

Nitroglycerin Patch in Traumatic Hemorrhagic Shock to Improve Signs of Poor Peripheral Perfusion

MEDHAT S. ALI, M.Sc.; HASSAN I.M. KOTB, M.D.; ALAA M. AHMED ATIA, M.D. and ABUALAUON M. ABD EL-MOHSEN, M.D.

The Department of Anesthesiology and Intensive Care, Assiut University Hospital, Assiut, Egypt

Abstract

Background: Microcirculatory function is the main prerequisite for adequate tissue oxygenation and organ function. It transports oxygen and nutrients to tissue cells, ensure adequate immunological function and, in disease, delivers therapeutic drugs to target cells. Recruiting microcirculation, i.e., non-perfused or intermittently perfused capillaries might improve tissue perfusion, mitigating the progression to organ failure and death. Nitroglycerin has been used in different shock states particularly in sepsis. The effect is variable and debatable suggesting an improvement of microcirculation.

Patients and Methods: 60 adult patients with hemorrhagic shock admitted to the Emergency Department within 6 hours of trauma event, resuscitation immediately started according to advanced trauma life support ATLS® protocol 2016 with control of the bleeding source. Nitroglycerine patch 5mg applied to patients after the first hour of resuscitation. The study period corresponded to the outcome of the first 48 hours of trauma unit or ICU resuscitation. Patients considered successfully resuscitated if they had normal lactate levels (≤ 2 mmol/L).

Results: 60 patients enrolled in this study, 10 patients were excluded; 3 of them due to uncontrolled bleeding and 7 due to marked hypotension. 50 patients continued in the study (38 men, 12 women) with mean age was (29.1 ± 10.8 ys); of them 45 survived (90%) and 5 did not survive (10%). Patients received mean crystalloid volume (6100 ± 1410.67 ml), mean colloid volume (490 ± 457.25 ml), mean packed RBCs (4.34 ± 1.33 units), mean fresh frozen plasma (3.08 ± 1.65 units) and mean nor-adrenaline dose (7.94 ± 10.55 μ g/kg/minute). Baseline perfusion index was (0.37 ± 0.21), mean heart rate (128.46 ± 18.18 beat/minute), systolic blood pressure (78.08 ± 7.47 mmHg), diastolic blood pressure (40.20 ± 7.39 mmHg), mean arterial pressure (53.44 ± 6.43 mmHg), central venous pressure (-1.46 ± 2.77 cmH₂O) and baseline modified shock index was (2.45 ± 0.56). Baseline serum lactate was (8.61 ± 1.86 mmol/L), base deficit was (-12.59 ± 5.57). Perfusion index showed statistically significant increase in survivors than non survivors at 12, 18, 24, 30, 36, 42, 48 hours ($p < 0.001$). Serum lactate level was significantly higher in non survivors group than survivor group ($p < 0.001$). Base deficit was significantly higher in non survivors than survivors ($p < 0.001$).

Conclusion: Use of nitroglycerin patch 5mg improved PI at 6 to 48 hours post resuscitation and reduce mortality rate (in this study was 10%) while in other previous studies with the same sample size of hemorrhagic shock patients without use of nitroglycerin it was higher (about 30%).

This study is registered at www.clinicaltrials.gov under number NCT03235921.

Key Words: Base deficit – Nitroglycerin – Perfusion index – Serum lactate.

Introduction

SHOCK is defined as acute circulatory with inadequate or inappropriately distributed tissue perfusion resulting in generalized cellular hypoxia [1].

Impaired tissue perfusion in hemorrhagic shock is due to both hypovolemia (decreased preload) and anemia (decreased arterial oxygen content). This has obvious therapeutic implications in that both volume oxygen carrying capacity must be restored [2,3].

The initial stages of shock are characterized by hypoperfusion and hypoxia resulting in cellular ischaemia as oxygen demand exceeds supply. Previously thought that cellular ischaemia is the underlying pathophysiological process, now it is appreciated that this is simply the trigger for a complex chain of events. Cellular hypoxia leads to local vasoconstriction, thrombosis and release of oxygen free radicals causing direct cellular damage and endothelial dysfunction [4].

Parameters related to macro-circulation, such as the mean arterial pressure, central venous pressure, cardiac output, mixed venous saturation and central oxygen saturation, are commonly used in hemodynamic assessment of critically ill patients. However, several studies have shown that there is

Correspondence to: Dr. Medhat Sayed Ali,
E-Mail: medhat_sayed69@yahoo.com

dissociation between these parameters and the state of microcirculation in this group of patients. Techniques that allow direct viewing of the microcirculation are not completely disseminated, nor are they incorporated into the clinical management in shock. The numerous techniques developed for microcirculation assessment include clinical assessment (e.g., peripheral perfusion index, capillary refill time and temperature gradient), laser Doppler flowmetry, tissue oxygen assessment electrodes, video-microscopy (orthogonal polarization spectral imaging, side-stream dark field imaging or incident dark field illumination) and near infrared spectroscopy. In the near future the monitoring and optimization of tissue perfusion by direct viewing and microcirculation assessment may become a goal to be achieved in the hemodynamic resuscitation of critically ill shock patients [5].

The microcirculation consists of the smallest blood vessels (<100 μ m diameter) where oxygen release to the tissues takes place, and consists of arterioles, capillaries and venules. The main cell types comprising the microcirculation are the endothelial cells lining the inside of the microvessels, smooth muscle cells (mostly in arterioles), red blood cells, leukocytes, and plasma components in blood. The structure and function of the microcirculation is highly heterogeneous in different organ systems. In general, driving pressure, arteriolar tone, hemorheology and capillary patency are the main determinants of capillary blood flow [6].

The regulatory mechanisms controlling microcirculatory perfusion are classed as myogenic (sensing strain and stress), metabolic (regulation based on O_2 , CO_2 , lactate and H^+), and neurohumoral. This control system uses autocrine and paracrine interactions to regulate microcirculatory blood flow to meet the oxygen requirements of tissue cells the endothelial cells lining the inside of the microvessels play a central role in this control system by sensing flow, metabolic, and other regulating substances to regulate arteriolar smooth-muscle-cell tone and capillary recruitment [7].

Endothelial cell-to-cell signaling transmits upstream information about hemodynamic conditions downstream. The endothelium is also important in controlling coagulation and immune function, both of which directly affect and define microcirculatory function [8].

Microcirculatory dysfunction is characterized by heterogeneous abnormalities in blood flow with some capillaries being under perfused, while others have normal to abnormally high blood flow. Func-

tionally vulnerable microcirculatory units become hypoxic, which explains the oxygen extraction deficit. In this condition, the microcirculatory partial pressure of O_2 (gpO_2) drops below the venous pO_2 . This disparity has been termed the "PO₂ gap", a measurement of the severity of functional shunting, the occurrence of which is more severe in sepsis than in hemorrhage. It is the main reason why monitoring systemic hemodynamic-derived and oxygen-derived variables is not able to sense such microcirculatory distress and mask this on-going process [7].

It has been postulated that interventions aiming to recruit microcirculation, i.e., open non-perfused or intermittently perfused capillaries might improve tissue perfusion, mitigating the progression to organ failure and death [9].

Nitroglycerin has returned back to clinical practice in different shock states particularly in sepsis. The effect is variable and debatable suggesting an instantaneous improving of microcirculation [10,11].

Basically loss of hemodynamic coherence due to injury to microcirculation after shock has raised attention to two major advances; first to restore coherence via real time monitoring of microcirculation and looking for pharmacological tools to resuscitate microcirculation. Among these tools are vasodilators of them recently studied is the nitroglycerin.

Bedside monitoring of peripheral circulation has gained importance after introduction of perfusion index and point of care monitoring of serum lactate level and both have been reported to have a good sensitivity to detect morbidity and mortality among shocked patients [10].

Tachon et al., (2014), showed that sublingual microcirculation was impaired up to 72 hours after traumatic hemorrhagic shock. The aim was to improve the microcirculatory flow adding NO as a mediator for vasodilatation to antagonize the vasoconstriction in shock states. Visualization of sublingual circulatory flow using SDM has drew the attention to the role of vasodilators in shock [12].

Two important studies in sepsis and septic shock showed improvement of sublingual microcirculation as evidenced by Peter E Spronk et al., [11,13], on the other hand Trzeciak S et al., study showed no benefit [14].

Lima claimed that monitoring of bedside peripheral circulatory parameters should be fully studied before wide clinical use of sublingual microcirculation [15].

In other studies intravenous nitroglycerin in a dose response study of small sized trial showed that nitroglycerin can revert peripheral circulatory changes associated with septic shock [10].

This study for the first time introduce nitroglycerin patch as a part of resuscitation protocol in a group of acute hemorrhagic shock patients due to trauma and observe the effects on peripheral perfusion parameters; perfusion index, modified shock index and serum lactate level and how these variables change during the first 48 hours post trauma. The primary endpoint is death within 48 hours.

Patients and Methods

This study was conducted in the Trauma Unit and Trauma ICU of Assiut University Tertiary Hospital from July 2016 to July 2017 after approval of the Local Research Ethics Committee of Faculty of Medicine, Assiut University. A written informed consent was obtained from each patient according to Institutional Ethical Committee Policy.

This trial was a prospective observational open trial of 60 adult poly-traumatized patients with hemorrhagic shock admitted to trauma unit within 6 hours of the trauma event fulfilling the inclusion criteria and underwent resuscitation according to advanced trauma life support ATLS® protocol 2016 [16] with control of source of bleeding.

This study is registered at www.clinicaltrials.gov under number NCT03235921.

Inclusion criteria:

Age: \geq 18 years old, systolic blood pressure below 90mmHg, mean blood pressure below 70 mmHg or decrease of systolic blood pressure 40 mmHg below normal value, metabolic acidosis with PH less than 7.35 due to hypoperfusion, capillary refill time $>$ 4 seconds, normal body core temperature, Injury Severity Score ISS \geq 25, Modified Shock Index MSI cut-off point of more than 1.5, serum lactate level more than 2mmol/L, perfusion index cut-off point of 0.4 or less.

Study protocol:

On admission, the Injury Severity Score ISS and Modified Injury Severity Score (MISS) were calculated. The Injury Severity Score (ISS) is an anatomical scoring system for patients with poly-trauma. Each injury is assigned as an Abbreviated

Injury Scale (AIS). Injuries are ranked on a scale of 1 to 6, with 1 being minor, 5 severe and 6 a non survivable injury. The ISS had values from 0 to 75. The ISS is the only anatomical scoring system in use with a linear correlation with mortality, morbidity, hospital stay and other measures of injury severity [17].

As multiple injuries in the same body region are assigned a single score, modification of the ISS, the "New Injury Severity Score" (NISS), has been proposed. This is calculated as the sum of squares of the top three scores regardless of body region. The NISS has been found to be statistically better than the traditional ISS. NISS was calculated in all patients in this study [18].

The study period had been corresponded to the outcome of the first 48 hours after resuscitation. Patients were considered to be successfully resuscitated if they had normal lactate levels (\leq 2mmol/L) in addition to stable hemodynamic parameters at the end of the study period.

All patients were resuscitated according to ATLS® algorithm (2016) aiming at normalizing perfusion parameters with aggressive bleeding source control and fluid loading by 1-2 liters of saline 0.9% or voluven, followed by Nor-Epinephrine (NE) as needed to maintain a Mean Arterial Pressure (MAP) \geq 65mmHg.

When the patient entered the resuscitation room, a primary survey with full exposure was done. Patients carefully inspected for external bleeding sources. A supine chest X-ray, pelvic X-ray and focused abdominal ultrasonography of trauma (FAST) were obtained within 10 minutes of arrival.

The following were done: Establish patient airway, ensure adequate ventilation and oxygenation, establish venous access by 2 wide bore canulae or central venous line and control source of bleeding by applying direct pressure and rapidly identify patients requiring surgical intervention to stop bleeding.

Crystalloid solutions were used for initial resuscitation with a target CVP (8-12) cmH₂O, saline 0.9% used. Low molecular weight colloid (voluven) solutions were also used to achieve intravascular volume expansion. The goal of resuscitation is to restore a normal blood pressure (systolic $>$ 90mmHg or mean arterial pressure $>$ 65mmHg).

Application of nitroglycerin patch 5mg occurred after the first hour of admission with immediate

start of resuscitation. To avoid significant hypotension during nitroglycerin administration each patient was evaluated for adequate intravascular volume as evidenced by repeated volume challenges (250ml of crystalloid over 10 minutes) up to a point at which central venous pressure raised by more than 2mmHg.

Nor-epinephrine was administered in cases with significant hypotension with MAP less than 50 mmHg and gradually withdrawn with improvement of hemodynamic parameters and normalization of serum lactate level ($\leq 2\text{mmol/L}$), total vasopressors requirements were calculated for each patient.

Measurements:

Protocol-related measurements were obtained at 0 hour (immediately after admission), 6, 12, 18, 24, 30, 36, 42 and 48 hours post resuscitation for metabolic perfusion parameters (serum lactate and base deficit). Perfusion index and hemodynamic parameters (heart rate, systolic, diastolic, mean blood pressure, modified shock index and central venous pressure) are obtained on admission and every hour thereafter. The outcome was recorded as survivor and non-survivor.

Peripheral Perfusion Index (PI):

Recorded using Massimo SET Rad-5 hand-held signal extraction oximetry (Massimo corporation, USA)®.

Modified Shock Index (MSI):

The ratio of heart rate to Mean Arterial Pressure (MAP).

$$\text{MAP} = \frac{[(\text{DBP} \times 2) + \text{SBP}]}{3}$$

Serum lactate:

Measured from a heparinized arterial sample using StatStrip® Lactate Xpress TM nova lactate point of care measuring system (Nova biomedical biosensor technologies)®.

Base deficit:

Measured from a heparinized arterial sample by blood gas analyzer. (Cobas b 221 Blood Gas System, Hoffmann-La Roche Ltd; Swiss).©

Statistical analysis:

Results for normally distributed continuous variables are expressed as mean value, standard deviation and inter-quartile range. Categorical data and dichotomous variables are shown as number and percentage. Comparisons of continuous varia-

bles were performed using independent *t*-test. Proportions were compared with chi-square test. All reported *p*-values are 2 sided with a significant α level of 0.05. Differences were considered to be statistically significant if the null hypothesis could be rejected with 95% confidence ($p < 0.05$).

The effect of nitroglycerin on the parameters of peripheral perfusion was shown by the significance of change in each parameter from baseline it was done with one way ANOVA test. Each parameter was compared in survivors and non survivors using independent *t*-test.

The SPSS Ver. 20 statistical software package (SPSS for Windows Release 20.0.0; SPSS Inc, Chicago, Ill, USA)® package was used for statistical analysis. It was used for all calculations, except ROC curve analysis which was done using "Medcalc 7" statistical software package available at <http://www.medcalc.org>.

Results

This study enrolled 60 adult poly-traumatized patients with hemorrhagic shock fulfilling the inclusion criteria, 10 patients were excluded; 3 of them due to uncontrolled bleeding (retroperitoneal hematoma) and the other 7 due to marked hypotension BP $< 60/20$ not responding to fluid therapy and vasopressors.

The other 50 patients upon whom the study continued (38 men and 12 women) with mean age was (29 ± 10.8 ys) of whom 45 survived (90%) and 5 non-survivors (10%). Patients received mean crystalloid volume ($6100 \pm 1410.67\text{ml}$), mean colloid volume ($490 \pm 457.25\text{ml}$), mean packed RBCs (4.34 ± 1.33 units), mean fresh frozen plasma (3.08 ± 1.65 units) and mean nor-adrenaline dose ($7.94 \pm 10.55 \mu\text{g/kg/minute}$).

As regard the baseline parameters of peripheral perfusion on admission; perfusion index was (0.37 ± 0.21), capillary refill time was (4.64 ± 1.15 seconds).

Baseline hemodynamics on admission; mean heart rate was (128.46 ± 18.18 beat/minute), systolic blood pressure was ($78.08 \pm 7.47\text{mmHg}$), diastolic blood pressure was ($40.2 \pm 7.39\text{mmHg}$), mean arterial pressure was ($53.44 \pm 6.43\text{mmHg}$), central venous pressure was ($-1.46 \pm 2.77\text{cmH}_2\text{O}$) and modified shock index was (2.45 ± 0.56). Baseline metabolic parameters of perfusion; serum lactate was ($8.61 \pm 1.86\text{mmol/L}$), base deficit was (-12.59 ± 5.57) (Table 1).

Parameters of peripheral perfusion:

Perfusion index:

There was a significant increase ($p<0.001$) from baseline at 6, 12, 18, 24, 30, 36, 42, and 48hrs post resuscitation (Table 2). Perfusion index showed a statistically significant increase in survivors than in non survivors at 12, 18, 24, 30, 36, 42 and 48hrs. Fig. (2).

Modified Shock Index (MSI):

There was a significant decrease ($p<0.05$) of MSI from baseline at 12, 18, 24, 30, 36, 42 and 48hrs post resuscitation (Table 3). Modified shock index was significantly higher in non survivors than in survivors ($p<0.001$) at 12, 18, 24, 30, 36, 42, and 48hrs. Fig. (3).

Serum lactate:

There was a significant ($p<0.05$) decrease in serum lactate from baseline at 6, 12, 18, 24, 30, 36, 42, and 48hrs post resuscitation (Table 4). Serum lactate was significantly higher in non survivors than survivors ($p<0.001$) at 6, 12, 18, 24, 30, 36, 42 and 48hrs. Fig. (4).

Base deficit:

There was a significant ($p<0.05$) decrease in base deficit from baseline at 18, 24, 30, 36, 42 and 48hrs post resuscitation (Table 5). Base deficit was significantly higher in non survivors than in survivors ($p<0.001$) at 18, 24, 30, 36, 42 and 48hrs. Fig. (5).

Table (1): Demographic data, baseline measurements and total requirements of fluids, blood products and vasopressors.

Variable	Value
Age	29.1 ± 10.8 (18-39)
Sex:	
Male	46 (92%)
Female	4 (8%)
RBCs	4.34 ± 1.33 (2-7)
Crystalloid. within 24h	6100 ± 1410.67 (5500-7511)
EP	10.98 ± 10.54 (0-35)
NE	7.94 ± 10.55 (0-32)
Colloid within 24h	490 ± 457.25 (0-1500)
FFP within 24h	3.08 ± 1.65 (1-6)
HR-0	128.46 ± 18.19 (106-176)
SBP-0	78.08 ± 7.48 (59-94)
DBP-0	40.2 ± 7.39 (28-52)
MAP-0	53.44 ± 6.44 (40-63)
CVP-0	-1.46 ± 2.77 (-10-3)
<i>Survival:</i>	
Survivor	45 (90%)
Non survivor	5 (10%)

Table (2): Change in Perfusion Index (PI) with time.

Item	Study group "n=50"
1- PI.0	0.37 ± 0.21
2- PI.6	0.55 ± 0.21 **
3- PI.12	0.94 ± 0.35 ***
4- PI.18	1.28 ± 0.62 ***
5- PI.24	1.49 ± 0.66 ***
6- PI.30	1.73 ± 0.69 ***
7- PI.36	1.93 ± 0.75 ***
8- PI.42	2.09 ± 0.79 ***
9- PI.48	2.29 ± 0.88 ***

Table (3): Change in Modified Shock Index (MSI) with time.

Item	Study group "n=50"
1- MSI.0	2.45 ± 0.56
2- MSI.6	2.01 ± 0.44
3- MSI.12	1.92 ± 0.69*
4- MSI.18	1.89 ± 0.76*
5- MSI.24	1.78 ± 0.80**
6- MSI.30	1.74 ± 0.88**
7- MSI.36	1.58 ± 0.96***
8- MSI.42	1.49 ± 0.96***
9- MSI.48	1.48 ± 1.03***

Table (4): Change of serum lactate with time.

Item	Study group "n=50"
1- Lactate.0	8.61 ± 1.86
2- Lactate.6	6.66 ± 2.48*
3- Lactate. 12	6.06 ± 3.10*
4- Lactate.18	5.23 ± 3.36**
5- Lactate.24	4.28 ± 1.41**
6- Lactate.30	3.49 ± 1.39***
7- Lactate.36	3.12 ± 1.51***
8- Lactate.42	3.03 ± 1.56***
9- Lactate.48	2.80 ± 1.70***

Table (5): Change of base deficit with time.

Item	Study group "n=50"
1- BEecf.0	-12.59 ± 5.57
2- BEecf.6	-11.52 ± 4.76
3- BEecf.12	-10.62 ± 4.84
4- BEecf.18	-8.56 ± 2.70*
5- BEecf.24	-7.68 ± 2.06**
6- BEecf.30	-5.89 ± 1.51***
7- BEecf.36	-3.92 ± 1.09***
8- BEecf.42	-2.76 ± 1.30***
9- BEecf.48	-2.41 ± 1.69***

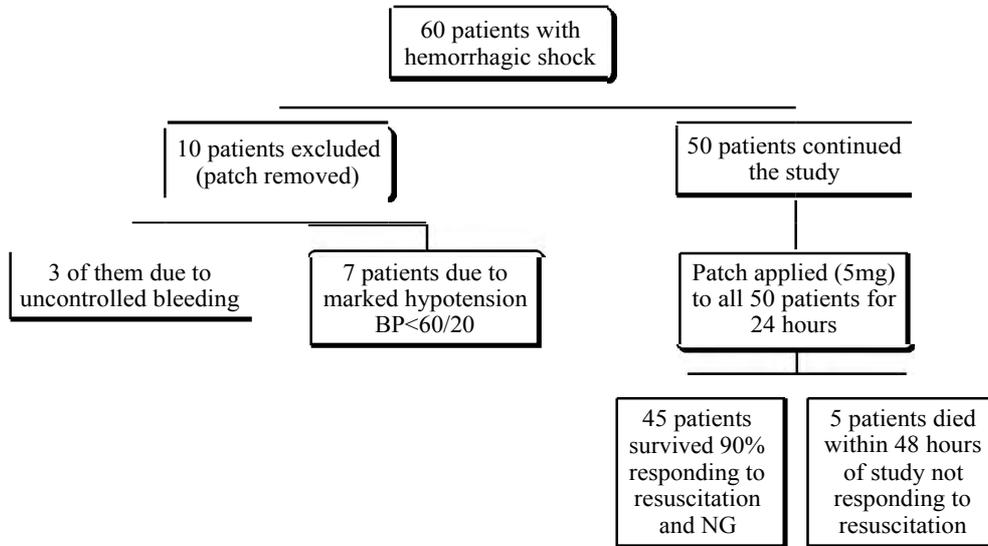


Fig. (1): Flow chart of 60 adult poly-traumatized patients with hemorrhagic shock enrolled in the study.

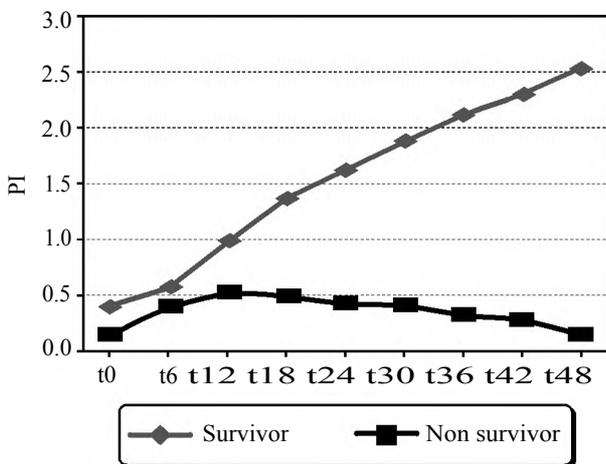


Fig. (2): Difference between survivors and non survivors in Perfusion Index (PI).

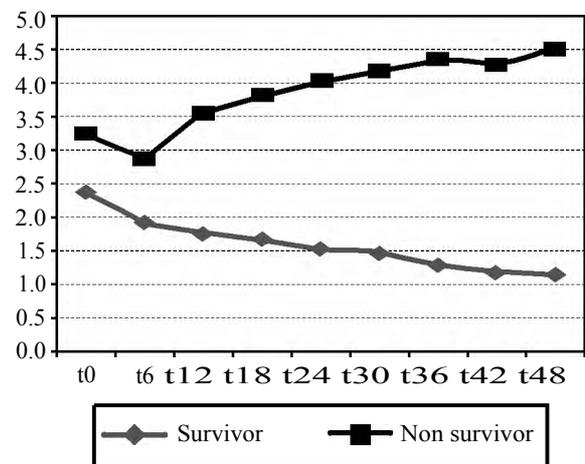


Fig. (3): Difference in MSI between survivors and non survivors.

Discussion

This trial demonstrates a favorable effect of nitroglycerin on Perfusion Index (PI), Modified Shock Index (MSI), base deficit and lactate level in patients with hemorrhagic shock.

The use of vasodilators in shock has been mentioned in septic shock with debatable and variable responses [10,11,19].

Many studies were based on the absence of hemodynamic coherence between macro and microcirculation. On the other hand there still a lot of suggestions for macro circulatory changes, anaerobic metabolism and peripheral perfusion changes to identify and predict mortality in patients with shock.

In a big study, International Study on Microcirculatory Shock Occurrence in Acutely Ill Patients (micro SOAP) including more than 500 patients with circulatory shock due to different etiologies using sublingual side stream Dark Field imaging, abnormal microvascular flow index was present only in 17% of patients and was not associated with mortality except in patients with tachycardia, this indicates that there is no direct relationship between perfusion and oxygenation [20].

In contrast to HR,MAP and lactate levels in micro SOAP study, a pathologic oral microvascular flow index is not independent risk factor for hospital mortality [20].

Lima et al., claimed that abnormalities in peripheral perfusion can predict outcome in shocked

patients and improving these abnormalities using vasodilators is a priority in resuscitation [10].

In this study a fixed dose of nitroglycerin patch 5mg was used to avoid rapid systemic effects such marked hypotension as absorption of the patch takes time and give a chance for resuscitation. We speculate that this can be a part of usual resuscitation protocol.

Comparison between baseline parameters; perfusion index, modified shock index and point of care serum lactate showed significant improvement in survivors than non survivors.

Perfusion index showed highly significant ($p < 0.000$) increase from baseline after 12 hours of patch application. In the other hand MSI showed highly significant ($p < 0.000$) decrease after 36 hours, while lactate level showed highly significant ($p < 0.000$) decrease after 30 hours post patch application.

Lactate in particular has gained a wide acceptance in clinical trials as a sensitive indicator of cellular dysoxia.

Recently Bakker suggested that lactate should be the target for early resuscitation in sepsis [21].

Vincet et al., reported in their review that all forms of circulatory shock having a decrease in lactate is associated with a more favorable outcome [22].

This study confirmed this concept from admission value of lactate and favorable outcome associated with lactate clearance and considered the high value of lactate on admission (6 hours) from traumatic event is due to inadequate oxygen delivery, this raised the possibility of considering lactate as a monitor after altered microcirculation in traumatic hemorrhagic shock.

Improving lactate under nitroglycerin patch treatment could be indirectly considered as an improvement of oxygen delivery to tissues.

Nitroglycerin in this trial showed this effect due to its effect on venous capacitance increasing microvascular flow.

Perfusion index showed a non significant change from baseline in the first 6 hours post resuscitation and post patch application, while after 6 hours onwards it showed a statistically significant difference ($p < 0.01$). Non-survivors had a significantly lower PI than survivors ($p < 0.001$).

Modified shock index reported in this study follow the other parameters as it decreased significantly from 12 hours onwards post patch application. A notable observation is that nitroglycerin patch caused no significant hypotension in all 50 patients continued the study due to gradual effect of patch and possibility of more slow absorption due to presence of hemorrhagic shock.

The mortality rate in this study was 10% with the use of nitroglycerin patch in resuscitation, while in our previous study with the same sample size of hemorrhagic shock patients without use of nitroglycerin it was 28% [23].

References

- 1- TEIRNEY P., et al.: Shock: Causes, initial assessment and investigations, *Anaesthesia and Intensive Care Medicine*, <http://dx.doi.org/10.1016/j.mpaic.2016.12.003>, 2016.
- 2- BRUN-BUISSON C., MESHAKA P., PINTON P. and VALLET B.: EPISEPSIS: A reappraisal of the epidemiology and outcome of severe sepsis in French Intensive Care Units. *Intensive Care Med.*, 30: 580-8, 2004.
- 3- MARTIN G.S., MANNINO D.M., EATON S. and MOSS M.: The epidemiology of sepsis in the United States from 1979 through 2000. *N. Engl. J. Med.*, 348: 1546-54, 2003.
- 4- CECCONI M., De BACKER D., ANTONELLI M., et al.: Consensus on circulatory shock and hemodynamic monitoring. Task Force of the European Society of Intensive Care Medicine. *Intensive Care Med.*, 40: 1795e815, 2014.
- 5- PHILIPPE FRANCO DO AMARAL TAFNERL, FELIPE KO CHEN¹, ROBERTO RABELLO FILHO², THIAGO DOMINGOS CORRÊA², RENATO CARNEIRO DE FREITAS CHAVES² and ARY SERPA NETO²: Recent advances in bedside microcirculation assessment in critically ill patients. *Rev. Bras. Ter. Intensiva*, 29 (2): 238-47. Doi: 10.5935/0103-507X.20170033, 2017.
- 6- INCE C.: The microcirculation is the motor of sepsis. *Crit. Care*, 9 Suppl 4: S13-9, 2005.
- 7- VALLET B.: Endothelial cell dysfunction and abnormal tissue perfusion. *Crit. Care Med.*, 30 (Suppl 5): S229-34, 2002.
- 8- LIDINGTON D., TYML K. and OUELLETTE Y.: Lipopolysaccharide-induced reductions in cellular coupling correlate with tyrosine phosphorylation of connexin. *J. Cell. Physiol.*, 193: 373-9, 2002.
- 9- De BACKER D., DONADELLO K., TACCONE F.S., OSPINA-TASCON G., SALGADO D. and VINCENT J.L.: Microcirculatory alterations: Potential mechanisms and implications for therapy. *Ann. Intensive Care*, 1 (1): 27, 2011.
- 10- LIMA A., VAN GENDEREN M.E., VAN B.J., KLIJN E., JANSEM T. and BAKKER J.: Nitroglycerin reverts clinical manifestations of poor peripheral perfusion in patients with circulatory shock. *Crit. Care*, 18 (3): R126, 2014.

- 11- SPRONK P.E., INCE C., GARDIEN M.J., MATHURA K.R., OUDEMANS-VAN STRAATEN H.M. and ZANDSTRA D.F.: Nitroglycerin in septic shock after intravascular volume resuscitation. *Lancet*, 360: 1395-6, 2002.
- 12- TACHON G., HARROIS A., TANAKA S., KATO H., HUET O., POTTECHER J., VICAUT E. and DURANTEAU J.: *Crit. Care Med.*, Jun., 42 (6): 1433-41, 2014.
- 13- HE X., SU F., VELISSARIS D., SALGADO D.R., De SOUZA B.D., LORENT S., TACCONE F.S., VINCENT J.L. and De B.D.: Administration of tetrahydrobiopterin improves the microcirculation and outcome in an ovine model of septic shock. *Crit. Care Med.*, 40 (10): 2833-40, 2012.
- 14- TRZECIAK S., GLASPEY L.J., DELLINGER R.P., DURFLINGER P., ANDERSON K., DEZFULIAN C., ROBERTS B.W., CHANSKY M.E., PARRILLO J.E. and HOLLENBERG S.M.: Randomized controlled trial of inhaled nitric oxide for the treatment of microcirculatory dysfunction in patients with sepsis. *Crit. Care Med.*, 42 (12): 2482-92, 2014.
- 15- LIMA A.P., BEELEN P. and BAKKER J.: Use of a peripheral perfusion index derived from the pulse oximetry signal as a noninvasive indicator of perfusion. *Crit.Care Med.*, 30: 1210-3, 2002.
- 16- American College of Surgeons Committee on Trauma Advanced Trauma Life Support 2016-2017 Series ATLS® University of Rochester Medical center Rochester, New York.
- 17- BAKER S.P. and O NEILL B.: The injury severity score: An update. *J. Trauma*, 16 (11): 882-5, 1976.
- 18- BALOGH Z., OFFNER P.J., MOORE E.E. and BIFFL W.L.: NISS predicts postinjury multiple organ failure better than the ISS. *J. Trauma*, 48: 634-628, 2002.
- 19- BOERMA E.C.: The microcirculation as a clinical concept: Work in progress. *Curr. Opin. Crit. Care*, 15 (3): 261-5, 2009.
- 20- VELLINGA N.A.R., BOERMA E.C., KOOPMANS M., DONATI A., DUBIN A., SHAPIRO N.I., et al.: International study on microcirculatory shock occurrence in acutely ill patients. *Crit. Care Med.*, 43: 48-56, 2015.
- 21- JAN BAKKER, et al.: Lactate is THE target for early resuscitation in sepsis *Rev. Bras. Ter. Intensiva*, 29 (2): 124-7, 2017.
- 22- VINCENT J.L., QUINTAIROS E. SILVA A., COUTO L. Jr. and TACCONE F.S.: *Crit Care.*, Aug 13, 20 (1): 257, 2016.
- 23- ALAA M. ATIA, ABUALAUON M. ALBEBLAWY, NAGWA M. IBRAHIM, MOHAMED Z. ABDELRHMAN, HESHAM A. ESMAEIL, NAWAL A. GAD EL-RAB and KOTB H.I.: Perfusion Index Derived from Pulse Oximetry, Serum Lactate, its Surrogates and Beta Type Natriuretic Peptide (Bnp) for Outcome Prediction in Poly-Traumatized Patients. A Prospective Observational Cohort Study *Anaesthesia & Critical Care Med. J.*, 1 (1): 000102, 2016.

إستخدام النيتروجلسرين لتحسين علامات قصور الدورة الدموية الطرفية فى حالات الصدمة النزفية الناتجة عن إصابات الحوادث

تعتبر الصدمة النزفية الناتجة عن حوادث الإصابة من أهم الأسباب المؤدية للوفاة والتي يمكن تجنب حدوثها إذا تم التعامل معها بأساليب العلاج المناسبة.

من أهم أهداف علاج حالات الصدمة النزفية الناتجة عن الإصابات المتعددة والتعامل مع الدورة الدموية الميكروسكوبية وإعادة إروائها بدافع تحسين إمداد الأنسجة والخلايا البينية بالأكسجين والمواد الغذائية اللازمة للحفاظ على وظائف الأعضاء فى مختلف أنحاء الجسم.

ونظرا لأهمية الدورة الدموية الميكروسكوبية إتجه العلم الحديث إلى إختراع تقنيات يمكن إستخدامها لمتابعة إرواء الدورة الدموية الطرفية الميكروسكوبية.

وتعد هذه التقنيات كمرآة تعكس مدى فعالية العلاج الموجه نحو الدورة الدموية الطرفية بإستخدام المحاليل ومنتجات الدم المختلفة مثل البلازما الطازجة المجمدة والبلازما الغنية بالصفائح الدموية.

بالإضافة إلى إنعاش الدورة الدموية الميكروسكوبية بالمحاليل ومنتجات الدم هناك بعض الدراسات الحديثة التي أضافت المواد الموسعة للأوعية الطرفية الدقيقة إلى العلاج، ومن أهم هذه المواد عقار النيتروجلسرين المعروف كيميائيا أنه من موانح جزئ أكسيد النيتريك NO الذى يعد من أقوى وأنتشط موسعات الأوعية الدموية والذي يمكن إستخدامه لإستعادة الإرواء الدموى للأوعية الدقيقة.

فى هذه الرسالة تحديدا تم إستخدام عقار النيتروجلسرين عن طريق اللاصقة وتركيزها ٥ ملجم فى كل حالات البحث وعددهم ٥٠ حالة.

أهداف البحث: إثبات فعالية عقار النيتروجلسرين فى تحسين علامات قصور الدورة الدموية الطرفية فى حالات الصدمة النزفية وتحسين إمداد الأنسجة بالأكسجين ومن ثم تقليل مستوى حمض اللاكتيك بالدم الناتج عن الأيض اللاهوائى.

المرضى والطرق: إشتملت الدراسة على ٦٠ مريض، عشرة مرضى منهم لم يكملو الفى الخضوع للدراسة بسبب فشل إستعادة الإرواء وهبوط حاد فى ضغط الدم.

النتائج: أثبتت الدراسة فعالية عقار النيتروجلسرين فى إستعادة الإرواء الدموى للدورة الدموية الطرفية فى المجموعة التى تم علاجها بلاصقة النيتروجلسرين حيث وجد أن هناك زيادة إحصائية ذات دلالات عالية فى معامل الإرواء الدموى PI فى مجموعة النيتروجلسرين ونقص مستوى حمض اللاكتيك بالدم.

وكان معدل الوفيات فى هذه الدراسة يساوى ١٠٪.

الإستنتاج: فعالية عقار النيتروجلسرين فى صورة اللاصقة عند إستخدامه فى علاج قصور الدورة الدموية الطرفية فى حالات الصدمة النزفية نتيجة حوادث الإصابة.