Evaluation of blood and serum markers in spinal cord injured patients with pressure sores

Eda Gurcay, MD, Ajda Bal, MD, Ahmet G. Gurcay, MD, Aytul Cakci, MD.

ABSTRACT

الأهداف: تقييم الدم وعلامات المصل لدى المرضى الذين يعانون من إصابة الحبل الشوكي (SCI) مع أو بدون قرحات ضاغطة.

الطريقة: أجريت هذه الدراسة المقطعية في وزارة الصحة ديسكابي يلدرم بيزيت ومستشفى نومون التعليمية ومراكز الأبحاث – أنقرة – تركيا، خلال الفترة ما بين عام 2006م وحتى 2008م. تم تقييم حالة 23 مريضاً يعاني من إصابة في الحبل الشوكي (SCI) مع قرحات ضاغطة (المجموعة الأولى) ومجموعة التحكم 25 مريضاً يعانون من إصابة في الحبل الشوكي (SCI) بدون قرحات ضاغطة. تم فحص خصائص التقرحات مع إعارة الانتباه للمدة، الموضع، الدرجة، نوع النسيج، منطقة السطح ومقدار النضح. تم تسجيل القياسات المخبرية وشملت: تعداد كريات الدم الحمراء ومعدل تنقلها (ESR) – تفاعل سلسلة الخمائر الناقلة للبروتين (CRP) – الهيموجلوبين (Hb) – والهيماتوكريت (Htc) – والخلايا اللمفاوية – كريات الدم البيضاء (WBC) – وكريات الدم الحمراء (RBC) – مصل الحديد – ناقلة الحديد – وسعة الحديد الكاملة (TIBC) – الفيريتين – البروتين الكامل – الألبومين – فيتامين (B12) والزنك.

النتائج: كان أكثر موضع للقرحة الضاغطة شيوعاً في العجز (38%). مقارنة مع مجموعة التحكم، ظهر على المرضى الذين يعانون من تقرحات ضاغطة أنيميا (فقر دم) مع انخفاض مصل الحديد وناقل الحديد وسعة الحديد الكامل (TIBC) وزيادة الفيريتين. كما كان لديهم زيادة في معدل نقل الكريات الحمراء (ESR) وتفاعل سلسلة الخمائر الناقلة للبروتين (CRP) وكريات الدم البيضاء (WBC)، وانخفاض الخلايا اللمفاوية، البروتين الكامل، والألبومين والزنك. تبين وجود علاقة إحصائية ملحوظة بين سلسلة الخمائر الناقلة للبروتين (CRP)، الهيموجلوبين (Hb)، الهيماتوكريت (Htc)، الخلايا اللمفاوية، كريات الدم الحمراء (RBC)، كريات الدم البيضاء (WBC)، مستويات مصل البروتين، ودرجة التقرحات الضاغطة.

خاتمة: يجب على الأطباء فحص المرضى باستمرار مع الأخذ بعين الاعتبار الدم وعلامات المصل لكي يتم تحديد أي مخاطر للتقرحات الضاغطة، كما يجب عليهم أيضاً القيام بالقياسات الوقائية الفورية بناءً على حالة المريض.

Objectives: To evaluate blood and serum markers in traumatic spinal cord injured (SCI) patients, with and without pressure sores.

Methods: This cross-sectional study was performed at the Ministry of Health Diskapi Yildirim Beyazit, and Numune Education and Research Hospitals, Ankara, Turkey, from 2006-2008. A total of 23 SCI patients with pressure sores (group I) and a control group of 25 SCI patients without pressure sores (group II) were evaluated. Characteristics of sores were examined with respect to duration, location, grade, tissue types, surface area, and exudate amount. Recorded laboratory parameters included erythrocyte sedimentation rates (ESR), C-reactive protein (CRP), hemoglobin (Hb), hematocrit (Htc), lymphocytes, white blood cells (WBC), red blood cells (RBC), serum iron, transferrin, total iron-binding capacity (TIBC), ferritin, total protein, albumin, vitamin B12, and zinc.

Results: The most common pressure sore location was the sacrum (38%). Compared to the control group, the patients with pressure sores showed anemia with reduced serum iron, transferrin, TIBC, and increased ferritin. They also had increased ESR, CRP, and WBC and reduced lymphocytes, total protein, albumin and zinc. Statistically significant correlations were found between CRP, Hb, Htc, lymphocytes, RBC, WBC, and serum protein levels, and grade of pressure sores.

Conclusion: Clinicians should regularly screen patients with respect to blood and serum markers, in order to determine any risks for pressure sores, and they should perform immediate preventive measures based on the patient's condition.

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From the Department of Physical Therapy and Rehabilitation (Gurcay E, Bal, Cakci), Ministry of Health Ankara Diskapi Yildirim Beyazit Education and Research Hospital, and Department of Neurosurgery (Gurcay A), Ministry of Health Ankara Numune Education and Research Hospital, Ankara, Turkey.

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Address correspondence and reprint request to: Dr. Eda Gurcay, Department of Physical Therapy and Rehabilitation, Ministry of Health Ankara Diskapi Yildirim Beyazit Education and Research Hospital, PO Box 06010, Ankara, Turkey. Tel. +90 (312) 5962000 Ext. 2994. Fax. +90 (312) 3230632. E-mail: dredagurcay@gmail.com

Pressure sore is a common condition most often seen in high-risk populations with physical impairments, particularly in those with severely limited mobility.[1] Patients are often bed-bound, paralyzed, elderly, and undergoing treatment for other diseases.[2] The incidence of pressure sores ranges from 0.4-38% in acute care, and from 2.2-23.9% in long-term care.[3] It is estimated that one-fourth of the approximately 200,000 people with spinal cord injuries (SCI) will develop pressure sore.[4] Although these sores can occur anywhere on the body, approximately 95% of them occur in the sacral and coccygeal areas, ischial tuberosities, and greater trochanteric areas.[2,5] Pressure sores can cause loss of therapy time, increase the duration of hospital stay, and impair quality of life.[6] Systemic factors such as anemia and vitamin, protein, or fluid deficiencies impair the healing process.[7] Pressure sore healing should be achieved as rapidly as possible for patients to quickly return to their activities.[4] However, with the available technique, healing of pressure sores can take several weeks to several months.[8] Pressure sores develop in most of the patients with SCI during their lifetime, increase in conjunction with time since injury and worsen prognosis. In patients with long-standing SCI, neurologically impaired skin with long-term structural and physiologic changes may play an important role in the development of pressure sores.[9,10] Assessing nutritional status is an important first step for optimal sore healing. Anemia, increased acute-phase proteins and decreased serum albumin and pre-albumin, often accompany pressure sores.[11,12] Although SCI patients with pressure sores receive significant attention in the literature, there are few reports assessing laboratory parameters in these patients. The aim of this study was to evaluate several blood and serum markers in traumatic SCI patients, with and without pressure sores.

Methods. Fifty subjects were initially recruited from January 2006 to January 2008, but only 48 eligible patients consecutively hospitalized at the Ministry of Health Diskapi Yildirim Beyazit, and Numune Education and Research Hospitals, Ankara, Turkey, during this cross-sectional study period were collected prospectively. Two subjects were unexpectedly discharged home. A total of 23 SCI patients with pressure sores (group I), and a control group of 25 SCI patients without pressure sores (group II) were examined. Pressure sores of stage II or higher, as defined by the National Pressure Ulcer Advisory Panel classification were included in the evaluations.[13] Subjects were excluded if they had neoplastic pathologies and chronic inflammatory or infectious diseases (such as collagenopathies, osteomyelitis, pneumonia), or if they had received immunosuppressive medications. All patients were informed on the nature of the study, and provided informed consent prior to beginning the trial, which was conducted in accordance with the Helsinki Declarations of 1975. Approval was obtained from the Local Ethics Committee prior to the commencement of the study. After inclusion, we recorded the demographic variables of age, gender, education duration, body mass index, duration and level of SCI, smoking habit, and route of nourishment. Pressure sores were examined with respect to duration, location, grade and surface area, and exudate amount was noted. Recorded laboratory parameters included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hemoglobin (Hb), hematocrit (Htc), red blood cells (RBC), white blood cells (WBC), lymphocytes, serum iron, transferrin, total iron-binding capacity (TIBC), ferritin, total protein, albumin, vitamin B12 and zinc. Severity of anemia was determined as: mild anemia (Hb 10.0-11.9 g/dl), moderate anemia (Hb 7.0-9.9 g/dl), and severe anemia (Hb <7 g/dl).

Data were analyzed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) statistical program. Descriptives were shown as the mean ± SD, or as frequency tables. Differences between the patient and control groups were investigated with independent samples t test, Mann-Whitney U test, or chi-square test. Pearson and Kendall's tau-ß coefficients of correlation were calculated for the relations among the parameters. *P*-value was set at 0.05.

Results. Demographic characteristics of each group are listed in **Table 1**. No statistically significant difference between the groups was identified regarding age, gender, education duration, duration of SCI, and smoking habits. All patients in the SCI group without pressure sores were nourished orally. Study participants ranged in age between 18 and 80 years, with a mean of 41.1 ± 15.0 years. Thirty-seven (77.1%) patients were male, 25 patients (52%) were paraplegic, and 23 (48%) were tetraplegic. Disease duration ranged between 1 and 24 years, with an average of 8.6 ± 6.5 years. Characteristics of pressure sores are described in **Table 2**. Twenty-three patients had a total of 42 pressure sores; 13 of these patients (56%) had multiple sores. The most common pressure sore location was the sacrum (38%). Blood and serum markers of the groups are shown in **Table 3**. Compared to the control group, the patients with pressure sores showed anemia with reduced serum iron, transferrin and TIBC, and increased ferritin. They also had increased ESR, CRP, and WBC, and reduced lymphocytes, total protein, and albumin. Patients showed mild to moderate anemia. Nineteen (82.5%) patients in group I, and 4 (16%) in group II had mild to moderate anemia according to

Table 1 - Demographic characteristics of patients.

Demographics	Group I (n=23)	Group II (n=25)	*P*-value
Age (years, mean±SD)	37.43±15.81	44.48±13.86	0.107
Gender			0.852
Male (%)	18 (78.3)	19 (76)	
Female (%)	5 (21.7)	6 (24)	
Education duration (years, mean±SD)	7.86±3.86	7.24±3.07	0.534
Body mass index (kg/m^2)	23.33±3.22	26.70±2.38	<0.001
Duration of SCI (month, mean±SD)	8.39±6.67	8.84±6.52	0.478
Level of injury			0.044
Tetraplegia (%)	15 (65.2)	8 (32)	
Paraplegia (%)	8 (34.7)	17 (68)	
Smoking status			
Yes (%)	10 (43.5)	8 (32)	0.602
No (%)	13 (56.5)	17 (68)	
Nourishment			0.022
Oral (%)	17 (73.9)	25 (100)	
Gastrostomy (%)	6 (26.0)	0 (0)	

SCI - spinal cord injury

Table 2 - Characteristics of pressure sores (N=42).

Characteristics	n (%)
Duration (month, mean ± SD)	1.3 ± 0.9
Location	
Sacral	16 (38)
Greater trochanter	10 (23.8)
Lateral malleolus	8 (19)
Ischial	4 (9.5)
Heel	4 (9.5)
Grade	
II	15 (35.7)
III	18 (42.8)
IV	9 (21.4)
Surface area (cm^2, mean ± SD)	20.6 ± 15.5
Exudate amount	
None	10 (23.8)
Light	18 (47.6)
Moderate	10 (23.8)
Heavy	4 (9.5)

Table 3 - Blood and serum markers of the groups.

Parameters	Group I (n=23) mean ± SD	Group II (n=25) mean ± SD	Difference	P-value
ESR (mm/h)	65.35±24.33	19.24±10.25	46.11	<0.001
CRP (mg/dl)	48.74±26.20	3.31±0.55	45.43	<0.001
Hb (g/dl)	10.57±1.52	13.70±1.92	-3.13	<0.001
Htc (%)	31.96±4.05	39.87±5.86	-7.91	<0.001
RBC/mm^3	3877400±568000	4475600±662280	-598.200	0.001
WBC/mm^3	11252.17±4191.21	6528.0±925.80	4724.17	<0.001
Lymphocytes/mm^3	1456.52±447.03	2432.0±752.06	-975.48	<0.001
Serum iron (µg/dl)	48.96±16.11	109.44±31.84	-60.48	<0.001
Transferrin (µg/dl)	141.13±28.96	206.28±39.66	-65.15	<0.001
TIBC (µg/dl)	230.17±36.19	314.96±45.98	-84.49	<0.001
Ferritin (µg/dl)	302.83±157.77	123.12±42.47	179.71	<0.001
Total protein (g/dl)	5.52±0.42	6.82±0.54	-1.30	<0.001
Albumin (g/dl)	3.23±0.35	3.81±0.43	-0.58	<0.001
Vitamin B12 (pg/ml)	378.13±392.85	523.52±201.87	-145.39	0.110
Serum zinc (µg/dl)	83.47±22.85	96.68±17.60	-13.21	0.007

ESR - erythrocyte sedimentation rate, CRP - C-reactive protein, Hb - hemoglobin, Htc - hematocrit, RBC - red blood cells, WBC - white blood cells, TIBC - total iron-binding capacity

Hb levels. Statistically significant positive correlations were found between grade of pressure sores (r=0.604, p=0.001), and CRP and WBC (r=0.677, p=0.001), while statistically significant negative correlations were found with Hb (r=-0.508, p=0.003), Htc (r=-0.519, p=0.002), lymphocytes (r=-0.612, p=0.001), RBC (r=-0.443, p=0.010), and serum total protein levels (r=-0.494, p=0.004).

Discussion. Our study was designed to evaluate the blood and serum markers of traumatic SCI patients, with and without pressure sores. This study showed mild to moderate anemia related to the presence of pressure sores. The most common pressure sore location was the sacral region, and exudate was present in the majority of sores.

Sacral pressure sores occur in the supine, bedridden, and acutely injured spinal cord patients. Ischial pressure sores are common in wheelchair-bound seated patient. Skin and tissue breakdown over the greater trochanter - the lateral prominence of the proximal femur - is most associated with prolonged lateral decubitus positioning, and with large patients in narrow wheelchairs.[5,14] Pieper et al[15] observed the most common sites such as sacrum-coccyx, left trochanter, right and left heel. The most common sore locations in our study population - sacral and trochanteric - were similar to those reported in other studies of SCI patients.[15,16] Smoking has a vasoconstrictive effect on the capillaries at the dermal level, which diminishes the amount of oxygenated blood reaching the tissues, further delaying the healing process of pressure sores.[17] Although the results showed no differences in parameters between the groups according to smoking habit, we definitely do not condone smoking by these patients.

A variety of factors are assumed to affect the outcome of pressure sore healing. Malnourished patients are prone to development of pressure sores, and low Hb was thought to be a predictor of poor sore healing. It is important to review complete blood count including RBC, WBC, and total amount of Hb, as they map directly to the sore healing process.[18-20] Serum measurement of visceral protein levels can help estimate the adequacy of the individual's nutritional intake. Serum albumin may be helpful in identifying chronic undernutrition. While it was stated that zinc has a key role in tissue growth and healing together with collagen synthesis and immune function, and that ferrous iron is necessary for normal collagen metabolism,[20-22] no randomized, controlled trial has shown an effect of zinc or ferrous iron in pressure ulcer healing. Severe fluid and protein loss from a pressure sore may lead to hypoproteinemia, or worsened malnutrition owing to the catabolic nature of these sores,[23] though there is currently no experimental data showing that hypoalbuminemia results from a pressure sore, or that patients with pressure ulcers are catabolic. To prevent this serious problem, evaluation of blood and serum markers should be carried out. Scivoletto et al[24] observed that patients with pressure sores suffered from anemia and serum protein alterations, but with a lack of correlation between metabolic alterations and pressure sore area. When we evaluated blood count, albumin, and total protein, the results indicated a deficiency in SCI patients with pressure sores, compared with SCI patients without pressure sores. Typical features of chronic inflammatory disorders were determined as normocytic, normochromic anemia associated with reduced serum iron and transferrin but elevated ferritin, total hypoproteinemia with hypoalbuminemia, lymphopenia, and higher ESR, CRP, and white cell counts. Chronic inflammatory status inhibits the use of iron stored in the reticuloendothelial system, and the hepatic synthesis of albumin.[25] The correlations between CRP, WBC, and serum total protein levels, and grade of pressure sores may permit us to attribute these outcomes to the inflammatory status, hypercatabolic nature of the sore, and loss of protein from the sore.

As malnutrition and weight loss play a role in the development and healing of sores,[15,20,21] it was not possible to draw any firm conclusions on the effect of enteral and parenteral nutrition, in the prevention and treatment of pressure ulcers.[26] Immune mediators, such as interleukin-1 (IL-1), tumor necrosis factor, interleukin-2 (IL-2), and interleukin-6 (IL-6) can also affect body composition.[27,28] Proinflammatory cytokines may also play an important role in the inflammatory response to traumatic central nervous system injury,[29,30] but they were not assessed in this study. Normal healing potential was reported as long as serum albumin was maintained above 2 g/dl. If the patient is unable to take an adequate amount of daily nutrition, supplemental means should be utilized.[24] Six patients in our study required percutaneous endoscopic gastrostomy for additional nutritional support.

The limitation of our study is that all data were cross-sectional in nature. Therefore, it was not possible to identify blood and serum markers after the healing process. Therefore, prospective studies should be performed to assess the nutritional status of SCI patients with pressure sores.

In conclusion, subjects with SCI are prone to developing pressure sores due to the chronic inflammatory state. Clinicians should regularly screen patients with respect to blood and serum markers in order to determine any risks for pressure sores. Immediate preventive measures for blood and serum markers should be performed based on the patient's condition. It is hoped that careful and early evaluation

of blood and serum markers may lead to a reduction in pressure sore incidence in SCI patients.

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