The value of 5-hydroxyindolacetic acid levels in spot urine in the diagnosis of acute appendicitis

Spot idrarda 5-hidroksi indol asetik asit düzeyinin akut apandisit tanısındaki değeri

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BACKGROUND

We investigated the value of 5-hydroxyindolacetic acid (5-HIAA) levels in spot urine in the diagnosis of acute appendicitis.

METHODS

Forty-three patients (11 females, 32 males; mean age 26.3 years; range 16 to 73 years) who were admitted to the emergency room with acute abdominal pain and suspected acute appendicitis were evaluated by means of physical examination, leukocyte counts, urine analysis, measurements of 5-HIAA in spot urine, abdominal x-rays, and sonography. Of these, 25 patients underwent appendectomy after a clinical diagnosis of acute appendicitis. Spot urine analyses were made in all the patients within the first hour of admission with the use of spectrophotometric and colorimetric methods; 5-HIAA levels were read at 540 nm.

RESULTS

At laparotomy, 22 patients (88%; 3 females, 19 males; mean age 26.18 years; range 15 to 38 years) were found to have acute appendicitis (11 phlegmonous, 11 gangrenous), whereas three patients (12%; 2 females, 1 male) had negative findings. No significant differences were found between patients with confirmed acute appendicitis, patients without appendectomy, and those with negative laparotomy with respect to the mean leukocyte counts and 5-HIAA levels ($p>0.05$). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 5-HIAA for the diagnosis of acute appendicitis were calculated as 22%, 93%, 71%, 62%, and 63%, respectively.

CONCLUSION

Measurement of 5-HIAA levels in spot urine is not helpful in the diagnosis of acute appendicitis.

Key Words: Appendectomy; appendicitis; diagnosis, differential; hydroxyindoleacetic acid; leukocyte count; urine.

AMAÇ

Bu çalışmada spot idrarda 5-hidroksi indol asetik asit (5-HİAA) düzeyinin akut apandisit tanısındaki değeri araştırıldı.

GEREÇ VE YÖNTEM

Karın ağrısı şikayetiyle acil cerrahiye başvuran ve akut apandisit olduğu düşünülen 43 hasta (11 kadın, 32 erkek; ort. yaş 26.3; dağılım 16-73) fizik muayene, lökosit sayımı, tam idrar tahlili, spot idrarda 5-HİAA düzeyi, direkt batın grafisi ve batın ultrasonografisi ile değerlendirildi. Yirmi beş hastada klinik olarak akut apandisit tanısı konduktan sonra apandektomi uygulandı. Spot idrar tahlili tüm hastalarda başvurunun ilk saati içinde yapıldı ve örnekler spektrofotometrik ve kolorimetrik yöntemlerle incelendi; 5-HİAA düzeyleri 540 nm'de okundu.

BULGULAR

Laparotomide 22 hastada (88%; 3 kadın, 19 erkek; ort. yaş 26.18; dağılım 15-38) akut apandisit olduğu görüldü (11 olguda flegmonöz, 11 olguda kangrenöz); üç hastada (12%; 2 kadın, 1 erkek) ise laparotomi bulguları negatif idi. Akut apandisit tanısı doğrulanan, apandektomi uygulanmayan ve negatif laparotomi sonucu alınan hastalar arasında ortalama lökosit sayımı ve 5-HİAA düzeyleri açısından anlamlı farklılık bulunmadı ($p>0.05$). Akut apandisit tanısında 5-HİAA düzeyinin ölçümünde duyarlık, özgüllük, pozitif öngörü değeri, negatif öngörü değeri ve doğruluk sırasıyla %22, %93, %71, %62 ve %63 bulundu.

SONUÇ

Spot idrarda 5-HİAA ölçümü akut apandisit tanısı koymada yardımcı bir yöntem değildir.

Anahtar Sözcükler: Apandektomi; apandisit; tanı, ayırıcı; hidroksi indol asetik asit; lökosit sayımı; idrar.

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Acute appendicitis which is the most common cause of acute abdomen is diagnosed mainly by clinical examination (history, physical examination).[1] There is no diagnostic test to detect acute appendicitis with 100% specificity and sensitivity; for this reason, many clinical studies have been performed in an attempt to decrease negative laparotomy rates.[2]

Seratonin is a local transmitter and a mediator of inflammation, which is released during inflammation and cell damage. It is metabolized to 5-hydroxyindolacetic acid (5-HIAA) by the liver and excreted in urine. It has been shown that, beneath the epithelial layer of the appendix, the lamina propria consists of cells containing seratonin in their eosinophilic granules,[3] which theoretically might be released during acute appendicitis.

In this study we aimed to measure 5-HIAA levels in spot urine and to evaluate its significance in the diagnosis of acute appendicitis.

MATERIALS AND METHODS

The study included 43 consecutive patients with suspected acute appendicitis, who were admitted to the 3rd General Surgery Department of Şişli Etfal Training and Research Hospital between November 2001 and 2002. There were 11 females, and 32 males with a mean age of 26.3 years (range 16 to 73 years). The patients were evaluated by physical examination, leukocyte count, urine analysis, 5-HIAA levels in spot urine, abdominal sonography and abdominal x-rays. Upon the diagnosis of acute appendicitis, appendectomy was planned for 25 patients. They were further divided into three groups as phlegmonous and gangrenous appendicitis (group A, n=22) and negative laparotomy. Those with a right lower quadrant pain, but without a diagnosis of acute appendicitis (n=18) were followed-up until their abdominal pain diminished (group B).

Spot urine analyses were made in all the patients within the first hour of admission with the use of spectrophotometric (Kontron Instruments, Zurich, Switzerland) and colorimetric methods; 5-HIAA levels were read at 540 nm.

Abdominal sonography findings showing a distended appendix with a diameter of more than 5 mm, an uncompressible appendix, appendicolithiasis, and fluid in the pouch of Douglas were regarded as diagnostic parameters of acute appendicitis. Plain films of the abdomen in acute appendicitis often reveal a distended loop or two of small bowel in the right lower quadrant, less often a distended cecum. A radiopaque fecalith when present in the right lower quadrant is nearly always associated with gangrenous appendicitis. Abdominal roentgenograms were regarded as positive in the presence of one or two distended loops of the small bowel in the right lower quadrant, a distended cecum, or a radiopaque fecalith in the right lower quadrant.

Statistical analyses were made with the use of the GraphPad Prism V3 program. Non-parametric tests were used for the parameters which could not be homogeneously grouped; the Mann-Whitney U-test was used to compare the groups of two and the chi-square test to compare the qualitative data.

RESULTS

All the patients had right lower abdominal pain; in 25 patients, physical examination showed maximal tenderness at or near the point described by McBurney[4] and rebound tenderness. After the clinical diagnosis of acute appendicitis, a decision for appendectomy was given for 25 patients. At laparotomy, 22 patients (88%; 3 females, 19 males; mean age 26.18 years; range 15 to 38 years) were found to have acute appendicitis (11 phlegmonous, 11 gangrenous), whereas three patients (12%; 2 females, 1 male) had negative findings (Table 1).

No significant differences were found between group A, B, and the patients with negative laparotomy with respect to the mean leukocyte counts and 5-HIAA levels ($p>0.05$) (Table 1). Similarly,

Table 1. Comparison of different parameters of patients with suspected acute appendicitis

	Group A (n=22)	Group B (n=18)	Normal laparotomy (n=3)	*p*
Mean age	26.18±11.68	26.62±8.34	28.92±9.31	>0.05
5-HIAA levels (mg/L)	15.59±11.36	11.60±6.95	13.24±8.72	>0.05
Leukocyte counts (/mm^3)	13,540.91±2,812.3	11,805±3,635.86	12,854±3,114.72	>0.05

patients with phlegmonous appendicitis, gangrenous appendicitis, and with negative laparotomy findings did not have significantly different 5-HIAA levels (14.74 mg/dl, 16.44 mg/dl, and 14.66 mg/dl, respectively; $p>0.05$).

The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 5-HIAA measurement for the diagnosis of acute appendicitis were calculated as 22%, 93%, 71%, 62%, and 63%, respectively.

Abdominal sonography was diagnostic in nine patients in group A (40.9%), and in three patients (14.3%) in group B ($x^2=3.78$; $p>0.05$). Sonography revealed normal findings in 13 patients (59.1%) in group A, and in 18 patients (85.7%) in group B ($x^2=3.78$; $p>0.05$). Abdominal x-rays were evaluated as positive in eight patients (36.4%) in group A, and in six patients (28.6%) in group B ($x^2=0.29$; $p>0.05$). There were no significant differences between the results of radiological investigations.

DISCUSSION

Patients with suspected acute appendicitis are usually assessed clinically with history and physical signs, both of which are subjective evaluations. An accurate diagnosis depends on the experience of the surgeon, sociocultural level of the patient, and interpretation of pain by the patient. The main reason for the search of a diagnostic parameter in acute appendicitis is to avoid negative laparotomies.[5] Negative laparotomy rates for appendectomy range between 9% to 19%,[6-9] being higher in women than in men.[7,8] In our study, three patients (12%) had negative laparotomy findings, with a female-to-male ratio of 2:1.

Leukocyte count, neutrophil count, C-reactive protein (CRP), interleukin-6, and phospholipase A_2 are some of the non-specific indicators of inflammation, which have been studied in acute appendicitis.[6,10-13] Leukocyte count is quite sensitive (60-90%) but less specific (46-70%) and is not more diagnostic than physical examination and observation.[14-17] Nonetheless, increased leukocyte levels support the clinical diagnosis.

A meta-analysis of 24 studies has shown that CRP levels provide a moderate accuracy for acute appendicitis, with sensitivity and specificity ranging between 40% to 60% and 27% to 90%, respectively.[16] Dueholm et al.[15] reported that CRP and leukocyte count, together with neutrophil count are insufficient for the diagnosis of acute appendicitis. However, when all the three are in normal ranges appendectomy may be avoided.

In cases of acute appendicitis, the sensitivity and specificity of abdominal sonography have been reported as 78% to 96% and 85% to 98%, respectively.[18-21] In our study, nine patients (40.9%) with acute appendicitis had normal sonographic findings and were evaluated as false negative, whereas three patients (14.3%) had false positive results.

5-Hydroxyindolacetic acid is a metabolite of seratonin and is used in the diagnosis of carcinoid tumors. Although the appendix is rich in seratonin (5-hydroxytryptamine) secreting cells, only a few studies have evaluated the relationship between seratonin levels and acute appendicitis. The first study, published in 1987, reported the sensitivity and specificity of high seratonin levels as 45% and 95%,[22] and another study as 93.8% and 95.7%,[23] respectively. Singh et al.[24] found higher seratonin specificity when gangrenous appendicitis was excluded. Ilkhanizadeh et al.[8] measured 5-HIAA levels in spot urine of patients with acute appendicitis and found sensitivity as 98% and specificity as 100%. In our study, the sensitivity of 5-HIAA levels in spot urine was very low (22%), though the specificity was 93%.

In conclusion, our data show that measurement of 5-HIAA levels in spot urine is not helpful in the diagnosis of acute appendicitis. In view of our findings and the reported data in the literature, the diagnosis of acute appendicitis should be based on clinical evidence provided by history and physical examination.

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