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The effects of topical epinephrine on haemodynamics and markers of tissue perfusion in burned and non-burned patients requiring skin grafting

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ARTICLE INFO

Article history:
Accepted 2 October 2008

Keywords:
Epinephrine
Skin grafting
Burn
Catecholamines
Haemodynamics
Lactate
LP-ratio

ABSTRACT

Objective: To compare the systemic effects in burn and non-burn patients undergoing skin grafting with or without the use of topical epinephrine to control bleeding.
Background: The effects of topical epinephrine on haemodynamics and bleeding are principally documented with burn patients. No reports are available on the effects of topical epinephrine on non-burn patients especially on markers of tissue perfusion.
Material and methods: A prospective study where topical epinephrine was used on burn and non-burn patients and five patients served as controls without epinephrine usage. Catecholamine concentrations were measured and to estimate the systemic effects of epinephrine, serum lactate and pyruvate concentrations were analyzed and perioperative haemodynamic changes recorded.
Results: Compared to the baseline values, there was a significant increase in the heart rate, serum epinephrine and lactate concentrations and LP-ratios in the burn patients and an increase in the epinephrine concentrations in the non-burn patients at 1 and 2 h. Epinephrine and lactate concentrations and LP-ratios were also higher in the burn patients compared to the other groups. Altogether, there were no changes in the control group.
Conclusion: This study showed that the use of topical epinephrine has systemic effects on haemodynamics and serum epinephrine concentrations. Increased epinephrine concentrations in burn patients suggest increased absorption properties in these patients. The increased lactate concentrations and LP-ratios suggest tissue ischaemia, likely in skin.

1. Introduction

Burn surgery is associated with great blood loss. This is typically controlled with electrocautery, tourniquet and the use of topical or clysed epinephrine and topical thrombin solutions. Although epinephrine solution is widely used, its effects on serum catecholamines is scarcely documented [1,2]. Most epinephrine studies on burn patients have concentrated on blood loss [3–10] or on haemodynamic effects [3,7,11–14]. However, there are no studies on catecholamine concentrations in non-burn patients undergoing surgical procedures with the use of topical epinephrine. In septic shock, the use of epinephrine as a systemic vasopressor may be associated with acidosis and hyperlactatemia [15]. Based on our clinical experience we hypothesized, in contradiction to present literature, that even locally administered epinephrine may

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0305-4179/$36.00
doi:10.1016/j.burns.2008.10.001

cause systemic effects leading to hyperlactatemia and haemodynamic changes.

In this study, we compared the systemic effects of topical epinephrine solution in burn and non-burn patients undergoing skin grafting with the use of topical epinephrine to control bleeding. Catecholamine concentrations were measured to assess whether epinephrine absorption from the wounds to systemic circulation is different in these patient categories. To estimate potential systemic effects of epinephrine, serum lactate and pyruvate concentrations were analyzed. In addition, perioperative haemodynamic changes were recorded. The two epinephrine groups were compared with a control group, where no topical epinephrine was used.

2. Materials and methods

This prospective study was approved by the ethical committee of Kuopio University Hospital. Burn ($N = 20$) and non-burn ($N = 10$) patients requiring skin grafting to an area greater than 200 cm^2 were enrolled in the study over a 4-year-period. Septic patients requiring vasopressor or inotropic treatment were excluded. Topical epinephrine solution was used to control bleeding both on donor sites and/or debrided areas. The required amount of epinephrine solution (Suprarenin®, 1 mg/ml epinephrine) was diluted 1:10 with saline (concentration 0.1 mg/ml). Soaked gauzes were applied to the wounds immediately after skin harvesting or wound debridement, replaced when needed and removed only after complete haemostasis was obtained. Additionally, there were five patients with identical surgical procedures in whom epinephrine was not used and haemostasis was obtained by starch powder (Arista®), warm saline compresses and electrocautery.

The following data was collected: age, gender, pre- and postoperative haemoglobin and haematocrit values, the estimated blood loss (ml), the amount of perioperatively given packed red cells (ml) and the surface area (cm^2) where topical epinephrine solution was used (epinephrine exposure area, EEA). Heart rate (HR), systolic (SAP) and mean systolic arterial pressures (SAPm), serum concentrations of lactate, pyruvate, epinephrine and norepinephrine, lactate to pyruvate (LP-) ratio and blood gases were documented prior to epinephrine application (0) and 5, 15, 30, 60, 120, 240 and 360 min post-application of first epinephrine gauze. The changes in lactate concentrations compared to the pre-application concentration (Δ-lactate) were calculated and the amount of patients who had serum lactate concentrations higher than 2.4 mmol/l was recorded, also. The results of the burn (B) patients were compared to the non-burn (NB) patients and both these groups were compared to the control (C) group.

3. Sample collection and substance analyses

Plasma samples were collected in 10 ml plastic tubes in ice containing EGTA (ethylene glycol-bis(2-aminoethylether)-*N*,*N*,*N*′,*N*′-tetraacetic acid) and reduced glutathione as a preservative. Samples were centrifuged immediately and plasma stored frozen at −70 °C until analyzed.

To a sample clean-up column 500 μl extraction buffer was transferred followed by 1000 μl plasma and 50 μl internal standards. Thereafter the column was shaken for 10 min. The cap from the bottom of the column was removed and the column was centrifuged and the eluate was discarded. The clean-up column was washed three times with 1000 μl of wash buffer. Finally, the catecholamines were eluted out of the clean-up column by centrifugation with 120 μl of elution buffer. An aliquot of 20 μl was injected for HPLC-system.

Chromsystems reagent kit for HPLC analysis of catecholamines in plasma (Chromsystems Instruments and Chemicals GmbH, Munich, Germany) was used. The kit (Chromsystems #5000) contained HPLC mobile phase, calibration standard, internal standard, sample clean-up columns, extraction buffer, wash buffer and elution buffer. Chromsystems Plasma Endocrine Controls, level I (#0010) and level II (#0020) were used to control the performance of the method. Running buffer was pumped 1.2 ml/min with the following detector settings: oxidation electrode 1: 70 mV; oxidation electrode 2: 280 mV; output 20 nA. The chromatographic system consisted of Shimadzu LC-10A pump (Shimadzu, Japan), Waters 717 Autosampler (Waters Corporation, Milford, MA, USA), Chromsystems #5100 HPLC column for plasma catecholamines (Chromsystems Instruments and Chemicals GmbH, Munich, Germany), and ESA, Coulochem II detector, equipped with Model 5011Analytical Cell (ESA, Bedford, MA, USA). The data were analyzed by HP ChemStation chromatography program. The chromatograms were printed out by HP LaserJet 4000 printer.

Absolute recovery of catecholamines was 70–72%, analytical recovery 96–99%, linear range of the method 0.06–40.0 nmol/l, intra-assay variation for norepinephrine 4.1–6.7% and for epinephrine 3.5–8.5%, and inter-assay variation for norepinephrine 7.1–7.2% and for epinephrine 7.6–10.1%.

4. Statistics

The results are presented as mean (±S.E.). The area under the curve was calculated for the serum lactate and catecholamine concentrations of each patient by taking the average of each two consecutive values (y axis) and multiplying that with the time between two samples (x axis). This was done at each time point followed by summarizing the values of the entire follow-up time. The one-way ANOVA was used to detect differences in different parameters between groups followed by student's t-test with a Bonferroni correction for additional statistical analysis when indicated. A p-value <0.05 was considered statistically significant.

5. Results

The demographic and perioperative data are presented in Table 1. There were 20 patients in the burn group, 10 in the non-burn group and 5 in the control group (3 burn and 2 non-burn patients) with no epinephrine exposure. There were no differences between the EEAs in the two epinephrine groups. The EEA in the B group, however, was bigger

Table 1 – Demographic and pre- and postoperative data of used epinephrine, blood loss, haemoglobin and hematocrit.

	Burn group	Non-burn group	Control group	*p*-value		
				B vs. NB	B vs. C	NB vs. C
Number of patients	20	10	5			
Age (years)	41 ± 5.3	47.2 ± 6.8	36.6 ± 10.4	ns	ns	0.044
Female:male	9:11	1:9	1:4			
Epinephrine soaks used (cm^2)	1932 ± 376	1364 ± 243		ns		
Surface area operated (cm^2)			963 ± 278		0.014	ns
Estimated blood loss (ml)	906 ± 127	166 ± 32	120 ± 46	0.02	0.013	ns
Packed red cells given (ml)	1292 ± 280	360 ± 133	0 ± 0	0.007	0.001	ns
Preoperative Hb (g/l)	99 ± 3.2	106 ± 5.9	115 ± 8.7	ns	ns	ns
Postoperative Hb (g/l)	96 ± 3.7	102 ± 5.1	107 ± 7.3	ns	ns	ns
Preoperative Hcr	0.29 ± 0.01	0.33 ± 0.01	0.33 ± 0.02	ns	ns	ns
Postoperative Hcr	0.30 ± 0.01	0.31 ± 0.01	0.31 ± 0.02	ns	ns	ns

Hb = haemoglobin; Hcr = hematocrit; values are presented as mean + S.E.; ns = non-significant.

than the surface area operated in the control group ($p = 0.014$). The estimated blood loss and the amount of given packed red cells were greater in the B group compared to the NB ($p = 0.02$ and 0.007, respectively) and the C ($p = 0.013$ and 0.001, respectively) group. There were no differences in pre- or postoperative values for Hb and Hct. The burn patients' operations included both early ($N = 11$) and late ($N = 9$) excisions and skin graftings with the operation on day 14 (±4) post-burn (Table 2).

5.1. *Differences compared to the baseline values*

No differences were found in the baseline (0) values for lactate, pyruvate, epinephrine and norepinephrine between the groups, but the LP-ratio was higher in burn patients compared to non-burn patients ($p = 0.0299$). Burn patients' heart rate was increased at 30–120 min ($p \leq 0.0001$–0.002) but there were no significant changes in the NB and C groups (Fig. 1a). Also, there were no significant changes in the SAP (Fig. 1b), SAPm or norepinephrine (Fig. 2a) concentrations in any group. The epinephrine concentrations were increased throughout the study in the B group ($p = 0.0001$–0.005) and at 60 and 120 min in the NB group ($p = 0.0016$ and 0.0024, respectively) with no changes in the control group (Fig. 2b). The peak concentrations of serum epinephrine in the B group were found at 4 h and in the NB group at 1 h with 59- and 8-fold increases, respectively, from the baseline values. The lactate concentrations were increased until 240 min in the B group ($p = 0.0006$–0.0123) and at 120 min in the NB group ($p = 0.0432$). There were no changes in the lactate concentrations in the C group (Fig. 3a).

Table 2 – Demographics on burn group.

Patient	TBSA	Age (years)	Gender	OR	EEA	Debridement
1	41	51	F	62	2580	Late
2	12	78	F	4	4383	Early
3	35	61	F	1	1000	Early
4	7	6	M	2	1252	Early
5	33	3	M	2	1000	Early
6	80	27	F	60	2770	Late
7	7	77	F	1	567	Early
8	72	28	M	1	1000	Early
9	48	39	M	19	1000	Late
10	12	29	F	22	1000	Late
11	45	30	M	17	4502	Late
12	5	78	M	7	750	Early
13	27	54	F	1	400	Early
14	20	45	F	20	2550	Late
15	5	14	M	7	950	Early
16	2	62	M	2	340	Early
17	34	55	F	23	2306	Late
18	27	52	M	19	2455	Late
19	49	24	M	18	4730	Late
20	34	10	M	2	6200	Early
Mean	29.75	41.2		14.5	1932	
S.E.	4.93	5.32		4.01	376	

TBSA = total burn surface area (%), OR = post-burn day when operation was performed, EEA = surface area where epinephrine soaks were used (cm^2), debridement = the type of surgery (early: ≤7 days post-burn; late: >7 days post-burn).

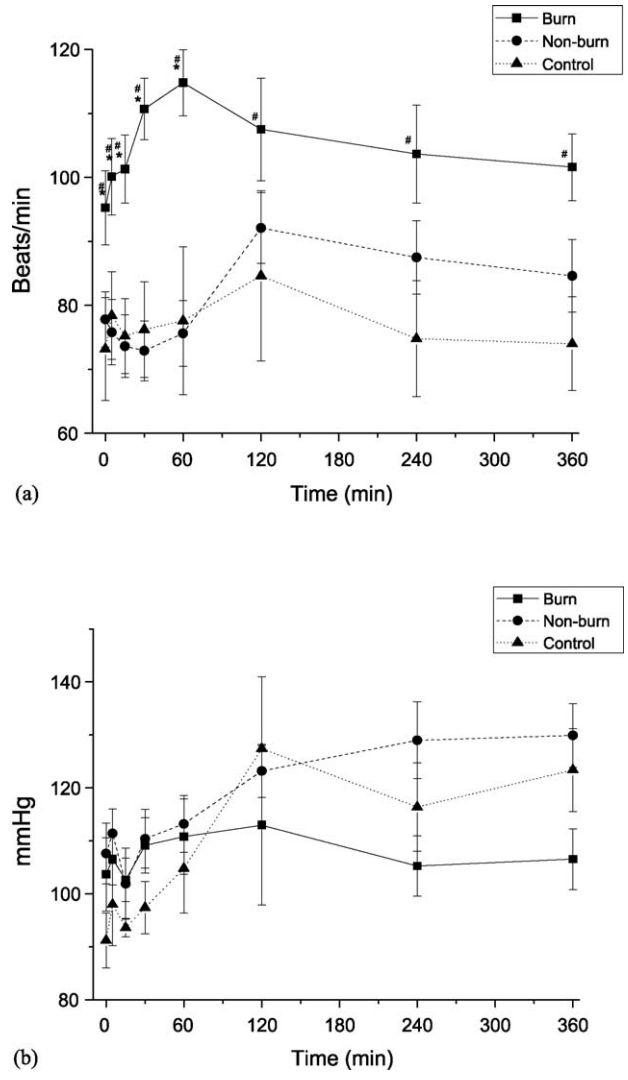


Fig. 1 – Heart rate (a) and systolic arterial pressures (b) (mean ± S.E.). $^{*}p < 0.05$ B vs. NB group and $^{\#}p < 0.05$, B vs. C group.

5.2. *Differences between groups*

The burn patients had higher heart rates than the NB group both prior to and during the first 60 min ($p = 0.000–0.0345$) and throughout the study against the control group ($p = 0.001–0.037$) (Fig. 1a). There were no differences in the SAP (Fig. 1b) or SAPm between any groups.

The serum concentrations of epinephrine were higher in the burn group at 15, 30, 120 and 240 min compared to the NB group ($p = 0.006–0.027$) and the control group ($p = 0.0001–0.001$). The NB group had higher epinephrine concentrations than the control group at 15, 30 and 120 min ($p = 0.001–0.042$) (Fig. 2b). As the intra-operative blood loss was the greatest in the burn group, the burn patients with blood loss greater than 500 ml were compared to burn patients with a blood loss less than 500 ml, the non-burn group and the control group. Interestingly, the burn patients with less than 500 ml blood loss had higher S-epinephrine concentrations than the burn patients with more significant blood loss (Fig. 2c).

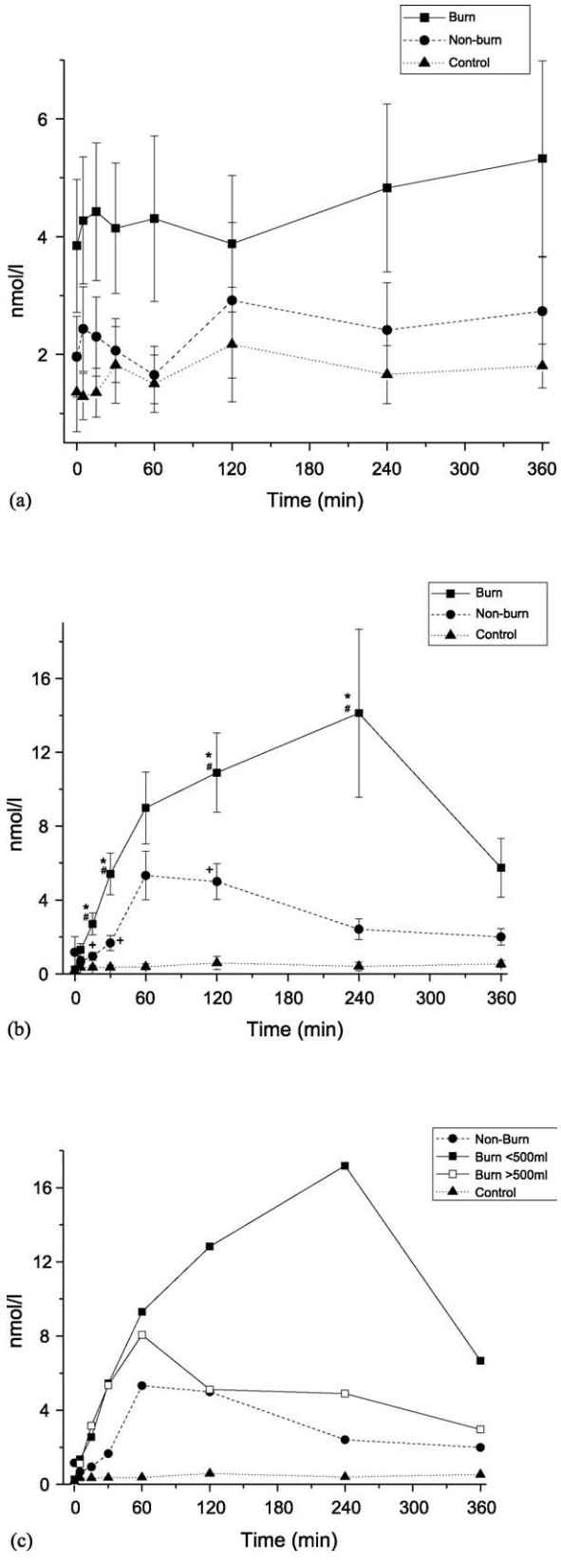
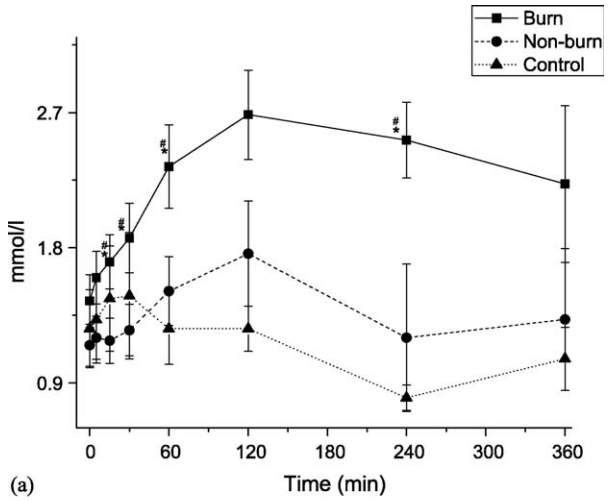


Fig. 2 – Serum (a) norepinephrine and (b) epinephrine concentrations (mean ± S.E.). $^{*}p < 0.05$ B vs. NB group, $^{\#}p < 0.05$, B vs. C group and $^{+}p < 0.05$ NB vs. C group. (c) Serum epinephrine concentrations. Burn patients are divided between the ones with >500 ml and <500 ml intra-operative bleeding.



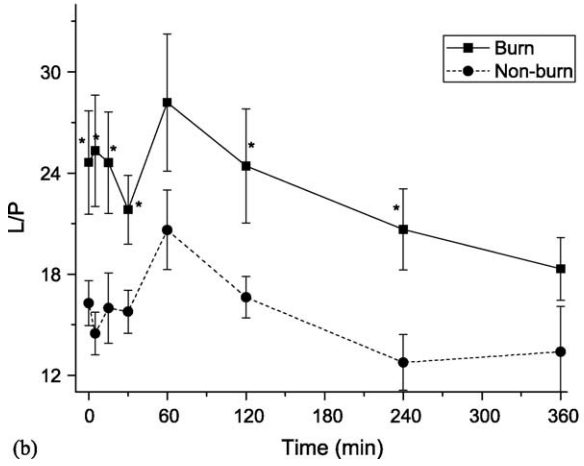


Fig. 3 – Serum lactate concentrations (mean ± S.E.). *$p < 0.05$ B vs. NB group and #$p < 0.05$, B vs. C group.

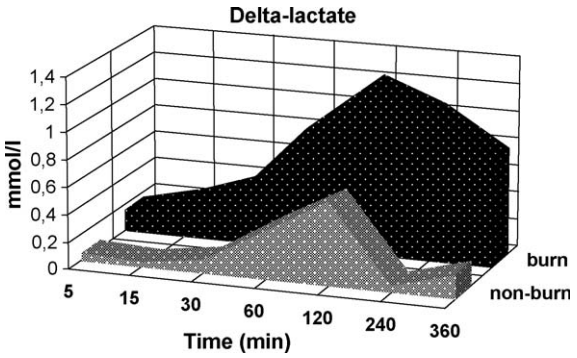


Fig. 4 – Mean changes in serum lactate concentrations compared to baseline values (Δ-lactate).

In the NB group only one patient had serum lactate concentrations >2.4 mmol/l during the study whereas as much as 70% (14/20) of the burn patients were hyperlactataemic. The lactate concentrations were higher in the B group at 15–60 and at 240 min (Fig. 3a) compared to the NB group ($p = 0.024$–0.046). The LP-ratio was higher in burn patients throughout the study except at 60 and 360 min compared to the NB group ($p = 0.007$–0.043) (Fig. 3b). Burn patients had greater Δ-lactate values than the non-burn patients after 120 min with the peak at 2 h in both groups (Fig. 4).

The area under the curve (AUC) values for lactate and epinephrine 'loads' are presented in Table 3. The lactate ($p = 0.026$) and epinephrine ($p = 0.008$) loads were higher in the B group compared to the NB group and also compared to the control group ($p = 0.001$ and $p = 0.0004$, respectively). The NB group had higher epinephrine loads compared to the control group ($p = 0.002$) but not in lactate loads ($p = 0.323$). There were no differences in the relative surface areas for lactate between groups, but the relative surface area for epinephrine loads were higher in both burn ($p = 0.004$) and non-burn ($p = 0.025$) groups compared to the control group (Table 3).

Table 3 – Absolute and relative surface areas under the curves of lactate, pyruvate, epinephrine, norepinephrine and LP-ratio with the respective *p*-values.

	B group	NB group	C group	*p* value		
				B vs. NB	B vs. C	NB vs. C
Surface areas						
S-Lactate	861 ± 119	504 ± 95	412 ± 43	0.026	0.001	ns
S-Pyruvate	38,251 ± 3836	32,933 ± 3832	nm	ns	nm	nm
S-Epinephrine	3570 ± 793	1157 ± 238	167.4 ± 74	0.008	0.0004	0.002
S-Norepinephrine	1622 ± 390	891 ± 310	640 ± 207	0.02	0.013	ns
L/P ratio	8019 ± 840	5463 ± 531	nm	0.047	nm	nm
Relative surface areas						
Lactate	0.6 ± 0.09	0.6 ± 0.16	0.58 ± 0.17	ns	ns	ns
Pyruvate	31.3 ± 4.60	41.9 ± 12.60	nm	ns	nm	nm
S-Epinephrine	3.9 ± 1.30	1.6 ± 0.60	0.19 ± 0.07	ns	0.004	0.025
S-Norepinephrine	1.4 ± 0.39	1.4 ± 0.83	0.75 ± 0.2	ns	0.036	0.042
L/P ratio	7.0 ± 1.92	6.5 ± 1.94	nm	ns	nm	nm

Values are presented as mean ± S.E.; ns = non-significant; nm = not measured; surface areas presented as (min × mmol/l) (lactate and pyruvate) and (min × nmol/l) (epinephrine and norepinephrine), relative surface areas presented as (min × mmol/l):cm^2 (lactate and pyruvate) and (min × nmol/l):cm^2 (epinephrine and norepinephrine).

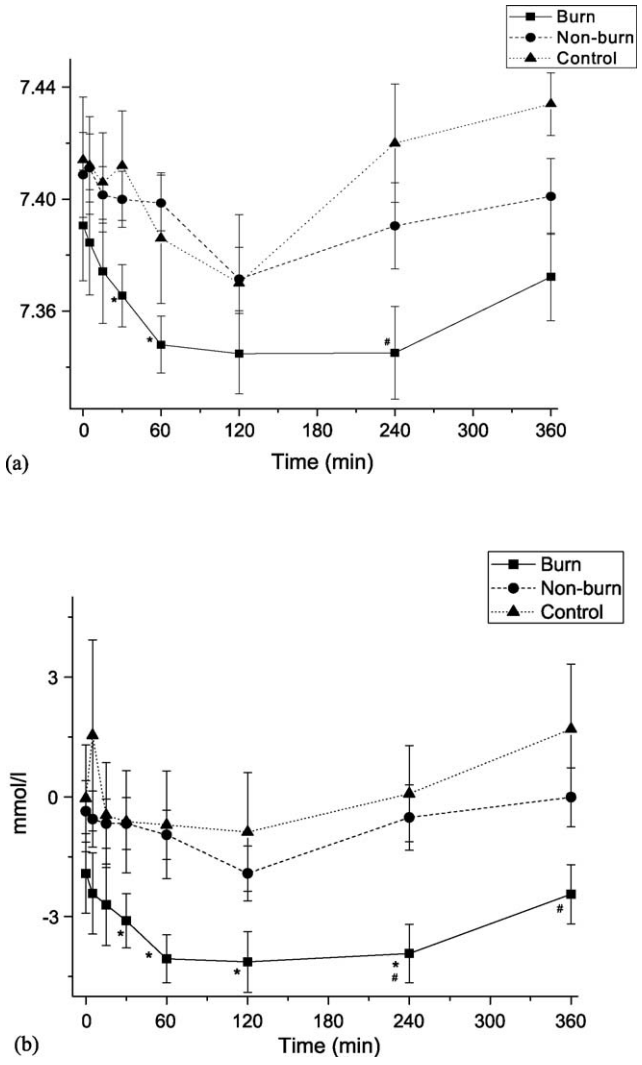


Fig. 5 – Results of blood gas analyses showing (a) pH and (b) base excess values (mean ± S.E.). $^{*}p < 0.05$ B vs. NB group and $^{\#}p < 0.05$, B vs. C group.

The pH was lower in the B group at 30 ($p = 0.046$) and 60 min ($p = 0.0018$) compared to the NB group and at 240 min compared to the control group ($p = 0.0134$). The burn patients had lower BE values between 30 and 240 min than the NB group ($p = 0.0018$–0.042) and at 240 ($p = 0.017$) and 360 min ($p = 0.044$) compared to the C group (Fig. 5a and b). The HCO_3^- was lower in burn patients at 240 ($p = 0.024$) and 360 min ($p = 0.046$) compared to the C group and at 30, 60, 240 and 360 min compared to the NB group ($p = 0.002$–0.045).

6. Discussion

The effects of topical epinephrine on non-burn patients requiring skin grafting have not been reported previously. The purpose of this study was to investigate the systemic effects of topically used epinephrine soaks on burn and non-burn patients and compare the groups with each other and with patients who received no epinephrine in skin grafting procedures of greater than 200 cm^2.

The main findings in this study were (1) topical epinephrine increases heart rate in the burn patients between 30 and 120 min, (2) compared to the baseline values the serum epinephrine concentrations are elevated in the burn patients up to 6 h and at 60 and 120 min in the non-burn patients, (3) 70% of burn patients have high (>2.4 mmol/l) lactate concentrations after epinephrine exposure and the hyperlactataemia lasts up to 4 h, (4) the heart rate is higher in the burn patients already prior to epinephrine exposure and during the first 60 min post-first epinephrine soak application, (5) the absolute lactate and epinephrine 'loads' are greater in the burn group and (6) the LP-ratio is higher in burn patients than in the non-burn patients. All these changes closely parallel the changes in the epinephrine concentrations.

Large burns produce a systemic inflammatory response with changes in autonomic nervous system activity, adrenergic receptor function, haemodynamics and pain. All these affect the levels of circulating catecholamines. Epinephrine has both alpha- and beta-adrenergic properties. The main clinical indications for epinephrine infusions are states of low cardiac output and septic shock. The actions of epinephrine are dose-dependent being mostly beta-stimulation with low concentrations and alpha-stimulation with high concentrations increasing systemic vascular resistance and possibly decreasing the cardiac output in the latter. The side effects include anxiety, tremor, palpitation, tachycardia and arrhythmias. Epinephrine may increase myocardial oxygen requirements and has a potential to cause ischaemia. It also has anti-insulin effects causing lactic acidosis and hyperglycaemia by increasing hydrolysis of glycogen to glucose in liver. Epinephrine is degraded by conjunction with glucuronic and sulphuric acids and is excreted in the urine.

Our findings differ significantly from several previous studies where no significant haemodynamic changes were found after using either clysed or topical epinephrine on burn patients [2,6,11,12,14]. The follow-up time in those studies was either not mentioned or was shorter than in the present study, ranging from 20 to 60 min [2,11,13,14]. The burn itself, with the injury-dependent increase in autonomic nervous system activity and adrenergic receptor function, might explain why the baseline heart rate and the perioperative epinephrine concentrations were higher in the burn patients. The peak values of HR in our study were found at 60–120 min after-epinephrine application in both burn and non-burn groups which is beyond the follow-up time in the previously mentioned studies. The half-life of epinephrine is only a few minutes but the contractive effect of vessels caused by intravenous epinephrine is 30–45 min [16]. The maximum concentration in plasma, on the other hand, is dependent on the route epinephrine is administered. In children with a history of anaphylaxis the maximum plasma epinephrine concentration was found at 8 ± 2 min in those children who received it intramuscularly and 34 ± 14 min in those who received it subcutaneously (range 5–120 min) [17]. Hence, the effect of topically applied epinephrine seems to be of slower nature relating most likely to the local vasoconstrictive effect of epinephrine in dermal vessels.

There was a maximum of a 59- and an 8-fold increase in the serum epinephrine concentrations in burn and non-burn patients and no increase in the control group (Fig. 2b). This differs significantly from the findings of Missavage et al. who found no changes in the catecholamine concentrations in serum even though the same concentration of epinephrine solution was used topically on almost identical sized areas compared to the present study [2]. It can be assumed that the use of topical epinephrine on large open wounds debrided down to healthy tissue would result in absorption of epinephrine from the wound site and increased serum epinephrine concentrations due to the good vascularity of the wound beds. Unfortunately, as epinephrine breakdown products were not analyzed in this study, we were unable to determine definitively the amount of endogenous (due to surgery itself) and exogenous (from topical soaks) epinephrine. On the other hand, as there was no increase in the serum epinephrine concentrations in the control group, who did not receive any exogenous epinephrine, it is likely, that the increase in the epinephrine concentration in the burn and non-burn groups' serum is mostly due to the topical epinephrine and not surgery or anaesthesia per se.

The burn patients with an intra-operative blood loss less than 500 ml had higher epinephrine concentrations than those with greater blood loss. This is interesting because it would seem logical that patients with greater blood loss would demonstrate a greater catecholamine surge than the ones with less bleeding. It is possible that as the blood loss in these patients is replaced with blood with no epinephrine it leads to lower serum epinephrine concentrations than suspected.

The burn patients' epinephrine load was 300% greater than the non-burn patients' load with the same external epinephrine exposure (Table 3). This is an interesting finding as the baseline values for epinephrine concentrations were identical. Burn patients regularly have increased catecholamine concentrations, but in this study it was seen likely due to the big portion of late excisions. The finding suggests that the burn patients have better absorption properties from their wound beds than the non-burn patients. It has been shown that the absorption properties of gall bladder wall increase after exposure to certain cytokines, such as TNF-α, prostaglandin E2 and interleukin 1α [18]. As burn injury triggers the release of various cytokines, they may have a role in the absorption properties of the wound bed in burn patients and hence lead to increased absorption of epinephrine from the soaked gauzes.

According to Clutter et al. tachycardia occurs with epinephrine concentrations of 50–100 pg/ml [19]. The peak concentrations in our study were greatly higher than that (B group mean maximum 14.1 nmol/l = 2582 pg/ml). Therefore, it is not surprising to see tachycardia in these patients. The mean heart rate in the burn group reached its peak at 1 h (115 b/min). Tachycardia was not seen in the non-burn and control groups most likely because of the lower epinephrine concentrations in these groups. There were no statistically significant changes in the SAP or SAPm in any group, which is different from previous findings [14]. As epinephrine has little or no effect on diastolic pressure, the effect on SAPm is smaller than on SAP and therefore more unlikely to be seen. When it comes to the systolic blood pressure, burn patients seemed to tolerate high epinephrine concentrations better than the non-burn group with no actual elevation in SAP at all. Additionally, the non-burn group showed a non-significant elevation in SAP between 15 and 360 min post-epinephrine application. In addition to the effect of topical epinephrine, there may be some role on surgery and anaesthesia as itself. Also, the fact that of burn patients often have vasodilatation and decreased peripheral resistance related to their injury must be taken in account. However, this was not studied as all patients were not invasively monitored.

The lactate concentrations increased until 2 h in both groups and closely paralleled that of epinephrine concentrations (Figs. 2b and 3). There was no difference between the groups in the pre-application concentrations and the increase (Δ-lactate) was more prominent in the burn group (Figs. 3a and 4). Serum lactate concentrations higher than 2.4 mmol/l were seen in 10% in the NB group whereas as much as in 70% in the burn group. The reason for this is not unambiguous. Lactataemia is, however, a relevant finding and clinically commonly seen in burn patients. The elevations in plasma lactate concentrations in hypermetabolic burn patients have been estimated to be, at least partly, related to increased glucose flux as a mass effect from increased pyruvate availability and not entirely a reflection of any deficit in oxygen availability [20]. Also, Levy et al. found in endotoxemic rats that epinephrine-induced hyperlactataemia was not related to cellular hypoxia [21]. In their study epinephrine induced increased lactate concentrations in plasma with stable L/P ratios. Patients with extensive burns have shown greater pyruvate concentrations in burned skin than in unburned skin or in non-burned control patients within the first 4 days post-burn [22]. There were no differences in the pyruvate concentrations between burn and non-burn patients in our study. However, the LP-ratios and serum lactate concentrations were higher in the burn patients relating to tissue ischaemia. As epinephrine is used to control bleeding from the wound beds via vasoconstriction it is likely that it causes transient hypoxia of the skin. This hypothesis is supported by the clinically often seen worsening of wound beds in patients with septic shock requiring systemic norepinephrine. Long-lasting hypoxia of the skin or wound bed may therefore compromise skin graft survival and delay healing in the donor sites. On that account the contingent object of ischaemia is the skin, where epinephrine locally causes vasoconstriction. Subsequently, the hyperlactatemia (and increased LP-ratios) seen in burn patients either questions their value as a traditional marker of tissue hypoxia or more likely are signs of decreased tissue perfusion somewhere in the body, most likely in the skin. In our study the hyperlactataemia and increased LP-ratios subsided without any treatment towards the end of the study.

A limitation of this study was that the absolute amount of epinephrine in the soaks was impossible to measure, a problem noted also in previous studies [14]. It is obvious, that the greater the surface area where epinephrine was applied, the more epinephrine is absorbed. However, the amount of absorption is not necessarily directly related to the surface area as the degree of vasoconstriction in the wound beds may vary between patients and the soaks may not be identically wet. Also, the concentration of epinephrine in our soaks is higher than what most burn units use. According to the

literature the concentrations used varies from 1:34 to 1:1,000,000 most being either 1:500,000 or 1:1,000,000. Even though this study showed no complications requiring treatment related to high epinephrine concentrations, lowering our concentration must be considered.

In conclusion, this study showed that the use of topical epinephrine has systemic effects on haemodynamics, serum lactate concentrations, LP-ratios and on blood gas values which all closely parallel the peak epinephrine concentrations. The elevated lactate concentrations and LP-ratios either question their value as markers of tissue perfusion, or more likely are signs of tissue hypoxia in these patients. As no specific treatment was needed for any of these changes the use of topical epinephrine still seems to be a safe way to obtain haemostasis in these patients.

Conflict of interest

None.

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