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Case Report

Refractory intraoperative hypotension: A case report to keep in mind

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ABSTRACT

Refractory intraoperative hypotension can be triggered by a complex interplay of perioperative factors, including anesthetic-induced vasodilation, patient positioning, surgical blood loss, autonomic dysfunction, and the prolonged effects of the patient's daily medications (such as long-acting irbesartan, amlodipine, and concomitant beta-blocker therapy). While the optimal approach to perioperative renin–angiotensin system inhibitor use remains uncertain, these combined agents can severely impair cardiovascular compensatory mechanisms and blunt vasopressor responsiveness under general anesthesia. A 66-year-old male with hypertension and diabetes underwent posterior spinal instrumentation under general anesthesia. Following induction and prone positioning, severe refractory hypotension developed despite aggressive fluid resuscitation guided by Pleth Variability Index, vasopressors, and inotropic support. Progressive lactic acidosis led to surgical termination at the 150th minute. Postoperative cardiac evaluations were normal. Further history revealed the patient had taken a long-acting triple combined antihypertensive regimen (irbesartan/amlodipine/hydrochlorothiazide) the night before surgery. Norepinephrine support was required for 36 hours postoperatively, followed by a full recovery. While diabetic cardiac autonomic neuropathy and prone positioning create a vulnerable baseline for hemodynamic instability, long-acting triple combination antihypertensive therapy acts as the definitive driver for severe, refractory vasoplegic shock. Concomitant use of renin-angiotensin system inhibitors, calcium channel blockers, and thiazide diuretics can severely impair compensatory vasoconstriction and blunt vasopressor responsiveness under general anesthesia. Perioperative antihypertensive management must be strictly individualized according to drug half-life, combination characteristics, and patient comorbidities.

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1. Introduction

We aimed to discuss the possible causes of refractory hypotension encountered during posterior instrumentation surgery, which persisted despite adequate volume replacement, inotropic and vasopressor support, ultimately leading to the termination of the procedure.

2. Case Presentation

Informed consent was obtained from the patient. A 66-year-old, 80 kg male patient with a history of hypertension for 18 years and diabetes mellitus for 12 years (ASA III) was scheduled for posterior spinal instrumentation. Informed consent was obtained from the patient in order to publish this case. Preoperative evaluation, in-

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cluding systemic examination, imaging, and laboratory findings, was unremarkable.

Preoperative blood pressure was 165/85 mmHg with a resting tachycardia (114 bpm). Due to these findings, cardiology consultation was requested, and oral bisoprolol (5 mg/day) was added to his regimen [metformin (1000 mg/day), acetylsalicylic acid (100 mg/day), and irbesartan/amlodipine/hydrochlorothiazide (150/10/12.5 mg)]. Echocardiography revealed a normal ejection fraction (EF 60%) and normal valvular functions.

Following routine monitoring and induction (propofol, fentanyl, rocuronium), the patient was intubated. Invasive arterial pressure and Pleth Variability Index (PVI) monitoring were established. Anesthesia was maintained with sevoflurane (0.8–1.0 MAC) in oxygen/air mixture and remifentanil infusion (0.05–0.20 mcg/kg/min) was titrated according to the hemodynamic response.

The patient was positioned prone using thoracic and abdominal supports. Airway pressures remained stable, and the abdomen was free of compression. Immediately post-positioning, profound refractory hypotension developed. Despite fluid resuscitation and ephedrine boluses, the collapse was non-reactive, requiring sequential norepinephrine and adrenaline infusions (Table 1). PVI (12–14%), oxygenation, and ECG remained stable.

Table 1. Patient's hemodynamic status and interventions performed.

Time point	Blood pressure (mmHg)	Heart rate (beats/min)	Intervention	Clinical response	Estimated blood loss (mL)	Fluid and blood replacement
Pre-induction	165/94	62	—	—	—	Crystalloid infusion
Post-induction	125/69	68	—	—	—	Crystalloid infusion
After prone positioning	80/42	78	500 mL colloid bolus	Normotension achieved within 15 min	—	Crystalloid infusion
5 min after colloid administration	52/35	61	Ephedrine 5 mg ×2; norepinephrine infusion initiated	No significant response	—	Crystalloid bolus and fluid challenge continued
Intraoperative 1st hour	92/52	70	Norepinephrine infusion 0.2 mcg/kg/min	Systolic blood pressure maintained between 90–100 mmHg	500	2400 mL crystalloid + 500 mL colloid
Intraoperative 90th min	62/36	75	Norepinephrine 0.3 mcg/kg/min + dopamine 20 mcg/kg/min	Systolic blood pressure increased to 90 mmHg; surgical team informed	750	1 unit erythrocyte suspension (ES); total crystalloid infusion 3500 mL
Intraoperative 120th min	65/38	78	Adrenaline infusion added to vasopressor and inotropic therapy	Systolic blood pressure reached 100 mmHg; surgical team warned about possible termination	1500	2 units ES administered; total crystalloid infusion 5500 mL
Intraoperative 150th min	82/48	73	Norepinephrine 0.5 mcg/kg/min + adrenaline 0.5 mcg/kg/min + dopamine 20 mcg/kg/min	Surgery terminated	2100	Total 7100 mL crystalloid + 500 mL colloid + 2 units ES replacement

Due to refractory hypotension unattributable to hypovolemia, cardiac, or pulmonary causes, surgery was terminated at the 150th minute. Intraoperative troponin, D-dimer, and fibrinogen were sampled. The patient was transferred intubated to the intensive care unit (ICU) (blood gas data in Table 2).

Table 2. Arterial blood gas and laboratory parameters during the perioperative period.

Time point	pH	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	Hemoglobin (g/dL)	Hematocrit (%)	Lactate (mmol/L)	Potassium (mmol/L)	Sodium (mmol/L)	HCO_3^- (mmol/L)	Base deficit (mmol/L)
Operating room 15th min	7.38	32.2	97	14.1	42.3	0.5	4.0	136	21.4	-3.9
Operating room 60th min	7.30	31.3	95	13.3	39.9	2.5	3.2	139	20.6	-5.3
Operating room 120th min	7.28	28.0	88	10.2	30.6	5.2	3.5	144	17.4	-8.5
Postoperative 0th hour	7.19	35.9	93	10.5	31.5	8.4	3.8	144	13.8	-13.3
Postoperative 1st hour	7.12	39.0	112	10.3	31.9	12.3	4.0	142	9.5	-16.2
Postoperative 6th hour	7.27	38.0	108	10.6	31.8	10.1	4.1	140	15.7	-11.4
Postoperative 12th hour	7.38	32.3	96	11.1	33.3	4.5	3.6	139	19.8	-6.3
Postoperative 24th hour	7.40	32.0	91	10.4	31.2	2.2	3.5	140	20.7	-4.5
Postoperative 48th hour	7.38	34.0	94	10.5	31.5	0.8	3.6	139	21.0	-4.8
Postoperative 72nd hour	7.39	35.0	98	10.4	31.2	0.6	3.5	139	21.3	-4.5

Postoperatively, ECG, chest X-ray, complete blood count, biochemistry, intraoperative and postoperative troponin levels were all within normal limits. Echocardiography again showed normal valvular functions and EF 60%.

Severe hypotension persisted for six hours, requiring maximum vasoactive support. Further questioning of the family revealed the patient had taken his triple antihypertensive combination the night prior to surgery. Spontaneous eye opening occurred at postoperative hour 7. Following extubation at hour 18 under low-dose norepinephrine (0.2 mcg/kg/min), vasoactive support was discontinued by hour 36, allowing a stable transfer to the ward at hour 72.

3. Discussion

Intraoperative refractory hypotension is a potentially life-threatening condition associated with increased perioperative morbidity and mortality. Multiple perioperative factors including advanced age, diabetes mellitus, antihypertensive medications, anesthetic agents, patient positioning, blood loss, cardiac autonomic neuropathy (CAN) and vasoplegic mechanisms may contribute to impaired hemodynamic stability during general anesthesia [1].

In our case, hypovolemia was ruled out as the primary cause of refractory hypotension, which emerged following anesthesia induction and remained unresponsive to volume replacement. This assessment was further supported by PVI values ranging between 12% and 14%; as demonstrated by Çelikalp et al. [2] PVI-guided monitoring serves as a valuable tool for assessing fluid responsiveness and excluding significant hypovolemia during spinal surgery.

Pulmonary causes were excluded as oxygenation/ventilation and respiratory parameters remained stable. While the inability to perform intraoperative echocardiography due to the prone position was a limitation in our case, cardiac causes for the refractory hypotension were ruled out by normal preoperative echocardiography and the absence of ECG findings, which was subsequently confirmed by normal intraoperative troponin values and normal postoperative echocardiographic findings. Although the lack of BIS monitoring is a limitation, our routine practice of titrating both sevoflurane and remifentanil maintained a conservative anesthetic depth, rendering deep anesthesia an unlikely cause for the refractory hypotension. The study by Ryu et al. [3] showed that although sevoflurane may cause hypotension up to 1 MAC, it is generally not severe enough to become clinically intolerable. Cardiac autonomic neuropathy is a serious complication of diabetes mellitus, characterized by the impairment of cardiovascular autonomic control, with a literature-reported incidence ranging from 7.7% to 90% [4].

By compromising heart rate, cardiac output, and vascular function, this condition disrupts hemodynamic stability, rendering the response to both vasopressor and inotropic agents highly unpredictable due to postganglionic norepinephrine depletion and denervation supersensitivity [5]. Here, the coexistence of a 12-year history of diabetes mellitus and preoperative resting tachycardia (114 bpm) served as a strong clinical indicator for CAN. Although preoperative bisoprolol therapy masked this presentation by lowering the heart rate to 62 bpm immediately prior to anesthesia induction, which initially led us to attribute the absence of intraoperative reflex tachycardia to beta-blockade, CAN should remain a critical consideration in the differential diagnosis of refractory hypotension. Previous studies have demonstrated that diabetes mellitus, particularly when accompanied by CAN, increases susceptibility to post-induction hypotension due to impaired cardiovascular autonomic control and altered compensatory vasoconstrictive responses, typically manifesting within the first 15–20 minutes after induction [1]. Similarly, our patient developed relative hypotension following induction, demonstrated by a 24% decrease in blood pressure. Considering the increasing prevalence of diabetes, a routine, cost-effective CAN screening involving the evaluation of effort capacity, resting tachycardia, and bedside orthostatic hypotension may be highly valuable, although it should be noted that subclinical diabetic autonomic dysfunction can easily be overlooked preoperatively [6].

Prone positioning during spine surgery contributes to transient hypotension by inducing hemodynamic instability through a combination of positionally induced mechanical load and blunted autonomic reflexes. Specifically, abdominal and thoracic compression restricts venous return, elevates intrathoracic pressure, and impairs right ventricular filling, ultimately reducing preload, stroke volume, and cardiac index [7,8]. Although volume replacement was administered to counteract the potential hypotensive effects of prone positioning, the patient remained unresponsive, a failure that may be explained by CAN preventing the compensatory response. Consequently, we consider it unlikely that prone positioning alone could explain this presentation. Despite aggressive management with volume replacement, vasopressors, and inotropic therapies, the patient's refractory hypotension persisted for a catastrophic duration, and ultimately, the surgery had to be terminated early.

Crucially, we hypothesize that the prolonged pharmacological effect of the triple combination therapy administered the night before surgery was the primary driver that converted this suspected baseline vulnerability into an irreversible state, thereby contributing to the refractory vasoplegic shock. A possible contributing factor to refractory hypotension may have been the prolonged effects of the antihypertensive combination therapy, consisting of irbesartan, amlodipine, and a thiazide diuretic [9,10]. Angiotensin II receptor blockers (ARB), calcium channel blockers, and thiazide diuretics may independently decrease vascular tone through distinct pharmacological pathways. When used together, these agents may potentiate vasodilatory responses during anesthetic induction, leading to prolonged and refractory hypotension. Literature reports indicate that a 24-hour washout period may be insufficient to eliminate the effects of long-acting ARBs and calcium channel blockers, as their pharmacological effects can persist for several days [11,12]. Sica et al. [12] reported that the pharmacodynamic effects of azilsartan/chlorthalidone therapy may persist beyond 24 hours, using a 1–2-week washout period to minimize residual antihypertensive activity.

Similarly, Lee et al. [11] demonstrated that refractory intraoperative hypotension developed despite 48-hour discontinuation of azilsartan but did not recur after extending the washout period to 96 hours. Consistent with these findings, refractory hypotension has also been reported with telmisartan despite 24-hour discontinuation, while Hojo et al. [13] showed that long half-life ARB and Angiotensin-Converting enzyme inhibitor (ACE-I) agents are associated with a significantly higher risk of induction-related hypotension compared with shorter-acting agents.

The patient's metabolic profile reflects the severity of this pharmacologically induced vasoplegia (Table 2). Hypoperfusion-induced lactic acidosis, compounded by high-dose adrenaline, blunted vasoactive responsiveness to create a dangerous vicious cycle. However, the complete normalization of metabolic parameters and lactate clearance by postoperative hour 24 closely corresponded to the gradual resolution of vasoplegia under norepinephrine support, confirming that this metabolic collapse was entirely secondary to prolonged cardiovascular paralysis.

4. Conclusions

In conclusion, this case highlights that while diabetic cardiac autonomic neuropathy (CAN) and prone positioning create a vulnerable baseline for hemodynamic instability, long-acting triple combination antihypertensive therapy acts as the definitive driver for severe, refractory vasoplegic shock. Concomitant use of RAS inhibitors, calcium channel blockers, and thiazide diuretics can severely impair compensatory vasoconstriction and blunt vasopressor responsiveness under general anesthesia. Although the optimal approach to perioperative RAS inhibitor use remains uncertain, our findings demonstrate that a standard 24-hour discontinuation period is insufficient. Therefore, perioperative antihypertensive management must be strictly individualized based on drug half-lives, specific combined regimens, and patient-specific autonomic comorbidities.

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Conflict of Interest

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Data Availability

The datasets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author upon reasonable request.

AI Assistance

No AI-based tools were used in the preparation of this manuscript.

Ethics Approval and Consent to Participate

Informed consent form was obtained from the patient.

Author Contributions

Mehmet Bulut: *conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, supervision, validation, visualization, writing – original draft, writing – review & editing.*

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