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

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

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Abstract

Purpose: Among 264 children suspected of GERD, acid gastroesophageal reflux (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 (in distal channel – above cardia) 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, of both sexes (140 boys – 53.0% and 124 girls – 47.0%), aged: 1.5-102 months; x=20.78±17.23 months, were enrolled in the study. In order to differentiate acid GER: primary from 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; x=25.2±27.28 months, with pathological primary GER. Group 2 – 62 patients (44.9%), aged: 4-74 months, mean age x=21.53±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 episodes of acid GER lasting more than 5 minutes, duration of the longest episode of acid GER, acid GER index: total and supine (distal 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.

Coclusions: The preliminary study of examined children confirmed that values of pH monitoring in distal channel were comparable and did not contribute to differentiation of GER into primary (group 1) and secondary (group 2). During prospective clinical observation and/or clinical treatment the intensity of reflux in these groups was assessed on the basis of the number of episodes of acid GER and episodes of acid GER lasting more than 5 minutes in distal channel. Acid GER index: total and supine appeared to be important diagnostic parameter but only after the first year of dietary and pharmacological treatment.

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]. In order to differentiate primary GER from GER secondary to cow milk allergy and/or other food allergy (CMA/FA), a complex differential diagnosis was performed on the basis of various examinations, e.g. immunoallergological tests [8-14]. Positive result of oral food challenge test (open or blind study) confirmed allergy being the cause of GER [13]. Positive result of oral food challenge test was crucial to assign children into study groups: 1 and 2,

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and these children underwent further prospective observation. Qualification of children to further comparative studies resulted from abnormalities of pH monitoring and clinical symptoms.

Aims of the study:

– comparative analysis of parameters of 24-hour intraesophageal pH monitoring with dual-channel probe (in distal channel – above cardia) 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 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, of both sexes (140 boys – 53.0% and 124 girls – 47.0%), aged 1.5 months to 102 months, mean age x=20.78±17.23 months, were enrolled in the study. According to anamnesis these children had various ailments of gastrointestinal tract reported in family histories.

1. 24-hour intraesophageal pH monitoring

The study was performed with dual-channel, antimony pH monitoring probe that measures intraesophageal pH in distal and proximal channel, and Digitraper MK III device, Synectics Medical, registering these values.

pH monitoring probe 2.1 mm diameter, was placed into esophagus of examined child through one of the nostrils and pharynx and distal channel (2) was situated 3-5 cm above upper edge of lower esophageal sphincter (LES).

Proximal channel (1) was 10, 15 or 20 cm above LES, depending on the length of esophagus.

To localize the probe Strobel's mathematical mode was used, and if difficulties in localizing occurred, radiological or manometric control of LES was performed [15-17].

Computer assessment of numerical measurements obtained from both channels: distal and proximal, concerned following pH monitoring parameters:

– number of episodes of acid GER (intraesophageal pH below 4.0),

– number of episodes of acid GER lasting more than 5 minutes (so-called "long episodes"),

– reflux index (RI), i.e. percentage of time that the pH is below 4.0 within 24-hour intraesophageal pH monitoring.

Pathological acid GER was diagnosed on the basis of ESPGHAN diagnostic criteria [1,2].

In children below 2 years of age results of esophageal pH monitoring were juxtaposed against borderline values summarized by Vandenplas et al. [3,4] and another authors [5,6].

In older children (above 2 years of age) the borderline values at qualitative and quantitative assessment of pathological GER in both channels were [1,2,18-20]:

total number of episodes of acid GER (pH<4.0/24 hrs) =50; number of episodes of acid GER lasting more than 5 minutes ≤2, percentage of time that the pH is below 4.0 (%) – acid GER

index total =5.0%: percentage of time that the pH is below 4.0 (%) – acid GER index in supine position =2.5%.

Pathological acid GER was diagnosed in 138 children of the examined group.

2. Differential diagnosis of pathological acid GER

A. In order to differentiate pathological GER in 138 children with GERD into primary (idiopathic) and secondary – triggered off or aggravated by CMA/FA, the following immunoallergologic tests were performed [11,13,21,22].

* Skin tests

Prick tests

• with12 native food allergens, i.e. fresh (cow's milk, soya, of hen's egg white, hen's egg yolk, chicken's meat, beef, wheat flour, peanuts, bananas, fish, orange, white sesame);

• with 9 commercial inhalant allergens (SmithKline Beecham – USA)(house dust mites, grass , trees, bushes and weeds pollens, dog's fur, cat's fur, mixed feathers, wool).

71 out of 138 children, of different age, with pathological acid GER and 32 children with CMA/FA exclusively, underwent these test once in order to confirm or exclude the ability of early IgE-dependent hypersensitivity to food allergens and/or inhalant allergens (atopic factor influence and or cross reactions) to trigger off symptoms observed.

Results of control tests were the point of reference in assessment of reaction to allergens.

The diameter of blister ≥3 mm assessed after 15-20 minutes of allergen placement was concerned a positive result of skin Prick tests, compared to negative result of negative control.

* Eosinophilia

One-time assessment of relative eosinophilia in full blood count and its analysis were performed in 138 children with pathological acid GER and in 32 children with CMA/FA exclusively. Improper percentage value of eosinophilia, determined in full blood count, was >5%.

* Total IgE concentration (c IgE) in serum – assessed with Fluoro-Fast method (3M Diagnostic Systems, USA).

One-time assessment of serum IgE concentration was done in 170 children – 138 with acid GER and 32 with CMA/FA exclusively. Serum c IgE concentration >50 IU/ml was considered as elevated in examined children.

Taking into consideration restricted specificity of one-time measurement of total IgE in diagnosis of atopy, this test was performed together with determination of specific Ig in this particular class for selected food allergens.

* Qualitative and quantitative assessment of specific IgE against food allergens (a-s IgE) and inhalant allergens (i-s IgE) with Fluro-Fast method (3M Diagnostic Systems, USA).

Assay of allergen specific Ig concentration in examined children enabled confirmation of IgE-dependent pathomechanism of food allergy and determination of food allergens.

These tests appeared to be helpful in cases where tests cannot be performed or their results are doubtful, due to various reasons.

103 patients suspected of allergy, with positive Prick tests results (food allergens and/or inhalant allergens and increased total serum IgE concentration) underwent qualitative and quantitative assessment of a-s IgE and i-s IgE.

Table 1. **General characteristics of 138 children with primary GER and GER secondary to CMA/FA, including age**

Examined groups	Sex	Number of patients		Age of patients			
				4-16 months		16-102 months	
		N	[%]	N	[%]	N	[%]
Group 1 Primary GER N=76	Boys	39	28.3	23	16.7	16	11.6
	Girls	37	26.8	21	15.2	16	11.6
	TOTAL	76	55.1	44	31.9	32	23.2
Group 2 GER secondary to CMA/FA N=62	Boys	33	23.9	16	11.6	17	12.3
	Girls	29	21.0	14	10.1	15	10.9
	TOTAL	62	44.9	30	21.7	32	23.2
	TOTAL	138	100.0	74	53.6	64	46.4

Positive results of specific IgE were:

a) a-s IgE against cow milk proteins, hen's egg white, hen's egg yolk, soy, fish, orange;

b) i-s IgE against grass, trees, bushes and weeds pollens, house dust mites and cat's fur, assayed in serum – presence supported in class ≥2-5.

B. Oral food challenge test [10,12,13,21,23].

Open or blind oral food challenge test (depending on the age of patient) was carried out in order to establish causative relationship between food and clinical symptoms, regardless of pathogenetic mechanisms of allergy (IgE-dependent or IgE-non-dependent) [8,13].

The first stage of diagnostic procedure preceding the beginning of oral food challenge tests was eliminatory diet implementation, lasting 4 weeks in 138 children with acid GER. Diet depended on elimination of the most common food allergens, suspected of triggering off symptoms in examined children.

Eliminatory diet was determined on the basis of information gathered from medical history of past nutrition and the results of additional tests (skin Prick tests, s IgE) [8,13,23].

At the time of study, patients didn't receive or had maximally reduced antillergic and/or antihistaminic medications.

138 children at various age, with pathological acid GER, after eliminatory diet implementation (milk-free and/or hypoallergic diet) underwent 204 biological oral food challenge tests; 138 (67.6%) with cow's milk and 66 (32.4%) with other food.

In order to establish primary diagnosis, open food challenge test was performed in 104 children (under 3 years of age) and blind food challenge test in 34 children (under 3 years of age) with mainly cow's milk (low-lactose Bebilon, Ovita Nutricia) or with other potentially noxious nutrients [13,23]. Further control challenge tests in 62 children at various age with acid GER secondary to CMA/FA were repeated during 9-year clinical observation and/or conservative treatment:

• after 1 year (open study in 33 children or blind study in 29 children),

• after 2 years (blind study in 47 children),

• after 4 and 9 years of treatment (blind study in 8 children).

Every time child spent 1-3 days at hospital (Laboratory of Allergy Diagnostics, of IIIrd Department of Pediatrics)

Time of appearance of biological reaction in examined child was counted from the last food challenge up to 48-72 hours after intake of specific nutrient in native, blind form.

Every patient examined received every day observation chart for reporting intensity of clinical manifestation.

In case of cow's milk allergy or soy milk allergy and/or other food allergy the time of challenge test lasted 4 weeks.

The first challenge test was performed at the time of enrollment, further challenge tests after 1, 2, 4, 9 years of treatment with eliminatory diet. Long-lasting clinical observation was conducted to determine the acquisition of children's tolerance towards previously noxious nutrient.

Positive result of food challenge test and/or positive results of immunoallergological tests enabled to qualify a selected 62 children into group 2 – children with GER secondary to FA.

C. In order to establish the cause of secondary GER, different from food allergy, the results of additional tests performed in these children were analyzed, i.e. chest X-ray and upper gastrointestinal tract X-ray with barium swallow, X-ray or CT of sinuses (exclusively in school children).

In some patients it was necessary to analyze; full blood count, sedimentation rate, CRP, ASO and protein fraction pattern, IgA, IgM, IgG, *Helicobacter pylori* antibodies of the IgG class, iron level in order to confirm or exclude infectious cause of the symptoms presented.

Bacteriological examinations were performed in some children (blood, urine, faeces, bile, pharyngeal and nasal excretion) and metabolic screening by assaying lactic acid, ammonia, acid-base balance parameters in blood. Pilocarpine test (chlorine concentration in perspiration) was performed to exclude cystic fibrosis [9,22,24,25].

3. Assignment of children into groups

Taking into consideration esophageal pH monitoring results, complex differential diagnosis, 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 (*Tab. 1*).

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 ±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 ±17.79 months), with pathological GER secondary to CMA/FA.

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 – duration of the longest episode of acid GER (minutes) Distal channel Range of values; mean (X); standard deviation (± 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 – 37.80 17.45±8.21 (76)	2.80 – 30.20 10.21±6.54 (76)	3.80 – 24.60 7.81±6.06 (46)	7.20 – 17.00 11.41±2.96 (12)	3.80 – 5.00 4.66±0.44 (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	8.50 – 41.50 14.61±7.68 (62)	3.20 – 30.20 10.03±5.83 (62)	3.30 – 27.60 6.23±4.89 (47)	8.20 – 16.30 10.19±2.71 (8)	3.90 – 9.80 5.28±1.86 (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

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 (distal 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.

pH monitoring parameters were defined as follows: in 76 children before treatment (preliminary study) 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 *Fig. 1-4* and in *Tab. 2* (distal channel – above cardia).

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

In children with primary GER (group 1) mean values of measured parameter, before administration of treatment, x=75.68±25.61, were similar to x=74.60±16.02 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=46.75±22.88 after 1 year; 35.20±13.00 after 2 years; 41.08±4.44 and 26.33±4.42 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=74.60±16.02) was observed. Its mean values made x=57.52±21.71 after 1 year; 45.49±15.99 after 2 years; 49.25±7.21 and 27.00±1.69 after 4 and 9 years, respectively. Mean number of episodes of acid GER, measured in distal 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 year than after 4 years.

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

In children with primary GER (group 1) mean values of measured parameter, before treatment administration,

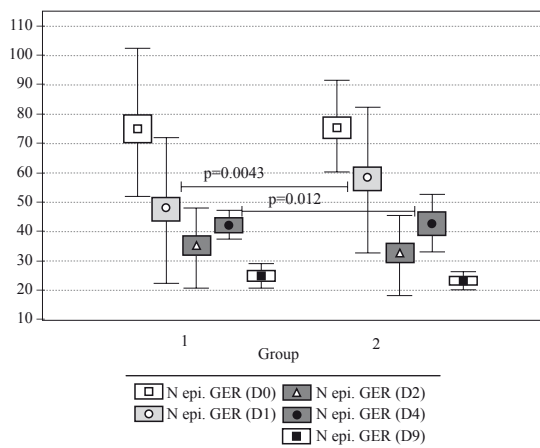*Figure 1.* **Prospective comparative analysis of number of episodes of acid GER between groups: 1 and 2 (distal channel)**

Figure 2. **Prospective comparative analysis of number of episodes of acid GER (pH<4) lasting >5 minutes between groups: 1 and 2 (distal channel)**
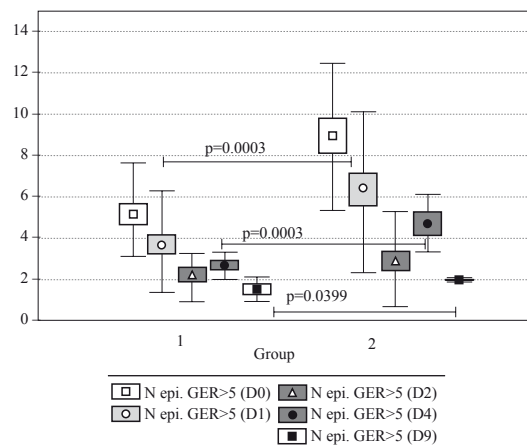

Figure 3. **Prospective comparative analysis of total acid GER index between groups: 1 and 2 (distal channel)**
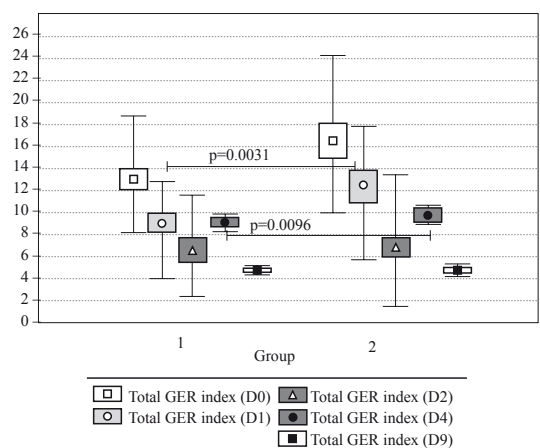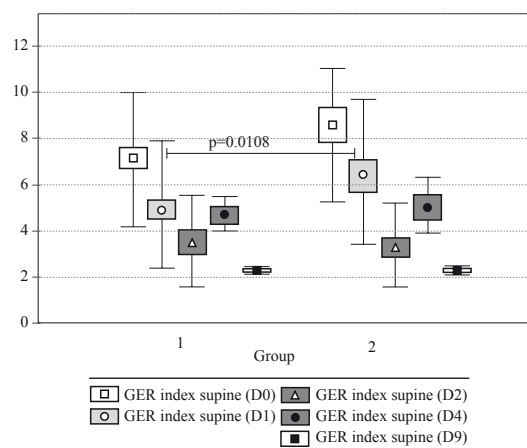

Figure 4. **Prospective comparative analysis of acid GER index (supine) between groups: 1 and 2 (distal channel)**

x=5.17±1.95 were lower than the values x=8.87±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=3.55±2.17 after 1 year; 2.17±1.18 after 2 years; 2.75±0.62 and 1.58±0.51 after 4 and 9 year, respectively.

In children with GER and CMA/FA (group 2) a downward tendency of mean number of episodes of acid GER lasting >5 minutes, measured before treatment (x=8.87±3.64) was observed. During clinical observation and/or treatment mean values accounted for x=5.87±3.75 after 1 year; 2.89±2.33 after 2 years; 4.88±0.99 and 2.00±0.00 after 4 and 9 years, respectively.

Mean number of episodes of acid GER lasting >5 minutes, measured in distal channel in both groups (1 and 2) constituted significant differentiation within 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 lasting >5 minutes between study groups (1 and 2) was confirmed. Statistical significance was higher in group 2, especially after 1 year and 4 years than after 9 years.

*** according to duration of the longest episode of acid GER (minutes) (*Tab. 2*)

In children with primary GER (group 1), mean values of the parameter measured before treatment administration x=17.45±8.21 were higher than the values in children with GER and CMA/FA x=14.61±7.68 (group 2).

During clinical observation and/or treatment in group 1, mean values were decreasing and accounted for x=10.21±6.54 after 1 year; 7.81±6.06 after 2 years; 11.41±2.96 and 4.66±0.44 after 4 and 9 years.

A downward tendency of mean value of duration of the longest episode of acid GER, measured before treatment (x=14.61±7.68) was observed in children with GER and CMA/FA.

During clinical observation and/or treatment mean values accounted for x=10.03±5.83 after 1 year; 6.23±4.89 after 2 years; 10.19±2.71 and 5.28±1.86 after 4 and 9 years, respec-

tively. Mean values of time of the longest episode of acid GER measured in distal 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 differentiation of mean values of duration of the longest episode of acid GER between study groups (1 and 2). Statistical significance was comparable in both groups: 1 and 2, in particular years.

**** according to total acid GER index (%) (*Fig. 3*)

In children with primary GER (group 1), before administration of treatment, mean values of measured parameter x=13.42±5.52 were lower than the values x=17.17±6.96 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=8.71±4.67 after 1 year; 6.99±4.24 after 2 years; 8.78±0.74 i 4.76±0.23 after 4 and 9 years, respectively.

In children with GER and CMA/FA (group 2) a downward tendency of mean values of total acid RI, measured before treatment (x=17.17±6.96) was observed.

During clinical observation and/or treatment mean values constituted x=11.83±5.85 after 1 year; 6.93±5.34 after 2 years; 10.21±1.12 i 4.59±0.24 after 4 and 9 years, respectively.

Mean values of total acid RI, measured in distal 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 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 higher in group 2, especially after 1 year than after 4 years.

***** according to acid RI, supine (%) (*Fig. 4*)

In children with primary GER (group 1), before treatment administration mean values of measured parameter x=6.96±2.64 were lower than values x=7.67±2.87 in children with GER and CMA/FA (group 2).

During clinical observation and/or treatment in group 1 mean values decreased and accounted for x=4.82±2.84 after 1 year; 3.46±2.06 after 2 years; 4.59±0.86 i 2.40±0.18 after 4 and 9 years, respectively.

In children with GER and CMA/FA a tendency of mean value of acid RI, in supine position, measured before treatment administration was observed (x=7.67±2.87).

During clinical observation and/or treatment mean values constituted x=5.92±2.81 after 1 year; 3.18±1.88 after 2 years; 5.06±0.92 and 2.40±0.09 after 4 and 9 years respectively. Mean values of acid RI, in supine position, measured in distal 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, between study groups (1 and 2) was seen. Statistical significance was higher in group 2, only after 1 year of treatment.

Discussion

Of 264 children with symptoms suggestive of GERD and various diseases of gastrointestinal system in family history, 138 children (52.3%) had pathological acid GER confirmed on the basis of 24-hour esophageal pH monitoring [1-7] and GERD diagnosed.

The results of immunoallergological tests and positive outcome of oral food challenge test [8-14,23] were pivotal in determining the cause of the disease, and acid GER was differentiated into primary (76 – 55.1%, group 1) and secondary to CMA/FA (62 – 44.9%, group 2) in 138 children.

Children with pathological acid GER diagnosed were included in a prospective study. The qualification of children was consequent upon the anomalies of pH monitoring recording and clinical manifestation. Both age and sex of 138 examined children of both study groups at diagnosis did not reveal statistically significant differences.

It was assumed that the higher positioning of the sensor of electrode in esophagus during 24-hour pH monitoring with dual-channel probe, the less number of shorter lasting reflux episodes were recorded. Total time of reflux is therefore shortened, which results from better efficiency of mechanism responsible for neutralizing gastric content retrograding into esophagus and the ability of esophagus to self-purification [5-7,19].

In both study groups (primary GER and secondary GER), the comparative analysis of mean values of pH monitoring parameters measured on the basis of 24-hour intraesophageal pH monitoring in distal lead was carried out. The measurements were done in preliminary study and during prospective clinical observation and conservative treatment.

The analysis showed significant differentiation of mean values between preliminary study and control study within groups in the case of: number of episodes of acid GER and episodes of acid GER lasting more than 5 minutes, duration of the longest episode of acid GER and acid GER index: total and supine. Statistical significance was higher in group with GER secondary to CMA/FA, especially during prospective clinical observation and treatment.

Differentiation of mean number of episodes of acid GER and episodes of acid GER lasting more than 5 minutes was shown during clinical observation and treatment.

Statistical significance of mean values of parameters mentioned was higher in group of GER secondary to CMA/FA after 1 year and 4 years.

Differentiation of mean values of total acid GER index within the groups was also statistically significant in this group after 1 year and 4 years. Similar mean values of supine acid GER index differed within the groups and were of higher statistical significance in group with GER secondary to CMA/FA but only after the first year of clinical observation and treatment. This is attributable to fast reduction of intensity of supine

GER at rest, especially during night sleep due to improvement of mechanisms responsible for neutralization and self-purification of esophagus under dietary and pharmacological treatment [12,14,19,21,22,25].

In the summary of the aforementioned comparative analysis, significantly higher values of pH monitoring parameters measured were shown during prospective studies, excluding duration of the longest episode of acid GER in children with GER secondary to CMA/FA in comparison with children with primary GER. Results obtained in patients with GER, in a study group with allergy are attributable to more intense to disorder of gastroesophageal junction arguably due to coexistent allergization of the upper gastrointestinal tract with noxious nutrient or food from children's regular diet [5-7,12,21,22,25].

Conclusions

In conclusion it was stated that values of pH monitoring parameters in distal channel in children at diagnosis were comparable, and results enabled to differentiate acid GER into primary and secondary.

During prospective clinical observation and/or conservative treatment the intensity of reflux in study groups was assessed on the basis of the results of episodes of acid GER and episodes of acid GER lasting more than 5 minutes in distal channel.

Acid GER index: total and supine appeared to be important diagnostic parameter but only after the first year of dietary and pharmacological treatment. It was therefore determined that GER secondary to CMA/FA was more intense than primary GER at that time.

References

1. 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.

2. Vandenplas Y, Loeb H. The interpretation of oesophageal pH monitoring data. Eur J Pediatr, 1990; 149: 598-602.

3. Vandenplas Y, Goyvaerts H, Helven R. Gastroesophageal reflux as measured by 24-hour monitoring, in 509 healthy infants screened for risk of sudden infants death syndrome. Pediatrics, 1991; 88: 834-40.

4. 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.

5. Arana A, Bagucka B, Hauser B, Hegar B, Urbain D, Kaufman L, Vandenplas Y. pH monitoring in the distal and proximal esophagus in symtomatic infants. J Pediatr Gastroenterol Nutr, 2001; 32: 259-64.

6. Bagucka B, Hegar B, Vandemaele K. Normal ranges of con-tinuous pH monitoring proximal esophagus. J Pediatr Gastroenterol Nutr, 2000; 31: 244-8.

7. Semeniuk J, Kaczmarski 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.

8. Kaczmarski M. Food allergy and intolerance. Milk, sugars, soya. Sanmedia, Warszawa, 1993.

9. Semeniuk J. Ethiopathogenic role of gastro-oesophageal reflux in developing of clinical symptoms in children. PhD thesis. Medical University of Białystok, 1990.

10. Staiano A, Troncone R, Simeone D. Differentiation of cow's milk intolerance and gastro-oesophageal reflux. Arch Dis Child, 1995; 73: 439-42.

11. 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.

12. Cavataio F, Iacono G, Montalto G, Soresi MM, Tumminello M, Campgna 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.

13. Kaczmarski M (editor). The stand of Polish Group of experts to food allergy and intolerance. Polish Society for Alergology, Symposium 1, Medical Convention Periodical, Unimed, 1997; 1: 21-31, 39-67.

14. Semeniuk J, Kaczmarski M, Nowowiejska B, Białokoz I, Lebensztejn D. Food allergy as the cause of gastrooesophageal reflux in the youngest children. Pediatr Pol, 2000; 10: 793-802.

15. Strobel CT, Byrne WJ, Marvin EA, Euler AR. Correlation of esophageal lengths in children with height: application to the Tuttle test without prior esophageal manometry. J Pediatr, 1979; 94: 81-3.

16. 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.

17. 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.

18. Gustafsson PM, Tibbling L. 24-hour esophageal two-level pH monitoring in healthy children and adolescents. Scand J Gastroenterology, 1988; 23: 91-4.

19. 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.

20. Little JP, Matthews BL, Glock MS. Extraesophageal pediatric reflux: 24-hour double-probe pH monitoring of 222 children. Ann Oto Thinol Laryngol, 1997; 196 (Suppl): S1-S16.

21. 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.

22. Semeniuk J, Tryniszewska E, Wasilewska J, Kaczmarski M. Food allergy-causal factor of gastrooesophageal reflux in children. Terapia, 1998; 6: 16-9.

23. Matuszewska E, Kaczmarski M, Semeniuk J. Doustne próby prowokacyjne w diagnostyce alergii i nietolerancji pokarmowej. Ped Współczesna Gastroenterol Hepatol i Żywienie Dziecka, 2000; 4: 239-43.

24. Semeniuk J, Wasilewska J, Kaczmarski M, Lebensztejn D. Non-typical manifestation of gastroesophageal reflux in children. Med Sci Monit, 1998; 4: 1122-30.

25. Salvatore S, Vandenplas Y. Gastroesophageal reflux and cow milk allergy: is there a link? Pediatrics, 2002; 110: 972-84.