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LACTIC ACIDOSIS FOLLOWING PROPOFOL ANESTHESIA: A CASE REPORT WITH LITERATURE REVIEW

Mehdi Nabil	Anesthesiology, Intensive Care Unit, Avicenna Military Hospital, Marrakech, Morocco. Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco
Said Khallikane*	Anesthesiology service, Cardiothoracic anesthesiology, Avicenna Military Hospital, Marrakech, Morocco. Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco *Corresponding Author
Bassam Bencharfa	Anesthesiology, Intensive Care Unit, Avicenna Military Hospital, Marrakech, Morocco. Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco
Ayoub Bouchama	Anesthesiology, Intensive Care Unit, Avicenna Military Hospital, Marrakech, Morocco. Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco
Mehdi didi	Anesthesiology, Intensive Care Unit, Avicenna Military Hospital, Marrakech, Morocco. Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco
Youssef Qamouss	Head of Department of Anesthesiology-ICU- Emergency Avicenna Military Hospital, Marrakech, Morocco. Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco

ABSTRACT The "Propofol-related Infusion Syndrome" (PRIS), first proposed in the early 1990 and clearly defined in 1998, is a rare clinical entity described in critical care settings. The complete form of PRIS includes hyperlactatemia, cardiac failure, and rhabdomyolysis. Elevated lactate levels during propofol anesthesia have been reported, potentially indicating early forms of PRIS. We present a case of early-onset lactic acidosis related to propofol during neurosurgery in a 13-year-old child with no notable medical history. The outcome was favorable after discontinuation of propofol.

KEYWORDS : lactic acidosis, propofol, anesthesia, infusion, syndrome.

INTRODUCTION

Propofol is widely used in healthcare settings, both for induction and maintenance in anesthesia and for sedation in mechanically ventilated patients. Its pharmacodynamic properties make it an agent of choice for neuroanesthesia.(1) PRIS is a rare clinical syndrome described since the early 1990s, characterized by metabolic acidosis with elevated lactate levels, rhabdomyolysis, and cardiac arrhythmias that may progress to asystole.(2) It is typically reported in critical care following prolonged, high-dose propofol administration. PRIS may also present as more heterogeneous entities, such as unexplained metabolic acidosis associated with continuous propofol infusion. Recently, cases of lactic acidosis occurring during propofol anesthesia have been described, which may represent early forms of PRIS. Here, we report a new case of early hyperlactatemia following propofol neuroanesthesia.

Case Observation

A 13-year-old child weighing 30 kg was admitted for endoscopic ventriculocisternostomy due to a pineal region tumor under general anesthesia. Pre-anesthetic evaluation revealed signs of increased intracranial pressure, including projectile vomiting, gait disturbances, and visual disturbances. Routine laboratory tests were unremarkable. The patient received preoperative corticosteroid therapy at a dose of 1.5 mg/kg for 5 days for edema management.

The anesthetic setup included two peripheral venous lines, urinary catheter placement, and monitoring of arterial blood pressure, SpO2, and ST segment. Rapid sequence induction involved 3 mg/kg of propofol, 3 µg/kg of fentanyl, and 1 mg/kg of rocuronium, followed by orotracheal intubation and controlled ventilation (air/oxygen mix). The patient received 2 mg/kg of solumedrol, 0.5 g/kg of 10% mannitol, and 1 g of cefazolin for antibiotic prophylaxis. Anesthesia was maintained with continuous propofol infusion at 10 mg/kg/h for 1 hour, then increased to 15 mg/kg/h, alongside 1.5 µg/kg of fentanyl. Perioperative hydration included 0.9% saline at 10 ml/kg/h, 5% dextrose at 10 ml/kg/h, with additional NaCl, KCl, and calcium supplementation (totaling 1000 cc). Hemodynamic status remained stable throughout the procedure, with a mean arterial pressure between 80 and 100 mmHg and negligible blood loss.

Extubation occurred 20 minutes after the procedure (total anesthesia duration: 2 hours, with normal clinical examination). An arterial blood gas analysis conducted 1 hour postoperatively revealed hyperlactatemia at 7.8 mmol/l, with a normal pH of 7.41 and HCO3- at 12. A second arterial blood gas analysis 2 hours later in the ICU showed a decrease in lactate to 4.2 mmol/l, and subsequently to 0.9 mmol/l at 12 hours postoperatively (Table 1). The remainder of the biological tests was unremarkable (Table 2). The total dose of propofol administered was 750 mg, averaging 12.5 mg/kg/h. No investigations for mitochondrial disorders were performed in this patient.

Table 1: Evolution of Blood Gas Parameters Postoperatively

Time	pH	Lactates	HCO3-	PaCO2	Base Excess
H1	7.41	7.8	12	30	-10
H3	7.39	4.2	22	32	-5
H12	7.36	0.9	25	35	1

Table 2: Postoperative Biological Assessment

Arrhythmias	Heart Failure	Metabolic Disorders
Asystole. Bradycardia. Pulseless electrical activity. Tachyarhythmias	Hypotension Weakness, Oliguria, anuria, Urine discoloration. Left ventricular dysfunction.	Muscle disorders/ rhabdomyolysis Acute renal failure. Respiratory failure. Dyspnea. Fever

DISCUSSION

We report a rare case of hyperlactatemia occurring during propofol neuroanesthesia in a previously healthy child. Exclusion of other etiologies (absence of underlying metabolic disorders, no hemorrhagic or hemodynamic events during surgery, and no medications that could

induce lactic acidosis) suggests a diagnosis of propofol infusion syndrome, with significant maintenance dosing potentially contributing as a risk factor.

In 1998, Bray defined PRIS after reviewing cases of children and adults in critical care(3). The classic form includes lactic acidosis, rhabdomyolysis, and cardiac failure. PRIS can arise in diverse situations, including neurocritical care for traumatic brain injury, ARDS, or sepsis, typically presenting after propofol infusion durations ranging from 42 to 96 hours.(4)

Table 3: Biochemical Characteristics of PRIS(5)

Parameter	Value
Urea (mmol/l)	3.58
Creatinine (µmol/l)	49
ASAT (U/l)	27
ALAT (U/l)	16
GGT (U/l)	30
PAL (U/l)	420
Total Cholesterol (g/l)	1.41
Triglycerides (g/l)	0.35
CK (U/l)	64
LDH (U/l)	203
Troponins (ng/l)	2
Chlorides	98

Table 4: Clinical Characteristics of PRIS

Metabolic Disorders	Muscular Disorders/ Rhabdomyolysis	Acute Kidney Injury
Hyperkalemia Hypocalcemia Lactic Acidosis Hyperlipidemia	Elevated CK Myoglobinuria Elevated troponins	Increased urea, Increased creatinine

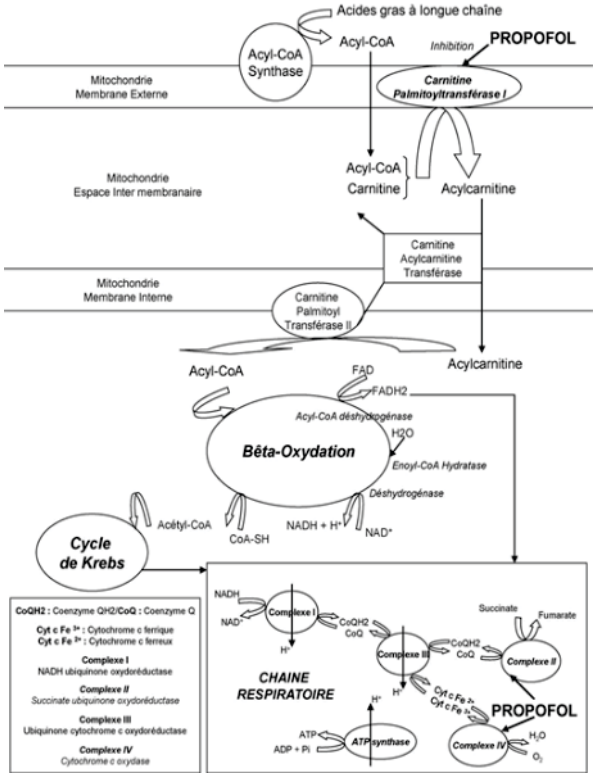
The administration of corticosteroids and catecholamines appears to be a risk factor associated with the occurrence of Propofol Infusion Syndrome (PRIS). In the field of anesthesia, the literature on the toxicity of propofol remains limited, with reported cases being sporadic. The circumstances of these cases have varied, including neuro-surgery, cardiac surgery, and urological procedures. A common feature among reported cases in anesthesia is the early onset of lactic acidosis, occurring between 3 to 6 hours after administration, with average doses of propofol ranging from 2.68 to 99 mg/kg/h. Diagnosis is often incidental, identified through routine blood gas analyses.(6)

One report noted tachycardia (100-110 bpm) preceding the onset of lactic acidosis, while another described rhabdomyolysis and acute kidney injury that evolved favorably.

The exact pathophysiology of PRIS is not well understood and remains widely debated. In vitro studies suggest that propofol can impair oxidative capacities in isolated liver mitochondria,(7) disrupting oxidative phosphorylation and energy production by increasing mitochondrial membrane permeability to protons.(8) It primarily inhibits Complex I and Complex II of the respiratory chain, contributing to reduced oxygen consumption and ATP synthesis.(9)

Furthermore, the effects of propofol on mitochondria are partly responsible for the clinical toxicity seen in patients with PRIS. Propofol significantly disrupts the transport and mitochondrial metabolism of fatty acids, leading to their accumulation and the buildup of intermediate metabolites. The lipid solvent in propofol elevates free fatty acid concentrations, which can promote ventricular arrhythmias and sudden cardiac death in the context of myocardial ischemia. Ultimately, the impairment of mitochondrial energy metabolism is a major contributor to cardiac failure and rhabdomyolysis, resulting in metabolic acidosis and acute kidney injury.(10)

In the case we report, the diagnosis of lactic acidosis was supported by several factors. First, there were risk factors associated with the development of PRIS, including corticosteroid therapy and the administration of propofol at a dose greater than 5 mg/kg/h. Furthermore, differential diagnoses were ruled out: hyperchloremic acidosis was excluded due to a high anion gap, especially considering the use of isotonic saline for perioperative rehydration. The possibility of acute renal failure was also dismissed, as urine output remained preserved and blood urea and creatinine levels were normal. Tissue hypoperfusion as a cause of hyperlactatemia was not supported by the absence of hemorrhagic events, hemodynamic instability, or pre-anesthetic hypoxia. Additionally, the lack of clinical and biochemical signs of liver failure indicated that there was no lactate excretion disorder. Finally, the decrease in blood lactate levels following the cessation of propofol infusion further supported the diagnosis.



Physiopathology of PRIS (11)

This clinical case is one of the few documented instances of hyperlactatemia due to propofol infusion occurring very early (approximately 2 hours into the infusion). In fact, a publication by Haase et al.(11) also reported lactic acidosis occurring 1 hour after propofol administration in a child in the postoperative period following surgery for craniosynostosis. Another case involving a 66-year-old adult during neuro-surgery for glioblastoma described hyperlactatemia occurring within less than 1 hour, as noted by Bordes et al.(12) In this case, hyperlactatemia was observed during the surgical procedure, and the outcome improved upon stopping the infusion. Salengros et al.(13) also reported hyperlactatemia at the fourth hour of propofol infusion (with normal lactate levels at the third hour). Previous adult cases reported are either later in onset or less documented, but events such as bleeding or rhythm disturbances requiring vasoactive drugs or electrical cardioversion raise questions about the responsibility of propofol.

There are also reports of early hyperlactatemia (<48 hours) associated with propofol in intensive care settings.(14-18) Some studies suggest that isolated lactic acidosis could be an early indicator of PRIS in both children and adults. At this stage, discontinuing propofol typically leads to a resolution of acidosis and a favorable outcome. In later stages, if propofol is not stopped, signs of multi-organ failure can develop, often leading to a fatal outcome. It is noteworthy that nearly all reported cases, whether in anesthesia or intensive care, share common risk factors, including the use of catecholamines and corticosteroids, along with propofol doses exceeding 5 mg/kg.

The observation of such cases advocates for more cautious use of propofol in anesthesia, particularly during maintenance. Prescribed doses should be minimized, and concentration-targeted delivery systems (AIVOC) should be employed, potentially alongside monitoring of anesthetic depth. Monitoring lactate levels through arterial blood gas analysis should be considered. Additionally, the presence of mitochondrial disease should prompt increased caution when using this agent, as some authors regard it as a predisposing factor. Finally, the discontinuation of propofol should be considered if hyperlactatemia occurs without an obvious cause.

Table 5: Key Cases of Metabolic Acidosis Reported in Anesthesia

Reference	Age	Inter-vention	Aver-age Propo-fol Dose (mg/kg/h)	Time to On-set of Metabolic Acidosis	Associated Signs	Treatment	Out-come
Observation	13	Ventriculocister nostomy	12.5	1 hour	Cortico-steroids, Tachycardia	Cessation of propofol	Favor-able
J. Bordes et al.(14)	66	Glioblastoma Excision	6.89	1 hour	-	Reduced doses	Favor-able
Liolios et al.(15)	42	Excision of Cavernous Angioma of Brainstem	9	3 hours	Cortico-steroids, Rhabdomyolysis, Renal Failure	Cessation of propofol	Favor-able
Salengros et al.(16)	64	Prostatectomy	7.8	4 hours	Tachycardia	Cessation of propofol	Favor-able
Burow et al.(17)	31	Radiofrequency Ablation	4.98	6 hours 35 minutes	-	Cessation of propofol	Favor-able
Hermanns(18)	16	Surgery for Scoliosis	9.1	ND	Catecholamines, Tachycardia, Hypotension, Rhabdomyolysis	Cessation of propofol; resuscitation (atropine, orciprenaline, fluids)	ND
Chukwemeka et al.(19)	45	Coronary Bypass	2.64	ND	Arrhythmias (VT, ST segment elevation, hypotension)	Catecholamines, Corticosteroids; Cessation of propofol, Cardioversion, Amiodarone, Fluids, Bicarbonates	Favor-able

CONCLUSION

PRIS (Propofol Infusion Syndrome) is a recently recognized clinical entity, traditionally described in intensive care settings but also reported in anesthesia. Our observation, along with existing medical literature, indicates that the onset of hyperlactatemia may be an early warning sign of its occurrence. Despite its widespread use, propofol should be administered with caution during maintenance, and anesthesia consultations should assess for risk factors associated with PRIS, particularly mitochondrial disorders. Larger studies are needed to determine the incidence of this syndrome in anesthesia and its relationship with mitochondrial disease.

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