16)	282 (19)	234 (18)	377 (28)**
IL-4	203 (11)	235 (12)	209 (11)	134 (8)*	573 (38)	548 (37)	594 (45)	416 (32)*
IL-10	168 (11)	186 (11)	180 (13)	106 (4)*	259 (10)	282 (12)	290 (13)	153 (8)*
IL-13	239 (12)	256 (13)	278 (12)	145 (9)*	465 (31)	433 (34)	491 (37)	352 (24)*

AD or AR patients embraced lovers or spouses without kissing (control study) or with kissing (kissing study) for 30 min while listening to music. Before and after each study, blood mononuclear cells were separated and cultured with JCP. Production of JCP-specific IgE, IgG₄ and IgA (A) and cytokines (B) was measured. Values are means (S.E.M.).

* $P < .01$, significant decrease compared to before.

** $P < .01$, significant increase compared to before.

All of the AR patients had no nasal symptoms at the time of study; thus, they did not take any oral medication. AD or AR patients were randomly assigned to two groups that contained 12 subjects each.

Study design

In the kissing study, subjects from one group kissed with their lover or spouse freely for 30 min alone in a room with closed door while listening to soft music (Beauty and the Beast, When You Wish Upon a Star, My Heart Will Go On, Love is a Many Splendored Thing, Moon River, Sunrise Sunset, Can You Feel the Love Tonight) [7]. In the control study, which was conducted after 2 weeks, each subject from two groups embraced a lover or spouse, but without

kissing, for 30 min in the same room while listening to the same music. Alternatively, the other 12 subjects from the AD or AR patients first conducted the control study, and after 2 weeks, they conducted the kissing study. Just before and immediately after each study, blood was sampled and mononuclear cells were separated, and they were cultured ($2 \times 10^4/0.2$ ml per well) with JCP (0.1 ng/ml) (Torii Pharm., Tokyo, Japan). Production of JCP-specific Ig was measured after 14 days by ELISA, while production of cytokines (IL-4, IL-10, IL-12, IL-13, and IFN- γ) was measured after 5 days by ELISA (R & D Systems, Minneapolis, MN) [4]. The culture medium was serum-free medium, DME, supplemented with Hams' Nutrient (DMA/F-12; Sigma, St. Louis, MO), 0.5% BSA, and 50 μ g/ml transferrin [2]. Moreover, mononuclear cells from

Table 2
Effect of kissing on HDM- or latex-specific immunoglobulin and cytokine

	Ig and cytokine production							
	HDM-simulated cultures				Latex-simulated cultures			
	Control study		Kissing study		Control study		Kissing study	
	Before	After	Before	After	Before	After	Before	After
(A) Allergen-specific immunoglobulin (ng/ml)								
IgE	4.5 (0.3)	4.8 (0.3)	4.1 (0.3)	2.6 (0.2)*	2.1 (0.2)	2.4 (0.2)	2.5 (0.2)	0.7 (0.1)*
IgG ₄	2.4 (0.2)	2.6 (0.2)	2.5 (0.2)	2.1 (0.2)	1.8 (0.2)	1.5 (0.2)	1.9 (0.2)	1.6 (0.2)
IgA ₁	1.0 (0.1)	0.8 (0.1)	1.2 (0.2)	1.4 (0.1)	0.8 (0.1)	1.1 (0.1)	1.2 (0.1)	0.9 (0.1)
(B) Cytokine (pg/ml)								
IFN- γ	124 (7)	117 (7)	129 (9)	245 (12)**	170 (10)	149 (9)	140 (9)	239 (11)**
IL-12	169 (11)	184 (11)	157 (10)	285 (13)**	237 (11)	270 (12)	281 (13)	420 (30)**
IL-4	215 (11)	206 (12)	243 (12)	109 (5)*	486 (41)	451 (39)	434 (34)	374 (29)*
IL-10	192 (10)	168 (10)	173 (11)	112 (4)*	154 (9)	125 (8)	170 (11)	71 (4)*
IL-13	281 (13)	291 (14)	252 (12)	169 (7)*	356 (27)	329 (25)	399 (30)	119 (8)*

AD patients embraced lovers or spouses with or without kissing as Table 1. Before and each study, blood mononuclear cells were separated and cultured with HDM or latex. Production of each allergen-specific IgE, IgG₄, and IgA (A) and cytokines (B) were measured. Values are means (S.E.M.).

* $P < .01$, significant decrease compared to before.

** $P < .01$, significant increase compared to before.

AD patients were cultured ($2 \times 10^4/0.2\text{ml/well}$) with HDM (0.1 ng/ml) (Torii Pharm.) or latex (0.1 ng/ml) (C-serum, kindly provided by Dr. Akira Akasawa, Department of Allergy and Immunology, National Research Institute for Child Health and Development, Tokyo, Japan) [4]. Production of each allergen-specific Ig and cytokine was measured after 14 and 5 days, respectively [2]. This study was approved by the Ethical Committee of Satou Hospital. Statistical analysis was performed with Wilcoxon signed rank test.

Results and discussion

As shown in Table 1, production of JCP-specific IgE, IgG₄, or IgA was not affected in the control study in AD or AR patients. In contrast, JCP-specific IgE production was decreased in the kissing study without affecting production of JCP-specific IgG₄ or IgA₁ in these atopic patients. Production of JCP-specific IgG₁, IgG₂, IgG₃, IgM, or IgA₂ was not induced (<0.15 ng/ml) in the control or kissing study in AD patients or AR patients as previously reported [8].

We and others have reported that allergen-specific IgE production was decreased by Th1 cytokine (IFN- γ and IL-12), while it was increased by Th2 cytokines (IL-4, IL-10, and IL-13) [8–10]. Thus, the effect of kissing on cytokine production was studied. As shown in Table 1, production of these cytokines was not affected in the control study in AD or AR patients. However, kissing significantly increased production of Th1 cytokine (IFN- γ and IL-12), while it significantly decreased production of Th2 cytokines (IL-4, IL-10, and IL-13), indicating that cytokine pattern was skewed toward Th1 type.

The effect of kissing was further studied for other allergen-stimulated responses. Since AD patients were allergic to HDM and latex, allergen-induced responses by HDM or latex were measured before and after kissing. As shown in Table 2, neither production of HDM-specific Ig nor latex-specific Ig nor production of cytokines by HDM or latex stimulation was affected in the control study. In contrast, kissing selectively decreased production of HDM-specific IgE and latex-specific IgE in HDM- and latex-stimulated cultures, respectively. This decrease in allergen-specific IgE production was associated with skewing cytokine pattern toward Th1 type in cultures stimulated with corresponding allergen, since kissing increased the production of Th1 cytokine (IFN- γ and IL-12), while it significantly decreased production of Th2 cytokines (IL-4, IL-10 and IL-13).

It has been suggested that modern medical therapeutic strategies may impair future ability to respond biologic disequilibria; thus, lifestyle approaches may expand the dynamic range of biologic experiences [11]. In addition, since many of AD patients have mood disorder, AD-related

perceptions of stigma are important in predicting AD-related quality of life over and above more general psychological factors, such as depression [12]. The impacts of psychologically mediated triggers on asthmatic children have also been reported [13]. On the other hand, stress-moderating effects of humor and laughter on physical health have been suggested [14].

Kissing induced earlier conflict resolution, thus mitigated emotional stress [15]. It is tempting to speculate that relaxation by kissing may decrease allergen-specific IgE production via skewing cytokine pattern toward Th1 type. Collectively, these results indicate for the first time that kissing may alleviate allergic responses.

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