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Comparison of pre-operative bilirubin level in simple appendicitis and perforated appendicitis

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Abstract

Background: Delay in diagnosis and treatment of perforated appendicitis may cause life-threatening complications. The aim of this study was to determine and compare pre-operative total and direct bilirubin levels in cases of simple and perforated acute appendicitis in order to improve the clinical decision making.

Methods: This prospective observational study included eighty patients who underwent open appendectomy, during a one-year period from March 2010 to March 2011 in the surgical department of Hazrat-e-Rasool Akram Hospital, an academic teaching hospital in Tehran- Iran. Pre-operative total and direct levels of bilirubin were compared in two groups of histologically proved appendicitis (simple and perforated), each including 40 patients.

Results: Eighty patients who underwent open appendectomy including 70% men and 30% women with a mean age of 34±11 years in Group I (perforated appendicitis) and 47.5% women and 52.5% men with a mean age of 33±14 in Group II (simple appendicitis) were included in this study. The mean bilirubin levels were higher for patients with perforated acute appendicitis compared to those with a non-perforated simple appendicitis (1.04±05 mg/dl vs 0.7±0.1 mg/dl) and this difference is highly significant ($p<0.01$).

Conclusion: Assessment of preoperative total bilirubin is useful for the differential diagnosis of perforated versus acute simple appendicitis and total bilirubin should be used as an independent parameter in the early diagnosis of appendix perforation

Keywords: Appendicitis, Bilirubin, Hyperbilirubinemia, Perforated appendicitis.

Introduction

Appendectomy for acute appendicitis (AA) is the most commonly performed emergency operation in the world. Appendicitis is a disease of the young with 40% of cases occurring in patients between the ages of 10 and 29 years (1). Delay in diagnosis and treatment results in an increased rate of perforation, postoperative morbidity, mortality and hospital length of stay. Several biochemical parameters including white blood cell (WBC) count, C-reactive protein (CRP), interleukin-6 (IL6) and Procalcitonin have been used to further improve the clinical diagnosis of AA (2). Recent studies have shown hyperbilirubinaemia to be a useful predictor of

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appendiceal perforation (3).

The aim of this study was to assess the value of hyperbilirubinemia as a preoperative laboratory marker for appendiceal perforation in patients with acute appendicitis in order to improve the clinical decision making and it might change the recent criteria designed for AA diagnosis and help to predict its prognosis.

Methods

This prospective observational study included eighty patients who underwent open appendectomy, based on the clinical diagnosis of acute appendicitis during a one-year period from March 2010 to March 2011 in the surgical department of Hazrat Rasool Hospital, an academic teaching hospital in Tehran- Iran.

Exclusion criteria included age less than 16 years - history of confirmed hepatitis or liver disease or icter - known elevated liver function tests (LFTs)- Gilbert syndrome- Dubin-Johnson syndrome – underlying diseases associated with intra or extra-hepatic cholestasis and finally hemolytic anemia.

Clinical and laboratory information of patients including age, sex, duration of symptoms, temperature, white blood cell counts (WBC) with total and differential leucocytes counts determination and Alverado score were recorded. Preoperatively patient's blood was also collected for serum bilirubin estimation and hyperbilirubinaemia was defined as a total bilirubin level greater than 1mg/dl.

All patients were informed about the aim of the study and an informed consent was obtained. Since the study was supported by a financial grant from the Tehran University of Medical Sciences, no extra cost regarding the bilirubin determination was imposed on the patients.

Patients who underwent conventional open appendectomy were grouped according to histologically proved acute appendicitis findings and comparisons were made between the groups. Patients were divided into two groups including simple (non-perforated) and perforated appendicitis.

Statistical Analysis: Statistical analysis including mean, standard deviation, and frequency percentages were calculated for all measurements. Data analysis was performed with SPSS version 14.0. Analysis of the data distribution was assessed by the Kolmogorov - Smirnov test. For normally distributed data the null hypothesis was based on the assumption that no difference in values existed between the two groups. In order to show whether the variance of data in two groups are equal or not, the Levene test was used. For normally distribute data, Independent-samples T test and for qualitative data Chi-square test was used. Less than 0.05 was accepted as indicating statistical significance.

Results

Eighty patients who underwent open appendectomy including 24 men (70%) and 12 women (30%) with a mean age of 34±11 years in Group I (perforated appendicitis) and 21 men (52.5%) and 19 women (47.5%) with a mean age of 33±14 in Group II (simple appendicitis) were included in this study. There was no significant difference in sex and age of patients between two groups (p-value>0.05).

Duration of symptoms from the onset of clinical discomfort to the time of the first visit by a surgeon was recorded which included a mean of 29±10 hours in Group I and 21±8 hours in Group II (p-value>0.05). Mean Alvarado score in Group I was 6.3±1.9 and 5.8±1.8 in Group II. Although Patients with perforated acute appendicitis had higher mean Alverado score, there was no significant difference in mean Alverado score between Group I and Group II (p>0.05). And the mean WBC value in all patients was 12338±8250 /mm^3 (range: 6500-19500/mm^3) and the patients had no underlying disease.

The mean bilirubin levels were higher for patients with perforated acute appendicitis compared to those with a non-perforated simple appendicitis (1.04±05 mg/dl vs 0.7±0.1 mg/dl) and this difference is highly

Table 1. Comparison of the measured variables in the study group.

Variable	Acute appendicitis with perforation (n=40)(First group)	Acute appendicitis without Perforation(n=40)(second group)	p
Age	34±11	33±14	0.9
Sex			0.9
Woman	12(30%)	19(47.5%)	
Man	24(70%)	21(52.5%)	
Serum total bilirubin levels	1.04±0.5	0.7±0.1	0.002
Alvarado Score	6.3±1.9	5.8±1.8	0.2
Duration of Symptoms	29±10	21±8	0.1

significant ($p<0.01$) (Table 1).

Discussion

The life time rate of appendectomy is 12% for men and 25% for women with 7% of all people undergoing appendectomy for acute appendicitis during their lifetime. Despite the increased use of sophisticated imaging and non-invasive diagnostic modalities such as graded compression sonography, high-resolution helical computed tomography (CT) and laparoscopy, the rate of misdiagnosis of appendicitis has remained constant (15%) as has the rate of appendiceal rupture (1). In addition, these procedures have a number of significant limitations including cost, radiation exposure, operator dependency, availability, contrast agent allergy, false positive and false negative diagnoses and exposure to anesthetics.

No single clinical or laboratory test is able to reliably predict acute appendicitis or appendiceal perforation (4). Rather, a combination of history, clinical examination and laboratory and radiological investigations is used to make the diagnosis and decide appropriate management. Those with less typical symptoms or signs warrant a period of observation and re-evaluation (5) a 'watch-and-wait' approach employed by many clinicians. However, this approach could result in unnecessarily prolonging patients' hospital stays and delaying their definitive treatment.

There have been several reports of hyperbilirubinaemia in appendicitis (6,7). Estrada et al hypothesised that hyperbilirubinaemia may be associated with appendiceal perforation and showed that more patients with a perforated or gangrenous appendix had hyperbilirubinaemia than those with simple acute appendicitis (8). Sand et al showed that hyperbilirubinaemia had a specificity of 86% for appendiceal perforation or gangrene, compared with a specificity of only 35% for CRP (3).

The development of jaundice in sepsis is well recognized and has been associated with a variety of causative bacteria, gram-negative bacteria being most commonly implicated (9).Several mechanisms leading to hyperbilirubinaemia in systemic infections have been described. Haemolysis causes an increased bilirubin load and has been associated with several bacteria including *Escherichia coli*. Another mechanism is reduced hepatic uptake and canalicular excretion of bilirubin caused by endotoxaemia (9). Bacterial endotoxin causes a cytokine mediated inhibition of bile salt transport mechanisms, leading to *cholestasis* (10). *Escherichia coli* is associated with the endotoxin lipopolysaccharide and is the most common organism cultured from intraperitoneal fluid in appendicitis (11,12). Hyperbilirubinaemia presumably occurs in appendicitis as a result of bacteraemia or endotoxaemia, which could occur both in simple appendicitis and perforated or gangrenous appendicitis albeit more commonly in the latter group.

The main finding of our study indicates that patients with perforation were significantly more likely to have hyper-

bilirubinemia (elevated total bilirubin levels>1 mg/dl) than those with acute simple appendicitis, but the limited number of patients in this study mandates that our results should be corroborated by larger studies.

In conclusion it seems that assessment of bilirubin level can help identify patients who are more likely to have appendicitis. It could be used together with clinical findings and other routine laboratory tests to definitively manage patients with acute appendicitis earlier. In addition hyperbilirubinaemia in patients with appendicitis indicates a higher likelihood of a perforated or gangrenous appendix.

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