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THE VALUE OF 5-HYDROXY INDOLE ACETIC ACID MEASUREMENT IN SPOT URINE IN DIAGNOSIS OF ACUTE APPENDICITIS

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ABSTRACT

Objective: To assess the role of 5-Hydroxy Indole Acetic Acid (5-HIAA) levels in spot urine in diagnosis of acute appendicitis.

Design: A prospective, controlled study.

Setting: Ankara Numune Teaching and Research Hospital, Ankara, Turkey.

Subject: Twenty six patients with histologically proven acute appendicitis following appendectomy were included in the study. Control group with consisted of patients prepared for hernia repair in the same duration. In the preoperative period, urine samples were collected from every patient for measurement of 5-HIAA.

Results: The study group comprised 26 patients; 15 of those had high urine 5-HIAA levels, whereas 11 patients had values within normal range. None of ten control patients displayed positive test result. The test had 58% sensitivity and 48% specificity. In histopathological examination only two of ten patients with gangrenous appendicitis showed positive test result, whereas 13 of 16 patients with no histopathological gangrenous changes had high values.

Conclusion: Urine 5-HIAA measurement has low sensitivity and specificity. The value of the test is even clearly lower in gangrenous appendicitis. This may be misleading in management of patients in late phase of appendicitis and in cases with perforation which is mainly responsible for morbidity.

INTRODUCTION

Despite recent improvements in diagnostic methods, to diagnose acute appendicitis (AA) grossly depends on the clinical judgement of the surgeon. Today, no single, safe laboratory method is available to help the surgeon in confirming the diagnosis. Also, imaging studies like ultrasound and computed tomography have high false negative rates(1).

Recently, it has been shown that blood serotonin levels confirm the diagnosis of AA(2-4). Serotonin is released by enterochromaffine cells in the lamina propria of the appendix(5). It may act as a local neurotransmitter as well as a mediator of inflammation. Therefore, serotonin may be a sign of acute inflammation of appendix. There have been few clinical studies assessing plasma serotonin level in AA(2-4). On the other hand, there is only one study in the English-based literature which reported the role of serotonin metabolite 5-Hydroxy indole acetic acid (5-HIAA) measurement in spot urine in this clinical condition(6). This study aimed to investigate the value of 5-HIAA levels in spot urine in the diagnosis of AA as a simple diagnostic method.

MATERIALS AND METHODS

Twenty six consecutive patients with histopathologically proven acute appendicitis were included in the study during

a one-month period in Ankara Numune Teaching and Research Hospital. Patients prepared for elective inguinal hernia repair in the same duration were also included in the study as the control group. The patients were questioned whether there was a history of recent ingestion of certain fruits or food and medications known to elevate blood level of serotonin. Preoperatively, spot urine samples were collected for 5-HIAA measurement from the patients in both groups and were acidified by hydrochloric acid under 4°C and then were centrifugated before the measurement. 5-HIAA levels were assessed with Ames Quick Lab Chemistry analyser in 546 nm by microcolon chromothographic and spectrophotometric method using byosystem kit(7,8). The cut-off value was accepted as 20 mmol/l for diagnosis of AA as mentioned in Ilkhanizadeh's study (6). All appendectomy specimens were evaluated histopathologically.

Statistical analysis was performed by SPSS 10.0 for windows programme. Chi-square test was used to evaluate the statistical differences. A p-value of 0.05 was accepted as significant.

RESULTS

The study group comprised twenty six patients (18 males, 8 females) with a mean age of 33 years (range: 9-72), while the control group was consisted of ten patients (eight males, two females) with a mean age of 48 years (range: 24-76). Spot urine 5-HIAA levels

were above reference range in 15 of 26 patients (57.7%) in the study group, whereas remaining 11 patients had levels below the cut-off value. In contrast, no patient in the control group had a high 5-HIAA value. The sensitivity of the test was calculated as 58%, and specificity was 48%.

All appendectomy materials revealed a variable degree of inflammation in histopathological examination. Ten cases had gangrenous appendicitis; two of these had positive urine 5-HIAA tests (20%). Sixteen cases showed no gangrenous changes; 13 of these cases had positive test results (81.3%). There was a significant difference between gangrenous and non-gangrenous cases ($p=0.003$). Among cases with gangrenous changes, three had perforation (11.5% of whole group); 5-HIAA levels of those three patients were also below the cut-off value.

DISCUSSION

Appendectomy is one of the most frequently performed surgical procedures in the emergency setting. The diagnosis of AA mainly depends on clinical findings and patient's history. Several diagnostic methods such as white blood cell count, C-reactive protein (CRP), and ultrasound have been useful in diagnosis of AA, but all these methods are neither sensitive nor specific and may be complicated with other inflammatory conditions. Limited diagnostic value has been reported for these tests(9), and today negative appendectomy rates still remain quite high (15-33%) in large series(1,10).

As a new diagnostic substrate, serotonin has been assessed both in plasma and urine as its 5-HIAA metabolite in limited number of recent studies. There are few reports searching the relation between AA and plasma serotonin and only one study has been reported measuring urine 5-HIAA levels so far. The earliest study showed the elevation of serotonin in plasma in AA with 95% specificity but only 45% sensitivity rates(4). Kalra *et al.* have suggested that serotonin level is a reliable marker for the diagnosis of AA especially in the first 48 hours with 93.8% sensitivity, 95.7% specificity rates (3). Similarly, Singh and colleagues reported that serotonin might be of value in confirming or excluding the diagnosis of AA (2). More recently, Ilkhanizadeh *et al.* showed that increased spot urine 5-HIAA levels have 98% sensitivity and 71% specificity rates in the diagnosis of AA. They also suggested that AA might be ruled out in the presence of its low levels with a 98.6% confidence interval(6). However, we found clearly lower specificity and sensitivity rates than those of the previous studies.

In the present study, no patient in the control group had elevated 5-HIAA level. It means that when a patient has a positive test result, this patient is not free

of disease. However, nearly half of the patients with acute appendicitis in the present study displayed negative test result, and this is the point largely restricting the usefulness and confidence of the test.

The value of 5-HIAA test has a limitation in the diagnosis of gangrenous form of AA. Singh *et al.* also reported that serotonin has a limited value in the diagnosis of gangrenous appendicitis(2). As serotonin has a short half time; when inflammatory process progresses to more severe form, namely gangrenous appendicitis, plasma serotonin level would decrease due to destruction of serotonin producing cells. Accordingly, the present study showed a similar pattern in gangrenous appendicitis cases and also in patients with perforation.

In conclusion, spot urine 5-HIAA measurement in confirming the diagnosis of AA has low sensitivity and specificity. As normal subject doesn't have a positive test, it may be used as an adjunct to classical diagnostic methods like patient history and physical examination in early phase of acute appendicitis. However, the test may be misleading when gangrenous changes occur in appendix; therefore, the surgeon should not rely on a negative test in the presence of clinical suspicion of acute appendicitis.

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REFERENCES

1. Lee, S.L., Alicia, J.W., and Hung, S. Computed tomography and ultrasonography do not improve and delay the diagnosis and treatment of acute appendicitis. *Arch. Surg.* 2001; **136**:556-562.
2. Singh, S.M., Dean, H.G., Dombal, T.D., Wilson, D.H., and Flowers M.W. Concentration of serotonin in plasma -a test for appendicitis. *Clin. Chem.* 1998; **34**:2572-2574.
3. Kalra, U., Chitkara, N., Dadoo, R.C., *et al.* Evaluation of plasma serotonin concentration in acute appendicitis. *Indian. J. Gastroenterol.* 1997; **16**: 18-19.
4. Rordam, P., Mortensen, P., Hindberg, I., and Christiansen, J. Acute appendicitis and plasm concentration of serotonin. *Acta. Chir. Scand.* 1987; **153**:437-439.
5. Rode, J., Dhillon, A.P., and Papadaki, L. Serotonin-immunoreactive cells in the lamina propria plexus of appendix. *Human Pathol.* 1983; **14**:464-469.
6. Ilkhanizadeh, B., Owji, A.E., Tavangar, S.M., *et al.* Spot urine 5-hydroxy indole acetic acid and acute appendicitis. *Hepato-Gastroenterol.* 2001; **48**:609-613.
7. Udentfriend, S. *et al.* *J. Biol. Chem.* 1955; **216**:499-505.
8. Constructor, S.F. *Biochem. Pharm.* 1966; **15**:1701-1706.
9. Dueholm, S., Bagi, P., and Bud, M. Laboratory aid in the diagnosis of acute appendicitis. A blinded, prospective trial concerning diagnostic value of leucocyte count, neutrophil differential count and c-reactive protein. *Dis. Colon. Rectum.* 1989; **32**:855-859.
10. Eryilmaz, R., Sahin, M., Alimoglu, O., Bas, G., and Ozkan, O.V. The value of c-reactive protein and leucocyte count in preventing negative appendectomies. *Ulus. Travma. Derg.* 2001; **7**:142-145.