Viewing Humorous Film Improves Night-time Wakening in Children with Atopic Dermatitis

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Manuscript received: August 26, 2006; Initial review completed: October 16, 2006; Revision accepted: December 11, 2006.

Introduction: *Patients with atopic dermatitis suffered from night-time wakening, but the exact mechanism of it was not known. Ghrelin was involved in growth hormone secretion, regulation of appetite, anxiety, night-time wakening and stress.* ***Methods:*** *Thus salivary ghreli levels during the night were measured in 40 healthy children or 40 patients with atopic dermatitis with night-time wakening. Salivary ghrelin levels at 02:00 h were markedly elevated in patients with atopic dermatitis compared to those in healthy children.* ***Results:*** *Neither viewing control non-humorous film nor viewing humorous film had any effect on healthy children. In contrast, viewing humorous film improved night-time wakening and reduced elevation of salivary ghrelin levels in patients with atopic dermatitis, while viewing control film failed to do so.* ***Conclusion:*** *Viewing humorous film may be useful in the treatment of night-time wakening in patients with atopic dermatitis.*

Key words: *Atopic dermatitis, Night-time wakening, Salivary ghrelin, Viewing humorous film.*

CHILDREN with atopic dermatitis (AD) often suffer from night-time wakening which is caused either by itching or mental stress, though exact mechanisms are not known(1-3). Night-time waking of children cause parental sleep disturbance, tiredness and exhaustion(3). Ghrelin is involved in growth hormone secretion, regulation of appetite, anxiety, night-time wakening and stress(4-6). Moreover, serum ghrelin levels are elevated in colicky infants(7). Salivary levels of ghrelin also correlate with plasma levels of ghrelin, and measurement of salivary ghrelin is non-invasive and useful in children(8). Therefore, salivary ghrelin levels were measured during the night in AD patients. On the other hand, we have previously reported that viewing humorous film reduces stress and allergic responses in AD patients(9). Therefore, the effect of viewing humorous film on night-time wakening and salivary ghrelin levels was also studied.

Subjects and Methods

After obtaining consent from parents, 40 non-obese healthy children (40 male, mean age 5 years, range 4-6 years, mean body mass index [BMI] 16, range 14-18) without night-time wakening and 40 non-obese patients with moderate AD (scoring atopic dermatitis [SCORAD] index: mean 29, range 20-36) (40 male, mean age 5 years, range 4-6 years, mean BMI 16, range 14-18) were studied(10). Since nocturnal ghrelin secretion is different between male and female(11) the study was conducted in male children(11). All of the AD patients complained night-time wakening. They were treated locally washing with povidone iodine and application of pinetar (Yoshida Pharmaceutical Co. Ltd. Tokyo, Japan) with zinc oxide ointment, but without oral medication(9).

At baseline study, 40 healthy children and 40 AD patients viewed no film, and they slept at sleep laboratory in the hospital at 21:00 hr and saliva was collected without stimulation at 23:00, 02:00 and 05:00 h during the night. Thereafter, randomly assigned 20 healthy children and 20 AD patients first viewed humorous film "The Best Bits of Mr. Bean" (72 min, Universal studios, 1996) at 19:00 h, and after 2 weeks, they viewed 72 min control non-humorous weather information film (72 min) at 19:00 h. Alternatively, another 20 healthy children and 20 AD patients first viewed control weather information film, and after 2 weeks they viewed humorous film. All of the subjects slept at

sleep laboratory at 21:00 h, and saliva was collected without stimulation. Each study was repeated three times (designated as study 1, 2 and 3), and each time number of subjects with night-time wakening was measured, although sampling of saliva was collected only once (study 1). Night-time wakening was assessed by staff who were blinded to study. Salivary active ghrelin levels were measured by radioimmunoassay (LINCO Research, St Charles, MO. USA) by staff who were blinded to study. As control, salivary amylase levels were measured by Kit α-amylase Colorimetric Test (Diagnostica, Merck, Germany). Statistical analysis was performed with repeated measures of ANOVA. Results were expressed as mean (95% CI). Statistical analysis was performed with repeated measured of ANOVA, and P values, Chohen's d and effect sizes (ES) were also calculated.

This study was approved by the Ethical Committee of Moriguchi-Keijinkai Hospital.

Results

As shown in *Table I*, viewing control film had no effect on night-time wakening in AD patients, while viewing humorous film improved night-time wakening in 36 AD patients out of 40. Therefore, only 4 AD patients had night-time wakening after viewing humorous film. None of healthy subjects had night-time wakening, and neither viewing control film nor viewing humorous film had any effect on night-time wakening on them (data not shown).

As shown in *Table II*, there was no difference of nocturnal salivary ghrelin levels at 23:00 h or at 00:50 h between healthy children and patients with AD at baseline (without viewing film). In contrast, nocturnal salivary ghrelin levels were significantly ($P < 0.01$) elevated at 00:20 h in patients with AD in comparison with those at 23:00 h, while they were not elevated in healthy subjects at 02:00 h. Neither viewing control film nor humorous film had any effect on salivary ghrelin levels in healthy children at any time measured during the night. In contrast, viewing humorous film significantly reduced elevation of salivary ghrelin levels in AD patients at 02:00 h, while viewing control film failed to do so. This was not non-specific effect, since viewing humorous film had no effect on salivary ghrelin levels at 23:00 h or 05:00 h, and moreover, salivary amylase levels were not reduced at any time measured (*Table III*).

Discussion

We have demonstrated that salivary ghrelin levels at 02:00 h are elevated in AD patients compared to healthy children. This nocturnal elevation of salivary ghrelin may cause night-time wakening in AD patients, since viewing humorous film improved night-time wakening and reduced elevation of ghrelin levels. Although the effect of

TABLE I– *Effect of Viewing Humorous Film on Night-time Wakening in Patients with Atopic Dermatiits*

	Number of subjects with night-time wakening					
	Baseline study		Viewing control film		Viewing humorous film	
	Before	After	Before	After	Before	After
Study 1	40	40	40	40	40	4
Study 2	40	40	40	40	40	4
Study 3	40	40	40	40	40	4
Mean*	40	40	40	40	40	4**
95% CI	40-40	40-40	40-40	40-40	40-40	4-4
P	NS		NS		<0.01	

Numbers of subjects having night-time wakening are shown.
* Values are the mean of three studies, and 95% CI, and p values in comparing "Before" and "After" shown. NS = not significant.
** Signifcant decrease compared to number of Baseline study.

TABLE II–*Effect of Viewing Humorous Films on Salivary Ghrelin Levels*

Time	Healthy children		Patients with atopic dermatitis	
	Mean (95% CI)	P	Mean (95% CI)	P
23:00 h				
Baseline	26.5 (23.4-29.6)		28.3 (24.8-31.8)	
Control film	27.3 (24.0-30.6)	NS	29.1 (25.4-32.8)	NS
Humorous film	25.8 (22.9-28.7)	NS	28.4 (24.5-32.3)	NS
02:00 h				
Baseline	27.6 (24.3-30.9)		39.5 (35.2-43.8)	
Control film	28.5 (24.8-32.2)	NS	40.1 (35.6-44.6)	NS
Humorous film	26.3 (23.2-29.4)	NS	29.1 (25.2-33.0)*	<0.01
00:50 h				
Baseline	25.7 (22.8-28.6)		29.2 (27.0-34.8)	
Control film	25.8 (23.4-28.2)	NS	30.9 (27.0-34.8)	NS
Humorous film	27.2 (23.9-30.5)	NS	28.6 (24.9-32.3)	NS

Values are the means of 40 subjects in each group, and 95% CI and P values in comparing "Baseline" and "Control film" or "Humorous Film" are shown. NS = not significant.
* Significant reduction compared to values of Baseline.

TABLE III*: Effect of Viewing Humorous Films on Salivary Amylase Levels*

Time	Healthy children		Patients with atopic dermatitis	
	mean (95% CI)	P	mean (95% CI)	P
23:00 h				
Baseline	73.0 (61.0-85.0)		74.5 (62.3-86.7)	
Control film	72.6 (62.0-84.2)	NS	76.8 (66.2-89.3)	NS
Humorous film	74.6 (62.4-86.8)	NS	77.0 (64.3-89.5)	NS
02:00 h				
Baseline	75.2 (63.0-87.4)		72.5 (60.7-84.3)	
Control film	76.9 (64.6-89.2)	NS	73.7 (61.5-85.9)	NS
Humorous film	77.1 (64.2-90.0)	NS	73.4 (61.4-85.4)	NS
00:50 h				
Baseline	73.9 (61.9-85.9)		77.1 (64.6-89.6)	
Control film	75.8 (63.5-88.1)	NS	75.2 (63.4-87.2)	NS
Humorous film	74.6 (62.3-86.2)	NS	78.0 (65.3-90.7)	NS

Values are the means of 40 subjects in each group, and 95% CI, and P values in comparing "Baseline" and "Control film" or "Humorous film" are shown. NS = not significant.

ghrelin on emotional responses remains to be elucidated, elevation of ghrelin levels were reported in sleep disturbance, anxiety and night-time wakening(3,4). Moreover, serum ghrelin levels were elevated in patients with epilepsy(12). Ghrelin injection in rats induces wakefulness(13). Stress increased ghrelin levels and patients with colicky pain had elevated serum ghrelin levels(6,7) Since AD patients are vulnerable to stress, it is tempting to speculate that chronic stress may elevate nocturnal

What this Study Adds

- Viewing humorous film improved night-time wakening with reduction of nocturnal elevation of salivary ghrelin in children with atopic dermatitis.

salivary ghrelin levels, which in turn may cause night-time wakening(14).

It was reported that there was a inverse correlation between plasma ghrelin levels and IgE levels, in which plasma levels of ghrelin in allergic patients (AD or bronchial asthma) only at one point were measured(15). We have sequentially measured salivary ghrelin levels during night and found no difference of salivary ghrelin levels at baseline between healthy children and AD patients, except nocturnal elevation at 02:00 h in AD patients. More detailed study should be carried out to elucidate the relationship of ghrelin in allergic diseases.

We also demonstrated that viewing humorous film reduced elevation of nocturnal salivary ghrelin and improved night-time wakening in AD patients. This is not surprising. We have previously reported that viewing humorous film counteracts (*i*) stress-induced enhancement of allergic responses and neurotrophin production in AD patients, (*ii*) allergen-induced IgE production, and (*iii*) bronchial responsiveness to methacholine or allergen in patients with bronchial asthma(5,16,17). It is possible that relaxation caused by viewing humorous film may reduce elevation of nocturnal salivary ghrelin levels, which in turn may improve night-time wakening. Study is currently in progress to elucidate the mechanisms.

Nocturnal ghrelin secretion were higher in female adults compared to those in male adults (11). Thus, we also measured nocturnal ghrelin levels in female healthy children without night-time wakening or female AD patients with night-time wakening. Salivary ghrelin levels (mean [95% CI] fmol/mL) at 02:00 h in baseline study in female healthy children (n = 40, mean age 5 years) and female moderate AD patients (n = 40, mean age 5 years) were 32.4 [28.3-36.5] and 46.5 [41.2-51.8], respectively, which were higher than those in male children. After viewing humorous film, night-time wakening was improved in 37 AD patients out of 40, while night-time wakening was not improved in any AD patients after viewing control film. Moreover, salivary ghrelin levels in female healthy children were not reduced after viewing control film or humorous film: salivary ghrelin levels after viewing control film and humorous film were 33.4 [29.1-37.7] and 32.9 [29.0-36.8], respectively. In contrast, viewing humorous film significantly reduced salivary ghrelin levels in female AD patients, while viewing control film failed to do so: salivary ghrelin levels in female AD patients after viewing control film and humorous film were 47.4 [41.9-52.9] and 33.6 [29.1-38.1] ($P<0.01$) compared to 46.5 [41.2-51.8] at 02:00 h in baseline as above), respectively.

Collectively, it would be tempting to speculate that ghrelin may be involved in stress responses, and alleviation of stress by viewing humorous film may improve nocturnal elevation of ghrein production and night-time wakening in AD patients. Measure-ment of salivary ghrelin levels is non-invasive and useful in the study of ghrelin production, and viewing humorous film may be useful in the treatment of night-time wakening in AD patients.

Funding: None.
Competing interests: None stated.

REFERENCES

1. Reuveni H, Chaonick G, Tal A. Sleep fragmentation in children with atopic dermatitis. Arch Pediatr Adolesc Med 1999; 153: 249-253.
2. Stores G, Burrows A, Crawford C. Physiological sleep disturbance in children with atopic dermatitis: a case control study. Pediatr Dermatol 1998; 15: 264-268.
3. Lewis-Jones MS, Finlay AY, Dykes PJ. The infants' dermatitis Quality of Life Index. Br J Dermatol 2001; 144: 104-110.

4. Carlini VP, Varas MM, Cragnolini AB, Schioth HB, Scimonelli TN, de Baroglio S. Differential role of the hippocampus, amygdala, and dorsal raphe nucleus in regulating feeding, memory, and anxiety-like behavioral responses to ghrelin. Biochem Biophys Res Commun 2002; 299: 739-743.

5. Taheri S, Lin L, Austin D, Young T, Mignot E: Short sleep duration associated with reduced leptin, elevated ghrelin, and increased body mass index. PLos Med 2004; 1: 210-217.

6. Kristenssson E, Sundqvist M, Astin M, Kjerling M, Mattson H, de la Cour CD, *et al.* Acute psychological stress raises plasma ghrelin in the rat. Regul Pept 2006; 134: 114-117.

7. Savino F, Grassino E, Guidi C, Oggero R, Silvestro L, Minero R. Ghrelin and motilin concentration in colicky infants. Acta Paediatr 2006; 95: 738-741.

8. Aydin S, Halifeoglu I, Ozercan IH, Erman F, Kilic N, Aydin S, *et al.* A comparison of leptin and ghrelin levels in plasma and saliva of young healthy subjects. Peptides 2005; 26: 647-652.

9. Kimata H. Laughter counteracts enhancement of plasma neurotrophin levels and allergic skin wheal responses by mobile phone-mediated stress. Behav Med 2004; 29: 149-152.

10. Kunz B, Oranje AP, Labreza L, Stalder J-F, Ring J, Taieb A. Clinical validation and guidelines for the SCORAD index: Consensus report of the European Task Force on atopic dermatitis. Dermatology 1997; 195: 10-19.

11. Schussler P, Uhr M, Ising M, Schmid D, Steiger A. Nocturnal ghrelin levels-relationship to sleep EEG, the levels of growth hormone, ACTH and cortisol-and gender differences. J Sleep Res 2005; 14: 329-336.

12. Berigen MS, Ungen B, Ustundag B, Demir C. Serum ghrelin levels are enhanced in patients with epilepsy. Seizure 2006; 15: 106-111.

13. Szentirmai E, Hajdu I, Obal Jr. F, Kruger JM. Ghrelin-induced sleep responses in ad libitum fed and food-restricted rats. Brain Res 2006; 1088: 131-140.

14. Buske-Kirschbaum A, Geiben A, Hollig H, Morschhauser E, Hellehammer D. Altered responsiveness of the hypothalamus-pituitary-adrenal axis and the sympathetic adrenomedullary system to stress in patients with atopic dermatitis. J Clin Endocrinol Metab 2002; 87: 4245-4251.

15. Matsuda K, Nishi Y, Okamatsu Y, Kojima M, Matsuishi T. Ghrelin and leptin: A link between obesity and allergy ? J Allergy Clin Immunol 2006; 117: 705-706.

16. Kimata H. Reduction of allergen-specific IgE production by laughter. Eur J Clin Invest 2004; 34, 76-77.

17. Kimata H. effect of viewing a humorous vs nonhumorous film on bronchial responsiveness in patients with bronchial asthma. Physiol Behav 2004; 81: 681-684.