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HOW MUCH PROCALCITONIN WE USE IN DIFFERENTIATION OF BACTERIAL PNEUMONIA IN CHILDREN?

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Abstract: *Procalcitonin is a new generation marker used to differentiate bacterial from viral pneumonia. Although it is not a test routinely used in practice, it can be included in diagnosis and treatment algorithm of pneumonia in children. Studies have shown the effectiveness of procalcitonin in determining of duration of antibiotherapy and hospitalization, too. The test is superior to the other laboratory parameters, compared to reactive C protein, inclusively. Depending on the result of the pulmonary x-ray (bacterial pneumonia) admitted patients were included in: study group – patients with increased values of procalcitonin, and control group – patients with normal values ones. The study proposed a comparative analysis; the correlation index was used to demonstrate how laboratory parameters can interact, and the evolutionary trend of studied parameters was analysed. The results are consistent with the literature data, validating the superiority of procalcitonin in establishing the etiologic diagnosis and the treatment evaluation in bacterial pneumonia in children.*

INTRODUCTION

Procalcitonin – a new generation marker of differentiation of bacterial from viral pneumonia, it is not a test often used in practice, although numerous studies appreciate it in bacterial infection diagnosis and treatment algorithm.(1)

The value of procalcitonin is directly proportional with the severity of bacterial infection, mainly being superior to reactive C protein.(2) The interest in procalcitonin is even greater as identification methods of pneumonia etiology in children are often invasive finally, the practitioner decision regarding antibiotherapy choice is theorized, and the duration of treatment seems random, one.(3)

Provided that the clinical examination became more and more subjective, and the x-ray exam conclusions sometimes differ from specialist to specialist, the final therapeutic decision it to move further and further away from the rigors of diagnosis and treatment algorithm of pneumonia in children.(1,4)

AIM

The study aims to evaluate the procalcitonin in pediatric patient diagnosed with community-acquired pneumonia established by x-ray criteria, mainly (the community-acquired pneumonia is considered the prototype of bacterial pneumonia in children). Thus, the following were studied:

- the role of procalcitonin in pneumonia evolution evaluation (hospitalization decision, duration of antibiotherapy and hospitalization) (5) and,
- the correlation between procalcitonin and clinical and the other laboratory data.

MATERIALS AND METHODS

Pediatric patients diagnosed with community-acquired pneumonia were included in the study. The diagnosis was established according to the definition of the Thoracic Society of Great Britain and the American Society of Infectious Diseases. Depending of the value of procalcitonin, two groups of patients were established: study group – patients with community-acquired pneumonia and increased values of procalcitonin and control group – patients with community-acquired pneumonia and normal values of procalcitonin.

Both groups were evaluated by general data (gender, environmental origin), clinical data (the presence of fever at the onset of disease), laboratory data (leukocyte count, neutrophil percentage, hemoglobin, platelet count, reactive C protein) and evolution data (length of stay).

The hemoglobin and platelet count were considered the inflammation markers, as included in the literature data, considering the extent of infectious anemia and reactive thrombocytosis from the evolution of pneumonia.(6)

The obtained data were statistically evaluated by odds ratio and correlation index.

RESULTS AND DISCUSSIONS

The study group included 54 patients, 26 males and 28 females, 29 from urban and 25 from rural origin, respectively.

The control group included only 4 patients, 3 males and 1 females, being homogeneous by environmental origin.

1. The comparative analysis of clinical, laboratory and evolution data of the groups

The fever was the only clinical parameter used in the study. The mean values of body temperature was 38,94^{0}C in the study group and 37,2^{0}C in the control group. The limit between normal value and hyperthermia is variable, so several possibilities were analysed:

- fever, corresponding to a value greater than 37,5^{0}C, was

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extremely statistically significant (p 0,00**)
- fever, corresponding to a value greater than 38^0C, was extremely statistically significant (p < 0,0001)
- fever, corresponding to a value greater than $38,6^0$C (according to the first quartile), was statistically significant (p < 0,003)
- fever, corresponding to a value greater than $38,9^0$C (according to the second quartile), was at the limit of statistical significance (p < 0,04)
- fever, corresponding to a value greater than $39,1^0$C (according to the third quartile), was without statistically significant (p = 0,26).

It is found that as the value of body temperature increase, the groups become less and less statistically significant.

The **leukocytes count** analysis (at the onset of pneumonia), old marker of differentiation of bacterial infection from viral one, showed the following results:
- the limit of 14.410/mmc (according to the first quartile) was not statistically significant (OR = 9,462 95% CI [0,9047-98,96], p < 0,059)
- the limits of 18.530/mmc (according to the second quartile) and 25.030/mmc (according to the third quartile) were not statistically significant (p < 0,08, p = 0,32, respectively).

The statistically significance of leukocytes count is only found to the limit of 14.000/mmc (OR = 13,2 95% CI [1,24-140,5], p = 0,032).

The mean leukocytes count was 20.200/mmc in the study group and 9.590/mmc in the control group.

The statistical analysis of **neutrophils percentage** (at the onset of pneumonia) found that the value of 63,8 % (according to the first quartile) has a statistical significance at the limit (p = 0,049). The statistical significance grows with the reduction of the limit to 61 % neutrophil percentage.

The mean neutrophils percentage was 73,2 % in the study group and 43,17 % in the control group.

The **hemoglobin** analysis proved that it does not exist any statistical significance between groups, even at values lower than 9,8 g/dL (p = 0,35).

The mean hemoglobin was 11,21 g/dL in the study group and 14,3 g/dL in the control group.

The **platelets count** analysis, another old inflammatory marker, showed that it does not exist statistical significance between groups even at values greater than 700.000/mmc.

The mean platelets count was 359.500/mmc in the study group and 385.500/mmc in the control group, almost homogeneous values.

The **reactive C protein** analysis, the most important differentiation marker, but considered inferior to procalcitonin, proved that a value greater than 55 mg/L (according to the first quartile) is extremely statistically significant (p < 0,005).

The mean reactive C protein was 115,07 mg/L in the study group and 6,25 mg/L in the control group.

The mean **length of stay** was 10,03 days in study group and 10,25 days in control group (homogeneous groups).

Considering the fact that the two groups are extremely heterogeneous, the analysis did not demonstrate statistical significance only for reactive C protein (since the first quartile).

2. The Pearson correlation index was studied only in study group, between procalcitonin and the other laboratory and evolution parameters in order to evaluate how parameters can interact.

It is found that of all of studied parameters the best interaction exists between procalcitonin and reactive C protein (figure no. 1). The interaction is a moderate one, both parameters changing in the same direction (growing, at the onset), followed by the relation with the length of stay, although a weak one, but statistical significant. Hemoglobin and platelets count shows a negative relation (table no. 1).

Table no. 1. The correlation index between procalcitonin and the other parameters (at the onset of pneumonia)

Parameter compared with procalcitonin at the onset of pneumonia	Relation		p value
	intensity	direction	
Leukocytes count	weak	positive	0,118
Neutrophils percentage	very weak	positive	0,104
Hemoglobin	very weak	negative	0,244
Platelets count	very weak	negative	0,410
Reactive C protein	moderate	positive	0,000057
Length of stay	weak	positive	0,00497

Figure no. 1. The correlation between procalcitonin and reactive C protein at the onset of pneumonia

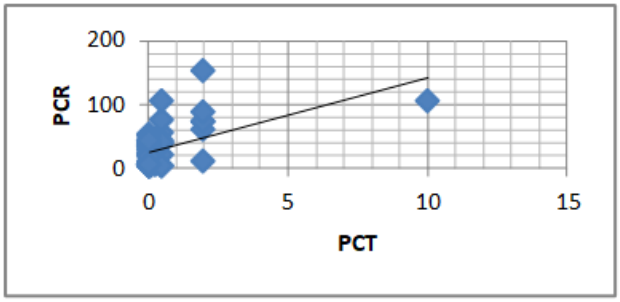

Table no. 2. The correlation index between procalcitonin and the other parameters (in evolution of pneumonia)

Parameter compared with procalcitonin, in evolution of pneumonia	Relation		p value
	intensity	direction	
Leukocytes count	very weak	positive	0,292
Neutrophils percentage	very weak	positive	0,351
Hemoglobin	very weak	positive	0,544
Platelets count	very weak	positive	0,410
Reactive C protein	weak	positive	0,00046
Length of stay	very weak	positive	0,243

In evolution, the interaction is found to be weaker than at the onset of pneumonia, reactive C protein normalizing later than procalcitonin. Although weak, the intensity of relation between procalcitonin and reactive C protein is statistically significant. It is also found a discordance of the direction of interaction between procalcitonin and hemoglobin, and platelets count, too: in evolution, the trend of hemoglobin and platelets count should be upward (with relieving anemia and reactive thrombocytosis), while the downward procalcitonin trend (table no. 2).

Considering the obtained results by correlation index it can be seen that in deliberation of the final diagnosis of community-acquired pneumonia the other parameters are necessary whose relation with procalcitonin is stronger.

3. The correlation between the evolution trend of procalcitonin and the other laboratory parameters.

Procalcitonin is the most accurate indicator of pneumonia evolution, dictating the duration of treatment, and healing, inclusively.

The results of the study were consistent with literature data. The study showed no statistical significance between the evolution of procalcitonin and those of the other laboratory parameters, as follows:
- leukocytes count does not normalize at the same time with procalcitonin (OR = 2,857 95 % CI [0,8854-9,433]; p = 0,07)
- neutrophils percentage does not normalize at the same time

with procalcitonin (OR = 1,768 95% CI [0,5611-5,57]; p = 0,24)
- hemoglobin does not normalize at the same time with procalcitonin (OR = 1,133 95% CI [0,3568-3,6]; p = 0,53)
- platelets count does not normalize at the same time with procalcitonin (OR = 2,779 95% CI [2,779 [0,7277-10,62]; p = 0,11)
- reactive C protein does not normalize at the same time with procalcitonin (OR = 1,086 95% CI [0,3293-3,579]; p = 0,56).

The study showed no statistical significance between the normalization trend of procalcitonin and the trends of the other parameters, as follows:
- leukocytes count does not tend to decrease at the same rate with the decrease of procalcitonin (p = 0,11)
- neutrophils percentage does not tend to decrease at the same rate with the decrease of procalcitonin (p = 0,16)
- hemoglobin does not tend to increase at the same rate with the decrease of procalcitonin (p = 0,43)
- platelets count does not tend to increase (reactive thrombocytosis) or decrease at the same rate with decrease of procalcitonin (p = 0,68)
- reactive C protein does not tend to decrease at the same rate with the decrease of procalcitonin (p = 0,91).

CONCLUSIONS

Since the study design (division into groups) depended almost exclusively on the result of pulmonary x-ray (considered until recently the diagnostic standard in pneumonia in children), the procalcitonin was requested only as laboratory marker, but most importantly, in differentiation of bacterial pneumonia from viral one.(7)

The study proved the superiority of procalcitonin in comparison with the other laboratory parameters.

The main inconvenience lies in the fact that procalcitonin is not considered a routine test in pediatric practice, and the other markers, with similar effectiveness (e.g. interleukin), are far too expensive to include themselves in diagnostic and treatment algorithm.

A hope could come from lung ultrasonography, as variant of x-ray, for the purpose of improvement etiologic differentiation in pneumonia in children.

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