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Effects of dopamine infusion on forearm blood flow in critical patients

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A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: In critical care, dopamine is administered by infusion at low doses (≤3 μg/kg/min) or at high doses (≥5 μg/kg/min) for assessment of hemodynamics. The present study was conducted to explore the effects of dopamine infusion on the vast microvascular network of skeletal muscle in the early phases of sepsis.

Material/Methods: An observational study was performed which included twelve critically ill patients. Patients' response to dopamine infusion (3 μg/kg/min) was studied within 24 hours from admission to the ICU. The forearm blood flow (FBF) and vascular resistance (FVR) were measured by near-infrared spectroscopy (NIRS).

Results: Dopamine did not ameliorate forearm regional oxygenation. The infusion of dopamine caused an increase in MAP, while FBF decreased with the resistance increase ($p>0.05$).

Conclusions: NIRS was suitable to measure bedside the vascular resistance and to test the effects of low doses of dopamine on forearm blood flow. A dopamine infusion of 3.0 μg/kg/min caused a reduction in forearm blood flow and an increase in vascular resistance in our patients.

key words: **NIR • dopamine • vascular resistance • critical closing pressure • forearm blood flow**

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Background

Critical ill patients show a variety of hemodynamic alterations that frequently result in cardiovascular collapse, marked decrease in tissue perfusion, acidosis and, ultimately, vital organ failure and death [1]. The vast micro-vascular network of skeletal muscle plays an important role in the compensatory phases of the ongoing insult. Studying the muscle perfusion in critical ill patients allows physicians to evaluate circulation defects and drug effects [2]. The basic premises to be outlined in this paper are the role of the microvasculature of muscle in the early phases of sepsis and the effects of dopamine on peripheral vascular resistance.

Material and Methods

An observational study was performed which included twelve patients admitted to our University Hospital ICU during year 2002 who consented to participating in the study (Table 1). The mean age was 64.5 years (range: 29–82 years) and two patients were female. Inclusion criteria were COPD exacerbation as the admission diagnosis and infusion of dopamine (3 μg/kg/min) during the first 24 hours of ICU stay. Exclusion criteria were mechanical ventilation at admission, continuous sedation, severe hypotension, or refusal to participate. The decision to start dopamine infusion to correct hemodynamic instability or acute renal failure was taken by the physician in charge on admission. The patients were divided in two groups: group 1 ('sepsis') and group 2 ('no sepsis') patients. Sepsis, according to the Bone's criteria was diagnosed in seven cases of the 12 [1]. Only two patients survived and were released home. All patients received on admission in the ICU invasive monitoring of arterial and central venous pressure and 50% O_2 by face mask.

We studied the patients' response to dopamine infusion (3 μg/kg/min) within 24 hours from ICU admission, as soon as clinical parameter stabilization was obtained. Forearm blood flow (FBF) and vascular resistance (FVR) were measured by near-infrared spectroscopy (NIRS) according to De Blasi et al. [2]. NIRS is a noninvasive technique aimed at monitoring oxygen availability and utilization at the tissue level based on the ability of near-infrared light (650–1000 nm) to pass through tissues [3]. The amount of light recorded after photons have passed through skin and muscles is dependent on the degree of scatter in the tissues and the amount of absorption by tissue chromophores (oxy- and deoxy-hemoglobin, myoglobin, and cytochrome *aa*3). This technology fits the need for forearm blood flow measurement noninvasively, since the amount of myoglobin is constant during the study and changes in total hemoglobin (oxy plus deoxy) can be related to changes in blood flow. To measure forearm blood flow, we positioned the NIR optodes (Critikon 2020, Johnson & Johnson, UK) on the brachioradialis muscle (on the arm were invasive radial pressure was monitored) and then performed a venous occlusion lasting 20 seconds by inflating a pneumatic cuff around the forearm to a pressure of 45 mmHg in a time shorter than 0.5 sec. The prompt increase in HbO_2 after each venous occlusion was due to arterial blood afflux ($d[HbO_2]/dT$). The temporary augmentation of deoxyhemoglobin ($d[Hb]/dT$) was related to tissue O_2 uptake. FBF was calculated as $d[HbO_2+HbH]/dT$ and measured as ml*100/g/min.

Table 1. Hemodynamic values at admission and patient mortality.

	Sepsis		No sepsis	
n	7		5	
Mean age (std. dev.) years	57	(14.4)	75	(4.3)
MAP (std. dev.) mmHg	68.3	(9.7)	62	(21)
WBC(std. dev.)	20361	(11140)	7980	(2310)
CVP (std. dev.) cm H_2O	9	(5)	14	(4)
Dead at discharge, n	5		5	

After each venous occlusion, rapid venous drainage was achieved by raising the patients' wrist 10 cm above the heart level. This maneuver was performed three times consecutively every 15 seconds. Five minutes later we performed a complete vascular occlusion by inflating the cuff to 240 mmHg. The pressure value recorded after a two-minute plateau was the critical occlusion pressure (CCP), an expression of arteriolar vascular tone. Forearm vascular resistance (FVR) was calculated by introducing the critical occlusion pressure as:

$$R0=(MAP-CCP)/FBF$$

FBF, CCP, FVR, and R0 measurements were performed at baseline and after dopamine infusion. Values of FBF, CCP, FVR, and R0 are expressed as the mean value of three consecutive measurements.

Statistical analysis

Data are expressed as mean value and standard deviation. Student's t test was used for statistical analysis.

Appendix

The relationship between flow, pressure, and resistance can be expressed mathematically as a variant of Ohms' law in which blood flow is directly proportional to the pressure drop across two points and inversely proportional to resistance. It is important to appreciate that the difference in pressure between two points, and not the absolute pressure, is the determinant of blood flow. Rearrangement of Ohms' formula emphasizes that resistance is directly proportional to pressure and inversely proportional to flow:

$$R=\Delta P/Q$$

where R = resistance; ΔP = pressure drop; Q = flow.

Furthermore, resistance is proportional to the viscosity of the blood and the length of the vessel and inversely proportional to the forth power of the radius of the vessel (Poiseuille's law).

$$R=\nu/r^4$$

where R = resistance; ν = viscosity; r = radius.

Systemic resistance to blood flow cannot be measured directly and is calculated as the difference between the mean arterial and right atrium pressure divided by cardiac output.

Table 2. Baseline values in septic and non-septic patients and statistical significance.

	Sepsis	No sepsis	Student's T
MAP mmHg	63.36	62.4	0.09
ΔHB µg/l	0.3	0.2	0.78
FBF ml*100/g/min	4.9	3.5	0.1
R0 mm Hg/ml*100/g/min	10.6	15	0.3
CCP mmHg	27.5	41.4	0.66

Peripheral resistance is considered as the resistance to the flow of a single conduit between the aorta and the caval veins. If the flow through a tube is equal to the difference in pressure across the tube divided by its resistance, then inflow and outflow pressure should be equal when the flow is zero, but it has been demonstrated that at zero flow, arterial pressure is greater than venous because a Starling resistance-like mechanism exists at the arteriolar level. This pressure was defined by Burton in 1951 [4] as critical closing pressure (CCP). When the flow pressure declines below the critical closure pressure, arterial vessels collapse. The average critical closing pressure is 40 mmHg.

The Starling resistor-like mechanism created by the arteriolar tone has some important implications.

Flow under this condition is similar to a natural waterfall in which the flow is determined by the difference in altitude between the upstream lake and the waterfall divided by the resistance of the river. It is not affected by the height of the fall or by the resistance of the river below the fall. Similarly, when a vascular waterfall is present, the pressure used to calculate resistance is the critical closing pressure and not the venous pressure.

Critical closure pressure is influenced by mechanisms that affect vascular tone, the perfusion pressure, the resistances, local myogenic response, metabolic and neurogenic factors, and endotelial-derived factor. Critical closing pressure is also influenced by the level of activity of the sympathetic nervous system: an inhibition of the sympathetic nervous system reduces CCP, while stimulation can increase vascular tone, reducing the dimensions of the circulatory system. Likewise, drugs such as dopamine act on the vascular tone.

Results

NIR spectroscopy was suitable for the bedside measurement of the vascular resistances and to test the effects of low doses of dopamine on forearm blood flow. Clinical parameters at baseline are shown in Table 2. Statistically significant differences between the two groups ('sepsis' and 'no sepsis') were not found in vital signs or in factors such as age, hemoglobin concentration, and arterial oxygen concentration at the baseline.

Hemodynamic effects of dopamine infusion are shown in Table 3: dopamine-related changes were not statistically significant (p>0.05). The R0 values at baseline were lower in the septic patients, but this difference was in the chance domain. Hemodynamic changes due to dopamine were not evidently different between the septic and non-septic patients (p>0.05). The infusion of dopamine caused a 10% MAP increase and a 15% FBF decrease in all the patients with no differences between group 1 (sepsis) and group 2 (no sepsis). The infusion of 3 µg/kg/min dopamine caused a 6.5% critical closing pressure increase and a larger R0 increment, with large inter-individual variability. Dopamine did not ameliorate forearm regional oxygenation.

Table 3. Hemodynamic effects of dopamine infusion and statistical significance.

	Basal	Dopamine	Student's T
ΔHB (std. dev.) µg/l	0.30 (0.18)	0.20 (0.15)	0.6
FBF (std. dev.) ml*100/g/min	4.36 (2.4)	3.70 (1.7)	0.53
MAP (std. dev.) mmHg	65.00 (15.3)	72.00 (24.3)	0.3
CCP (std. dev.) mmHg	33.15 (10.1)	35.33 (5.3)	0.07
R0 (std. dev.) mmHg/ml*100/g/min	6.4 (12.5)	9.00 (6.8)	0.4

Discussion

Correct appraisal of distrectual vascular resistances would allow estimating the perfusional state of the organs. Particularly in case of critical illness it is of great advantage for the physician to know how the cardiac output redistributes to the different 'systems'. Only a few regions, such as the forearm or quadriceps [5], are suitable for easy, reproducible, and noninvasive measurements.

Dopamine did not ameliorate forearm oxygenation in this critical patient series. Our result confirms Schwarte's recently published study on intestinal perfusion under dopamine treatment [6]. The results of the present study demonstrated that in critical patients the infusion of small doses of dopamine causes a reduction in blood flow to the forearm associated with an increase in local arteriolar resistance, with large inter-individual variability. Dopamine dose-dependent effects are not easily predictable for the single patient [7–9]. Dopamine infusion at 5.0 µg/kg/min or lower is traditionally considered responsible for dopaminergic receptor activation, in a lower grade of beta-adrenergic receptor, but not of alpha 1 adrenergic receptor activation [10]. Alpha 1 agonism can cause regional vasoconstriction, counterbalancing the vasodilating effects of DA1 receptor activation. In this series, dopamine did not cause a significant hemodynamic change, even though a mean 40% R0 increase was recorded.

In this series, the infusion of dopamine at 3 µg/kg/min was not compared to placebo or to a different infusion rate (because of the observational nature of the study), but it would be important to perform a case-control study to define the role of dopamine more precisely. We were not able to distinguish a difference between septic and non-septic patients where dopamine infusion was concerned, probably because of the small size of the sample.

Conclusions

NIR is a noninvasive, bedside available, easy to use device that allows forearm blood flow measurements. The protocol of De Blasi et al. [2] is suitable for studying vascular resistance and blood flow changes related to drug infusion in critical patients using the critical closing pressure value. A dopamine infusion of 3 μg/kg/min caused an increase in vascular resistance (6.5% critical closing pressure increment) and a 15% reduction in forearm blood flow, even though these changes were in the chance domain. The lack of a gold standard for blood flow measurement does not allow us to draw definitive conclusions.

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