Sleep-related breathing disorders in small children with nocturnal acid gastro-oesophageal reflux

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Abstract

Purpose: Coincidence of gastroesophageal reflux disease with obstructive sleep apnea/hypopnea syndrome has been discussed in recent years. Treatment with nasal continuous positive airway pressure (nCPAP) reduces gastroesophageal reflux (GER) in adult patients with obstructive sleep apnea (OSA). Moreover, treatment of gastroesophageal reflux with omeprazole can reduce the severity of obstructive sleep in selected individuals. The aim of the study was to test the hypothesis that gastroesophageal reflux does not influence sleep quality and breathing pattern during sleep in children.

Material and methods: 24 children (14 boys, 10 girls, aged 2 months-3 years) with sleep disturbances indicating GER were studied. Standard polysomnography with parallel recording of 24-h oesophageal monitoring was performed. Apnea/hypopnea index (AHI) in active/REM sleep and quiet/NREM sleep was compared between nocturnal acid GER children (13 children; 7 boys, 6 girls; aged 1.28±0.95y; FRT-18.63±11.83%) and nocturnal acid GER-free controls (11 children; 7 boys, 4 girls; aged 1.64±0.97y; FRT-2.93±2.08%). Exclusion criteria were: 1. laboratory signs of infection (↑OB, ↑CRP, ↑α2-globulin); 2. clinical symptoms of infection in the respiratory tract, the alimentary tract or in the urinary tract.

Results: In children with nocturnal GER higher incidence of obstructive apnea/hypopnea during REM sleep was found: AHI=23.35/h±19.1; (CI 95%11.81-34.89) vs AHI=4.99/h±3.12 in children without nocturnal GER. We found no differences between the groups in saturation <90% time during sleep.

Conclusions: The study confirms coincidence of nocturnal gastroesophageal reflux and sleep-related breathing disorders in children. Higher number of apnea/hypopnea during REM sleep was found in children with nocturnal gastroesophageal reflux.

Key words: sleep apnea, gastroesophageal reflux disease, ALTE, SIDS, polysomnography.

Abbreviations:
ALTE – Apparent Life Threatening Event
CI – confidence interval
FRT – Fractional reflux time
nGER – nocturnal gastroesophageal reflux
OSAHS – obstructive sleep apnea/hypopnea syndrome
SaO2 – arterial oxygen saturation
SIDS – Sudden Infant Death Syndrome
TST – Total Sleep Time.

Introduction

Coincidence of gastroesophageal reflux disease with obstructive sleep apnea/hypopnea syndrome (OSAHS) has been discussed in recent years [1-3]. Obstructive sleep apnea may predispose to nocturnal GER by lowering intrathoracic pressure and increasing arousal and movement frequency. Nasal continuous positive airway pressure (nCPAP) can correct these predisposing factors and may be an effective form of antireflux therapy leading to reduce GER in adult patients with OSAHS [4-6]. Moreover, treatment of gastroesophageal reflux with omeprazole can reduce the severity of obstructive sleep in selected individuals [2].

The role of gastroesophageal reflux in apnea/breathing

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Table 1. **Population characteristics and polysomnographic findings**

	Group I nGER (+)	Group II nGER (-)	p
n	13	11	ns
Age (range, y) (Mean) (CI 95%)	0.08-2.9 1.28 ± 0.95 (0.71-1.85)	0.16-3.08 1.64 ± 0.97 (0.98-2.29)	ns
Male, n (%)	7 (53.8)	7 (63.6)	ns
Body weight >95%	0	0	ns
Total recording time (min)	1324 ± 43	1287 ± 39	ns
Total sleep time (TST) (min)	698 ± 72	591 ± 84	ns
Fractional Reflux Time (FRT) (%) (CI 95%)	18.63 ± 11.83 (11.47-25.78)	2.93 ± 2.08 (1.53-4.33)	p<0.0003
Mean intra-oesophageal pH during sleep (CI 95%)	5.01 ± 0.48 (4.72-5.31)	5.78 ± 0.36 (5.53-6.03)	P<0.0003
Mean intra-oesophageal pH during wakefulness (CI 95%)	5.21 ± 0.57 (4.86-5.55)	5.56 ± 0.32 (5.39-5.82)	ns
Apnea / hypopnea Index AHI (n/h TST) (CI 95%)	23.35 ± 19.1 (11.81-34.89)	4.99 ± 3.12 (2.89-7.09)	p < 0.004
Apnea / hypopnea Index AHI (n/h TST) (active/REM sleep) (CI 95%)	24.84 ± 19.64 (12.97-36.71)	8.54 ± 8.55 (2.79-14.28)	p < 0.018
Apnea / hypopnea Index AHI (n/h TST) (quiet/NREM sleep) (CI 95%)	4.00 ± 3.43 (1.93-6.08)	3.23 ± 2.43 (1.59-4.85)	ns
SaO2<90% (%TST)	3.1 ± 1.4	1.1 ± 0.9	ns

nGER – nocturnal gastroesophageal reflux

difficulties in children has long been studied [7-11]. Despite a large number of studies, a direct causal relationship has not been consistently shown. The aim of the study was to test the hypothesis that gastroesophageal reflux does not influence sleep quality and breathing pattern during sleep in children.

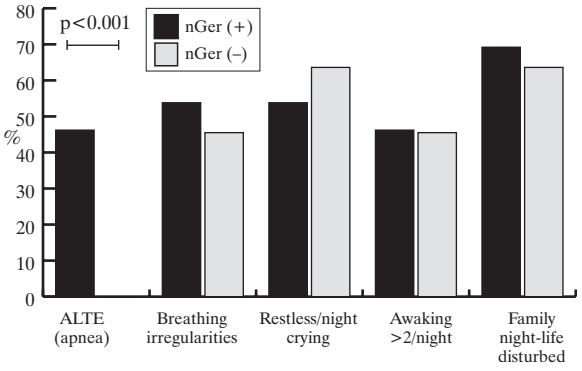
Material and methods

Prospective, nonrandomized study involved 24 children (13 boys, 11 girls) aged 2 months-3 years with chronic sleep disturbances, suspected of nocturnal gastroesophageal reflux (*Tab. 1*, *Fig. 1*). The history, clinical examination, blood tests and polysomnographic study were performed in all the children. Complete polysomnography (Alice 4, Respironics USA) in addition to a 24-hour pH probe (single channel) was performed at the sleep laboratory, in III Department of Pediatrics, Medical University of Białystok. The following parameters were recorded: 2 channels of electroencephalogram (F4A2, F3A1), the bilateral electro-oculogram (LEOG, REOG), chin electromyogram (EMG), nasal and oral airflows detected using a termistor (FLW), chest and abdominal wall movement by respiratory impedance (THO, ABD, Imp), heart rate by electrocardiogram (ECG), arterial oxygen saturation (SaO2) assessed by pulse oximetry with simultaneous recording of the pulse wave form (PLR), body position (Body), actimeter and a digital time-synchronized video recording (*Fig. 2*). All measures were digitized using a commercially available polysomnography system.

Apnea was defined as the cessation of oronasal flow for >5 s and hypopnea was defined as a reduction ≥50% in the oronasal flow for at least 20 seconds associated with a 3% decrease in oxygen saturation. The apnea/hypopnea index (AHI) was defined as the number of obstructive and mixed apnea/hypopnea per hour of total sleep time. Sleep studies were interpreted according to pediatric criteria [12].

The pH probe was introduced through the nose and the tip was sited at 87% of the distance from the nares to the lower

Figure 1. **Clinical symptoms of sleep disturbances**



Sleep disturbances	nGER (+) n=13		nGER(-) n=11	
	n	%	n	%
ALTE (apnea)	6	46,2	0	0
Breathing irregularities	7	53,8	5	45,5
Restless/night crying	7	53,8	7	63,6
Awaking > 2 / night	6	46,2	5	45,5
Family night-life disturbed	9	69,2	7	63,6

Figure 2. **Acid GER event leading to a drop in oxygen saturation (85%) and arousal (↑↓)**

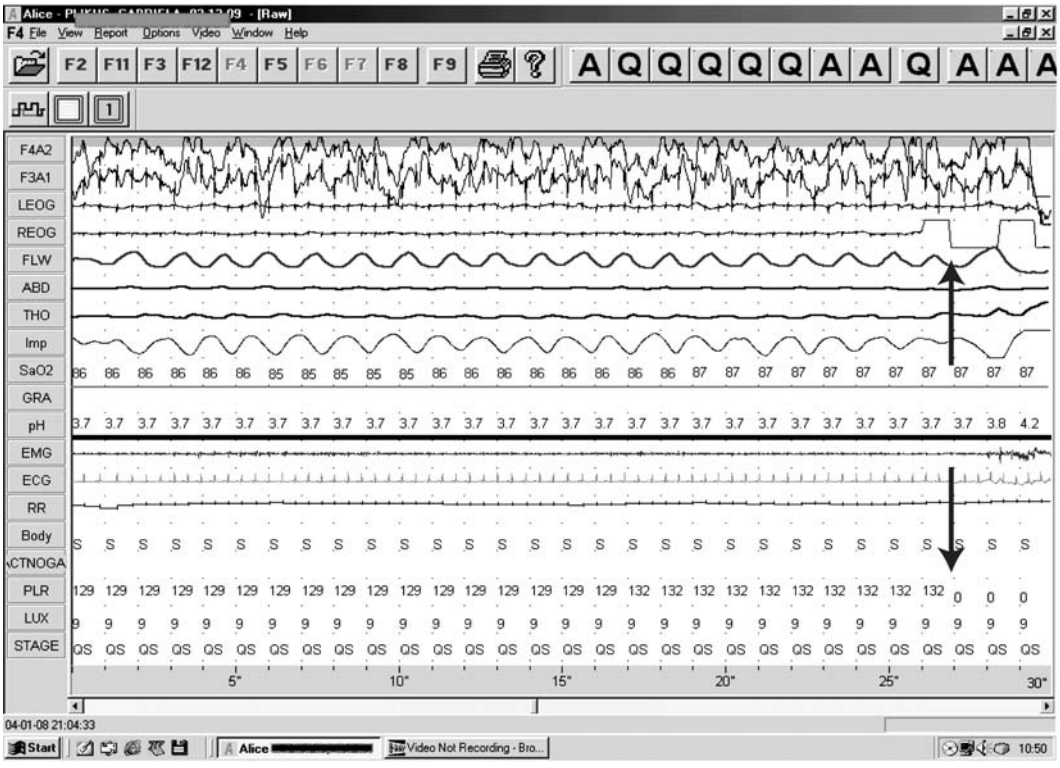
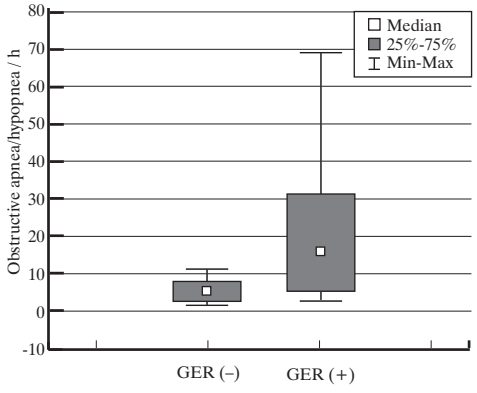


Figure 3. **Sleep-disordered breathing in GER children**



oesophageal sphincter. The reference electrode was attached to the anterior chest wall. Fractional reflux time (FRT), which represents the proportion of the total time of the recording for which the esophageal pH was less than 4.0 was calculated and expressed as a percentage value. When FRT was ≥7% during total sleep time (TST) the diagnosis of nocturnal gastroesophageal reflux was made. None of the study patients took medications at the study time. Exclusion criteria were: 1. laboratory signs of infection (↑OB, ↑CRP, ↑α2-globulin); 2. clinical symptoms of infection in the respiratory tract, in the alimentary tract or in the urinary tract.

Statistical analysis

The Mann-Whitney nonparametric test was used to compare the results in patients with nocturnal gastroesophageal reflux and in control subjects.

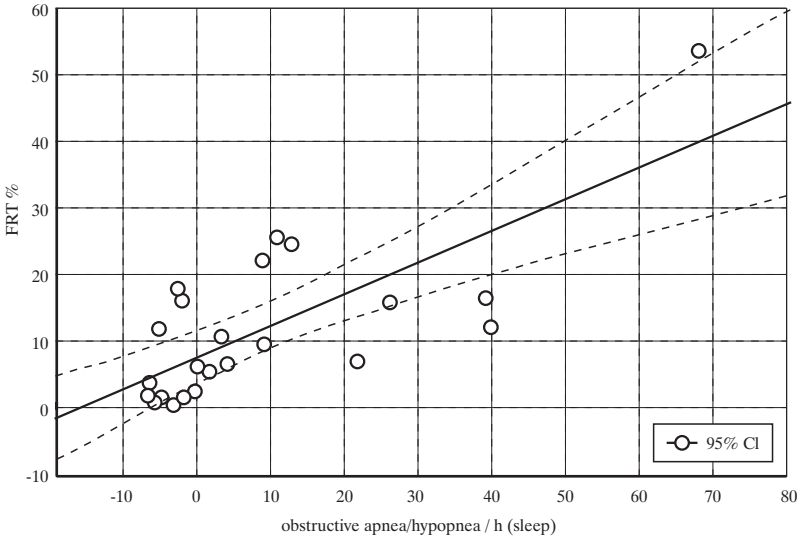
Results

In 13 children (7 boys, 6 girls; aged 1.28 ± 0.95 y) with FRT-18.63 ± 11.83% we recognized nocturnal acid GER (*Tab. 1*). In 11 controls (7 boys, 4 girls; aged 1.64 ± 0.97 y) with FRT-2.93 ± 2.08% we excluded exposure to esophageal acid at night. In children with nocturnal GER the mean intra-oesophageal pH during sleep was higher than in controls. The groups differ significantly in the number of obstructive apnea and hypopnea episodes (*Fig. 3*). This difference referred to the active/REM sleep but not to the quiet/NREM sleep. A strong positive correlation between the intensity of nocturnal acid GER (FRT) and degree of sleep-related breathing disorders (AHI) was found (*Fig. 4*). The total time of saturation < 90% did not differ between the groups.

Discussion

The main finding of this study is that infants and small children with intensive acid nocturnal GER (nGER) present

Figure 4. **Fractional reflux time (FRT) and apnea/hypopnea index (r=0.74482)**



more obstructive apnea and hypopnea during sleep than controls. Obstructive sleep apnea (OSA) is a condition characterized by repetitive, sleep-related obstruction of the upper airway resulting in oxygen desaturation and arousals from sleep. Overnight polysomnography is conducted to assess respiratory, cardiac and neurological abnormalities during sleep and is the optimal standard investigation when sleep apnea is suspected [12,13]. Parallel recording of intraoesophageal pH makes detection of acid gastroesophageal reflux possible. Gastroesophageal reflux with an esophageal pH in the physiological range (pH 5-6.8) is unrecognized by pH-metry and the intraluminal impedance technique is recommended as a diagnostic method [10,14].

The role of gastroesophageal in apnea/breathing difficulties in infants has long been studied, but a direct causal relationship has not been consistently shown [9,13,15]. A high prevalence of GER has been found to be present in adult patients with OSAHS [4-6]. Subjects with OSAHS had more frequent and prolonged reflux episodes than matched control subjects [1]. Nocturnal GER may precipitate symptoms suggestive of OSA, including awaking, nocturnal choking and reduced sleep efficiency. GER symptoms in OSAHS patients are reversed by nasal CPAP treatment, probably by increasing the intrathoracic pressure [4,6]. Moreover, the treatment of GER with omeprazole improves the apnea index (AI) and respiratory disturbances index (RDI) in patients with OSAHS [2].

Obesity which is a common risk factor for OSAHS and nGER in adults, was not found in our study. The nGER group and the control group did not differ in anthropometric parameters. Other predisposing factors, including immaturity of neuro-muscular mechanisms of breathing and swallowing should be considered in this group of age [10,16,17]. The process of inspiration and expiration (the breathing cycle) is precisely linked with the swallowing reflex via the supralaryngeal nerve. It is suggested that OSA is a primary disorder that leads to an abnormality in the swallowing reflex [18]. Patients with OSAHS are likely to exhibit an impaired swallowing reflex, probably due to the perturbed neural and muscular function of the upper airways, resulting in an increased vulnerability to aspiration. During OSA there is an increased respiratory effort by diaphragm, which is transmitted to the lower esophageal sphincter by the phrenoesophageal ligament.

There is evidence that obstructive apneas might cause hypoxia during sleep in infants at risk of sudden infant death syndrome (SIDS). Characteristically petechiae are found on the surface of the lungs and intrathoracic organs such as the thymus at SIDS victims. It has been speculated that these petechiae are due to the highly negative pressure in the thoracic cavity that is generated by the inspiratory effort against an obstructed airway [16]. Polysomnography studies showed more frequent and longer obstructive episodes during sleep in the future SIDS victims [19]. Central apneas were not distinctive. According to the last consensus document of the European Society for the Study and Prevention of Infant Death (ESPID, 2003) digestive disorders are the most frequent problems associated with apparent life threatening events (ALTE) (about 50%) [13]. Gastrooesophageal reflux is one of the main causes identified in ALTE infants (in 28-95% patients) [7,8,20]. When reflux and apnea are associated, the latter is predominantly of the obstructive type. In this study ALTE symptoms were present in 46,2% of nGER patients, but not in the control group.

The present study did not determine a direct relationship between gastroesophageal reflux and sleep-disordered breathing. However, we confirmed their coexistence in small children. Recognition and treatment of GER should help improve the quality of sleep and quality of life in patients having both conditions. It is an important aspect in the management of sleep-related breathing disorders in pediatric patients.

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References

1. Ing AJ, Ngu MC, Breslin AB. Obstructive sleep apnea and gastroesophageal reflux. Am J Med, 2000; 108 (4a): 120-5.
2. Senior BA, Kahn M, Schwimmer C, Rosenthal L, Benninger M. Gastroesophageal reflux and obstructive sleep apnea. Laryngoscope, 2001; 111: 2144-6.
3. Penzel T, Becker HF, Brandenburg U, Labunski T, Pankow W, Peter JH. Arousal in patients with gastro-oesophageal reflux and sleep apnea. Eur Resp J, 1999; 14: 1266-70.
4. Kerr P, Shoenut JP, Millar T, Buckle P, Kryger MH. Nasal CPAP reduces gastroesophageal reflux in obstructive sleep apnea syndrome. Chest, 1992; 101: 1539-44.
5. Tawk MM. Effect of one week of CPAP on esophageal reflux in patients with obstructive sleep apnea. Chest, 2003; 124: 73.
6. Green BT, Broughton WA, O'Connor JB. Marked improvement in nocturnal gastroesophageal reflux in a large cohort of patients with obstructive sleep apnea treated with continuous positive airway pressure. Arch Intern Med, 2003; 13: 41-5.
7. Sacre L, Vandenplas Y. Gastroesophageal reflux associated with respiratory abnormalities during sleep. J Pediatr Gastroenterol Nutr, 1989; 1: 28-33.
8. Newman LI, Russe J, Glassman MS, Berezin S, Halata MS, Medow MS, Dozor AJ, Schwarz SM. Patterns of gastroesophageal reflux (GER) in patients with apparent life-threatening events. J Pediatr Gastroenterol Nutr, 1989; 8: 157-60.
9. Peter CS, Sprodowski N, Bohnhorst B, Silny J, Poets CF. Gastroesophageal reflux and apnea of prematurity: no temporal relationship. Pediatrics, 2002; 109: 8-11.
10. Wentzl TG, Schenke S, Peschgens T, Silny J, Heimann G, Skopnik H. Association of apnea and nonacid gastroesophageal reflux in infants: Investigations with the intraluminal impedance technique. Pediatr Pulmonol, 2001; 31: 144-9.
11. Arad-Cohen N, Cohen A, Tirosh E. The relationship between gastroesophageal reflux and apnea in infants. J Pediatr, 2000; 137: 321-6.
12. American Thoracic Society. Standards and indications for cardiopulmonary sleep studies in children. Am J Respir Crit Care Med; 1996, 153: 866-78.
13. Kahn A. Recommended clinical evaluation of infants with an apparent life-threatening event. Consensus document of the European Society for the Study and Prevention of Infant Death, 2003. Eur J Pediatr, 2004; 163: 108-15.
14. Kwiecień J, Fyderek K. 24-godzinna pH-metria przełyku w diagnostyce choroby refluksowej przełyku u dzieci. Standardy Medyczne 2002, 6, 412-7.
15. Kahn A, Rebuffat E, Sottiaux M, Dufour D, Cadranel S, Reiterer F. Lack of temporal relation between acid reflux in the proximal oesophagus and cardiorespiratory events in sleeping infants. Eur J Pediatr, 1992; 151: 208-12.
16. Engelberts AC. The role of obstructive sleep apnea in sudden infant death syndrome and apparent life threatening event. International J Ped Otorhinolaryngol, 1995; Suppl 32: 59-62.
17. Wennergren G, Bjure J, Hertzberg T, Lagercrantz H, Milerad J. Laryngeal reflex. Acta Paediat, 1993; Suppl 389: 53-6.
18. Teramoto S, Sudo E, Matsue T, Ogha E, Ishii T, Ouchii Y, Fukuchi Y. Impaired swallowing reflex in patients with obstructive sleep apnea syndrome. Chest, 1999; 116: 17-21.
19. Kahn A, Groswasser J, Rebuffat E, Sottiaux M, Blum D, Foerster M, Franco P, Bochner A, Alexander M, Bachy A. Sleep and cardiorespiratory characteristics of infant victims of sudden death: a prospective case-control study. Sleep, 1992; 15: 287-92.
20. Wasilewska J, Kaczmarski M, Semeniuk J, Wysocka I. Charakterystyka kliniczna zespołu ALTE u dzieci hospitalizowanych. Przeg Pediatr, 2001; 31: 25-8.