Praćenje broja trombocita u bolesnika s opeklinama

Platelet count monitoring in burn patients

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Sažetak

Uvod: Kod bolesnika s opeklinama dolazi do bitnog narušavanja hemostatskog i imunološkog odgovora u kojem trombociti imaju značajnu ulogu. Cilj ispitivanja bio je praćenje broja trombocita u bolesnika s opeklinama, ovisno o težini opeklinske ozljede (postotak opečene površine tijela bolesnika – %TBSA) i ishodu bolesti (preživljenje/smrt).

Materijali i metode: Ukupno smo ispitali 68 bolesnika: skupina A (32 bolesnika s lakšim opeklinama, ≤ 10% TBSA) i skupina B (36 bolesnika s umjerenim/težim opeklinama, > 10% TBSA). Broj trombocita odredili smo na hematološkom brojaču Sysmex XT-1800i, 1., 4., 7., 14., 21. i 28. dana nakon ozljede, ovisno o dužini boravka bolesnika u Klinici.

Rezultati: Broj trombocita 4. i 7. dana u bolesnika s obzirom na težinu ozljede značajno se razlikovao između skupina A i B, a niži su bili u skupini B ($P < 0,001$; $P = 0,045$). U objema skupinama 4. u odnosu na 1. dan došlo je do pada broja trombocita, ali značajan pad bio je prisutan samo u skupini B. Značajan porast broja trombocita u objema skupinama zabilježen je 7. u odnosu na 4. dan, kao i 14. u odnosu na 7. dan. S obzirom na ishod bolesti preživjelo je 56, a umrlo 12 bolesnika. U bolesnika sa smrtnim ishodom, u usporedbi s preživjelima tijekom cijelog perioda praćenja, dobivena je značajna razlika u broju trombocita ($P < 0,05$). U umrlih je bolesnika bio značajno niži broj trombocita svih dana praćenja, osim prvoga dana kada su bili značajno viši u odnosu na preživjele bolesnike.

Zaključak: Dobivene značajne razlike u broju trombocita 4. i 7. dana između skupina prema težini opeklinske ozljede, kao i značajan pad trombocita 4. u odnosu na 1. dan u skupini umjerenih/težih opeklina, upućuje na potrebu uvođenja učestalijeg praćenja broja trombocita u tom periodu radi pravovremenog određivanja pada njihovog broja. U bolesnika sa smrtnim ishodom u odnosu na preživjele značajno su bile niže vrijednosti trombocita tijekom cijelog perioda praćenja, osim prvoga dana kada su bile značajno više. Usprkos prisutnim razlikama prema ishodu bolesti, ali sličnoj dinamici trombocita (porast i pad) u objema skupinama te malog broja umrlih ispitanika, potrebna su dodatna istraživanja.

Ključne riječi: trombociti, bolesnici s opeklinama, %TBSA, ishod bolesti

Abstract

Introduction: Platelets play an important role in severe hemostasis disorders and immune response impairments in burn patients. The aim of this study was platelet count monitoring in burn patients in relation to the severity of burn injury (percentage of total body surface area burned - %TBSA) and disease outcome (survival/death).

Materials and methods: We investigated a total of 68 patients: group A (32 patients with mild burns, ≤ 10% TBSA) and group B (36 patients with moderate/severe burns, > 10% TBSA). Platelet count was determined on Sysmex XT-1800i automated hematology analyzer on the 1st, 4th, 7th, 21st and 28th day after burn injury, depending on the length of hospital stay.

Results: Platelet count was significantly different on the 4th and 7th day comparing group A and B according to the severity of injury**;** platelet count was lower in group B ($P < 0.001$; $P = 0.045$). When the 4th day was compared to the 1st day, a platelet count decrease was observed in both groups, but was significant only in group B. In both groups, a significant increase in platelet count was observed on the 7th day compared to the 4th day, and on the 14th compared to the 7th day. In relation to disease outcome, 56 patients in our study group survived and 12 died. Comparison between surviving and non-surviving patients showed a significant difference throughout the whole period of observation ($P < 0.05$).

Conclusion: The significant between-group differences observed in platelet count on the 4th and 7th day in relation to severity of injury, as well as the significant decrease in platelet count on the 4th day as compared to the 1st day in patients with moderate/severe burns, suggest the need to increase the frequency of platelet count monitoring in this particular period in order to timely identify the decrease in platelet count. Comparing surviving and deceased patients, a significantly lower platelet count was observed in the group of patients with lethal outcome throughout the whole period of observation, with the exception of the 1st day when platelet count was higher in this group. Despite the between-group differences in platelet count in relation to disease outcome (but similar time-dependent changes in, i.e. increase and decrease) and because of a low number of the examined deceased patients, additional investigations are needed.

Key words: platelet, burn patient, total body surface area percentage, disease outcome

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Uvod

Na Odjel za opekline Klinike za traumatologiju u razdoblju od 2003. do 2005. godine primljeno je ukupno 442 bolesnika s opeklinskim ozljedama (godišnje prosječno oko 147 bolesnika). Uzroci su bili plamen (vatra) u 41% slučajeva te vruća tekućina u 31% slučajeva, a zatim kontaktne opekline, opekline uzrokovane električnom strujom i eksplozijama te kemijski izazvane opekline.

Opekline su izrazito složene traumatske ozljede koje se dijele prema dubini ozljede, veličini opečene tjelesne površine, mjestu opekline, dobi, kao i općem stanju bolesnika (1-3). Prilikom odabira terapije neophodna je procjena opsega opečenog područja koje se izražava u obliku postotka opečene ukupne površine tijela (%TBSA, engl. *total body surface area*). U tu svrhu u odraslih se najčešće primjenjuje tzv. pravilo devetki: tijelo se podijeli na regije te se svakoj regiji pripiše višekratnik broja devet. Glava s vratom i ruke imaju površinu od po 9%, prednja i stražnja strana trupa i svaka noga po 18% ukupne površine tijela, dok preostalih 1% odgovara površini spolnih organa i perineuma. Prilikom toplinske traume dolazi do narušavanja strukture i gubitka funkcije kože. Oštećenje tkiva posljedica je toplinom izazvane koagulacije strukturnih proteina, a daljnja oštećenja ovise o lokalnom oslobađanju medijatora, promjenama u mikrocirkulaciji, edemu tkiva, te pojavi infekcije (1,2). U bolesnika s opeklinama značajno su narušeni hemostatska ravnoteža i imunološki odgovor, a u moduliranju tih odgovora bitno mjesto zauzimaju trombociti.

Trombociti su mali fragmenti citoplazme megakariocita. Imaju temeljnu ulogu u primarnoj i sekundarnoj hemostazi, na njihovoj fosfolipidnoj površini odvijaju se bitne reakcije koagulacijske kaskade. Rana faza akutne opekline obilježena je sklonošću krvarenju, dok je kasnija faza u znaku hiperkoagulabilnosti (4). Iako je funkcija trombocita primarno hemostatska, oni djeluju i kao upalne stanice. Oslobađaju upalne medijatore, očituju proupalne površinske molekule, međudjeluju s leukocitima i endotelnim stanicama, te na taj način sudjeluju u poticanju akutnog i kroničnog imunološkog odgovora (5-7). Ako je TBSA veći od 30%, oslobođeni medijatori upale i citokini prelaze u sistemsku cirkulaciju, čime se potiče sistemski upalni odgovor. Vodeći uzrok smrtnosti bolesnika koji prežive početni period liječenja predstavljaju infekcije, koje su u bolesnika s teškim opeklinama posljedica poremećaja staničnog i humoralnog imunološkog odgovora (1,2).

Ispitivanja koja se odnose na ulogu trombocita i vrijednosti broja trombocita u opeklinskih ozljeda vrlo su rijetka, starijeg su datuma i pretežito se radi o prikazima slučaja. Kako je Odjel za opekline Klinike jedan od vodećih centara u Hrvatskoj specijaliziran za takvu vrstu ozljede, razumljivo je da su istraživanja patofizioloških poremećaja u takvih bolesnika od velikog interesa ne samo u razumijeva-

Introduction

During the 2003–2005 period, 442 patients with burn injuries (an average of 147 per year) were admitted to the Department of Burn Injuries, University Hospital of Traumatology in Zagreb. The most common causes of burn injury were flame (fire, 41%) and hot liquids (scalds, 31%), followed by contact burns, electrical burns, explosions and chemical burns.

Burns are extremely complex traumatic injuries that can be classified according to burn depth, size and area involved in injury, age and general health status (1-3). In treatment planning, it is essential to estimate the extent of burn wound which is expressed by means of percentage of total body surface area (%TBSA). The so-called rule of nines is most commonly applied in adults to estimate the extent of burn wound: the body is divided into areas and each area is attributed a multiple of the number nine. The head with the neck and the upper limbs account for 9% each, anterior and posterior trunk 18% each, each lower limb 18% of body surface, the remaining 1% accounts for the genitalia and perineum. Thermal trauma leads to impairment of skin structure and loss of skin functions. Tissue damage is the direct result of heat coagulation of structural proteins, while further progression of injury depends on the release of local mediators, changes in microcirculation, tissue edema and infection (1, 2). Burned patients are characterized by severe impairment of hemostatic balance and immune response, and platelets play an important role in the modulation of both these responses.

Platelets are small fragments of megakaryocyte cytoplasm. They play a fundamental role in primary and secondary hemostasis, as crucial reactions of the coagulation cascade occur on their phospholipid surface. The early phase of acute burn is characterized by a bleeding tendency, whereas the late phase is characterized by hypercoagulability (4). Although the platelet primary function is hemostatic regulation, they also act as inflammatory cells. They release inflammatory mediators, express proinflammatory surface molecules, interact with leukocytes and endothelial cells, thus taking part in the induction of acute and chronic immune response (5-7). If TBSA exceeds 30%, the released inflammatory mediators and cytokines migrate to the systemic circulation, inducing systemic inflammatory response to injury. Infections are the leading cause of death in patients who survive the initial period of treatment; they are the consequences of impairments in cellular and humoral immune responses in patients with severe burns (1, 2).

Studies investigating the role of platelets and platelet count in burn patients are rare, rather old and mostly presenting case reports. The Department of Burn Injury of our University Hospital is one of the leading centers in Croatia

nju kliničkog tijeka ozljede, već i u praćenju uspješnosti primijenjene terapije i ranom predviđanju komplikacija, odnosno ishoda bolesti. Cilj ovoga istraživanja bio je praćenje broja trombocita u skupinama bolesnika s različitim postotkom opečene površine tijela (≤ 10% TBSA – skupina A; > 10% TBSA – skupina B), te s obzirom na ishod bolesti (preživljenje/smrt).

Materijali i metode

Ispitanici

Retrospektivno u periodu od tri godine, u kojem je obrađeno 442 bolesnika s opeklinskom ozljedom odabrali smo 68 bolesnika s odgovarajućom dinamikom vađenja uzoraka krvi, odnosno 1., 4., 7., 14., 21. i 28. dana nakon ozljede, ovisno o dužini njihova boravka na Odjelu za opekline Klinike za traumatologiju. Iz ispitivanja smo isključili sve bolesnike koji su na daljnju skrb i zbrinjavanje u Kliniku bili upućeni iz drugih ustanova (nisu primljeni odmah po ozljeđivanju), kao i bolesnike koji nisu imali odgovarajuću dinamiku vađenja uzoraka krvi. Ukupno smo ispitali 49 muških i 19 ženskih ispitanika prosječne dobi od 55 (35–70) godina (medijan, interkvartilni raspon). Bolesnike s opeklinama podijelili smo u skupine A i B ovisno o postotku opečene površine tijela. Skupina A sastojala se od 32 bolesnika s lakšim opeklinama (≤ 10% TBSA), a skupina B od 36 bolesnika s umjerenim/težim opeklinama (> 10% TBSA). U skupini B bilo je 20 bolesnika s 11–20% TBSA, 9 s 21–40% TBSA, 6 s 41–60% TBSA i 1 s > 61% TBSA. Ovisno o ishodu opeklinske ozljede, ispitanike smo svrstali u dvije skupine: skupinu preživjelih činilo je ukupno 56 bolesnika, a skupinu umrlih 12 bolesnika. Osnovne karakteristike ispitivanih skupina prikazane su u Tablici 1. Istraživanje je odobrilo Etičko povjerenstvo Klinike za traumatologiju, Zagreb.

Metode

Broj trombocita odredili smo u sklopu rutinske obrade i praćenja bolesnikovog stanja, u uzorcima pune krvi s K_3EDTA kao antikoagulansom na automatiziranom hematološkom brojaču Sysmex XT-1800i (Sysmex Corporation, Kobe, Japan).

Statističke metode

Za ispitivanje normalnosti raspodjele podataka koristili smo Kolmogorov-Smirnovljev test. Podatke koji slijede normalnu raspodjelu prikazali smo aritmetičkom sredinom i standardnom devijacijom, uz pridružene 95%-tne intervale pouzdanosti, a podatke s asimetričnom raspodjelom prikazali smo medijanom i interkvartilnim rasponom, uz pridružene 95%-tne intervale pouzdanosti. Statističku značajnost razlike među skupinama ispitali smo t-testom (za normalnu raspodjelu), odnosno Mann-Whitneyevim testom (za asimetričnu raspodjelu). Statističku

specialized in this type of injury, thus it is understandable that investigations of pathophysiologic disorders in burn patients are of great interest, not only in understanding the clinical course of burn wound, but also in monitoring the efficacy of treatment applied and early prognosis of complications and disease outcome. The aim of the present study was to monitor platelet count in groups of patients with different percentage of body surface area burned (≤ 10% TBSA – group A; > 10% TBSA – group B), and with regard to the outcome of disease (survival/death).

Materials and methods

Patients

Retrospectively, of a total of 442 burn patients who were treated in a 3-year period, we selected and included in the study 68 patients with appropriate blood sampling dynamics on days 1, 4, 7, 14, 21, 28 after burn injury, and depending on the length of hospital stay at the Department of Burn Injury, University Hospital of Traumatology Zagreb. Patients referred to our University Hospital from other institutions for additional care and treatment (those that were not admitted immediately after being injured), and patients with inappropriate blood sampling dynamics were excluded. A total of 49 male and 19 female patients, mean age 55 (35-70) years (median, interquartile range), were investigated. Burn patients were divided in groups A and B, depending on the percentage of total body surface area burned. Group A consisted of 32 patients with mild burns (≤ 10% TBSA), whereas group B consisted of 36 patients with moderate/severe burns (> 10% TBSA). Group B consisted of 20 patients with TBSA 11–20%, 9 patients with TBSA 21–40%, 6 patients with TBSA 41–60% and 1 patient with TBSA > 61%. Depending on disease outcome, patients were subsequently divided into two groups: 56 patients who survived, and 12 patients who died as a consequence of burn injury. Basic burn patient group characteristics are shown in Table 1. This study was approved by the Ethics board of the University Clinic of Traumatology, Zagreb.

Methods

Platelet count was determined as a part of routine patient work-up and follow up, in whole blood samples with the addition of K_3EDTA as anticoagulant, using the automated hematology analyzer Sysmex-XT 1800i (Sysmex Corporation, Kobe, Japan).

Statistical analysis

Variables were tested for normality using the Kolmogorov-Smirnov test. Parametric data were expressed as arithmetic mean and standard deviation, with the pertaining 95% confidence interval, whereas nonparametric data were expressed as median and interquartile range, with

značajnost razlike broja trombocita u svim vremenskim točkama unutar skupina testirali smo RM ANOVOM. Za usporedbu razlike broja trombocita u pojedinačnim vremenskim točkama unutar skupina koristili smo *post hoc* test (Holem Sidak). Vrijednost P < 0,05 odabrali smo kao statistički značajnu. Za statističku obradu podataka koristili smo statistički program Sigmastat for Windows, verzija 3.5, Systat Software Inc.

Rezultati

U ispitivanim skupinama s obzirom na težinu opeklinske ozljede A i B nije dobivena značajna razlika u dobi bolesnika (P = 0,840), za razliku od skupina ispitanika s obzirom na ishod bolesti gdje je takva razlika bila prisutna. Ispitanici sa smrtnim ishodom bili su značajno stariji u odnosu na preživjele (P = 0,014) (Tablica 1). U skupini umrlih bolesnika samo je jedan pripadao skupini A, a taj je bolesnik bio star 70 godina. Ostalih jedanaest bilo je iz skupine B (3 s 11–20% TBSA, 2 s 21–40% TBSA, 5 s 41–60% TBSA i 1 s > 61% TBSA).

Vrijednosti broja trombocita u ispitivanim skupinama opeklinskih bolesnika s obzirom na težinu ozljede navedene su u Tablici 2. Broj trombocita prvoga dana ispitivanja nalazio se u referentnom intervalu (158–424 x 10^9/L), a između skupina nije postojala značajna razlika u broju trombocita (P = 0,170). Suprotno tomu, 4. i 7. dana praćenja broja trombocita dobivena je značajna razlika između skupina, bili su niži u skupini B (P < 0,001; P = 0,045). 14., 21. i 28. dana broj trombocita između ispitivanih skupina nije se značajno razlikovao (P = 0,199; P = 0,253; P = 0,333). Vršni broj trombocita dobiven je 14. dan u skupini B (492 x 10^9/L), odnosno 21. dan u skupini A (536 x 10^9/L). Ispitivanjem promjene broja trombocita u svim vremenskim točkama unutar skupine A, odnosno B, zabilježena je statistički značajna razlika (P < 0,001). *Post-hoc* testiranje pokazalo je u skupini A statistički značajan porast broja trombocita 7. u odnosu na 4. dan, kao i 14. u odnosu na 7. dan. Ostalih dana praćenja unutar skupine A (4. u odnosu na 1., 21. u odnosu na 14. i 28. u odnosu na 21.) nisu postojale značajthe pertaining 95% confidence interval. The t-test and Mann-Whitney test were used for between-group difference testing of parametric and nonparametric data, respectively. Differences in platelet count between multiple time points within groups were tested using the RM ANOVA. Differences in platelet count between paired time points within groups were tested using a post hoc test (Holem Sidak). Values of P < 0.05 were considered statistically significant. Analyses were performed using the Sigmastat for Windows software, version 3.5, Systat Software Inc.

Results

No significant difference was observed in patient age (P = 0.840) comparing group A and B according to severity of burn injury, but the difference in patient age was found comparing groups according to disease outcome. Patients with lethal outcome were significantly older compared to surviving patients (P = 0.014) (Table 1). Only one patient from group A died**;** he was 70 years old. The remaining 11 patients who died were from group B (3 with TBSA 11-20%, 2 with TBSA 21-40%, 5 with TBSA 41-60% and 1 with TBSA > 61%).

Platelet count in investigated burn patient groups according to severity of injury is shown in Table 2. On the first day of investigation, platelet count was within the reference range (158-424 x 109/L), showing no significant difference between groups (P = 0.170). On the contrary, on the 4th and 7th day of platelet count monitoring, there was a significant between-group difference, platelet count was lower in group B (P < 0.001; P = 0.045). No significant between-group difference in platelet count was found on days 14, 21 and 28 (P = 0.199; P = 0.253; P = 0.333). Peak platelet counts were recorded on the 14th day in group B (492 x 109/L), and on the 21st day in group A (536 x 109/L). A significant difference was obtained testing changes in platelet count at all time points observed within group A, and group B, respectively (P < 0.001). Post hoc testing showed significant increase in platelet count on day 7 compared to day 4 in group A, as well as on day 14 com-

Tablica 1. Značajke ispitanika prema skupinama

Table 1. Characteristics of burn patient groups

Group characheristics	A (TBSA ≤ 10%)	B (TBSA > 10%)	Survived	Deceased
N (male/female)	32 (23/9)	36 (26/10)	56 (43/13)	12 (6/6)
Age (Years)	52 ± 19 *	53 ± 21 *	50 ± 19 *	70 (68-75) §
P	0.840		0.014	

* $\bar{x}$ ± SD; § Median (interquartile range)

Tablica 2. Vrijednosti trombocita u ispitivanim skupinama

Table 2. Platelet count in burn patient groups

Day	Platelet count (x10⁹/L)						P
	Group A (TBSA ≤ 10%)			Group B (TBSA > 10%)			
	N	$\bar{x}$ ± SD	95%CI	N	$\bar{x}$ ± SD	95%CI	
1	32	232 ± 73	206–258	36	261 ± 97	228–294	0.170
4	32	212 ± 56	192–232	35	155 ± 65	133–177	< 0.001
7	26	298 ± 91	261–335	36	250 ± 92	219–281	0.045
14	16	425 ± 148	346–504	35	492 ± 179	430–554	0.199
21	7	536 ± 112	432–640	25	434 ± 224	342–526	0.253
28	4	441 ± 43	373–509	20	359 ± 167	281–437	0.333

ne promjene u broju trombocita. U skupini B zabilježen je značajan pad broja trombocita 4. u odnosu na 1. dan, a zatim je došlo do značajanog porasta broja trombocita 7. u odnosu na 4. dan, kao i 14. u odnosu na 7. dan. Ostalih dana praćenja unutar skupine B (21. u odnosu na 14. i 28. u odnosu na 21.) nisu postojale značajne promjene u broju trombocita.

Vrijednosti broja trombocita s obzirom na ishod bolesti (preživljenje/smrt) prikazane su u Tablici 3. S obzirom na ishod bolesti među skupinama nađena je značajna razlika u broju trombocita tijekom cijelog perioda praćenja ($P < 0,05$). Vrijednosti trombocita u bolesnika sa smrtnim ishodom bile su značajno niže svih dana praćenja, osim prvoga dana kada su dobivene vrijednosti bile značajno više u odnosu na preživjele bolesnike. Ispitivanjem razlike među brojem trombocita u svim vremenskim točkama unutar skupine preživjelih, odnosno umrlih, zabilježena je statistički značajna razlika ($P < 0,001$). *Post-hoc* testirapared to day 7. No significant difference in platelet count was observed in the remaining monitoring days in group A (day 4 vs. day 1, day 21 vs. day 14, and day 28 vs. day 21). In group B, a significant decrease in platelet count was observed on day 4 compared to day 1, followed by a significant increase in platelet count on day 7 compared to day 4, as well as on day 14 compared to day 7. No significant difference in platelet count was observed in the remaining monitoring days in group B (day 21 vs. day 14 and day 28 vs. day 21).

Platelet count according to disease outcome (survival/death) is shown in Table 3. A significant difference was found throughout the whole monitoring period by comparing surviving and deceased patients ($P < 0.05$). Significantly lower platelet count was observed in patients with lethal outcome on all monitoring days, except on day 1, when significantly higher platelet count was obtained compared to surviving patients. A significant difference

Tablica 3. Vrijednosti trombocita s obzirom na ishod bolesti

Table 3. Platelet count in relation to disease outcome

Day	Platelet count (x 10⁹/L)				P
	Survived (N=56)		Deceased (N=12)		
	$\bar{x}$ ± SD	95%CI	$\bar{x}$ ± SD	95%CI	
1	233 ± 78	212–254	314 ± 102	249–379	0.003
4	193 ± 66	175–211	133 ± 48	103–163	0.004
7	285 ± 91	259–311	208 ± 82	156–260	0.009
14	501 ± 168	447–555	362 ± 146	264–460	0.012
21	517 ± 206	426–608	323 ± 142	222–424	0.012
28	450 ± 135	372–528	264 ± 113	183–345	0.002

njem u skupini preživjelih zabilježen je značajan porast broja trombocita 7. dana u odnosu na 4. dan kao i 14. u odnosu na 7. dan. Ostalih dana praćenja unutar skupine preživjelih (4. u odnosu na 1., 21. u odnosu na 14. i 28. u odnosu na 21.) nisu postojale značajne promjene u broju trombocita. U skupini umrlih 4. u odnosu na 1. dan zabilježen je značajan pad broja trombocita. Do značajnog porasta broja trombocita u umrlih došlo je 14. u odnosu na 7. dan. Ostalih dana praćenja unutar skupine umrlih (7. u odnosu na 4., 21. u odnosu na 14. i 28. u odnosu na 21.) nisu postojale značajne promjene u broju trombocita.

Rasprava

Ovo je istraživanje pokazalo da u bolesnika s opeklinama, ovisno o težini opeklinske ozljede, postoji značajna razlika u broju trombocita 4. i 7. dana praćenja; trombociti su bili niži u skupini s umjerenim/težim opeklinama. Četvrtoga u odnosu na 1. dan dobiven je značajan pad broja trombocita u skupini B (umjerene/teže opekline), broj trombocita bio je ispod donje granice referentnog intervala. Zabilježen je značajan porast broja trombocita u objema skupinama 7. u odnosu na 4. dan. Trend značajnog porasta broja trombocita unutar skupina nastavio se i 14. u odnosu na 7. dan, ali nije bilo značajne razlike između ispitivanih skupina.

Postoji vrlo malo radova u kojima je istraživana dinamika broja trombocita u bolesnika s opeklinama. Prema radu Takashima i sur. koji su pratili vrijednosti broja trombocita u pet teže opečenih bolesnika, pad broja trombocita pojavio se u periodu od 7–12 dana, a nakon toga vrijednosti su bile unutar referentnog intervala ili je došlo do njihova porasta. Vrijednosti broja trombocita ustalile su se tek nakon dva mjeseca (8). Promjena broja trombocita u našem ispitivanju sličnija je kretanjima trombocitnih vrijednosti koje su objavili Sarda i sur. (9) te Bartlett i sur. (4). Bartlett i sur. pratili su koagulacijske promjene u 11 bolesnika s opeklinama, kod kojih se trombocitopenija pojavila u vrijeme prva tri dana nakon ozljede. Najniži broj trombocita postignut je trećega dana, uz značajan pad u teže opečenih bolesnika. Broj trombocita dosegnuo je bazalne vrijednosti oko prvoga tjedna. Nakon toga došlo je do preokreta, broj trombocita je porastao. U našem radu, 4. u odnosu na 1. dan dobiven je značajan pad trombocita samo u skupini umjerenih/težih opeklina. Uzroci smanjenja broja trombocita mogu biti višestruki i najčešće su međusobno povezani, bilo da se radi o pojačanom uništavanju trombocita, prisutnoj hemodiluciji, sekvestraciji trombocita (npr. u slezeni) ili njihovoj smanjenoj sintezi. Nekoliko je radova koji ukazuju na povezanost trombocitopenije u kritičnih bolesnika i skraćenog životnog vijeka trombocita (10,11). Osim toga, trombocitopenija često prati bakterijsku sepsu koja može biti prisutna kod ovakvih bolesnika. U našem radu 7. u odnosu na 4. dan, kao i 14. u odnosu na

was obtained testing changes in platelet count at all the time points in the surviving patient group, as well as within the group of deceased patients ($P < 0.001$). *Post hoc* testing showed a significant increase in platelet count on day 7 compared to day 4 in the surviving group, as well as on day 14 compared to day 7. No significant difference in platelet count was observed in the remaining monitoring days in survived patients group (day 4 vs. day 1, day 21 vs. day 14 and day 28 vs. day 21). A significant decrease in platelet count was observed on day 4 compared to day 1 in patients with lethal outcome. No significant difference in platelet count was observed in the remaining monitoring days in patients with lethal outcome (day 7 vs. day 4, day 21 vs. day 14, and day 28 vs. day 21).

Discussion

The results of this investigation revealed a significant difference in platelet count on the 4th and 7th day during monitoring in burn patient groups according to severity of injury; platelet count was lower in group B. A significant decrease in platelet count was observed in group B (moderate/severe burns) on day 4 compared to day 1, platelet count was below the reference range. A significant increase in platelet count was observed on day 7 compared to day 4 in both groups according to severity of burn injury. A rising platelet count tendency further continued on day 14 compared to day 7, but with no significant difference between groups.

Investigations dealing with time-dependent changes in platelet count in burn patients are rare. Takashima *et al.* recorded platelet count in five severely burned patients during clinical course after burn injury. They observed that platelet count decreased during 7-12 days, and after that stage numbers returned within the reference range or increased markedly. Platelet count stabilized just after two months (8). The time-dependent changes of platelet count in our investigation are similar to platelet count trend found by Sarda *et al.* (9) and Bartlett *et al.* (4). Bartlett and al. monitored coagulation and platelet changes in a group of 11 burn patients who manifested a progressive thrombocytopenia during the first three days after injury. Thrombocytopenia reached its maximum on the third day, the decrease being significant only in severely burned patients. Platelet count reached baseline values in the first week, followed by a reversal to abnormally high levels. In our investigation, a significant decrease in platelet count was observed only in the moderate/severe group of burn patients if day 4 was compared to day 1. Decrease in platelet count is caused by multiple and mostly interrelated factors. Platelet destruction is intensified, hemodilution is present, along with platelet sequestration (e.g., in the spleen) and their reduced production. A number of studies emphasize the relationship between

7. dan došlo je do značajanog porasta broja trombocita u objema skupinama ispitanika, što se najvjerojatnije može objasniti njihovim doprinosom upalnoj reakciji na opeklinsku ozljedu. Naime, patofiziološke promjene uzrokovane opeklinskom ozljedom ne zahvaćaju samo mjesto opekline, već se djelovanjem oslobođenih upalnih citokina i endotoksina razvija sistemski upalni odgovor. Povećanje broja trombocita predstavlja normalan odgovor organizma na upalni podražaj, a moguća prisutnost trombocitopenije jedan je od problema u kritičnih bolesnika i smatra se da ima značajnu ulogu u pogoršanju tijeka bolesti (12). Primarni pokazatelji smrtnosti nakon termalne ozljede su %TBSA zahvaćene opeklinom, dob te eventualna prisutnost inhalacijske ozljede (3). Ispitivanja su pokazala da je i broj trombocita koristan pokazatelj ishoda opeklinske ozljede (9,13). U našem istraživanju bolesnici sa smrtnim ishodom bili su značajno stariji u odnosu na preživjele. S obzirom na ishod bolesti u ovim dvjema skupinama dobivena je značajna razlika u broju trombocita tijekom cijelog perioda praćenja. Vrijednosti trombocita u bolesnika sa smrtnim ishodom bile su značajno niže svih dana praćenja osim prvoga dana kada su trombociti bili značajno viši u odnosu na preživjele bolesnike. Više vrijednosti trombocita u skupini umrlih prvoga dana mogu biti posljedica hemokoncentracije. Niži broj trombocita u skupini umrlih bolesnika ostalih dana praćenja najvjerojatnije je posljedica teže opeklinske ozljede i bakterijske infekcije, koji djeluju na stimulaciju koagulacijske kaskade u smjeru stvaranja mikrotromba i njihove pojačane potrošnje. Osim toga, težina ozljede i infekcija mogu djelovati i na depresiju koštane srži. U radu El-Sonbaty i sur. (13) zabilježeno je značajno povećanje broja trombocita sedmoga dana u preživjelih opeklinskih bolesnika, a u umrlih je došlo do progresivnog smanjenja. Suprotno njima, prema našim podatcima 7. u odnosu na 4. dan u objema skupinama s obzirom na ishod bolesti dobiven je porast broja trombocita, koji je bio značajan samo u skupini preživjelih.

Svjesni smo ograničenja naše studije koje predstavlja s jedne strane mali broj ispitanika (skupina umrlih, skupina lakših opeklina – ranije otpuštanje s bolničkog liječenja), a s druge strane nedostupnost vrijednosti srednjeg volumena trombocita (MPV) koji bi nam mogao pružiti potpuniju informaciju o patofiziološkoj podlozi promjene broja trombocita u određenoj vremenskoj točki praćenja u odgovoru na opeklinsku ozljedu.

Prisutne značajne razlike u broju trombocita 4. i 7. dana između skupina prema težini opeklinske ozljede, kao i značajan pad trombocita 4. u odnosu na 1. dan u skupini umjerenih/težih opeklina upućuje na potrebu uvođenja učestalijeg praćenja trombocita u tom razdoblju radi pravovremenog određivanja pada njihovog broja. U bolesnika sa smrtnim ishodom u odnosu na preživjele bile su značajno niže vrijednosti trombocita tijekom cijelog perioda praćenja, osim prvoga dana kada su te vrijednosti bile značajno

thrombocytopenia in critically ill patients and platelet reduced life expectancy (10,11). Additionally, thrombocytopenia is frequently associated with bacterial sepsis present in these patients. In our investigation, a significant increase in platelet count was observed in both groups of patients on day 7 compared to day 4, and on day 14 compared to day 7, which can probably be explained by platelet contribution to the inflammatory reaction caused by burn injury. In fact, pathophysiological changes caused by burn injury are not localized to the site of burn injury, systemic inflammatory response results from the effects of released cytokines and endotoxins. An increase in platelet count represents normal response to a variety of inflammatory stimuli, whereas thrombocytopenia is considered to be an important issue concerning critically ill patients and is thought to play an important role in worsening the course of disease (12).

The percentage of TBSA, age and possible presence of inhalation injury are the major mortality determinants after thermal injury (3). Several investigations indicated the role of platelets as useful outcome indicators in burn patients (9, 13). Patients with lethal outcome followed up in our investigation were significantly older compared to surviving patients. A significant difference in platelet count throughout the entire monitoring period was observed in groups of patients according to disease outcome. Significantly lower platelet count was observed at all the monitored time points in patients with lethal outcome, except on day one when platelet count was significantly higher in this group of patients compared to those who survived. Higher platelet count in patients with lethal outcome on the 1st day can be caused by hemoconcentration. Furthermore, lower platelet count in patients with lethal outcome found in the remaining monitored days is probably caused by more serious burn injury and bacterial infection, the processes that stimulate thrombus formation in the coagulation cascade and intensive platelet consumption. Moreover, severity of injury and infection can depress bone marrow activity. El Sonbaty *et al.* (13) reported a significant platelet count increase on the 7th day in survivors after burn injury, while in those with lethal outcome a progressive decrease was recorded. In contrast, our results showed a platelet count increase in both groups in relation to disease outcome on the 7th day compared to the 4th day, but it was significant only in survivors.

We are aware of our study limitations: a limited number of investigated patients (especially in the group of patients with lethal outcome, and the group of mild burns where early hospital discharge was present), and on the other hand, unavailability of mean platelet volume (MPV) data, valuable for generating more complete information about the pathophysiological background of platelet count change at a given time point during monitoring of platelets in burn injury.

više. Usprkos prisutnim razlikama prema ishodu bolesti, ali sličnoj dinamici trombocita (porast i pad) u objema skupinama te vrlo malom broju umrlih ispitanika potrebna su dodatna istraživanja. Buduća bi istraživanja trebala ispitati korisnost poznavanja i praćenja dinamike trombocitne krivulje u liječenju te smanjivanju rizika komplikacija prilikom primjene kožnih presadaka kao i u mogućnosti procjene ishoda bolesti.

Zahvale

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In conclusion, significant between-group differences recorded on the 4th and 7th day in groups of patients according to severity of injury, and significant decrease in platelet count recorded on the 4th day compared to the 1st day in moderate/severe burn patients in our study address the necessity for more frequent platelet count monitoring in this particular period of burn injury management in order to timely determine its decline. Significantly lower platelet count was observed throughout the whole monitoring period in patients with lethal outcome compared to survivors, except on day one, when platelet count was higher in this group. Despite the between-group differences in platelet count according to disease outcome, similar time-dependent changes in platelet count (increase and decrease) in both groups, and a limited number of study group patients, additional investigations are needed. Future investigations should address the usefulness of knowing platelet values and platelet curve monitoring in treatment, reducing the risk of complications during skin grafting, and disease outcome estimation.

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