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Thiol–disulfide Homeostasis in Acute Appendicitis

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SUMMARY

This study aimed to assess the diagnostic value of thiol–disulfide homeostasis in patients with acute appendicitis (AA). A total of 43 patients diagnosed with acute appendicitis in the emergency department and 59 healthy individuals were evaluated. Age, gender, white blood cell count, and thiol–disulfide homeostasis parameters (native thiol, total thiol, disulfide, disulfide/native thiol, native thiol/total thiol, and disulfide/total thiol ratios) were compared between groups. Thiol–disulfide homeostasis was determined using a newly developed method by Erel and Neşelioğlu. White blood cell counts were statistically significantly higher in the AA group, but no significant difference (P = 0.742) was found between native thiol, total thiol, and disulfide levels of the patient and control groups. Also, no statistically significant difference was observed in disulfide/native thiol, disulfide/total thiol, and native thiol/total thiol ratios (P = 0.117) between groups. This was thought to be a result of early diagnosis of AA in patients at the emergency department. Hence, the inflammatory response did not increase significantly at the time of diagnosis.

Key words: Appendicitis, oxidative, stress, thiols

INTRODUCTION

Acute appendicitis (AA) is the most common cause of acute abdominal pain, which requires appendectomy (1). The diagnosis of AA is primarily based on clinical symptoms, physical examination, and history. Despite the clinical preliminary diagnosis, negative appendectomy rate of 12% and missed perforated appendicitis rate of 3.4% have been reported in the literature (2,3). However, no specific diagnostic technique is available for AA. Therefore, new markers are urgently required (4).

It is well known that the balance between oxidants and antioxidants is crucial in the pathogenesis of AA (5). However, whether oxidative stress is caused by an inflammatory response or an increase in free radicals is sufficient for activating the enzymatic defense system is not clear (6). A few experimental and clinical studies have investigated the association between AA and oxidative stress (6-8).

Thiols, which are also known as mercaptans, include sulfhydryl (SH) group. Briefly, they are compounds of carbon, sulfur, and hydrogen (9). Thiol–disulfide (TDR) homeostasis is critical in detoxification, and involved in enzymatic regulation, apoptosis, cellular signaling mechanisms, and antioxidant protection (10,11). The role of thiol–disulfide in many disorders has been explored. Until 2014 this homeostasis was measured only one sided (12). This balance can be determined bilaterally using a novel and automated assay described by Erel and Neşelioğlu (13).

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This study aimed to investigate a novel, easily calculated oxidative stress parameter, thiol–disulfide homeostasis, in patients diagnosed with AA compared with healthy controls. In this study, it was hypothesized that oxidant–antioxidant balance was impaired in the pathogenesis of AA.

MATERIALS AND METHODS

This prospective study was approved by the local research ethics committee of Yıldırım Beyazıt University Atatürk Training and Research Hospital. It included 109 participants, aged more than 18 years, between January 2015 and December 2016. Fifty patients diagnosed with AA underwent surgery, and the tissue samples were examined pathologically. Forty-three of them were included in the study group (Group 1). Seven patients were excluded because three had normal samples, two had lymph node hyperplasia, one had diverticulitis, and one had an abscess. Fifty-nine healthy individuals were included in the control group (Group 2). Blood samples are taken from all participants.

Patients aged less than 18 years and having a history of certain diseases that might affect the thiol–disulfide ratio were excluded from the study. These diseases were diabetes mellitus, neoplastic diseases, inflammatory diseases (autoimmune diseases, etc.), chronic renal impairment, ischemic cardiac diseases, and chronic/acute hepatic failure.

Statistical analysis

The data were analyzed using the SPSS package program (version 20, Inc., IL, USA). Kolmogorov–Smirnov test was used to determine whether the distribution of continuous variables was normal. Descriptive statistics were expressed as mean ± standard deviation and the number of cases (n) and (%) as categorical variables. Categorical variables were assessed using the chi-square test. Two independent-sample t tests were used to determine the statistically significant difference in the mean values of the patient and control groups, if any. A statistically significant level was considered as $P < 0.05$.

RESULTS

Demographic features of 43 patients (group 1) and 59 healthy individuals (group 2) in the study are shown in Table 1. The average age was 34.7 years in the patient group and 35.6 in the control group ($P = 0.307$). No statistically significant difference was found between the patient and control groups in terms of age and gender (Table 1).

White blood cell (WBC), Total thiol, native thiol, and disulfide levels and ratios are shown in Table 2.

Table 1: Demographic features of groups.

	Group 1 n = 43	Group 2 n = 59	*P* value
Age	34.76 ± 14.14	35.59 ± 10.06	0.307
Gender			
Female, n (%)	16 (37.2)	32 (54.2)	0.089
Male, n (%)	27 (62.8)	27 (45.8)	

Table 2: Native thiol, total thiol, and disulfide levels and ratios of patients with AA and control group.

	Group 1 n = 43	Group 2 n = 59	*P* value
WBC (µL)	14.3 ± 6.6	7.5 ± 1.8	0.001
Native thiol (µmol/L)	430.19 ± 60.39	436,22 ± 41,73	0.742
Total thiol (µmol/L)	468.1 ± 60.94	480.65 ± 41.27	0.485
Disulfide (µmol/L)	18.95 ± 8.52	22.22 ± 5.7	0.51
Disulphide/Native thiol ratio (%)	4.53 ± 2,27	5.16 ± 1.52	0.108
Disulphide/Total thiol ratio (%)	4.08 ± 1.88	4.65 ± 1.24	0.108
Native thiol/Total thiol ratio (%)	91.84 ± 3.76	90.71 ± 2.47	0.108

Table 2 shows that WBC levels were statistically significantly higher in the AA group, but no significant difference (P = 0.742) was found between the native thiol levels of acute appendicitis cases and control group. Also, no statistically significant difference was observed in the levels of total thiol and disulfide, disulfide/native thiol ratios, disulfide/total thiol ratios, and native thiol/total thiol ratios between the groups.

DISCUSSION

The present study found no significant difference in the levels of native thiol, total thiol and disulfide and their ratios between the groups. Dynamic thiol–disulfide homeostasis is crucial in organisms. Exchanges in thiol–disulfide homeostasis are key in antioxidant protection, detoxification, organization of enzymatic activity, and parts of cellular signaling mechanism (10, 11). Thiol–disulfide homeostasis is linked to many disorders such as diabetes mellitus, cancer, migraine, hyperemesis gravidarum, and chronic renal impairment (14-17). Cysteine and cysteine components are the main thiol–disulfide structures. Cysteine has a role in structural functions as well as exchanges of thiol–disulfide in redox systems (18). Disulfides such as cysteines are members of redox systems such as thiol–disulphide exchanges (19).

AA still poses a problem for clinicians. The balance of oxidant/antioxidant systems has a role in the pathogenesis of AA (10). However, clinical and experimental studies performed on this topic are quite limited (5,20-22).

Dumlu et al. showed that total thiol levels and total antioxidant status were higher in patients with AA compared with the control groups (5). Özdoğan et al. observed that a decrease in plasma total antioxidant capacity might be a predictor of the progression of inflammation to the perforation in AA (20). Similarly, the study by Köksal et al. performed on 73 patients and 30 healthy individuals showed that an increase in the oxidative status (total oxidant and antioxidant status) was related to the progression of inflammation to the perforation in AA (22).

In a study performed in 2016, lower levels of antioxidants (antioxidant glutathione, lactate dehydrogenase) were observed in patients with AA compared with healthy controls (23).

Yılmaz et al. found a decrease in thiol levels of patients diagnosed with AA (25). Özyazıcı et al. found that dynamic thiol/disulfide homeostasis shifted toward disulfide formation as a result of thiol oxidation in patients with AA (24).

In the present study, the levels of thiol–disulfide, one of the significant antioxidant systems, were evaluated. However, no significant difference was found between the groups of patients diagnosed with AA and healthy individuals. This was thought to be a result of early diagnosis of patients with AA at the emergency department. Therefore, the inflammatory response did not increase significantly at the time of diagnosis.

This study had some limitations. First, the sample size was small and it was a singled-center study. Also, blood samples of the patients were taken only at the time of diagnosis and serial measurements of the levels of thiol–disulfide and other antioxidants were not performed. Limited studies have been conducted so far on this subject and hence it is hard to compare the results.

CONCLUSIONS

No difference was found in the thiol/disulfide homeostasis between patients with AA and healthy individuals. This was thought to be related to the fact that only blood samples from the patients at the time of diagnosis were studied, leading to lack of time for the balance to be distorted. Randomized, controlled, and prospective trials are needed to confirm the role of thiol/disulfide homeostasis in patients with AA.

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