Thooft et al. Critical Care 2011, 15:R222
http://ccforum.com/content/15/5/R222

CRITICAL CARE

RESEARCH Open Access

Effects of changes in arterial pressure on organ perfusion during septic shock

Aurélie Thooft, Raphaël Favory, Diamantino Ribeiro Salgado, Fabio S Taccone, Katia Donadello, Daniel De Backer, Jacques Creteur and Jean-Louis Vincent*

2012.4.17 PGY 紀博仁
Supervisor CR 曾理銘 VS 王瑞芳

Introduction

- Septic shock - alteration in tissue perfusion generally defined as a systolic arterial pressure of less than 90 mm Hg despite adequate fluid resuscitation
- Systemic hemodynamic variables inadequate to identify tissue perfusion influenced by additional microvascular factors

Introduction

- an increased number of non-perfused small vessels (release of mediators and cytotoxic substances like oxygen radicals, various cytokines, and prostanoids
- By vasoactive effects, norepinephrine (NE) could contribute to alter the microcirculation and impair cellular metabolism.

Introduction

- Recommendations suggest that a mean arterial pressure (MAP) of around 65 mm Hg
- arterial pressure that is too low induces a loss of autoregulation, so that tissue perfusion directly dependent on arterial pressure

Introduction

- whether a higher MAP should be targeted is a matter of debate (negative in urinary output, blood lactate levels, individual response was highly variable. positive in oxygen delivery and microvascular flow)
- optimal MAP level remains unclear
- hypothesis was that increasing MAP by increasing NE doses would improve microvascular function in patients with septic shock

Materials and methods

- a single-center study conducted over a 1-year period
- 13 adult patients who had had septic shock for less than 48 hours

Materials and methods

- arterial catheter, central venous catheter, and a Swan-Ganz
- hypotension resistant to fluid, therapy change in pulse pressure (ΔPP) of less than 13%
- mechanical ventilation and received an infusion of midazolam for sedation and morphine for analgesia

Materials and methods

- dobutamine when judged necessary by the attending physician
- Exclusion: severe head trauma, recent stroke, Child-Pugh C cirrhosis, scleroderma or drepanocytosis, significant arrhythmias, pregnancy

Protocol

- NE doses maintain a baseline MAP of 65 ± 2 mm Hg, basal measurements were performed twice, 15 minutes apart

↓

- NE doses were increased to obtain an MAP of 75 ± 2 mm Hg, 30 minutes taking measurements

↓

- increased to reach an MAP of 85 ± 2 mm Hg within 15 minutes

↓

- then decreased to return to an MAP of 65 ± 2 mm Hg (no other change in treatment was allowed)

Measurements

- near-infrared spectroscopy (NIRS) on the thenar eminence to measure tissue hemoglobin oxygen saturation (StO2)
- vascular occlusion test (VOT) was used to measure different variables reflecting local metabolic demand and microcirculatory function

Measurements

- inflating a pneumatic cuff around the upper arm to 50 mm Hg above the systolic pressure for 3 minutes
- The descending slope of the StO2 and the nirVO2I (the reverse descending slope multiplied by the average THI during the first occlusion minute) estimate regional tissue oxygenconsumption (VO2).
- The ascending slope of the StO2 and the reactive hyperemia reflect microcirculatory reactivity

Measurements

- In six patients, assessed the sublingual microcirculation using the SDF imaging technique (two perfusion indices: the microvascular flow index (MFI) and the vessel density

Results

Table 1 Clinical data

Parameter	Value
Age in years, mean (95% CI)	63.3 (55.0-71.6)
Males/females	9/4
Weight in kilograms, mean (95% CI)	80 (69-91)
Body mass index, mean (95% CI)	27.3 (22.6-32.0)
APACHE II score, mean (95% CI)	22.7 (18.9-26.5)
SOFA score, mean (95% CI)	12.8 (11.4-14.2)
Source of infection, number (percentage)	
Abdominal	6 (46)
Lung	5 (39)
Unknown	2 (15)
Comorbidities, number (percentage)	
Chronic hypertension	8 (62)
Diabetes	5 (38)
Chronic renal failure	2 (15)
ICU length of stay in days, median (25-75% IQR)	17 (6-27)
28-day mortality, number (percentage)	2 (17)

APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; SOFA, Sequential Organ Failure Assessment; CI: confidence interval; IQR: interquartile range

Hemodynamic and metabolic variables

Table 2 Norepinephrine doses and hemodynamic variables

	65 mm Hg	75 mm Hg	85 mm Hg	65 mm Hg
Norepinephrine, μg/minute	17.3 (5.9-28.6)	24.5 (9.5-39.5)[a]	32.7 (14.0-51.4)[a]	22.4 (11.0-33.8)
Mean arterial pressure, mm Hg	66.0 (65.1-66.8)	75.9 (73.5-78.3)[a]	86.3 (84.3-88.4)[a]	66.2 (65.1-67.3)
Heart rate, beats per minute	93.5 (83.9-103.1)	91.4 (81.4-101.5)	92.8 (82.1-103.6)	94.2 (81.7-106.7)
Cardiac output, liters per minute	6.1 (5.4-6.8)	6.5 (5.7-7.3)	6.7 (5.9-7.6)[a]	6.1 (5.4-6.8)
Mean pulmonary arterial pressure, mm Hg	29 (24.9-33.1)	30.3 (26-34.7)	32.2 (27.9-36.5)[a]	29.4 (24.8-34.0)
Pulmonary artery occlusion pressure, mm Hg	15.3 (12.7-18)	15.4 (12.7-18.2)	16.1 (13.5-18.6)	14.6 (12.2-17.1)
Central venous pressure, mm Hg	12.0 (9.8-14.3)	12.8 (10.3-15.2)	13.4 (11.1-15.7)[a]	12.4 (10.3-14.5)
Systemic vascular resistance, dyne/second per cm^{-5}	716 (647-786)	803 (711-896)[a]	902 (793-1,010)[a]	726 (645-806)
Pulmonary vascular resistance, dyne/second per cm^{-5}	181 (141-222)	188 (141-234)	197 (150-244)	184 (134-234)
Change in pulse pressure, percentage	2 (1.5-4.5)	2.5 (1-8)	1.5 (0-4)	4 (3-7)

[a]P <0.05 versus baseline.

Hemodynamic and metabolic variables

Table 3 Metabolic variables

	65 mm Hg	75 mm Hg	85 mm Hg	65 mm Hg
Hemoglobin, g/dL	8.9 (8.0-9.7)	9 (8.2-9.9)	8.9 (7.9-10.0)	8.8 (7.8-9.8)
Temperature, °C	37.3 (36.5-38.0)	37.3 (36.5-38.1)	37.3 (36.6-38.1)	37.4 (36.6-38.2)
Lactate, mEq/L	2.3 (1.5-3.1)	2.2 (1.4-2.9)[a]	2.1 (1.4-2.8)[a]	2.2 (1.5-3.0)
SaO_2, percentage	97.2 (96.4-98.1)	97.5 (96.7-98.3)	97.9 (96.9-98.9)	97.8 (96.9-98.7)
SvO_2, percentage	70.6 (67.9-73.2)	72.3 (69.3-75.3)	75.9 (71.7-80.1)[a]	69.0 (65.8-72.2)
DO_2, mL/minute	728 (633-824)	806 (678-933)	826 (687-965)[a]	721 (623-819)
VO_2, mL/minute	197 (175-220)	203 (173-232)	177 (149-204)	208 (179-238)
EO_2, mL/minute	27.5 (24.6-30.4)	25.8 (22.6-29.0)	22.5 (18.3-26.7)[a]	29.4 (26.1-32.7)

[a]P <0.05 versus baseline. DO_2, oxygen delivery; EO_2, oxygen extraction ratio; SaO_2, arterial hemoglobin saturation; SvO_2, mixed venous oxygen saturation; VO_2, oxygen consumption.

Near-infrared spectroscopy variables

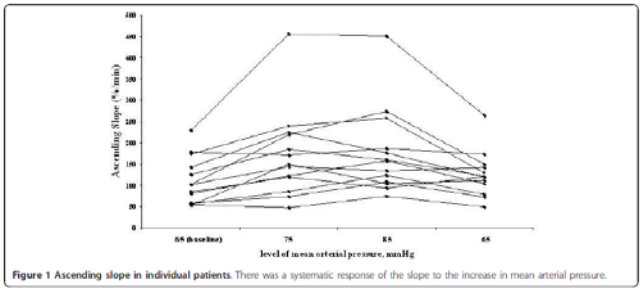

Figure 1 Ascending slope in individual patients. There was a systematic response of the slope to the increase in mean arterial pressure.

Table 4 Near-infrared spectroscopy and sidestream dark field variables

	65 mm Hg	75 mm Hg	85 mm Hg	65 mm Hg
NIRS variables				
StO_2, baseline, percentage	82.5 (79.0-85.9)	81.0 (77.0-85.0)	81.2 (77.6-84.7)	77.8 (73.6-82.1)
Descending slope, percentage/minute	−14.8 (−18.0 - −11.6)	−14.5 (−18.9 - −10.0)	−16.4 (−22.0 - −10.9)	−15.7 (−21.9 - −9.4)
$nirVO_2I$, arbitrary units	139 (114-165)	122 (98-146)	153 (109-196)	129 (93-165)
Delta StO_2, percentage	7.4 (5.3-9.5)	8.4 (5.2-11.6)	7.7 (5.4-9.9)	7.4 (5-9.7)
AUC ratio, percentage	0.11 (0.05-0.16)	0.12 (0.09-0.15)	0.10 (0.08-0.14)	0.10 (0.07-0.15)
Ascending slope, percentage/minute	111 (80-141)	172 (115-228)[a]	177 (122-232)[a]	114 (94-134)
SDF variables				
Total vessel density	12.8 (10.5-15.0)	13.2 (11.1-15.3)	14.3 (12.9-15.7)	13.7 (11.0-16.4)
Small vessel density	10.7 (8.5-12.9)	11 (8.5-13.4)	11.6 (10.1-13.1)	11.7 (9.0-14.3)
PVD, vessels/mm	11.0 (8.6-13.3)	12.0 (9.4-14.5)	13.2 (11.9-14.5)[a]	12.1 (9.2-14.9)
Small PVD, vessels/mm	9.1 (6.4-11.9)	9.8 (6.9-12.8)	10.7 (9.0-12.3)	10.3 (7.1-13.5)
All PPV, percentage	85.9 (80.1-91.6)	89.5 (83.7-95.2)	92.6 (89.9-95.3)	87.7 (79.9-95.6)
Large PPV, percentage	95.5 (93.6-97.4)	95.4 (88.8-102.0)	97.5 (95.2-99.7)	89.8 (82.7-96.9)
Small PPV, percentage	83.6 (76.1-91.0)	87.9 (81.8-94.0)	91.1 (87.9-94.3)	86.4 (76.3-96.5)
Microvascular flow index	2.4 (2.2-2.7)	2.7 (2.4-2.9)	2.9 (2.8-2.9)[a]	2.5 (2.2-2.9)

[a]P <0.05 versus baseline. AUC, area under the curve; NIRS, near-infrared spectroscopy; $nirVO_2I$, reverse descending slope multiplied by the average tissue hemoglobin index during the first occlusion minute; PPV, proportion of perfused vessels; PVD, perfused vessel density; SDF, sidestream dark field; StO_2, thenar muscle oxygen saturation.

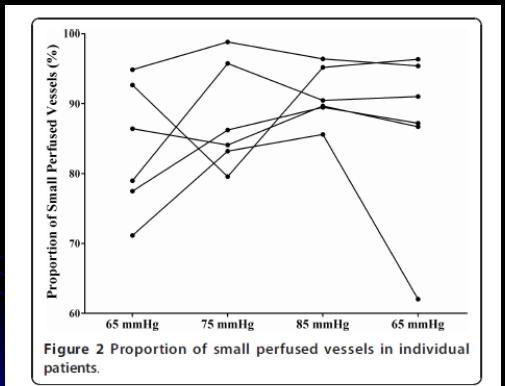

Figure 2 Proportion of small perfused vessels in individual patients.

Discussion

- The major finding: MAP from 65 to 75 and 85 mm Hg by titrating NE an increase in cardiac output, a decrease in blood lactate level, and an improvement in microcirculatory function
- NE, strong alpha-adrenergic properties, whether this vasoconstriction is not deleterious for the microcirculation
- increase in cardiac output could be explained by the beta-1 adrenergic action of NE

Discussion

- no significant increase in VO2 in our study, blood lactate concentrations decreased slightly
- With NIRS, impairment in tissue reperfusion after hypoxia has been shown to be correlated with the severity of sepsis and with outcome

Discussion

- StO2 was not affected by the different arterial pressure levels and remained lower than in a healthy population . The absence of changes in StO2 suggests that NIRS changes were not the consequence of the increase in cardiac output
- Our results contradict those of some previous studies, dopamine in addition to NE, fluid repletion or in the timing of the study, patient selection

Discussion

- a relatively small number of patients, had strict enrollment criteria, to all patients may be problematic
- this study investigated only immediate changes, the MAP is maintained above 65 mm Hg for longer would be difficult
- these data cannot be extrapolated to other vasopressor agents

Conclusions

- Increasing MAP above 65 mm Hg with higher doses of NE can result in increased cardiac output, improved microcirculatory function, and decreased lactate concentrations
- Additional studies should to develop criteria for determining an individually adapted arterial pressure and to evaluate the long-term effects