available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

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

Anthony A. Papp [a,*], *Ari V. Uusaro* [b], *Esko T. Ruokonen* [b]

[a] *BC Professional Firefighters' Burn Unit, Vancouver General Hospital, Vancouver, Canada*
[b] *Department of Anaesthesia and Critical Care, Kuopio University Hospital, Kuopio, Finland*

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

* *Corresponding author at*: BC Professional Firefighters' Burn Unit, Vancouver General Hospital, JPP 2, 899 W. 12th Avenue, Vancouver, BC V5Z 1M9, Canada. Tel.: +1 604 875 4084.
E-mail address: anthony.papp@ubc.ca (A.A. Papp).
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