

24-hour esophageal pH monitoring in children with pathological acid gastroesophageal reflux: primary and secondary to food allergy

Part II

Intraesophageal pH values in proximal channel; preliminary study and control studies – after 1, 2, 4 and 9 years of clinical observation as well as dietary and pharmacological treatment

Semeniuk J, Kaczmariski M*

III Department of Pediatrics, Medical University of Białystok

Abstract

Purpose: Among 264 children suspected of GERD, acid GER was confirmed in 138 children on the basis of 24-hour pH monitoring.

Aims of the study: Comparative analysis of parameters of 24-hour intraesophageal pH monitoring with dual-channel probe (in proximal channel) in children with acid GER: primary and secondary to cow milk allergy and/or other food allergy (CMA/FA) diagnosed; comparison of examined values of pH monitoring parameters with regard to duration of the disease (preliminary study and prospective studies – after 1, 2, 4 and 9 years of clinical observation and/or conservative treatment).

Material and methods: 264 children suspected of GERD, aged: 1.5-102 months; $\bar{x}=20.78\pm 17.23$ months, were enrolled in a study. In order to differentiate acid primary GER from GER secondary to CMA/FA in 138 (52.3%) children with GERD immunoallergological tests were performed. Positive result of oral food challenge test confirmed the allergy being the cause of GER.

138 children with pathological acid GER were qualified into two groups: 1 and 2.

Group 1 – 76 patients (55.1%), aged: 4-102 months; $\bar{x}=25.2\pm 27.28$ months, with pathological primary GER. Group 2 – 62 patients (44.9%), aged: 4-74 months; $\bar{x}=21.53\pm 17.79$ months, with pathological GER secondary to CMA/FA.

Results: Significant differentiation of the mean values of these parameters between preliminary study and control studies within groups was shown in the case of: number of episodes of acid GER and duration of the longest episode of acid GER,

acid GER index: total and supine (proximal channel). Statistical significance ($p<0.05$) was higher in group 1, especially during prospective clinical observation and/or conservative treatment. At the same time significant differentiation of the mean values of: number of episodes of acid GER and episodes of acid GER lasting more than 5 minutes and mean values of acid GER index: total and supine was shown between the groups. Statistical significance ($p<0.05$) was higher in group 2.

Conclusions: The preliminary study of examined children confirmed that values of pH monitoring in proximal channel were comparable to those in distal channel and did not contribute to differentiation of GER into primary and secondary. During prospective clinical observation and/or clinical treatment, on the basis of consecutive measurements, especially the number of episodes of acid GER and episodes of acid GER lasting more than 5 minutes, and also supine acid GER index it was stated that GER secondary to CMA/FA was of wider extent (higher) in comparison with primary GER in these patients.

Key words: children; GER: primary, secondary; CMA/FA; 24-hour esophageal pH monitoring; oral food challenge test.

Introduction

Among 264 children suspected of gastroesophageal reflux disease (GERD), acid gastroesophageal reflux (GER) was confirmed in 138 (52.3%) children on the basis of 24-hour intraesophageal pH monitoring [1-7].

Aims of the study

– comparative analysis of parameters of 24-hour intraesophageal pH-monitoring with dual-channel probe (in proximal channel) in children with acid GER: primary and secondary to CMA/FA diagnosed,

– comparison of examined values of pH monitoring parameters with regard to duration of the disease (preliminary study

* CORRESPONDING AUTHOR:

III Department of Pediatrics, Medical University of Białystok
ul. Waszyngtona 17, 15-274 Białystok, Poland
Fax: +48 85 742 3841
e-mail: Janexik@poczta.onet.pl (Janusz Semeniuk)

Table 1. Values of selected parameter of 24-hour esophageal pH monitoring in 138 children with pathological primary GER and GER secondary to CMA/FA, before and during treatment and/or clinical observation (prospective study)

Groups of examined children with specific ailment N= 138	pH monitoring parameter – number of episodes of acid GER (pH<4) Proximal channel				
	Range of values; mean (X); standard deviation (\pm SD); statistical significance (p); number of patients (N)				
	Before treatment (0)	Treatment and/or clinical observation in progress			
		after 1 year	after 2 years	after 4 years	after 9 years
Group 1 Primary GER	31.00 – 107.00 61.45 \pm 20.43 (76)	10.00 – 78.00 34.13 \pm 16.71 (76)	10.00 – 49.00 22.17 \pm 12.40 (46)	24.00 – 37.00 31.00 \pm 3.77 (12)	10.00 – 19.00 15.00 \pm 3.02 (12)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0054; 0 – 9, p=0.0022; 1 – 2, p=0.0001; 1 – 4, p=0.0022; 1 – 9, p=0.0022; 2 – 4, p=0.0022; 2 – 9, p=0.0022; 4 – 9, p=0.0022				
Group 2 GER+ CMA/FA	32.00 – 93.00 62.48 \pm 14.67 (62)	19.00 – 79.00 45.60 \pm 16.70 (62)	21.00 – 65.00 30.11 \pm 10.58 (47)	36.00 – 49.00 41.13 \pm 4.29 (8)	21.00 – 27.00 23.50 \pm 1.77 (8)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0117; 0 – 9, p=0.0117; 1 – 2, p=0.0001; 1 – 4, p=0.0117; 1 – 9, p=0.0117; 2 – 4, p=0.0117; 2 – 9, p=0.0117; 4 – 9, p=0.0117				
Statistical significance between the groups (p)	ns	p=0.0001	p=0.0001	p=0.0003	p=0.0002

and prospective studies – after 1, 2, 4 and 9 years of clinical observation and/or conservative treatment).

Detailed diagnostic procedure is presented in 'Material and methods' section, Part I of the study [8-25].

Assignment of children into study groups

Taking into consideration esophageal pH-monitoring results, complex differential diagnostics, oral food challenge tests and nutrition analysis in 264 children, pathological acid GER was confirmed in 138 of them (52.3%). These children were assigned into group 1 and group 2.

Group 1 – 76 patients (55.1%), of both sexes (39 boys – 28.3%, 37 girls – 26.8%), aged 4-102 months (mean age $x=25.2\pm 27.28$ months), with pathological primary GER.

Group 2 – 62 patients (44.9%), of both sexes (33 boys – 23.9%, 29 girls – 21.0%), aged 4-74 months (mean age $x=21.53\pm 17.79$ months), with pathological GER secondary to CMA/FA.

Statistical analysis

The statistical analysis of the results comprised arithmetical mean, standard deviation, minimal and maximal values and median – for measurable features and quantitative percentage distribution for qualitative features.

To compare the groups, features compatible with normal distribution, assessed with Kolomogorov compatibility test, were assessed together with the post hoc Bonferroni one-way analysis of variance. Features non-compatible with the distribution underwent Kruskal-Wallis test followed with Mann-Whitney test. T-Student pair test or Wilcoxon matched pairs test, respectively were used for the comparison between the two tests within each group at time interval. Statistical significance was $p<0.05$. Calculations were performed with the help of statistical package SPSS' 12.0 PL.

Results

Prospective analysis of values of parameters measured during 24-hour intraesophageal pH monitoring with dual-channel probe (proximal channel) was performed in 138 children. Assessment concerned preliminary study and control studies (during clinical observation and/or conservative treatment). 76 children had acid primary GER (group 1) and 62 children GER secondary to CMA/FA (group 2).

pH-monitoring parameters were defined as follows:

in 76 children before treatment (preliminary examination) and after 1 year of treatment, in 46 children – after 2 years, and in 12 children after 4 and 9 years of clinical observation and/or dietary and pharmacological treatment (group 1) and in 62 children – before treatment (preliminary examination) and after 1 year, in 47 children after 2 years and in 8 children after 4 and 9 years of clinical observation and treatment (group 2).

The analysis is presented in tables (proximal channel; *Tab. 1-5*).

* according to number of episodes of acid GER (pH<4) (*Tab. 1*)

In children with primary GER (group 1) mean values of parameter measured before treatment $x=61.45\pm 20.43$ were similar to the values $x=62.48\pm 14.67$ in children with GER and CMA/FA (group 2).

During clinical observation and/or treatment mean values in group 1 were decreasing and accounted for $x=34.13\pm 16.71$ after 1 year; 22.17 ± 12.40 after 2 years; 31.00 ± 3.77 and 15.00 ± 3.02 after 4 and 9 years, respectively.

In children with GER and CMA/FA (group 2) during clinical observation and/or treatment, a downward tendency of number of episodes of acid GER measured before treatment administration ($x=62.48\pm 14.67$) was observed. Its mean values

Table 2. Values of selected parameter of 24-hour esophageal pH monitoring in 138 children with pathological primary GER and GER secondary to CMA/FA before and during treatment and/or clinical observation (prospective study).

Groups of examined children with specific ailment N=138	pH monitoring parameter – number of episodes of acid GER lasting >5mins (pH<4) Proximal channel				
	Range of values; mean (X); standard deviation (\pm SD); statistical significance (p); number of patients (N)				
	Before treatment (0)	Treatment and/or clinical observation in progress			
		after 1 year	after 2 years	after 4 years	after 9 years
Group 1 Primary GER	1.00 – 7.00 3.96 \pm 1.37 (76)	0.00 – 6.0 2.62 \pm 1.60 (76)	0.00 – 4.00 1.37 \pm 1.10 (46)	1.00 – 3.00 2.08 \pm 0.79 (12)	1.00 – 2.00 1.17 \pm 0.39 (12)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0209; 0 – 9, p=0.0033; 1 – 2, p=0.0001; 1 – 4, p=0.0022; 1 – 9, p=0.0022; 2 – 4, p=0.0277; 2 – 9, p=0.0022; 4 – 9, p=0.0117				
Group 2 GER + CMA/FA	1.00 – 15.00 5.87 \pm 3.64 (62)	0.00 – 12.00 4.24 \pm 3.09 (62)	0.00 – 8.00 2.40 \pm 1.94 (47)	3.00 – 6.00 4.38 \pm 1.19 (8)	1.00 – 2.00 1.75 \pm 0.46 (8)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0117; 0 – 9, p=0.0117; 1 – 2, p=0.0001; 1 – 4, p=0.0117; 1 – 9, p=0.0117; 2 – 4, p=0.0117; 2 – 9, p=0.0117; 4 – 9, p=0.0117				
Statistical significance between the groups (p)	ns	p=0.0039	p=0.0046	p=0.0005	p=0.011

made $x=45.60\pm 16.70$ after 1 year; 30.11 ± 10.58 after 2 years; 41.13 ± 4.29 and 23.50 ± 1.77 after 4 and 9 years, respectively. Mean number of episodes of acid GER, measured in proximal channel in both groups (1 and 2) revealed significant differentiation within the groups, between preliminary study (0) and control studies. Statistical significance was higher in group 1, especially during prospective clinical observation and treatment.

During clinical observation and treatment, differentiation of mean number of episodes of acid GER between study groups (1 and 2) was observed. Statistical significance was higher in group 2 after 1, 2, 4 and 9 years.

**** according to the number of episodes of acid GER (pH<4), lasting >5minutes (Tab. 2)**

In children with primary GER (group 1) mean values of measured parameter, before treatment administration, $x=3.96\pm 1.37$ were lower than the values $x=5.87\pm 3.64$ in children with GER and CMA/FA (group 2).

During clinical observation and/or treatment in group 1 mean values were decreasing and accounted for $x=2.62\pm 1.60$ after 1 year; 1.37 ± 1.10 after 2 years; 2.08 ± 0.79 and 1.17 ± 0.39 after 4 and 9 years, respectively.

In children with GER and CMA/FA (group 2) downward tendency of mean number of episodes of acid GER lasting >5 minutes, measured before treatment ($x=5.87\pm 3.64$) was observed. During clinical observation and/or treatment mean values accounted for $x=4.24\pm 3.09$ after 1 year; 2.40 ± 1.94 after 2 years; 4.38 ± 1.19 and 1.75 ± 0.46 after 4 and 9 years, respectively.

Mean number of episodes of acid GER lasting >5 minutes, measured in proximal channel in both groups (1 and 2) constituted significant differentiation within the groups between preliminary study (0) and control studies. Statistical significance

was higher in group 1, especially during prospective clinical observation and treatment (exception: higher significance in group 2 between preliminary study and control study – after 4 years and between control studies: after 2 and 4 years).

During clinical observation and treatment, differentiation of mean number of episodes of acid GER lasting >5 minutes between study groups (1 and 2) was observed.

Statistical significance was higher in group 2, the highest after 4 years and the lowest after 9 years.

***** according to duration of the longest episode of acid GER (minutes) (Tab. 3)**

In children with primary GER (group 1), mean values of the parameter measured before treatment administration $x=12.91\pm 5.14$ were higher than the values in children with GER and CMA/FA $x=9.51\pm 3.78$ (group 2).

During clinical observation and/or treatment in group 1 mean values were decreasing and accounted for $x=7.61\pm 4.80$ after 1 year; 5.32 ± 3.96 after 2 years; 7.90 ± 1.09 and 3.96 ± 0.73 after 4 and 9 years.

A downward tendency of mean value of duration of the longest episode of acid GER, measured before treatment ($x=9.51\pm 3.78$) was observed in children with GERD and CMA/FA (group 2).

During clinical observation and/or treatment mean values accounted for $x=7.17\pm 3.40$ after 1 year; 4.61 ± 2.68 after 2 years; 7.85 ± 1.11 and 3.90 ± 0.37 after 4 and 9 years, respectively. Mean values of duration of the longest episode of acid GER measured in proximal channel in both groups (1 and 2) were significantly different within the groups, between preliminary examination (0) and control examinations. Statistical significance was higher in group 1, especially during prospective clinical observation and treatment.

During clinical observation and treatment there was no dif-

Table 3. Values of selected parameter of 24-hour esophageal pH monitoring in 138 children with pathological primary GER and GER secondary to CMA/FA before and during treatment and/or clinical observation (prospective study)

Groups of examined children with specific ailment N=138	pH monitoring parameter – duration of the longest episode of acid GER (mins) Proximal channel				
	Range of values; mean (X); standard deviation (\pm SD); statistical significance (p); number of patients (N)				
	Before treatment (0)	Treatment and/or clinical observation in progress			
		after 1 year	after 2 years	after 4 years	after 9 years
Group 1 Primary GER	5.50 – 24.10 12.91 \pm 5.14 (76)	1.20 – 21.00 7.61 \pm 4.80 (76)	1.10 – 16.90 5.32 \pm 3.96 (46)	6.60 – 9.90 7.90 \pm 1.09 (12)	2.60 – 5.00 3.96 \pm 0.73 (12)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0022; 0 – 9, p=0.0022; 1 – 2, p=0.0001; 1 – 4, p=0.0022; 1 – 9, p=0.0022; 2 – 4, p=0.0022; 2 – 9, p=0.0022; 4 – 9, p=0.0022				
Group 2 GER + CMA/FA	5.60 – 21.50 9.51 \pm 3.78 (62)	2.30 – 19.30 7.17 \pm 3.40 (62)	2.20 – 14.70 4.61 \pm 2.68 (47)	6.30 – 9.30 7.85 \pm 1.11 (8)	3.50 – 4.50 3.90 \pm 0.37 (8)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0117; 0 – 9, p=0.0117; 1 – 2, p=0.0001; 1 – 4, p=0.0117; 1 – 9, p=0.0117; 2 – 4, p=0.0117; 2 – 9, p=0.0117; 4 – 9, p=0.0117				
Statistical significance between the groups (p)	ns	ns	ns	ns	ns

Table 4. Values of selected parameter of 24-hour esophageal pH monitoring in 138 children with pathological primary GER and GER secondary to CMA/FA before and during treatment and/or clinical observation (prospective study)

Groups of examined children with specific ailment N=138	pH monitoring parameter – total acid GER index (%) Proximal channel				
	Range of values; mean (X); standard deviation (\pm SD); statistical significance (p); number of patients (N)				
	Before treatment (0)	Treatment and/or clinical observation			
		after 1 year	after 2 years	After 4 years	after 9 years
Group 1 Primary GER	5.20 – 20.20 11.26 \pm 4.18 (76)	2.70 – 16.40 7.28 \pm 3.78 (76)	2.90 – 14.10 6.48 \pm 4.92 (46)	6.40 – 8.80 7.36 \pm 0.66 (12)	3.20 – 5.00 4.11 \pm 0.55 (12)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0022; 0 – 9, p=0.0022; 1 – 2, p=0.0001; 1 – 4, p=0.0022; 1 – 9, p=0.0022; 2 – 4, p=0.0022; 2 – 9, p=0.0022; 4 – 9, p=0.0022				
Group 2 GER + CMA/FA	5.20 – 19.20 10.47 \pm 3.80 (62)	3.00 – 14.40 7.99 \pm 3.13 (62)	2.90 – 11.90 4.84 \pm 2.47 (47)	6.00 – 8.50 7.48 \pm 0.88 (8)	3.30 – 4.30 3.81 \pm 0.41 (8)
Statistical significance within the groups (p)	0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0117; 0 – 9, p=0.0117; 1 – 2, p=0.0001; 1 – 4, p=0.0117; 1 – 9, p=0.0117; 2 – 4, p=0.0117; 2 – 9, p=0.0117; 4 – 9, p=0.0117				
Statistical significance between the groups (p)	ns	ns	ns	ns	ns

ferentiation of mean values of duration of the longest episode of acid GER between study groups (group 1 and 2). Statistical significance was comparable in both groups: 1 and 2, in particular years.

****** according to total acid GER index (%) (Tab. 4)**

In children with primary GER (group 1), before administration of treatment, mean values of measured parameter $x=11.26\pm 4.18$ were lower than the values $x=10.47\pm 3.80$ in children with GER and CMA/FA (group 2).

During clinical observation and/or treatment in group 1 mean values were decreasing and accounted for $x=7.28\pm 3.78$

after 1 year; 6.48 ± 4.92 after 2 years; 7.36 ± 0.66 and 4.11 ± 0.55 after 4 and 9 years, respectively.

In children with GER and CMA/FA (group 2) a downward tendency of mean values of total acid reflux index (RI), measured before treatment ($x=10.47\pm 3.80$) was observed.

During clinical observation and/or treatment mean values constituted $x=7.99\pm 3.13$ after 1 year; 4.84 ± 2.47 after 2 years; 7.48 ± 0.88 and 3.81 ± 0.41 after 4 and 9 years, respectively.

Mean values of total acid RI, measured in proximal channel, in both groups (1 and 2) revealed significant differentiation within the groups, between preliminary examination (0) and control examinations. Statistical significance was higher in

Table 5. Values of selected parameter of 24-hour esophageal pH monitoring in 138 children with pathological primary GER and GER secondary to CMA/FA before and during treatment and/or clinical observation (prospective study)

Groups of examined children with specific ailment N=138	pH monitoring parameter – acid GER index (supine position) (%)				
	Proximal channel				
	Range of values; mean (X); standard deviation (\pm SD); statistical significance (p); number of patients (N)				
	Before treatment (0)	Treatment and/or clinical observation in progress			
		after 1 year	after 2 years	After 4 years	after 9 years
Group 1 Primary GER	2.70 – 13.80 6.41 \pm 2.64 (76)	1.00 – 12.10 4.07 \pm 2.59 (76)	1.30 – 8.00 3.03 \pm 2.02 (46)	2.90 – 5.10 3.93 \pm 0.53 (12)	1.80 – 2.50 2.13 \pm 0.19 (12)
Statistical significance within the groups (p)		0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0022; 0 – 9, p=0.0022; 1 – 2, p=0.0001; 1 – 4, p=0.0022; 1 – 9, p=0.0022; 2 – 4, p=0.0022; 2 – 9, p=0.0022; 4 – 9, p=0.0022			
Group 2 GER + CMA/FA	3.30 – 15.00 7.16 \pm 2.76 (62)	1.80 – 11.50 5.35 \pm 2.59 (62)	1.70 – 8.30 2.85 \pm 1.78 (47)	3.50 – 5.50 4.60 \pm 0.70 (8)	1.80 – 2.50 2.16 \pm 0.24 (8)
Statistical significance within the groups (p)		0 – 1, p=0.0001; 0 – 2, p=0.0001; 0 – 4, p=0.0117; 0 – 9, p=0.0117; 1 – 2, p=0.0001; 1 – 4, p=0.0117; 1 – 9, p=0.0117; 2 – 4, p=0.0117; 2 – 9, p=0.0117; 4 – 9, p=0.0117			
Statistical significance between the groups (p)	ns	p=0.0011	ns	p=0.0637	ns

group 1, especially in prospective clinical observation and treatment.

During clinical observation and treatment, differentiation of mean values of total acid RI between study groups (1 and 2) was observed. Statistical significance was comparable in both groups 1 and 2, in particular years.

****** according to acid RI, supine position (%) (Tab. 5)**

In children with primary GER (group 1), before treatment administration mean values of measured parameter $x=6.41\pm 2.64$ were slightly lower than values $x=7.16\pm 2.76$ in children with GER and CMA/FA (group 2).

During clinical observation and/or treatment on group 1 mean values decreased and accounted for $x=4.07\pm 2.59$ after 1 year; 3.03 ± 2.02 after 2 years; 3.93 ± 0.53 and 2.13 ± 0.19 after 4 and 9 years, respectively.

In children with GER and CMA/FA a downward tendency of mean value of acid RI, in supine position, measured before treatment administration was observed ($x=7.16\pm 2.76$).

During clinical observation and/or treatment, mean values constituted $x=5.35\pm 2.59$ after 1 year; 2.85 ± 1.78 after 2 years; 4.60 ± 0.70 and 2.16 ± 0.24 after 4 and 9 years respectively. Mean values of acid RI, supine measured in proximal channel in both groups (1 and 2) revealed significant differentiation within the groups, between preliminary examination (0) and control examinations.

Statistical significance was higher in group 1, especially during prospective clinical observation and treatment.

During clinical observation and treatment differentiation of mean values of acid RI, in supine position was statistically significant between study groups (1 and 2). Statistical significance was higher in group 2, only after 1 year of treatment.

Discussion

The comparative analysis of mean values of pH monitoring parameters recorded in 24-hour intraesophageal pH monitoring in proximal channel of both study groups: children with primary GER and children with GER secondary to CMA/FA was conducted [1-7].

The measurements were done before the treatment and during prospective clinical observation and treatment.

The analysis showed statistically significant differentiation of mean values of episodes of acid GER and episodes of acid GER lasting more than 5 minutes, the longest episode of acid GER duration and acid GER index (total and supine) between preliminary study and control study. Statistical significance of these differences was higher in group 1, especially during prospective, long-term clinical observation.

This is attributable to higher effectiveness of classical antireflux treatment rather than combined treatment (antiallergic and antireflux) in eliminating the results of reflux and the causative and pathogenic role of food allergy in secondary GER [9,10,14,21,26-28].

Statistically significant mean value of episodes of acid GER lasting more than 5 minutes, higher in group 2 in preliminary study and control study after 4 years and in control studies after 2 and 4 years of clinical observation and treatment seems to be an exception.

The higher number of episodes of GER lasting more than 5 minutes constituted a characteristic feature of GER secondary to FA.

During clinical observation differentiation of mean number of episodes of acid GER and episodes of acid GER lasting more than 5 minutes, especially after 4 years was shown. Statistical significance of mean values mentioned was higher in group with GER secondary to CMA/FA.

In the case of acid GER index only supine mean values were differentiated within the groups and had higher statistical significance in group 2, exclusively after the first year of clinical observation and treatment.

The results may suggest that the reduction of the intensity of supine GER, especially during night sleep is due to improvement of mechanism responsible for neutralization and self-purification of esophagus under dietary and pharmacological treatment [5,7,10,14,19,21,22].

The comparative analysis of examined pH monitoring parameters measured in proximal channel showed significantly higher mean values of episodes of acid GER and acid GER lasting more than 5 minutes and supine acid GER index in children with GER secondary to CMA/FA than in children with primary GER during the study.

The results obtained in patients of group 2 are attributable to more clearly expressed dissociation of motor activity of gastroesophageal junction, which could be the result of coexistent allergization of upper gastrointestinal system triggered off by noxious nutrient from the patients' diet [12,14,21,22,25].

During 24-hour esophageal pH monitoring with dual-channel probe it was assumed that the higher the positioning of the sensor of the electrode the lower number of short-term reflux episodes.

It was also assumed that the total reflux time is shortened, which results from the better efficiency of the mechanism responsible for neutralisation pH gastric content and the ability of esophagus to self-purification [5,7,19,20].

The results of our studies do not confirm the stated hypothesis completely because the mean values of analyzed pH monitoring parameters in proximal channel were not lower (not statistically significant) than in distal part of esophagus in children with GERD of both study groups with GERD. The results are comparable with pH-metric esophageal results obtained by Cucchiara et al. [19] and another authors [5,6,20].

The percentage values of the number of episodes of acid GER registered in preliminary study and after 1 year and 9 years of treatment accounted for 81%, 73% and 57% in proximal channel, respectively (group 1) and 84%, 79% and 87% in distal channel, respectively (group 2).

The number of episodes of acid GER lasting more than 5 minutes recorded in proximal channel accounted for 76% to 74% (group 1) and 66%, 72% and 87% (group 2) in distal channel, in preliminary study and control studies.

Also the duration of the longest episode of acid GER recorded in proximal channel reached 74% and 75% (group 1) and in distal channel 65%, 71% and 74% (group 2), respectively in preliminary study and control studies.

Total acid GER index recorded in proximal channel accounted for 84% and 86% (group 1), whereas in distal channel 61%, 67% and 83% (group 2), in preliminary study and control studies after 1 year and 9 years of treatment, respectively.

Supine acid GER index recorded in proximal channel made 92%, 84% and 89% (group 1) and 93% and 90% (group 2) in distal channel, in preliminary study and control studies.

During prospective studies the gradual tendency of mean values of pH monitoring parameters in both channels to return to normal values. Although the reflux was diminishing in consecutive pH recordings in examined children with primary and

secondary GER, mean values of parameters were comparable and did not show significant difference between both channels (distal and proximal).

In both groups the values of pH monitoring parameters obtained in proximal channel constituted more than 50% of the values obtained in distal channel. This may appear due to considerable range of reflux (high reflux), persisting regardless of the normalisation of pathological pH monitoring recording under antireflux or combined treatment (antireflux and antiallergic) [5,7,10,14,19,21,22].

On the basis of the results obtained in preliminary study and control studies in these groups there were no significant quantitative differences in episodes of acid GER reaching both distal and proximal channel, regardless of the age of the children.

The preliminary study in children with primary GER showed that mean values of pH monitoring parameters measured in proximal channel were similar.

However, the control pH monitoring in proximal channel showed that mean values of episodes of acid GER and episodes of acid GER lasting more than 5 minutes during clinical observation and/or treatment, similarly to mean values of supine acid GER index – only after the first year of observation were significantly higher in group with GER secondary to FA than in group with primary GER ($p < 0.05$).

The high GER, reaching proximal esophagus is important in children of both groups, but in children with atypical symptoms, especially of respiratory tract (latent reflux) may suggest microaspiration of gastric content into bronchial tree [5-7,9].

In children below 3 years of age, who had recurrent inflammations of upper respiratory tract reported, latent GER was confirmed with pH esophageal monitoring with single-channel probe in 56% and 57% of other gastroenterological centers in Poland, respectively [29,30].

On the basis of 24-hour esophageal pH monitoring with dual-channel probe in children with symptoms outside the gastrointestinal tract, in the same age group, in own studies, the percentage of high GER in both study groups was reported accounting for 77.4% and 88.3%, respectively.

The results of own studies contribute to intensity of acid GER reaching distal and proximal esophagus, and mean values of pH monitoring parameters in proximal and distal channel show statistical significance between the groups, especially during the prospective clinical observation and administered treatment.

The comparable mean values of duration of the longest episode of acid GER in both channels, supine acid GER index in distal channel and total acid GER index in proximal channel constitute the exception.

This differentiation of examined pH monitoring parameters between the groups could be important in predicting who of the examined children is at risk of primary GER and who is at risk of GER secondary to CMA/FA.

Conclusions

In conclusion, the values of all pH monitoring parameters in proximal channel recorded during the preliminary study (before treatment) were comparable (similarly to distal channel) and

did not serve as a source to differentiate GER into primary and secondary to CMA/FA.

During clinical observation and/or treatment of the patients the dynamics of acid GER, especially its range, and its intensity was assessed at control studies, in proximal channel.

The results of control studies, especially the number of episodes of acid GER and episodes of GER lasting more than 5 minutes, and supine acid GER index it showed that the range of GER secondary to CMA/FA was higher than primary GER range in these patients.

Acknowledgement

The study was supported by Grant of State Committee for Scientific (KBN) No 4P05E 04719.

References

- Vandenplas Y (Coordinator). A standardized protocol for the methodology of esophageal pH monitoring and interpretation of the data for the diagnosis of gastroesophageal reflux. (ESPGHAN – society statement). *J Pediatr Gastroenterol Nutr*, 1992; 14: 467-71.
- Vandenplas Y, Loeb H. The interpretation of oesophageal pH monitoring data. *Eur J Pediatr*, 1990; 149: 598-602.
- Vandenplas Y, Goyvaerts H, Helven R. Gastroesophageal reflux as measured by 24-hour monitoring, in 509 healthy infants screened for risk of sudden infant death syndrome. *Pediatrics*, 1991; 88: 834-40.
- Vandenplas Y, Sacre-Smith L. Continuous 24-hour esophageal pH monitoring in 285 asymptomatic infants 0-15 months old. *J Pediatr Gastroenterol Nutr*, 1987; 6: 220-4.
- Arana A, Bagucka B, Hauser B, Hegar B, Urbain D, Kaufman L, Vandenplas Y. pH monitoring in the distal and proximal esophagus in symptomatic infants. *J Pediatr Gastroenterol Nutr*, 2001; 32: 259-64.
- Bagucka B, Hegar B, Vandemaële K. Normal ranges of continuous pH monitoring proximal esophagus. *J Pediatr Gastroenterol Nutr*, 2000; 31: 244-8.
- Semeniuk J, Kaczmarek M, Krasnow A, Sidor K, Matuszewska E, Daniluk U. Dual simultaneous esophageal pH monitoring in infants with gastroesophageal reflux. *Pol Merk Lek*, 2003; 83: 405-9.
- Kaczmarek M. Food allergy and intolerance. Milk, sugars, soya. Sanmedia, Warszawa, 1993.
- Semeniuk J. Ethnopathogenic role of gastro-oesophageal reflux in developing of clinical symptoms in children. PhD thesis. Medical University of Białystok, 1990.
- Staiano A, Troncone R, Simeone D. Differentiation of cow's milk intolerance and gastro-oesophageal reflux. *Arch Dis Child*, 1995; 73: 439-42.
- Iacono G, Carroccio A, Cavataio F. IgG antibetalactoglobulin: its use in the diagnosis of cow's milk allergy. *Ital J Gastroenterol*, 1995; 27: 355-60.
- Cavataio F, Iacono G, Montalto G, Soresi MM, Tumminello M, Campagna P, Notarbartoloo A, Carroccio A. Gastroesophageal reflux associated with cow's milk allergy in infants: Which diagnostic examinations are useful? *Am J Gastroenterol*, 1996; 91: 1251-60.
- Kaczmarek M (editor). The stand of Polish Group of experts to food allergy and intolerance. Polish Society for Allergology, Symposium 1, Medical Convention Periodical, Unimed, 1997; 1: 21-31, 39-67.
- Semeniuk J, Kaczmarek M, Nowowiejska B, Białokoz I, Lebensztejn D. Food allergy as the cause of gastroesophageal reflux in the youngest children. *Pediatr Pol*, 2000; 10: 793-802.
- Strobel C T, Byrne W J, Marvin E A, Euler A R. Correlation of esophageal lengths in children with height: application to the Tuttle test without prior esophageal manometry. *J Pediatr*, 1979; 94: 81-3.
- Mc Cauley RGK, Darling DB, Leonidas JC. Gastroesophageal reflux in infants and children: A useful classification and reliable physiologic technique for its demonstration. *Am J Roentgenol*, 1987; 130: 47-52.
- Thor P, Herman R, Plebankiewicz S, Bogdał J. Esophageal manometry and pH-metry in gastroesophageal reflux disease; their role in preoperative evaluation. *Acta Endosc Pol*, 1994; 6: 167-73.
- Gustafsson PM, Tibbling L. 24-hour esophageal two-level pH monitoring in healthy children and adolescents. *Scand J Gastroenterology*, 1988; 23: 91-4.
- Cucchiara S, Santamaria S, Minella R. Simultaneous prolonged recordings of proximal and distal intraesophageal pH in children with gastroesophageal reflux disease and respiratory symptoms. *Am J Gastroenterol*, 1995; 90: 1791-6.
- Little JP, Matthews BL, Glock MS. Extraesophageal pediatric reflux: 24-hour double-probe pH monitoring of 222 children. *Ann Oto Rhinol Laryngol*, 1997; 196 (Suppl): S1-S16.
- Iacono G, Carroccio A, Cavataio F. Gastroesophageal reflux and cow milk allergy in infants: a prospective study. *J Allergy Clin Immunol*, 1996; 97: 822-7.
- Semeniuk J, Tryniszewska E, Wasilewska J, Kaczmarek M. Food allergy – causal factor of gastroesophageal reflux in children. *Terapia*, 1998; 6: 16-9.
- Matuszewska E, Kaczmarek M, Semeniuk J. Doustne próby prowokacyjne w diagnostyce alergii i nietolerancji pokarmowej. *Ped Współczesna Gastroenterol Hepatol i Żywnie Dziecka*, 2000; 4: 239-43.
- Semeniuk J, Wasilewska J, Kaczmarek M, Lebensztejn D. Non-typical manifestation of gastroesophageal reflux in children. *Med Sci Monit*, 1998; 4: 1122-30.
- Salvatore S, Vandenplas Y. Gastroesophageal reflux and cow milk allergy: is there a link? *Pediatrics*, 2002; 110: 972-84.
- Vandenplas Y (Coordinator). A proposition for the diagnosis and treatment of gastro-oesophageal reflux disease in children: a report from a working group on gastro-oesophageal reflux disease. *Eur J Pediatr*, 1993; 152: 704-11.
- Vandenplas Y (Coordinator). Diagnosis and treatment of gastroesophageal reflux disease in infants and children. *J Gastroenterol Hepatol*, 2000; 15: 569-72.
- Orenstein SR. Management of supraesophageal complications of gastroesophageal reflux disease in infants and children. *Am J Med*, 2000; 108 (4A): 139S-143S.
- Fyderek K, Stopyrowa J, Śladek M. Refluks żołądkowo-przelykowy jako czynnik patologiczny w wybranych schorzeniach u dzieci. *Przegl Lek*, 1991; 48: 385-9.
- Zielińska I, Czerwionka-Szaflarska M. Wartość badań pH-metrycznych w diagnostyce nawracających zapaleń oskrzeli i płuc. *Przegl Pediatr*, 1999; (Suppl 1): 52-4.