



A Mild Type Propofol Infusion Syndrome Presentation in Critical Care

Yoğun Bakımda Hafif Şiddetli Bir Propofol İnfüzyon Sendromu

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ABSTRACT

Propofol infusion syndrome (PRIS) is a rare but fatal disease. It was occurred mostly after high dose of propofol infusions for long times. Metabolic acidosis, hypotension, myoglobinuria, elevated muscle and liver enzymes, cardiac arrhythmias, cardiac arrest are common manifestations of the syndrome. This case report concluded a mild type of PRIS which was presented after low dose (25–50 mcg/kg/min) infusion for long time. In this case significant metabolic acidosis, hypotension and arrhythmias were not detected during drug infusion. Syndrome was manifested with only significantly elevated AST, ALT, CK, CKMB, LDH levels. Persistence of these findings during propofol infusion without patient's further clinical impairments defined as mild type of PRIS. In addition, the improvements in the biochemical parameters deteriorated after the drug was discontinued proved the validity of our diagnosis.

Key words: propofol; critical care; sedation

ÖZET

Propofol infüzyon sendromu (PRİS) nadir ama ölümcül bir hastalıktır. Bu sendrom çoğunlukla ilacın yüksek dozda uzun süreli infüzyonundan sonra oluşur. Metabolik asidoz, hipotansiyon, miyoglobinüri, artmış karaciğer ve kas enzimleri, kardiyak aritmiler ve kalp durması sendromun genel özellikleridir. Bu olgu sunumunda uzun süreli düşük doz (25–50 mcg/kg/dk) ilaç infüzyonundan sonra ortaya çıkan hafif tipte bir PRİS tartışılmıştır. Bu olguda ilaç infüzyonu esnasında ciddi metabolik asidoz, hipotansiyon yada aritmi gözlenmemiştir. Sadece AST, ALT, CK, CKMB, LDH düzeylerinde artış saptanmıştır. Propofol infüzyonu boyunca hastanın hiç klinik durumunda bozulma olmadan sadece bahsedilen parametrelerdeki bozukluğun devam etmesi olguyu hafif tipte bir PRİS olarak tanımlamamıza neden oldu. Ek olarak ilacın kesilmesi sonrası bozulan kimyasal parametrelerdeki düzelmeler teşhisimizin doğruluğunu da kanıtlamış oldu.

Anahtar kelimeler: propofol; yoğun bakım; sedasyon

Introduction

Propofol is a widely used anesthetic and sedative drug that with its safety profile in critical care. Minimal side effects, short half-life, minimum residual cognitive effects are the reason of the propofol selection. Frequently, propofol is used via intravenous infusion in critical care and long term infusion may cause a fatal complication named as propofol infusion syndrome (PRIS). Lactic acidosis, hypotension, myoglobinuria, rhabdomyolysis, cardiac arrhythmia and cardiovascular collars are the clinical findings of the syndrome¹. Even the exact therapy of the syndrome is unknown, early diagnosis may increase survival rate. We try to demonstrate an early diagnosed mild type PRIS in critical care.

Case Report

46 year old male patient was brought to the hospital for sudden loss of consciousness. His physical examination showed that his glasgow coma scale was 3E (patient was intubated in ambulance and mechanically ventilated), direct and consensual pupillary reflexes were negative, spontaneous breathing was weak and irregular. In history, there is none of systemic comorbidities and trauma. His blood pressure was 190/100 mmHg, pulse rate was 99/min, peripheral oxygen saturation was 94%. Cranial computed tomography (CT) demonstrated mesencephalic hemorrhage and significant brain edema. The patient was scheduled for external ventricular drainage system (EVD) placement. After surgery, patient was sedatized in critical care with midazolam infusion. In critical care, all vital signs (electrocardiogram, blood pressure, pulse rate, peripheral oxygen saturation, temperature) and

urine output were monitorized. Daily complete blood count, biochemical variables, arterial blood gases were measured (myoglobin levels could not be measured in our hospital). For significant brain edema, daily mannitol and dexamethasone therapy was initiated. Ceftriaxone is administered for postoperative antibiotic prophylaxis. Intravenous antihypertensive therapy was administered for brain perfusion protection. Intraarterial catheterization was applied for closed blood pressure monitorization. None of cerebral edema reduction was detected in control cranial CT in the third day of the hospitalization. Secondary of significant brain edema and resistant hypertension, propofol infusion was added to the therapy. The intravenous infusion was maintained between 25–50 mcg/kg/min. Patient was evaluated daily by neurosurgeons. Biochemical parameter analyses showed significant elevations in creatine kinase (CK), muscle band of creatine kinase (CKMB), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels at the second day of the propofol infusion. (CK=6524 IU/L, CKMB=73 U/L, LDH=584 IU/L, AST=311 U/L, ALT=109 U/L). Lactic acidosis or troponin level elevation was not demonstrated at this day. At the second day deep hypotension was not demonstrated and secondary to significant brain edema propofol infusion was continued. Similar clinical and laboratory findings were recorded in the third day of the infusion. At the fourth day of the infusion CK, CKMB, LDH, ALT, AST levels elevated more significantly (CK=11014 IU/L, CKMB=104 U/L, LDH=883 IU/L, ALT=214 U/L, AST=660 U/L). At the fourth day lactic acidosis or troponin level elevation was not demonstrated still. Hemodynamic variables were still stable. Secondary to these biochemical parameters' alteration, propofol infusion was terminated. The biochemical parameters started to decrease at the 24th hour of the infusion cessation. Five days after the infusion termination biochemical parameters reached almost baseline levels. Unchanged mesencephalic hematoma, slightly decreased brain edema was demonstrated by control cranial CT scans but none of clinically neurologic impairment was detected. Daily clinical and laboratory assessments continued. At the 19th day of the hospitalization, hypotension was occurred secondary to sepsis and dopamine, norepinephrine infusions were initiated. And at the 20th day of the hospitalization sudden cardiac arrest occurred and patient died.

Discussion

Several case reports were published about PRIS. In these reports; lactic acidosis, rhabdomyolysis, elevated liver enzymes, hypotension, fatal cardiac arrhythmias were most seen clinical presentations¹⁻⁵. Authors concluded that PRIS occurred after long term infusions (48 hours) and high drug doses (>4 mg/kg/h)⁶. In our case report patient received lower doses of propofol but infusion persisted for longer than mentioned above. Laboratory parameters' alteration started at the second day of the infusion as mentioned in literature but any clinical deterioration could not be observed. Hypotension or malignant arrhythmias were not observed. The clinical and hemodynamic stability encourage the clinicians to continue propofol infusion because there was still need to sedate the patient for significant brain edema. But significantly daily increasing liver enzymes, CK and CKMB alterations resulted the termination of propofol infusion at fourth day. The absence of the clinical impairment or lactic acidosis may be secondary to low doses of the drug. Authors concluded that clinicians must be aware of PRIS by following all these biochemical markers mentioned above and absence of lactic acidosis do not exclude PRIS. In this case report patients biochemical parameters were decreased to baseline values in a few days after the termination of the drug. But patient had a fatal disease like mesencephalic hemorrhage still and sepsis added to the process which caused the death of the patient.

In critical care to be male, younger than 18yr old, to receive vasopressor drugs, metabolic acidosis, rhabdomyolysis are the main mortality risk factors of PRIS⁶. Our case consists only one risk factor such being male during propofol infusion. Besides, our patient was collapsed thirteen days after propofol infusion termination. Authors concluded that not propofol infusion, intracranial pathology and sepsis were the reasons of the death. It was thought that propofol impaired mitochondrial respiratory chain reactions and energy production get insufficient especially in heart and muscle cells. These pathophysiology manifested with high AST, CK, CKMB, LDH levels and myoglobinuria like our case. The most important deficiency of our case report was not to demonstrate myoglobin levels secondary to hospital's laboratory limitations. The literature can not demonstrate exact therapy for the PRIS. Cessation of the drug infusion and supportive therapies were recommended⁷. In this case, these recommendations were applied and sufficed to get better laboratory findings with stable hemodynamic changes.

In conclusion, we want to emphasize that, clinicians must be aware of different degrees of PRIS like our case. PRIS may not be always manifest as its perfect definition which was defined above. Muscle enzymes' alterations alone may be the early signs of the syndrome. In these conditions; closed follow up, consideration of mortality risk factors and true timing for cessation of the drug infusion may increase survival.

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