

Suckling Reduces Allergic Skin Responses and Plasma Levels of Neuropeptide and Neurotrophin in Lactating Women with Atopic Eczema/Dermatitis Syndrome

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Key Words

Suckling · Skin prick test · Substance P · Vasoactive intestinal peptide · Nerve growth factor · Atopic eczema/dermatitis syndrome

Abstract

Background: Lactation is associated with an inhibited hypothalamic-pituitary-adrenal axis response to physical and psychological stress in women and female rats. However, suckling also improved mood and calmness in nonatopic lactating women. Relaxation by humor reduced allergen-induced skin wheal responses, while various forms of stress enhanced those responses in allergic patients. Moreover, enhancement and reduction in allergen-induced skin wheal responses are associated with up- and down-regulation of plasma levels of substance P (SP) and vasoactive intestinal peptide (VIP), respectively. In addition, plasma levels of SP, VIP and nerve growth factor (NGF), but not neurotrophin-3 (NT-3), are elevated in allergic patients. Therefore, the effects of suckling on allergic responses and plasma levels of neuropeptides and neurotrophins were studied in lactating women with atopic eczema/dermatitis syndrome (AEDS). **Methods:** Before and after suckling, allergic skin responses to allergens were studied by skin prick test; simultaneously plasma levels of substance P, vasoactive

intestinal peptide, nerve growth factor and neurotrophin-3 were measured in lactating women with atopic eczema/dermatitis syndrome. **Results:** Suckling reduces allergen-induced, but not histamine-induced, skin wheal responses, while holding infants without suckling failed to do so. Suckling also reduced plasma levels of SP, VIP and NGF, but not NT-3 in these patients, while holding infants without suckling failed to do so. **Conclusions:** These results indicate that suckling reduces allergic responses with a concomitant reduction in plasma levels of SP, VIP and NGF. Collectively, suckling may have some implication in the study of maternal allergy in atopic patients.

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Introduction

It has been reported that lactation is associated with restraint of hypothalamic-pituitary-adrenal axis response to physical and psychological stress in women and female rats [1, 2]. It has also been reported that suckling improved mood and calmness in nonatopic lactating women, while holding the infants without suckling failed to do so [3]. However, the effect of suckling on allergic responses has not been reported. In patients with atopic eczema/dermatitis syndrome (AEDS), hypothalamic-pi-

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tuitary-adrenal axis responses are blunted [4]. I previously reported that relaxation by humor reduced allergen-induced skin wheal responses, while various forms of stress enhanced them in patients with AEDS or allergic rhinitis [5–7]. Moreover, enhancement and reduction of allergen-induced skin wheal responses are associated with up- and down-regulation of plasma levels of substance P (SP) and vasoactive intestinal peptide (VIP), respectively [7]. In addition, plasma levels of SP, VIP and nerve growth factor (NGF), but not neurotrophin-3 (NT-3), are elevated in allergic patients [7–9]. Moreover, plasma levels of NGF, but not SP or VIP, were also elevated during lactation [10]. These reports prompted me to study the effect of suckling on allergic skin responses and plasma neuropeptides and neurotrophins in lactating women with AEDS.

Methods

After obtaining informed consent, 60 lactating women with AEDS who were between 8 and 12 weeks postpartum were studied. All of the patients were treated at our outpatient clinic with azulene ointment, but without any oral medication, and were recruited by advertisement at the hospital. They were randomly assigned to two groups. One group (control group) consisted of 30 women (mean age 25 years, range 22–28 years; mean 9.4 weeks postpartum), while the other group (suckling group) consisted of 30 women (mean age 25 years, range 21–29 years; mean 9.6 weeks postpartum). All of the patients had mild AEDS according to the SCORAD index and there was no difference in the SCORAD index between the control group (mean 11, range 7–13) and the suckling group (mean 11, range 8–13) [11]. All of the patients were allergic to house dust mite and Japanese cedar pollen as proven by a skin prick test and anti-house dust mite and anti-Japanese cedar pollen serum IgE levels. There were no significant differences in the clinical severity of the skin symptoms, skin wheal responses to house dust mite and Japanese cedar pollen by the skin prick test, and anti-house dust mite and anti-Japanese cedar pollen serum IgE levels between the two groups. They took no oral medication for 72 h prior to the study. In the control group, 30 AEDS patients bottle-fed their infants for 15 min, while in the suckling study another 30 AEDS patients breast-fed their infants for 15 min. Twenty minutes before and immediately after the study, skin prick tests were performed using commercial house dust mite allergen, Japanese cedar pollen allergen (Torii Pharm. Co., Ltd., Tokyo) as well as control solution and histamine (10 mg/ml) (Sigma Chemical Co., St. Louis, Mo., USA), and 15 min later, the wheal size was measured by staff who were blinded to the suckling status of the mothers [7]. The concentration of allergen extract for the skin prick test was titrated by comparison with the histamine control of each patient, and the optimal concentration was found to be the undiluted one. Therefore, undiluted allergen extract was used. All of the 30 patients were studied at the same time as a group. Immediately after the prick test, i.e., 20 min before and immediately after suckling or bottle-feeding, blood was drawn and plasma levels of SP, VIP, NGF and NT-3 were measured by ELISA according to the manufacturer's protocol:

plasma levels of SP and VIP were measured by ELISA purchased from Peninsula Laboratories Inc. (Calif., USA), while plasma levels of NGF and NT-3 were measured by ELISA purchased from Boehringer Mannheim Corp. (Mannheim, Germany) by staff who were blinded to the suckling status of the mothers [7–9]. In some experiments, plasma prolactin levels were measured by ELISA (IBL, Hamburg, Germany) by staff who were blinded to the suckling status of the mothers. Control mothers breast-fed their babies at other times. This study was approved by the Ethical Committee of our hospital. Statistical analysis was performed with the nonparametric Wilcoxon t test.

Results

As shown in table 1, the wheal responses induced by house dust mite, Japanese cedar pollen and histamine were not changed in the controls. In contrast, the wheal responses to house dust mite and Japanese cedar pollen were significantly reduced by suckling. This was not due to a nonspecific effect of the skin, as no reduction in wheal responses were induced by histamine in these subjects. Moreover, plasma levels of SP, VIP and NGF were significantly decreased by suckling but not in the controls. Again, this was not due to a nonspecific effect of suckling, since plasma levels of NT-3 were not reduced (table 1). Moreover, each decline in SP, VIP or NGF correlated with a reduction in skin wheal responses to house dust mite ($p < 0.0001$) or Japanese cedar pollen ($p < 0.0001$) by the χ^2 test.

In 20 AEDS patients, plasma prolactin levels [median (interquartile ranges) ng/ml] measured at baseline and after 15, 60 and 120 min of suckling were 16.1 (10.1–21.7), 41.9 (33.5–51.6), 31.2 (24.6–40.2), and 19.0 (13.4–25.8), respectively. The skin wheal responses [median (interquartile ranges) mm] by house dust mite at baseline and after 15, 60 and 120 min of suckling were 6.8 (4.8–8.1), 5.1 (3.8–6.6), 5.8 (4.1–7.0), and 6.6 (4.7–8.0), respectively.

In contrast, plasma prolactin levels were not elevated in controls [16.3 (10.5–22.1) at baseline vs. 16.0 (10.1–23.4) after 15 min vs. 17.4 (10.9–23.8) after 60 min vs. 16.9 (10.8–24.1) after 120 min].

I have also studied the effect of suckling in lactating women with allergic rhinitis ($n = 25$) or bronchial asthma ($n = 17$). Suckling significantly ($p < 0.001$) reduced skin wheal responses to Japanese cedar pollen from 6.5 (5.4–7.8) mm to 4.0 (3.3–4.8) mm in patients with allergic rhinitis and the responses to house dust mite from 7.3 (5.6–8.8) to 5.3 (4.6–6.0) mm in patients with bronchial asthma.

Table 1. Effect of suckling on skin wheal responses and plasma neuropeptides and neurotrophins

	Control		Suckling	
	before	after	before	after
<i>Skin wheal responses, mm</i>				
House dust mite	6.2 (4.9–7.0)	6.4 (5.6–7.1)	6.8 (5.6–7.7)	4.7 (4.0–5.8)*
Japanese cedar pollen	5.2 (4.6–6.2)	5.5 (4.9–6.3)	5.3 (4.7–6.2)	4.1 (3.6–4.7)**
Histamine	5.5 (4.7–6.8)	5.7 (4.6–6.9)	6.1 (4.8–7.2)	6.3 (4.7–7.1)
Control solution	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)
<i>Plasma, pg/ml</i>				
SP	84 (79–92)	85 (73–96)	89 (80–97)	66 (59–69)**
VIP	33 (28–39)	34 (27–42)	35 (24–41)	21 (17–25)**
NGF	825 (660–935)	800 (640–999)	841 (690–975)	640 (558–801)#
NT-3	589 (510–686)	593 (518–692)	557 (482–673)	566 (491–680)

AEDS patients fed infants by bottle feeding (control) or breast feeding (suckling).

Skin wheal responses to house dust mite, Japanese cedar pollen, histamines or control solution were studied before and after bottle feeding or breast-feeding. Simultaneously, plasma levels of SP, VIP, NGF and NT-3 were measured.

Values are medians (interquartile ranges are shown in parentheses). * $p = 0.001$, ** $p < 0.0001$, and # $p = 0.0009$, significant reduction (compared to before).

Discussion

These results suggest that suckling reduces allergen-induced skin wheal responses in association with a reduction in plasma levels of SP, VIP and NGF, but not NT-3. The mechanisms of differential modulation of plasma levels of SP, VIP, and NGF vs. NT-3 remain to be elucidated, but this is not surprising. It has been reported that various forms of stress enhance allergen-induced skin wheal responses and plasma levels of SP, VIP and NGF, but not NT-3 in humans [5–9]. SP, VIP, and NGF were involved in mast cell degranulation, while the role of NT-3 in mast cell degranulation remains to be elucidated [12]. It was also reported that immobilization stress enhanced SP expression in rats, while it had no effect on NT-3 expression [13]. Collectively, SP, VIP and NGF may be involved in allergic and stress responses, while NT-3 may not be involved in those responses.

It was reported that suckling improved mood and calmness in lactating nonatopic women, while holding the infants without suckling failed to do so [3]. Suckling also leads to positive physiologic changes [14]. These results indicate that suckling may alleviate stress. It has been reported that humor reduces allergen-induced skin wheal responses, while stress enhances those responses and plasma SP, VIP and NGF levels [5–7]. Therefore, it would be tempting to speculate that suckling reduces allergic re-

sponse with concomitant reduction of plasma levels of SP, VIP and NGF by alleviating stress.

It should be pointed out that the effect of suckling may be due to a rise in plasma prolactin levels [3], since prolactin may contribute to adaptive changes in stress responsiveness in rats [15]. Plasma prolactin levels were elevated in suckling AEDS patients, while plasma prolactin levels were not elevated in the control study, which is in accordance with previous reports [3]. A detailed study is currently in progress.

These findings indicate that suckling may have some implication in the study of maternal allergy in atopic patients.

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