Sublingual microcirculatory shock and loss of haemodynamic coherence during subarachnoid anaesthesia

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Dear Editor,

Optimization of tissue perfusion is one of the primary goals of perioperative care and its adequacy is often assumed based on systemic measures, such as mean arterial pressure (MAP). However, microcirculatory alterations may occur even when global haemodynamic variables are within normal targets and are associated with the development of organ dysfunction. Indeed, perfusion-related complications are a main cause of morbidity and mortality in the surgical population, especially within the first thirty postoperative days [1, 2].

Although several studies have emerged in the last years providing important data that highlight the relationship between intraoperative hypotension and organ injury [3, 4], intraoperative microcirculatory endpoints and the impact of microcirculatory-guided therapeutic interventions have not yet been well defined [5]. In this report, we present a case of intraoperative loss of haemodynamic coherence in a patient with normal systemic haemodynamics during subarachnoid anaesthesia.

A 51-year-old white woman with a body mass index of 33.3 kg m^{-2}, American Society of Anesthesiologists Physical Status Classification II, and stable general condition was scheduled to undergo total knee arthroplasty under subarachnoid anaesthesia. Her medical history was remarkable for well-controlled hypothyroidism and chronic psychosis managed with L-thyroxine (112 μg per day), nebivolol hydrochloride (5 mg per day), trazodone (150 mg per day), olanzapine (2.5 mg per day), agomelatine (25 mg per day), and prazepam (10 mg per day). Physical cardiopulmonary examination before surgery was unremarkable. Preoperative electrocardiogram and laboratory blood tests were also unremarkable except for haemoglobin of 10.6 g dL^{-1} and creatinine of 0.46 mg dL^{-1}. Preoperative calculated plasma volume status was 0.32.

Upon arrival at the operating room, she was awake with a Glasgow Coma Scale score of 15 and no neurological deficiencies. Standard monitoring was placed. The patient was haemodynamically stable with heart rate 89 beats min^{-1}, arterial blood pressure 126/82 mmHg, respiratory rate 14 min^{-1}, peripheral oxygen saturation 99% on room air, and body temperature 36.4°C. Two large-bore (17G) intravenous cannulae were inserted. She received 5 mL kg^{-1} of a balanced crystalloid solution to compensate for preoperative fasting and vasodilation associated with anaesthesia followed by an infusion of 2 mL kg^{-1} h^{-1}.

The patient was placed seated on the operating table with the assistance of one nurse. The puncture area was strictly disinfected and covered with a sterile sheet. After anaesthetizing the puncture site with 1.5 mL of 2% lidocaine, the anaesthesiologist performed spinal anaes-

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thesia through the L4–L5 space with a 25G spinal atraumatic needle. When positive reflux of cerebrospinal fluid was observed, a single bolus dose of 2.2 mL (15 mg of 0.75% ropivacaine plus 0.02 mg of fentanyl) was administered. The patient was placed supine and a T7 sensory blockade was confirmed by pinprick test at the 8th minute after intrathecal injection.

Intraoperative systemic haemodynamics remained stable without vasopressor use, and the procedure was evolving smoothly. Approximately 15 minutes after the surgical incision, the patient complained of anxiety and sweating. At that time, a reduction of heart rate (sinus rhythm, 64 beats min^{-1}) was observed with arterial blood pressure being 105/67 mmHg. Arterial blood gas analysis was unremarkable except for increased lactate (2.7 mmol L^{-1} [normal range: 0.93–1.65]) and a base deficit of −2.1 mmol L^{-1} (normal range: −2 to +2).

Fifteen minutes later, haemodynamic stability was maintained (sinus rhythm, 67 beats min^{-1}; blood pressure 108/65 mmHg), but the patient complained of anxiety and dry mouth. Based on the available clinical and laboratory data, and after exclusion of other potential causes including surgery-related blood losses, a second sample for arterial blood gas testing was collected, revealing a lactate level of 3.2 mmol L^{-1} and a base deficit of −3.4 mmol L^{-1}. As the next diagnostic step, sublingual microcirculation was visualized and assessed, revealing plugged vessels next to vessels with flowing cells (type 3 microcirculatory alterations, Figure 1). Taking into consideration the anaesthesia-induced sympathetic nervous system blockade (resulting in a decrease in systemic vascular resistance), the possibility of a subsequent Bezold-Jarisch reflex [6, 7], and the evidence suggesting that impairment of microcirculatory flow should be taken as a serious warning sign for an imminent deterioration [8], the infusion of crystalloids was accelerated and three 50 µg doses of phenylephrine were administered with 5-min intervals (150 µg in total).
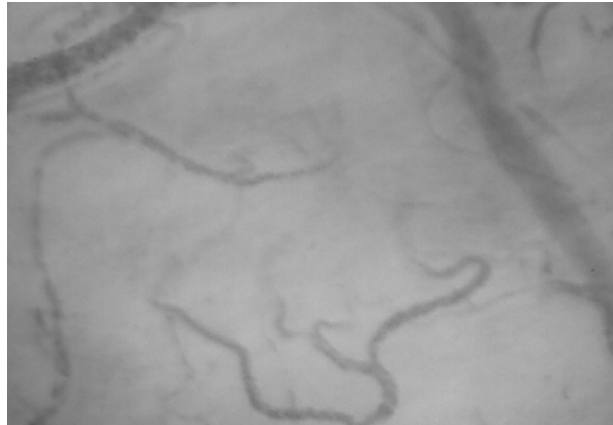

FIGURE 1. Plugged vessels next to vessels with flowing cells (type 3 microcirculatory alterations)

FIGURE 2. Aggravation of microcirculatory flow due to excessive vasoconstriction (type 1 and type 3 microcirculatory alterations)
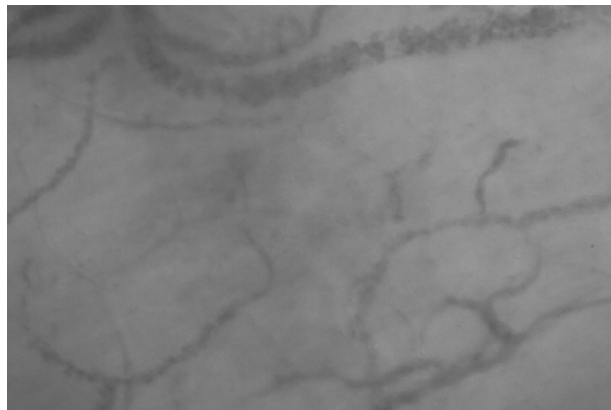

FIGURE 3. A small improvement in microcirculatory flow was observed 20 min after the start of glyceryl trinitrate infusion

A second assessment of sublingual microcirculation performed five minutes after the third dose of phenylephrine revealed further deterioration of microcirculatory flow with complete stagnated capillaries (type 1 alterations) in addition to type 3 alterations (Figure 2), suggesting microcirculatory shock due to excessive vasoconstriction. An intravenous dose of 1.5 mg of midazolam was administered to the patient and the radial artery was cannulated and connected to a pressure transducer to directly measure arterial blood pressure. Thereafter, an infusion of glyceryl trinitrate was started at 0.11 µg kg^{-1} min^{-1}.

Twenty minutes later, a third assessment of sublingual microcirculation revealed a small improvement

TABLE 1. Perioperative fluctuation of anaesthetic, haemodynamic, and metabolic variables

Factor	Arrival at the operating room	Onset of symptoms	Before phenyl ephrine	After the last dose of phenylephrine	20 min after glyceryl trinitrate	30 min after admission to PACU
Heart rate (beats min⁻¹)	89	64	67	71	72	70
Systolic arterial pressure (mmHg)	126	105	108	131	77	79
Diastolic arterial pressure (mmHg)	82	67	65	84	58	60
Mean arterial pressure (mmHg)	97	80	79	100	64	66
Capillary refill time (s)	2	3	3	5	2	1
SpO$_2$ (%)/FiO$_2$	99/0.21	98/0.21	98/0.21	96/0.21	99/0.21	99/0.21
pH	NA	NA	7.36	7.34	7.35	7.38
Lactate (mmol L⁻¹)	NA	2.7	3.2	3.3	3.2	2.1
Base deficit (mmol L⁻¹)	NA	−2.1	−3.4	−3.6	−3.5	−1.6
De Backer score (mm⁻¹)	NA	NA	5.4	3.1	5.8	7.3
Consensus PPV (%)	NA	NA	59	42	64	83
Consensus PPV (small) (%)	NA	NA	41	34	53	78
Total amount of crystalloids (mL)	NA	650	700	1100	1200	1500
Glyceryl trinitrate (µg kg⁻¹ min⁻¹)	–	–	–	0.11	0.35	0.3

PACU — post-anaesthesia care unit, SpO$_2$ — peripheral oxygen saturation, FiO$_2$ — fraction of inspired oxygen, PPV — proportion of perfused vessels
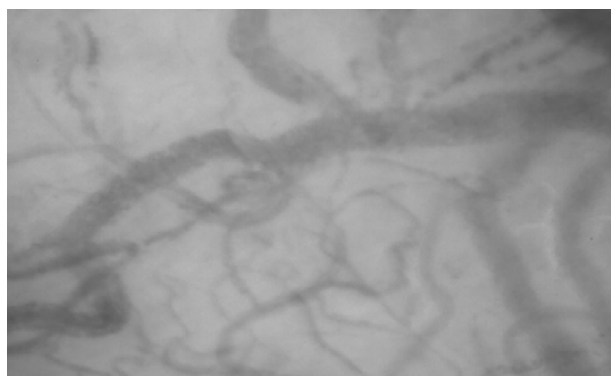

FIGURE 4. Increasing the dose of glyceryl trinitrate significantly improved microcirculatory flow

in microcirculatory flow (Figure 3). The dose of glyceryl trinitrate was titrated up to 0.46 µg kg⁻¹ min⁻¹, with the blood pressure ranging between 76/54 mmHg and 80/62 mmHg and the patient's symptoms progressively subsiding without any adverse sequalae during the remaining intraoperative period (Table 1). The surgery was uneventful, and the patient was transferred to the post anaesthesia care unit (PACU). Another assessment at that time (glyceryl trinitrate 0.42 µg kg⁻¹ min⁻¹) revealed improved sublingual microcirculatory flow (Figure 4). The patient remained in the PACU for four hours and she was discharged to the ward after gradual tapering and weaning from glyceryl trinitrate infu-

sion. Postoperative calculated plasma volume status at the ward was 3.

The postoperative course was uneventful, and the patient was discharged from the hospital after four days. In the follow-up consultations at 6 months, 1 year, and 2 years, she was in perfect condition. No evidence of myocardial, renal, or other injury was observed during hospitalization and follow-up.

Perioperative calculated plasma volume status was obtained by determining actual and ideal plasma volume levels, as previously reported [9]. Mean arterial pressure was initially measured intermittently using a non-invasive oscillometric device every three minutes. Thereafter, MAP was directly measured

with a 20-gauge radial arterial catheter connected to the anaesthesia monitor. Before taking measurements, we confirmed that the transducers were correctly levelled and zeroed, while the system's dynamic response was confirmed with fast-flush tests [10]. Sublingual microcirculation was monitored using SDF+ imaging (Microscan; Microvision Medical BV, Amsterdam, The Netherlands). To optimize video quality, we tried to avoid pressure and movement artefacts, optimized focus and illumination, and cleaned saliva and/or blood from the sublingual mucosa [11, 12].

To our knowledge, this is the first report of microcirculatory shock with type 1 and type 3 alterations during subarachnoid anaesthesia. This case highlights the diagnostic value of intraoperative monitoring of sublingual microcirculation, which may provide information about the mechanisms of tissue hypoperfusion and aid in the determination of an appropriate therapeutic strategy.

Subarachnoid anaesthesia may induce significant systemic haemodynamic impairment due to sympatholytic action and peripheral vasodilation in the blocked area, which decrease systemic vascular resistance and arte-

rial blood pressure. However, its effects on sublingual microcirculation have not been studied extensively. A study investigating the impact of subarachnoid anaesthesia on maternal sublingual microcirculation reported no statistically significant difference in pre- and post-spinal microvascular flow index [13]. Another prospective observational study with patients undergoing elective surgery under subarachnoid anaesthesia reported a significantly decreased microvascular reperfusion rate in the blocked area, although an increase in tissue oxygen saturation was observed due to its sympatholytic effects [14]. In the present case, the impairment of sublingual microcirculatory flow together with the observed metabolic deterioration indicate splanchnic hypoperfusion [4, 12, 15, 16].

Microcirculatory shock is the failure of microcirculation to support tissue perfusion and oxygenation despite normal systemic haemodynamics [5]. Different types of sublingual microcirculatory alterations have been described. Type 1 alterations include complete stagnated capillaries due to circulatory arrest or excessive use of vasopressors, and/or raised venous pressures. In type 3 alterations, plugged vessels are seen next to vessels with flowing cells (sepsis, haemorrhage, and/or haemodilution). Taking into consideration that the patient was normovolaemic, the most likely cause of microcirculatory impairment was extreme anxiety and the associated catecholamine-induced vasoconstriction. Experimental and clinical research have shown that psychological stress may result in dysfunction of microcirculation, tissue hypoperfusion, and organ damage, especially in women [17–20]. Notably, the microcirculatory impairment was evident in our patient despite the vasodilatory/protective effects of nebivolol and thyroxine [21, 22].

Based on the available perfusion data at the onset of symptoms (normal macrohaemodynamics, capillary refill time, and oxygen saturation), the sym-pathetic nervous system blockade, the possibility of a Bezold-Jarisch reflex, and the evidence suggesting that impaired microcirculatory flow should be taken as a serious warning sign for imminent deterioration, the anaesthesia team acted pre-emptively and administered a total dose 150 μg of phenylephrine. The latter further worsened sublingual microcirculatory flow, which was subsequently improved with glyceryl trinitrate infusion. Although the available evidence suggests a non-linear relationship between the macro- and microcirculation, our case indicates a linear relationship until a certain physiological point, beyond which an increase in MAP does not translate into better microcirculatory perfusion.

Intact coherence between the macro- and microcirculation facilitates oxygen delivery to the parenchymal cells. In this context, tissue perfusion is very important because hypoxia does not equate to a specific oxygen concentration. Indeed, many tissues function physiologically at levels equivalent to an atmosphere of 5% oxygen and some at levels as low as 1% oxygen [23, 24]. Furthermore, other phenomena, such as capillary rarefaction or reduced vascular density in individuals with chronic hypertension, may jeopardize tissue oxygenation [10]. The present case confirms that complex mechanisms of haemodynamic coherence are required to maintain homeostasis over a very wide range of oxygen concentrations and/or perfusion changes.

Extreme anxiety and psychological stress may impair microcirculatory flow in patients with normal systemic haemodynamics. The present paper highlights the importance of visualization of microcirculation for optimizing perioperative cardiovascular dynamics and improving outcomes.

ACKNOWLEDGEMENTS

REFERENCES

1. Chalkias A, Laou E, Kolonia K, et al. Elevated preoperative suPAR is a strong and independent risk marker for postoperative complications in patients undergoing major noncardiac surgery (SPARSE). Surgery 2022; 171: 1619-1625. doi: 10.1016/j.surg.2021.10.012.

2. Ackland GL, Brudney CS, Cecconi M, et al; Perioperative Quality Initiative-3 workgroup; POQI chairs; Physiology group; Preoperative blood pressure group; Intraoperative blood pressure group; Postoperative blood pressure group. Perioperative Quality Initiative consensus statement on the physiology of arterial blood pressure control in perioperative medicine. Br J Anaesth 2019; 122: 542-551. doi: 10.1016/j.bja.2019.01.011.

3. Mascha EJ, Yang D, Weiss S, Sessler DI. Intraoperative mean arterial pressure variability and 30-day mortality in patients having noncardiac surgery. Anesthesiology 2015; 123: 79-91. doi: 10.1097/ALN.0000000000000686.

4. Chalkias A, Papagiannakis N, Mavrovounis G, et al. Sublingual microcirculatory alterations during the immediate and early postoperative period: a systematic review and meta-analysis. Clin Hemorheol Microcirc 2022; 80: 253-265. doi: 10.3233/CH-211214.

5. Ince C, Boerma EC, Cecconi M, et al; Cardiovascular Dynamics Section of the ESICM. Second consensus on the assessment of sublingual microcirculation in critically ill patients: results from a task force of the European Society of Intensive Care Medicine. Intensive Care Med 2018; 44: 281-299. doi: 10.1007/s00134-018-5070-7.

6. Langesaeter E, Rosseland LA, Stubhaug A. Continuous invasive blood pressure and cardiac output monitoring during cesarean delivery: a randomized, double-blind comparison of low-dose versus high-dose spinal anesthesia with intravenous phenylephrine or placebo infusion. Anesthesiology 2008; 109: 856-863. doi: 10.1097/ALN.0b013e31818a401f.

7. Campagna JA, Carter C. Clinical relevance of the Bezold-Jarisch reflex. Anesthesiology 2003; 98: 1250-1260. doi: 10.1097/00000542-200305000-00030.

8. Scheuzger JD, Zehnder A, Yeginsoy D, Siegemund M. Sublingual microcirculation: a case report. J Med Case Rep 2019; 13: 179. doi: 10.1186/s13256-019-2118-4.

9. Maznyczka AM, Barakat MF, Ussen B, et al. Calculated plasma volume status and outcomes in patients undergoing coronary bypass graft surgery. Heart 2019; 105: 1020-1026. doi: 10.1136/heartjnl-2018-314246.

10. Chalkias A, Xenos M. Relationship of effective circulating volume with sublingual red blood cell velocity and microvessel pressure difference: a clinical investigation and computational fluid dynamics modeling. J Clin Med 2022; 11: 4885. doi: 10.3390/jcm11164885.

11. Chalkias A, Papagiannakis N, Saugel B, et al. Association of preoperative basal inflammatory state, measured by plasma suPAR levels, with intraoperative sublingual microvascular perfusion in patients undergoing major non-cardiac surgery. J Clin Med 2022; 11: 3326. doi: 10.3390/jcm11123326.

12. Chalkias A, Laou E, Mermiri M, et al. Microcirculation-guided treatment improves tissue perfusion and hemodynamic coherence in surgical patients with septic shock. Eur J Trauma Emerg Surg 2022; 48: 4699-4711. doi: 10.1007/s00068-022-01991-2.

13. George RB, Boyd C, McKeen D, Abdo IS, Lehmann C. Possible impact of spinal anesthesia and phenylephrine on sublingual microcirculation of cesarean delivery patients. J Clin Med Res 2019; 11: 543-549. doi: 10.14740/jocmr3778.

14. Cho AR, Kim HJ, Lee HJ, et al. Changes in the microvascular reactivity during spinal anesthesia. Microvasc Res 2021; 137: 104176. doi: 10.1016/j.mvr.2021.104176.

15. Bouattour K, Teboul JL, Varin L, Vicaut E, Duranteau J. Preload dependence is associated with reduced sublingual microcirculation during major abdominal surgery. Anesthesiology 2019; 130: 541-549. doi: 10.1097/ALN.0000000000002631.

16. Bansch P, Flisberg P, Bentzer P. Changes in the sublingual microcirculation during major abdominal surgery and post-operative morbidity. Acta Anaesthesiol Scand 2014; 58: 89-97. doi: 10.1111/aas.12204.

17. Wang C, Wang XR, Song DD, et al. The establishment of rat model in myocardial ischemia with psychological stress. Ann Transl Med 2020; 8: 322. doi: 10.21037/atm.2020.02.128.

18. Hammadah M, Kim JH, Al Mheid I, et al. Coronary and peripheral vasomotor responses to mental stress. J Am Heart Assoc 2018; 7: e008532. doi: 10.1161/JAHA.118.008532.

19. Vaccarino V, Sullivan S, Hammadah M, et al. Mental stress-induced-myocardial ischemia in young patients with recent myocardial infarction: sex differences and mechanisms. Circulation 2018; 137: 794-805. doi: 10.1161/CIRCULATIONAHA.117.030849.

20. Sullivan S, Hammadah M, Al Mheid I, et al. Sex differences in hemodynamic and microvascular mechanisms of myocardial ischemia induced by mental stress. Arterioscler Thromb Vasc Biol 2018; 38: 473-480. doi: 10.1161/ATVBAHA.117.309535.

21. Velasco A, Solow E, Price A, et al. Differential effects of nebivolol vs. metoprolol on microvascular function in hypertensive humans. Am J Physiol Heart Circ Physiol 2016; 311: H118-H124. doi: 10.1152/ajpheart.00237.2016.

22. Oflaz H, Kurt R, Sen F, et al. Coronary flow reserve after L-thyroxine therapy in Hashimoto's thyroiditis patients with subclinical and overt hypothyroidism. Endocrine 2007; 32: 264-270. doi: 10.1007/s12020-008-9037-2.

23. Keeley TP, Mann GE. Defining physiological normoxia for improved translation of cell physiology to animal models and humans. Physiol Rev 2019; 99: 161-234. doi: 10.1152/physrev.00041.2017.

24. Schödel J, Ratcliffe PJ. Mechanisms of hypoxia signalling: new implications for nephrology. Nat Rev Nephrol 2019; 15: 641-659. doi: 10.1038/s41581-019-0182-z.