C-Reactive Protein and Leukocyte Count in the Diagnosis of Acute Appendicitis in Children

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PURPOSE: The aim of this study was to analyze the diagnostic accuracy of C-reactive protein and its possible advantage, if any, over leukocyte counts in acute appendicitis in children. METHODS: We performed a retrospective study of 124 children (72 males) with a mean age of 9.3 (range, 2-14) years operated on under a clinical diagnosis of acute appendicitis. The diagnosis of acute appendicitis, confirmed by pathologic examination of the removed appendix, was then correlated with C-reactive protein, leukocyte count, and a combination of both C-reactive protein and leukocyte count, with a logistic regression model. C-reactive protein serum measurements were performed by an immunoturbidimetric test. The patients were divided into two groups according to the pathologic features of the removed appendix: Group A (n = 104), patients with acute appendicitis, and Group B (n = 20), patients without acute appendicitis. To assess the accuracy of C-reactive protein, leukocyte counts, and a combination of both parameters, receiver operating characteristic curves were used. The areas under the curve were compared using the maximum likelihood estimation method. RESULTS: There were 95 cases (76.6 percent) of nonperforated appendicitis, 9 cases (7.3 percent) of perforated appendicitis and 20 cases (16.1 percent) of normal appendix. Mean C-reactive protein in Group A was 4.3 (standard deviation, 6.6) and in Group B was 1.2 (standard deviation, 1.7; P = 0.03). The C-reactive protein and leukocyte count values were correlated with the pathologic diagnosis of acute appendicitis. Mean C-reactive protein values increase as the pathologic inflammation type progresses (P = 0.007). The C-reactive protein receiver operating characteristic curve shows that the C-reactive protein value with highest accuracy was 1.7 mg/dl. The sensitivity, specificity, and accuracy rates calculated in the 1.7 cutoff were 58, 80, and 83.8 percent, respectively. A comparison of the respective receiver operating characteristic curves demonstrates that C-reactive protein, leukocyte count, and the combination of both tests all have a good diagnostic value but without any significant difference (P = 0.2). CONCLUSIONS: In children, 1) serum C-reactive protein is increased in acute appendicitis; 2) such increase is related to the severity of the appendiceal inflammation; and 3) although serum C-reactive protein has an adequate diagnostic accuracy, neither individually nor in combination with the leukocyte count is it significantly better than the leukocyte count alone. [Key words: Appendicitis; Diagnosis; Leukocytes; C-reactive protein]
tions: Does a cutoff value exist to accurately diagnose AA? When does the CRP increase happen after symptom onset? Is CRP or a combination of CRP and leukocyte count superior to leukocyte count alone?

**PATIENTS AND METHODS**

We performed a retrospective study of 124 consecutive patients operated on with a clinical diagnosis of AA. There were 52 females. The clinical diagnosis was established preoperatively by a staff surgeon in every patient by means of clinical history, physical examination, and laboratory tests, including total leukocyte count, leukocyte differential count, CRP, and abdominal plain films. CRP serum concentration was measured by immunoturbidimetry (Tina-quant® CRP, Boehringer-Mannheim GmbH, Mannheim, Germany; normal value < 0.5 mg/dl). The removed appendix was studied histologically in every case, and the patients were divided into two groups: Group A (n = 104), AA confirmed, and Group B (n = 20), normal appendix.

A logistic regression model was used to decode whether CRP offers information in addition to the leukocyte count. Logistic regression provides a model for the variables that could predict a diagnosis of appendicitis. Through use of these variable coefficients the risk of having appendicitis can be estimated for each variable level.

Because reporting only one value for sensitivity and specificity may result in a misleading simplification of diagnostic accuracy, we used the receiver operating characteristic (ROC) curves to measure the clinical performance of the tests. Briefly, a ROC curve is a graphic representation of multiple pairs of sensitivity and 1 − specificity calculated at several cutoff values of the test. To establish these values, CRP and leukocyte counts were stratified in ten levels, then the ROC curves were calculated using the ROC Curve Analyzer program (Version 6; Richmond, Virginia). If the area under the curve is close to 1, the test discrimination is very good, but if the area is close to 0.5, the discrimination is very poor.

The areas under the curve were compared using the maximum likelihood estimation method. Other numeric values were analyzed by Student's t-test and variance analysis.

**RESULTS**

The mean age of the patients was 9.3 (range, 2–14) years. Average evolution time between symptom onset and CRP and leukocyte sampling was 28.2 (range, 3–166; standard deviation (SD), 25.5) hours. The age, gender, and preoperative evolution time were comparable between the two groups (Table 1).

Histologic examination revealed 20 cases of normal appendix (16.1 percent), 64 cases of simple appendicitis (51.6 percent), 31 cases of gangrenous appendicitis (25 percent), and 9 cases of perforated appendicitis (7.3 percent). Thus, the diagnosis was confirmed in 104 patients (83.9 percent). Mean evolution time between symptom onset and CRP and leukocyte sampling was 22.4 (SD, 18.6), 29 (SD, 15.5), and 63.7 (SD, 50.8) hours in simple, gangrenous, and perforated appendicitis, respectively. It was 23.8 (SD, 27.9) hours in cases of normal appendix. CRP values are represented in Figure 1. Mean value in Group A was 4.3 (SD, 6.6) mg/dl, and in Group B it was 1.2 (SD, 1.7) mg/dl (P = 0.05). CRP mean value increased proportionally with more advanced degree of inflammation (Fig. 2), with significant differences between every appendicitis type and the normal appendix (P = 0.007).

Logistic regression analysis showed that a model including both CRP and leukocyte count has a better predictive value than any other model, including either of the variables. The model gave the following formula:

\[
\text{Probability} = \frac{1}{1 + e^{(-1.00+0.40\times CRP+0.12\times \text{leucocyte})}}
\]

The coefficients indicate the risk increase for each variable value increase (Table 2). In Table 3 a risk estimation has been represented for several values of CRP and leukocyte count, using the aforementioned formula. The risk of having appendicitis increases with higher levels of either CRP or leukocyte count, but is greatest with the highest levels of both variables.

Concerning ROC analysis, in the CRP ROC curve (Fig. 3) two points having the greatest areas can be seen: 1.7 and 3.8, with both high positive predictive value (94 and 97 percent, respectively) but low negative predictive value (26 and 22 percent, respectively). From a clinical point of view a cutoff of 1.7 mg/dl

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<tr>
<th>Table 1. Features of Patients with Appendicitis (Group A) and Without Appendicitis (Group B)</th>
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<tbody>
<tr>
<td>Age (yr)</td>
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<td>Group A</td>
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<td>Group B</td>
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