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Serum Hs-CRP level and clinical significance of patients with stress ulcer caused by massive blood loss after trauma

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Stress ulcer refers to a specific type of irritation of the inner wall of the gastrointestinal tract that occurs rapidly due to acute physiological stress such as severe disease, infection, or trauma. This study investigated the serum Hs-CRP level and clinical significance of patients with stress ulcers caused by massive blood loss after trauma. For this purpose, we studied 113 patients with enormous blood loss after trauma. During the study, 26 patients developed stress ulcers. Therefore, patients with massive blood loss after trauma were divided into two groups with and without stress ulcers. In addition to clinical and demographical evaluations, serum Hs-CRP levels were measured by ELISA test method in all patients at baseline, 6, and 12 days after starting the study. Results showed that 24 patients were excluded from the study due to termination of cooperation or death. Finally, 89 patients participated in the final analysis. Of these 89 patients, 26 developed stress ulcers. There was a significant difference between the two groups with stress and non-stress ulcers in terms of mean age (P=0.001) and gender (P=0.041). Also, there was a significant difference between the two groups regarding re-bleeding (P=0.012), the number of hospitalization days (P=0.001), and a decrease in hemoglobin (P=0.035). But there was no difference between the two groups regarding the need for re-surgery (P=0.276). The results of this study showed that increased serum hs-CRP levels are directly related to stress ulcers. Patients with higher serum Hs-CRP levels were more likely to develop stress ulcers than patients without stress ulcers during six days (P=0.04) and twelve days after starting the study (P=0.001). Current research results also show that the prevalence of stress ulcers occurs in men more than women. The risk of stress ulcers increases among older patients. People with stress ulcers also lose more hemoglobin, and finally, patients with more trauma and more extended hospital stays have a higher chance of developing stress ulcers.

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Introduction

Stress ulcers can occur when tissues in the mouth, stomach, esophagus or other parts of the gastrointestinal tract are damaged (1, 2). This area becomes irritated and inflamed, causing holes or pain (3). There is a risk of bleeding from the wound, so the stomach and intestinal ulcers should be monitored (4). Stress comes in many forms (mental, psychological, or physiological). The type of ulcer that is commonly known as a stress ulcer is believed to be caused by physiological stress (5).

Physiological stress can occur in some forms, such as serious long-term illness, surgery, severe burns, damage to the central nervous system, and trauma to the brain or body (1). Any shock, injury, or accident to the body is considered trauma in medical science, which has entered the body from the outside, and the internal factor is not the cause of the injury. In other words, trauma is any injury caused by an increase in energy entering the body (3, 6). This energy may be of the impact type, mechanical, thermal (burn), chemical, or other types. Trauma can be classified according to the mechanism of injury (traffic accidents, falls, home accidents, etc.), the location of the damage (head, abdomen, etc.), or based on the characteristics of the trauma cause (penetrating trauma, penetrating trauma, trauma Thermal, compressive trauma, etc.) (7). Today, trauma is an important issue that is seriously considered in most developed countries (8). Because it is the fourth leading cause of death worldwide and the first leading cause of death in the first four decades of life. Thousands of deaths and millions of injuries from

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various traumas occur each year. This mortality is increasing year by year (9).

One of the complications of trauma is stress ulcers. The most common symptom of a stomach ulcer is usually pain. Another problem is internal bleeding (10). Bleeding may not be noticeable to some people. But if the bleeding becomes severe, surgery is needed to stop it (7). Symptoms of gastrointestinal ulcers include burning sensation, heartburn, nausea, weight loss, and loss of appetite (11).

Serious complications are not common in stress ulcers, but there are some things to be aware of. Some mouth sores are a type of oral cancer (12). A sore that does not heal even after treatment and may develop on the tongue, between the cheeks, and under the gums, or under the tongue is a sign of oral cancer (13). In some cases, untreated stomach ulcers may cause severe symptoms such as loss of appetite and weight, difficulty breathing, fainting, vomiting, nausea, black stools, internal bleeding, and stomach obstruction (5). High-stress ulcers occur when a patient is under medical care for a particular illness, such as surgery, trauma, or injury (14). Stress ulcers cause another complication to other medical conditions that can lead to ulcers. Like gastric ulcers, the most severe complication is internal bleeding or obstruction (15).

Elevated CRP levels, one of the hallmarks of malnutrition-inflammation-atherosclerosis syndrome, are a risk factor for disease and mortality from stress ulcers (16). In these patients, early diagnosis can be made by assessing CRP levels, which depends on the severity of the disease. The Hs-CRP (High-sensitivity CRP) test is much more sensitive than conventional CRP tests and can measure very accurate CRP values (17). Therefore, in the current study, serum Hs-CRP level and clinical significance were investigated on patients with stress ulcers caused by massive blood loss after trauma.

Materials and methods

Demographic and clinical evaluations

This study was performed on 113 patients with massive blood loss after trauma referred to the emergency department or hospitalized. In addition to clinical evaluations such as endoscopy, blood cell count, and abdominal diagnostic imaging, serum Hs-CRP levels were measured in all patients at baseline, 6, and 12 days after baseline. Then, patients were evaluated for stress ulcers for one year at each visit. 26 patients developed stress ulcers. For this reason, patients with massive blood loss after trauma were compared into two groups with and without stress ulcers. To comply with ethical considerations in this study, the purpose of the study was explained to selected patients, and informed consent was obtained. Then the checklist, including demographic information (age, sex, length of hospital stay, re-bleeding, and hemoglobin loss), was completed by the researcher with an interview and reading the history in the medical record.

ELISA test method

To measure serum Hs-CRP levels, 2ml blood samples were taken 6 hours after fasting. Hs-CRP was measured by immunoturbidimetric using the bionic kit (Germany) and ELISA technique. The technique involved coating specific antibodies to the bottom of the wells by the kit manufacturer. In the blocking phase, the voids between the antibodies coated on the bottom of the well were filled with a neutral protein, which is made by the kit manufacturer. Bovine series albumin is one of the most common blockers. During the sampling stage, the patient's serum or other reagents such as standards and controls were poured into the wells from the ELISA test. Incubation was then performed at 37°C. React with the antibodies in the wells. In the next step, the conjugate enzyme was added to label the antibody reactions. In the washing step, the well was washed inside the wells to remove non-specific antibodies that did not react and produced false ODs from the wells. This step was performed by the ELISA washer. Then another reagent was added to the wells called TMB-Substrate. The substrate reacts with the conjugate to form a dye inside the wells. Following the ELISA test, another reagent called Stop is added to the wells. This reagent stops the enzymatic reaction and thus prevents the increase of color inside the wells. Finally, the adsorption rate of the wells was measured with the help of the ELISA reader at specific wavelengths. The ELISA reader that was used in the current study was Synergy H1 (Biotek, USA).

Statistical analysis

In order to analyze the data, in addition to using descriptive statistics to provide demographic and

clinical information, Chi-square, ANOVA, and Kruskal-Wallis tests were used by SPSS software version 18 to analyze other data. P <0.05 was considered statistically significant.

Results and discussion

A total of 113 patients with massive blood loss after trauma were included in the study. Twenty-four of them were excluded from the study due to termination of cooperation or death. Finally, 89 patients participated in the final analysis. Of these 89 patients, 26 developed stress ulcers.

The study results showed that out of 89 patients with massive blood loss after trauma, 65 (73.03%) were male, and 24 (26.96%) were female. The minimum age was 15 years, and the maximum was 87 years. There was a significant difference between the two groups with stress and non-stress ulcers in terms of mean age (P=0.001) and gender (P=0.041) (Table 1). There was a significant difference between the two groups regarding re-bleeding which more patients in the stress ulcer group had re-bleeding (P=0.012). There was a significant difference between the two groups in terms of the number of hospitalization days (P = 0.001). Patients in the stress ulcer group were hospitalized longer (more than four days). People in the stress ulcer group also had a more significant decrease in hemoglobin (P = 0.035). But there was no difference between the two groups in terms of the need for re-surgery (P=0.276).

Table1. The demographic and clinical characteristics of patients with massive blood loss after trauma in stress ulcer group and non-stress ulcer group

Variable		Stress Ulcer Group (n=26)	Non-stress Ulcer Group (n=63)	P-value
Gender	Male	16 (61.54%)	49 (77.78%)	0.041
	Female	10 (38.46%)	14 (22.22%)	
Age	0-30 years old	4 (15.38%)	20 (31.75%)	0.001
	31-60 years old	7 (26.92%)	35 (55.55%)	
	61-90 years old	15 (57.70%)	8 (12.70%)	
Re-bleeding	Have	14 (53.85%)	23 (36.51%)	0.012
	Not Have	12 (46.15%)	40 (63.49%)	
Days of Hospitalization	<4 days	1 (3.84%)	15 (23.81%)	0.001
	4-8 days	10 (38.46%)	43 (68.25%)	
	>8 days	15 (57.70%)	5 (7.94%)	
Decreased Hemoglobin	Less than 2 units	9 (34.62%)	30 (47.62%)	0.035
	More than 2 units	17 (65.38%)	33 (52.38%)	
Re-surgery	Need	13 (50%)	31 (49.21%)	0.276
	Not Need	13 (50%)	32 (50.79%)	

The results of this study also showed that increased serum Hs-CRP levels are directly related to stress ulcers. Patients with higher serum Hs-CRP levels were more likely to develop stress ulcers than patients without stress ulcers during six days (P=0.04), and twelve days after starting the study (P=0.001) (Figure1).

Although gastric and duodenal ulcers are the most common diseases, there are still many unknowns about them (18). The onset of gastric mucosal lesions can be caused by various invasive pepsin, bile acids, and hydrogen ions. In particular, increasing the concentration of hydrogen ions can disrupt platelet function and increase pepsin activity (19, 20).

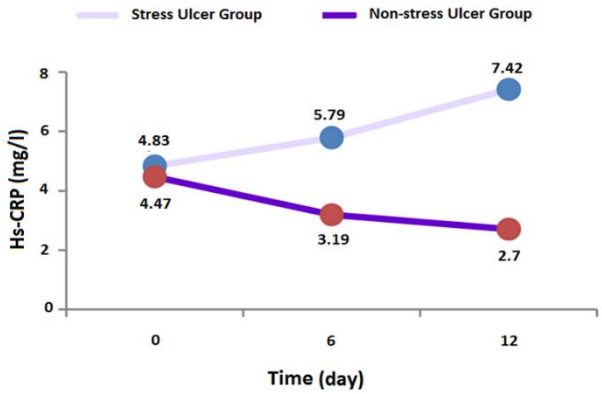

Fig1. Changes in High-sensitivity C-reactive protein (Hs-CRP) levels in patients with massive blood loss after trauma in the Stress Ulcer Group and the Non-stress Ulcer Group

Concentrations of hydrogen ions can disrupt platelet function and increase pepsin activity (21). On the other hand, the hydrophobicity of the mucosal layer, which is caused by the phospholipid layer adhering to the mucosal surface and as a defense barrier prevents the redistribution of hydrogen into the mucosa, protects the mucosa against these invasive agents (22, 23). If the invasive factors are strengthened, or the defense barrier is weakened, wounds will form (24).

Decreased mucosal circulation, stress, and various chemicals such as ASA can break down this barrier (25). In recent years, research has shown that gastric mucosa contains high concentrations of the enzyme phospholipase A2 (26). It was initially thought that the function of this enzyme was to digest phospholipids that enter the stomach through bile into the diet (27). But it has now been shown that phospholipases are involved in many other events, such as signal transduction, cell activity, and inflammatory reflexes (28). There are many reasons to suggest that mucosal damage is caused by stress and various chemical agents (29).

Stress ulcers are a variety of superficial erosions, which mainly occur in the fundus and body of the stomach (1). They can cause aftershocks, sepsis, and trauma and are common in patients with peritonitis and other chronic diseases (2, 28). In a study by Herzig *et al*. (30), About 58% of patients with peritonitis had elevated CRP levels. Serum CRP levels are a well-known and important predictor in patients. Other studies have shown that as serum CRP levels increase, the risk of peritonitis also increases (31-34).

The results of this study showed that increased serum Hs-CRP levels are directly related to stress ulcers. Patients with higher serum Hs-CRP levels were more likely to develop stress ulcers than patients without stress ulcers during six days (P=0.04), and twelve days after starting the study (P=0.001). CRP is the most widely used clinical marker among pro-inflammatory markers for monitoring micro-inflammation in patients with stress ulcers (2). Current research results also show that the prevalence of stress ulcers occurs in men more than women. The risk of stress ulcers increases among older patients. People with more trauma and longer hospital stays have a higher chance of developing this complication. People with stress ulcers also lose more hemoglobin.

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