Acute-Phase Proteins in Acute Appendicitis

To the Editor:

After tissue injury or inflammation there may be increased synthesis of several "acute-phase" proteins. Although this response is nonspecific, increases in these proteins in serum are commonly interpreted as a sign of inflammation. Assessment of the diagnostic value of acute-phase proteins in this setting is hampered by the lack of reliable, definitive criteria to establish the presence of inflammation.

We chose to evaluate the diagnostic value of measuring five acute-phase proteins (haptoglobin, α1-antitrypsin, α1-acid glycoprotein, ceruloplasmin, and C-reactive protein) for the detection of acute appendicitis. By utilizing defined histological criteria to establish the presence of appendicitis after surgery, the sensitivity and specificity of each protein for the diagnosis of acute appendicitis could be evaluated with reasonable certainty.

We studied 98 patients admitted to the emergency room with the clinical designation of "rule-out" appendicitis who subsequently underwent surgery. Blood was sampled on admission to the emergency room. During the period of study, no patient who was discharged without surgery was subsequently re-admitted for an appendectomy. The diagnosis of acute appendicitis, made by an anatomical pathologist, was based on standard criteria (1). If initial sectioning failed to show inflammation, the remainder of the specimen was sectioned and microscopically examined in toto.

α1-Antitrypsin, α1-acid glycoprotein, haptoglobin, ceruloplasmin, and C-reactive protein were determined by nephelometry with an ICS Analyzer (Beckman Instruments, Fullerton, CA 92634), according to the manufacturer's procedure.

The diagnostic sensitivity and specificity (2) of each acute-phase protein for the detection of appendicitis were determined at multiple discrimination levels. The decision levels tested ranged from the lower limit of the suggested reference interval to fivefold the upper limit. These data were evaluated by generating a family of receiver operating characteristic curves (3), shown in Figure 1. These curves clearly demonstrate that none of the proteins evaluated exhibited a high sensitivity at specificities greater than 20%. C-reactive protein and α1-antitrypsin were more sensitive than the other proteins at specificities from 20 to 90%, but remained less than 90% sensitive for acute appendicitis. At maximal levels of sensitivity, no protein exhibited a positive predictive value of greater than 90%.

Acute appendicitis without rupture is a relatively focal inflammatory disease of unclear etiology. It is a surgically correctable condition, which incurs a significant morbidity if left untreated. The surgical approach to acute appendicitis has resulted in a reported diagnostic error rate (removal of a normal appendix) of 15 to 25% (4, 5). This error is weighed against the risk of delayed surgery and appendiceal perforation. In this study, the clinical diagnostic error was 18% and the perforation rate 8%. We found no evidence of clinical false-negative (missed case) workups. Therefore, the "clinical" diagnostic sensitivity was apparently 100% with a positive predictive value of 82%.

To provide additional diagnostic information, laboratory tests for acute appendicitis should possess 100% sensitivity (no false negatives) and 100% negative predictive value, and a significant increase in positive predictive value above that found without testing. Any significant false-negative ratio is unacceptable, owing to the potential complications of appendiceal rupture if surgery is delayed, especially when the clinical diagnosis is made with such high sensitivity. The acute-phase proteins we tested fail to demonstrate this required sensitivity. Lowering the decision levels to a point where sensitivities approached 90% resulted in a marked loss of specificity and in positive predictive values similar to those seen without testing. We conclude that determination of individual acute-phase proteins does not provide the clinician with any additional information that could decrease the proportion of normal appendices surgically removed while ensuring that all true cases of appendiceal inflammation received prompt surgical treatment.

Figure 1. Receiver operating characteristic curves for acute-phase proteins in the diagnosis of appendicitis

True positive ratio (sensitivity) is plotted against false positive ratio (1-specificity) at various decision levels. Proteins evaluated were C-reactive protein (closed circles), α1-antitrypsin (open circles), α1-acid glycoprotein (open triangles), haptoglobin (closed triangles), and ceruloplasmin (closed squares).

References

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Supplier Misidentified

To the Editor:

In a review of hemostatic disease markers (1), Table 4 incorrectly states that New England Nuclear offers a kit for measurement of leukotrienes. Ours is the only company currently manufacturing and marketing kits for quantification of lipooxygenase products. Currently we have kits for 5-HETE, 12-HETE, and 15-HETE. Additionally Seragen's kits for measurement of thromboxane B2 and 5-ketoPGF1α (both 3H-RA or 125I-RA) were not mentioned. In fact, Seragen has the world's most extensive line of kits for prostaglandin measurement.

Reference

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Improved Liquid-Chromatographic Determination of 5-Hydroxyindoles

To the Editor:

Recently, we described a liquid-chromatographic method for determining indole-3-acetic acid and 5-hydroxyindole-3-acetic acid (5HIAA) in human plasma (1). The procedure involves addition of 40 μL of a 20 g/L solution of