Propofol Infusion Syndrome Associated with Short-Term Large-Dose Infusion During Surgical Anesthesia in an Adult

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In this case report we describe a case of propofol infusion syndrome in an adult after a short-term infusion of large-dose propofol during a neurosurgical procedure. Large-dose propofol (9 mg · kg^{-1} · h^{-1}) was given for only 3 h during surgery and was followed by a small-dose infusion (2.3 mg · kg^{-1} · h^{-1}) for 20 h postoperatively. The patient had also received large doses of methylprednisolone. He developed a marked lactic acidosis with mild biological signs of renal impairment and rhabdomyolysis but no cardiocirculatory failure. There were no other evident causes of lactic acidosis as documented by laboratory data. We believe this is the first report of reversible lactic acidosis associated with a short duration of large-dose propofol anesthesia.

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Propofol infusion syndrome (PRIS) is reported with an increasing frequency in adults (1,2). As the pathophysiology remains poorly understood, accurate documentation of new cases is essential (3). This report describes a case of reversible lactic acidosis in an adult after short-term propofol infusion of doses larger than 5 mg · kg^{-1} · h^{-1}. Consecutive determinations of blood lactate and electrolytes allowed a better interpretation of propofol-associated metabolic acidosis.

Case Report

A 42-yr-old man (77 kg weight) without a medical history underwent elective surgery for a brainstem cavernous angioma. Preoperative routine laboratory investigation was normal. Anesthesia and surgery were uneventful. Anesthesia was achieved by the administration of sevoflurane. Propofol was added as required to achieve adequate anesthesia as dictated by intraoperative neuromonitoring (somatosensory evoked potentials). Propofol was initially infused at a rate of 400 mg/h (5.2 mg · kg^{-1} · h^{-1}). A first arterial blood gas analysis, including lactate levels obtained 1 h later, was normal. After 90 min, propofol infusion was increased to 700 mg/h (9 mg · kg^{-1} · h^{-1}) for a period of 3 h to achieve adequate anesthesia and was then tapered down to 180 mg/h (2.3 mg · kg^{-1} · h^{-1}) at the end of surgery. Surgery lasted for 7.5 h. IV fluid therapy during the procedure included 1 L 0.9% NaCl and 2 L hydroxyethyl starch, 6%. Arterial blood gas values at the end of the rapid propofol infusion rate were normal but there was an increasing lactate level (3.4 mmol/L) (Table 1). No hypothermia was observed during the procedure and the minimal rectal temperature during the procedure was 36.4°C. Two episodes of moderate hypertension were noted (systolic blood pressure, 160 mm Hg) and were treated by small doses of urapidil and clonidine. The patient was also given methylprednisolone (30 mg/kg initially and 5.4 mg · kg^{-1} · h^{-1} for 23 h thereafter) at the end of surgery because there was suspicion of spinal cord injury during surgery as judged by the evoked potentials, which revealed worsening of somatosensory conduction. He was then transferred to the intensive care unit (ICU) for postoperative management. Admission and follow-up blood gas analysis and other laboratory data appear in Table 1. Lactic acidosis progressed without evidence of hemodynamic instability, tissue hypoxia or severe inflammation (C-reactive protein 0.9 mg/L). Nine hours after starting propofol infusion, lactate levels reached a plateau of approximately 6.0 mmol/L with an isolated spike of 10.8 mmol/L at 13 h after the beginning of the infusion (normal lactate levels, <1.3 mmol/L). Serum chloride remained near baseline values and the anion gap progressively increased in parallel with the increasing serum lactate values. Laboratory results 10 h after the end of the procedure revealed creatinine kinase 3384 IU/L (MM isoenzyme) (normal, <400 IU/L; admission value, 389 IU/L; peaked at 3480 IU/L 44 h after the procedure, decreased to 1303 IU/L 48 h after propofol was stopped), serum creatinine 1.6 mg/dL (normal, <1.4 mg/dL; admission value, 1.30 mg/dL), and normal blood glucose. Serum potassium concentration remained within normal range. Urinary output was adequate

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Table 1. Laboratory Data in the Operating Room and Intensive Care Unit

	OR Jan 6 10:33	OR Jan 6 14:30	ICU Jan 6 16:49	ICU Jan 6 19:22	ICU Jan 6 21:05	ICU Jan 7 0:50	ICU Jan 7 6:40	ICU Jan 7 13:10	ICU Jan 7 18:37	ICU Jan 8 1:18
Delay after the start of propofol infusion	1 h after infusion	3 h	7 h	10 h	22 h	15 h	21 h	28 h	33 h	38 h
Propofol ($mg/kg \cdot h^{-1}$)	5.2	9	2.3	2.3	2.3	2.3	2.3	–	–	–
pH	7.44	7.42	7.36	7.50	7.50	7.29	7.33	7.35	7.41	7.41
$Paco_2$ (mm Hg)	39	37	40	24	26	29	34	33	31	35
HCO_3^- (mmol/L)	26	24	22	18	20	13	18	18	19	22
Lactate (mmol/L)	1.8	3.4	4.4	6.1		10.8	5.5	5.7	4.2	2.4
Base excess (mmol/L)	2	0	−2	−3	−2	−11	−7	−6	−4	−2
Creatinine kinase (IU/L)						3384	3470			
Na^+ (mmol/L)	137	135	137	134		137	140	139	140	141
K^+ (mmol/L)	4.0	3.7	3.7	3.5		4.2	4.0	3.6	4.1	4.2
Cl^- (mmol/L)	103	104	104	104		104	104	104	104	104
Anion gap (mmol/L)	12	11	15	18		24	22	21	21	19

throughout the patient's course. Myoglobinuria was detected once but ketonuria was absent. Propofol infusion was continued after ICU admission at rates shown in Table 1. Propofol was stopped 21 h after admission. After stopping propofol, serum creatinine returned to preoperative values within 24 h and arterial lactate completely normalized after 48 h. Electrocardiogram was normal throughout the patient's stay. The patient recovered uneventfully from his surgery.

Discussion

Initially observed in children, PRIS was subsequently described in adults (1–9). The syndrome consists of cardiac failure, rhabdomyolysis, severe metabolic acidosis, and renal failure (5,6). The adults were mostly patients with acute neurological illnesses or acute inflammatory diseases with or without sepsis. Most patients received catecholamines and steroids (5). Impaired fatty acid oxidation at the level of the mitochondria, antagonism of β-receptors, and impaired myocardial oxygen use are plausible mechanisms of this syndrome (5,10). Although prolonged large-dose propofol infusions are typically required to produce the syndrome, readministration of regular doses of propofol has been associated with the death of a 3-year old patient when a large-dose infusion was initially administered (11).

Our patient had a neurosurgical intervention and received steroids. Large-dose propofol was given for <3 hours, followed by a small-dose infusion for 20 hours postoperatively. He developed lactic acidosis, increased levels of creatinine kinase consistent with rhabdomyolysis, and laboratory evidence of mild renal function impairment, all probably as a result of PRIS. Although he did not receive vasopressors, he developed intraoperative hypertension, in all probability as a result of catecholamine surge. Even though lactic acidosis is commonly a result of hypoperfusion and anaerobic glycolysis in the critically ill patient, our patient had no signs of organ hypoperfusion. Lactate levels remained increased during propofol infusion and returned to normal 48 hours after propofol was stopped. Furthermore, ketoacidosis and hyperchloremic acidosis were excluded. Additionally, the patient developed laboratory evidence of rhabdomyolysis and renal impairment without any clear precipitating factors other than propofol infusion. Furthermore, he rapidly improved and the laboratory values returned to normal after propofol was withdrawn.

Although PRIS has been defined as a highly lethal clinical syndrome of cardiac and metabolic failure occurring after large cumulative doses of propofol, we believe that the observed unexplained metabolic acidosis in our case represents an episode of early PRIS. Our patient received short-term (<3 hours) large-dose propofol infusion without the concurrent administration of vasopressors. This is among the shortest large-dose propofol infusions associated with the syndrome. Current recommendations suggest caution when using prolonged (>48 hours) propofol sedation at doses larger than 5 $mg \cdot kg^{-1} \cdot h^{-1}$ (5). Marinella et al.(12) have described PRIS developing in an adult after 12 hours and Koch et al.(13) after a 6-hour large-dose infusion in a child. Propofol dose, bicarbonate level, and lactate level shortly before propofol infusion were not provided in the adult case. Furthermore, the adult patient was experiencing an asthma attack with resultant respiratory failure that may have contributed to the observed increase in lactate. In their more recent reports, Salengros et al.(1) and Burow et al. (2) describe cases of PRIS in which large-dose propofol was administered to adults. In the first case, an average of 7.8 $mg \cdot kg^{-1} \cdot h^{-1}$ of propofol was administered over 4.5 hours intraoperatively (calculations based on the data provided in the report: 2500 mg of propofol infused over 4.5 hours to a 71-kg man). The patient received propofol postoperatively but the total dose and duration of propofol administration are unclear

(1). In the report by Burow et al.(2), a total of 4.98 $mg \cdot kg^{-1} \cdot h^{-1}$ of propofol was given for more than 6 hours. Although boluses and doses as large as 7.5 $mg \cdot kg^{-1} \cdot h^{-1}$ were given, the exact timing and duration are unclear (2).

Physicians using propofol for sedation should be aware of the potential occurrence of the syndrome even when large doses are used briefly. If a patient receiving propofol develops unexplained lactic acidosis, rhabdomyolysis, or renal failure, propofol infusion should be stopped and an alternative sedating drug should be considered, especially in the context of neurological injury when steroids are commonly used, as they may be considered as an additional triggering factor (5).

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