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Sensitivity and Specificity of Procalcitonin to Determine Etiology of Diarrhea in Children Younger Than 5 Years

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ABSTRACT

Aim: The aim of this study is to assess the sensitivity and specificity of procalcitonin to determine bacterial etiology of diarrhea. **The examinees and methods:** For this purpose we conducted the study comprising 115 children aged 1 to 60 months admitted at the Department of Pediatric Gastroenterology, Pediatric Clinic, divided in three groups based on etiology of the diarrhea that has been confirmed with respective tests during the hospitalization. Each group has equal number of patients – 35. The first group was confirmed to have bacterial diarrhea, the second viral diarrhea and the third extra intestinal diarrhea. The determination of procalcitonin has been established with the ELFA methods of producer B.R.A.H.M.S Diagnostica GmbH, Berlin, (Germany). **Results**: From the total number of 1130 patient with acute diarrhea procalcitonin was assessed in 105. 67 (63.8%) of these patient were male. More than one third (38.14%) of the children in our study were younger then 12 months. Approximately the same was the number of children 13-24 months (33 patients or 31.43%) and 25-60 months (32 patients or 30.43%). The mean value of PRC in children with viral diarrhea was 0.13±0.5 ng/mL in children with bacterial diarrhea was 5.3±4.9 ng/m Land in children with extra intestinal diarrhea was 1.7±2.8 ng/mL. When measured using ANOVA and Turkey HSD tests, results have shown the statistical significance when comparing viral with bacterial and extra intestinal diarrhea but were statistically insignificant when comparing bacterial and extra intestinal diarrhea. **Conclusion**: Procalcitonin is an important but not conclusive marker of bacterial etiology of acute diarrhea in children younger than 5 years.
Key words: acute diarrhea, procalcitonin.

1. INTRODUCTION

Since clinical features alone are not enough good to determine etiology of acute diarrhea in children the ongoing attempts are made to find fast and reliable markers to serve this purpose. Some of the potential markers assessed were C reactive protein, erythrocyte sedimentation rate, blood white cells count and procalcitonin. Unfortunately results are inconclusive.

2. AIM

Our study is an attempt to test the ability of the procalcitonin to determine the etiology of diarrhea. This is a study conducted at the Department of Gastroenterology in Pediatric Clinic of the University Clinical Center of Kosova

3. THE EXAMINEES AND METHODS

From the total number of 1130 patient with acute diarrhea procalcitonin was assessed in 105. Children age 1 to 60 months with acute diarrhea was included in the study comprising three different groups: one with diarrhea caused by bacteria, the second caused by Rotavirus and the third with extra intestinal diarrhea. Each group had 35 children in while the etiology of diarrhea has been established during the course of the hospitalization. Data to be tested are taken at the moment of the admission to the hospital. The blood sample for procalcitonin testing has been taken using "Sarstedt" monovettes. After serum separation, biochemical parameters were immediately determined. The determination of procalcitonin has been established employing ELFA method produced by B.R.A.H.M.S Diagnostica GmbH, Berlin, Germany**.** Statistical analysis has been performed employing ANOVA and Turkey HSD tests.

4. RESULTS

Of 105 children comprised in the study 38 (36.2%) were girls and 67 (63.8%) were boys. Figure 1 explains the gender of the children and their age presented by the etiology of diarrhea More than one third (38.14%) of the children in our study were younger then 12 months. Approximately the same was the number of children 13-24 months (33 patients or 31.43%) and 25-60 months (32 patients or 30.43%).

The mean value of PRC in children with viral diarrhea was

0.13±0.5 ng/mL in children with diarrhea cause by bacteria was 5.3±4.9 ng/mL with maximum 18 ng/mL and in children with extra intestinal diarrhea was 1.7±2.8 ng/mL with maximum 12 ng/mL . (Figure 2)

When measured using ANOVA and Turkey HSD tests, and when subjected to variance analysis results have shown the statistical significance of presented values of procalcitonin when comparing viral with bacterial and extra intestinal diarrhea but were statistically insignificant when comparing bacterial and extra intestinal diarrhea (Figure 2,3 and 4).

Parameters	Viral		Bacterial		Extraintestinal		Total	
	N	%	N	%	N	%	N	%
Gender								
Male	17	48.57	26	74.26	24	68.57	67	63.8
Female	18	51.43	9	25.74	11	31.43	38	36.2
Age								
0 – 6 months	7	20	3	8.58	12	34.28	22	21
7 – 12 months	6	17.14	7	20	5	14.28	18	17.14
13 – 24 months	11	31.43	12	34.28	10	28.57	33	31.43
25 – 60 months	11	31.43	13	37.14	8	22.87	32	30.43

Figure 1. Patients according to the gender and age

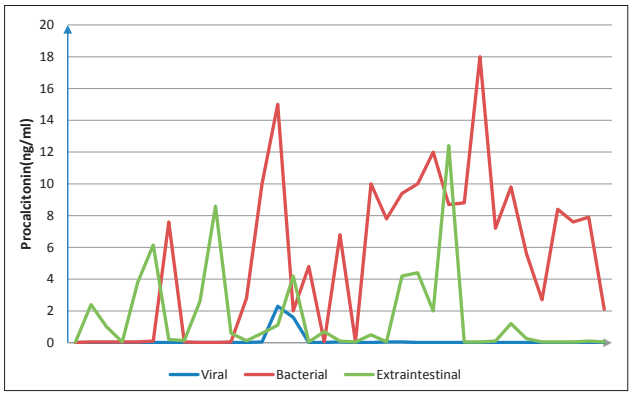

Figure 2. Values of procalcitonin in children with diarrhea according to etiology

	Valid Number	Mean	Minimum	Maximum	Standard Deviation
Viral diarrhea	35	0.133714	0.020000	2.30000	0.461641
Bacterial diarrhea	35	5.301714	0.020000	18.00000	4.947147
Extraintestinal diarrhea	35	1.658000	0.050000	12.40000	2.766602

Figure 3. Values of procalcitonin in children with diarrhea according to etiology

Variance analysis							
SS	df	MS	SS	df	MS	F	p
493.5971	2	246.7986	1099.610	102	10.78049	22.89308	0.000000

Table 4. Variance analysis of the values of procalcitonin in children with diarrhea according to etiology

Tukey HSD test			
	Viral diarrhea	Bacterial diarrhea	Extra intestinal diarrhea
Viral diarrhea		0.000104	0.132305
Bacterial diarrhea	0.000104		0.000131
Extra intestinal diarrhea	0.132305	0.000131	

Table 5. Tukey HSD analysis of the values of procalcitonin in children with diarrhea according to etiology

Table 3 presents the values of procalcitonin in children with diarrhea according to the etiology. In patients with diarrhea caused by viruses the mean values of procalcitonin was 0.133 ng/ml with peak in 2.30 ng/mL. In patients with diarrhea caused by bacteria the mean values of procalcitonin was 5.30 ng/ml with peak in 18.0 ng/mL and in patients with extra intestinal diarrhea the mean values of procalcitonin was 1.658 ng/ml with peak at 12.40 ng/mL. Table 4 presents analysis of variance for acquired data and table 5 data acquired employing Turkey HSD on the values of procalcitonin in children with different etiology of diarrhea.

5. DISCUSSION

Not all children with acute diarrhea require laboratory examination. Acute diarrhea of childhood has a short course and is easily managed by parents alone in majority of cases. This is through for most of cases. However there are also situation when laboratory investigation is very important (1), especially when baring in mind the fact that diarrhea may be a manifestation of the food poisoning and food intolerance, extra intestinal infection or surgical disease (2).

In these cases, stool investigation remains the "gold standard" for the diagnosis of diarrhea, since the similarity of the symptoms does not allow the establishment of the causative diagnosis based on clinical presentation only(3). Unfortunately the result of a stool examination are available only after 48 to 72 hours and this may delay the initiation in time of the antimicrobial therapy. The test is also not fully reliable due to a large percent of false negative and false positive results (4). As a consequence, doctors initiate the antimicrobial therapy empirically, very often aware of the risk for the bacterial flora of the intestines and the development of bacterial resistance (6). In some paper the prescription rate has arrived to unbelievable percentage of 99% (7-17). This phenomenon is global and has been reporter to very close to these figures to be present in Europe and United States (18-24). Republic of Kosovo, our country according to the National Institute of Public Health is at the tenth place for the use of antibiotics in Europe and in the fits for the use of cephalosporines.

The occurrence became so widely spread to influence Spielberg and coauthors (25) to found the world in the middle of the crisis characterized by the increase of the antibiotic resistance in every field of medicine. This includes pediatric gastroenterology as well.

In order to fight this tendency the need for simple, fast and accurate markers to distinguish between different etiological agents of acute diarrhea in children has become an imperative. Some of the potential markers are C reactive protein, erythrocyte sedimentation rate, blood white cells count and procalcitonin.

First two potential markers were the subject of analysis in a study conducted in Italy by Borgnolo and coauthors (26), Lin and coauthors from Taiwan/China (27) and Marcus and coauthors from Israel (28). Leukocyte count as a potential marker, on the other hand, was assessed by Ashkenazi and coauthors

(29). Although all of these markers have demonstrated the high specificity and sensitivity, their value is questionable (1). These because although their increase may suggest the bacterial etiology of diarrhea there were many occasion when either CRP or leukocyte count was within normal range.

Procalcitonin, that has been confirmed as excellent marker of sepsis (30-36), was assessed as a potential marker of bacterial gastroenteritis in several studies. In sepsis, compared with C reactive protein it has been shown not only much reliable but also in relation with the aggressiveness of the disease (37,13) and time required for the result to be obtained is also only two hours (38). Korczowski and Szybist [37] have tested the procalcitonin in 129 children divided in groups with extra intestinal diarrhea (sepsis, meningitis), bacterial diarrhea, rotavirus diarrhea and diarrhea due to an inflammatory intestinal disease. They compared the results with the values in healthy individuals. The results have shown for procalcitonin to be more reliable marker of the systemic infection then C reactive protein the has been shown also more specific but less sensitive for non bacterial etiology of diarrhea.

Procalcitonin has been shown important by Decaluwe and coauthors [13] and Thia and coauthors [39] that compared the values of procalcitonin in children with diarrhea caused by Escherichia coli O157:H7 and complicated with uremic hemolytic syndrome with the values of procalcitonin in children with inflammatory intestinal disease. Value of procalcitonin has been confirmed in multicentre studies as a qualitative test of inflammation in emergency departments [40]. It is also a subject of ongoing studies that will definitively explain its importance on this issue (36).

In our study values of procalcitonin were significantly different among the groups. ANOVA, Turkey HSD and variance tests when employed established the strong relation of the procalcitonin with bacterial diarrhea when compared with extra intestinal and viral diarrhea (bacterial vs. viral p= 0.000104 and bacterial vs. extra intestinal 0.000131)

6. CONCLUSION

Despite worldwide interest in developing simple and fast test to distinguish between various etiologies of diarrhea this has not been achieved jet. However, elevated values of procalcitonin may be an important indicator of bacterial nature of diarrhea, especially when considered in addition to the clinical features of the disease. Further studies will have to look into the value of elevated procalcitonin in addition to other tests like C reactive protein, erythrocyte sedimentation rate, interleukins and blood white cells count to serve this purpose.

Conflict of interest: NONE DECLARED.

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