CASE REPORT
https://doi.org/10.26432/1809-3019.2022.67.015

Propofol infusion syndrome in severe COVID: a case report

Síndrome da infusão de propofol em COVID grave: relato de caso

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ABSTRACT

Introduction: Propofol infusion syndrome (PIS) consists of symptoms at 48 h following the infusion of a dose ≥ 5 mg kg^{-1} h^{-1} and/or cumulative dose (CD) > 240 mg kg^{-1} of propofol. **Objective:** This study aimed to present the clinical observations and evolution of a patient with severe involvement by COVID-19 and who presented PIS after continuous infusion of propofol. **Case report:** Seven days after sedation with propofol at 2,857 mg kg^{-1} h^{-1} and CD of 480 mg kg^{-1}, a male patient diagnosed with SARS-CoV-2 presented with classic PIS signals. **Conclusion:** In the current context of the COVID-19 pandemic, PIS should always be considered in prolonged hospital stays, as should new sedation strategies.
Keywords: Propofol infusion syndrome, COVID-19, Propofol

RESUMO

Introdução: A Síndrome de infusão de propofol (SIP) consiste em sintomas que se iniciam após 48 h de infusão de dose ≥ 5 mg/kg/h e/ou dose acumulada (DA) > 240 mg kg^{-1} de propofol. **Objetivo:** Apresentar as observações clínicas e a evolução do paciente com acometimento grave pela COVID-19, o qual apresentou SIP após infusão contínua de propofol. **Relato de caso:** Um paciente do sexo masculino diagnosticado com SARS-COV-2 demonstrou, após sete dias de sedação com Propofol à mg kg^{-1} h^{-1} e DA de 480 mg kg^{-1}, sinais clássicos da SIP. **Conclusão:** No atual contexto da pandemia de COVID-19, a SIP deve sempre ser aventada em internações prolongadas e novas estratégias de sedação devem ser consideradas.
Palavras-chave: Síndrome da infusão de propofol, COVID-19, Propofol

INTRODUCTION

Propofol is a hypnotic drug launched on the market in 1977 that revolutionized anesthesiology regarding anesthetic induction, maintenance thereof, and sedation of patients receiving care in the intensive care unit (ICU)[1]. Its rapid onset of action as well as its short half-life have made this medication one of the most commonly used in anesthesia and intensive care[2].

Due to its wide use — and for increasingly longer periods of infusion — the first cases of propofol infusion syndrome (PIS) began to be reported in the 1990s[1]. PIS consists of a set of symptoms, the pathophysiology of which still remains poorly defined, and usually starts 48 h following the infusion of a dose ≥ 4–5 mg kg^{-1} h^{-1}. A cumulative dose (CD) > 240 mg kg^{-1} of propofol increases the risk of developing the syndrome in adults[2]. Even though it is a rare and potentially serious condition, most common in children, PIS also affects adults. The most common clinical and laboratory parameter changes are heart failure, cardiac dysrhythmias, metabolic acidosis, hyperkalemia, hypertriglyceridemia, hepatobiliary disorders, rhabdomyolysis, and acute renal failure[2].

Prevention is the best way to avoid this syndrome by avoiding overdoses. In addition, in established cases, immediate discontinuation of the medication infusion and treatment of hyperkalemia, acute renal failure, arrhythmias, and metabolic acidosis are essential[1-3].

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Article received: May 9, 2022. Article approved: August 10, 2022. Article published: October 19, 2022.
Responsible Editor: Prof. Dr. Eitan Naaman Berezin (Editor-in-Chief).

This case report aims to present the clinical observations and progression of a patient severely affected by COVID-19 and who presented with PIS 7 days into continuous infusion of propofol.

A CASE REPORT

A 68-year-old male patient, weighing 70 kg, without comorbidities, was admitted to the emergency department, screened by the respiratory ward with dyspnea, cough, tachypnea, use of accessory muscles, O_2 saturation of 84%, and mental confusion. COVID-19 was detected by an RT-PCR test. The patient progressed with respiratory failure and opted for orotracheal intubation.

He was transferred to the COVID-ICU, and sedation and analgesia were maintained for 7 days with propofol at 2,857 mg kg^{-1} h^{-1} (CD of 480 mg kg^{-1}) and midazolam at 1.42 mg kg^{-1} h^{-1} and fentanyl at 1.42 µg kg^{-1} h^{-1}, in addition to the administration of vasoactive medications, antibiotic therapy, and corticosteroids. The patient then progressed with fever, hyperkalemia refractory to pharmacological measures, and a mild acidosis, all of which were associated with an increase in the levels of liver enzymes and triglycerides, changes in renal function, and an increase in creatine phosphokinase (CPK). Given the suspicion of PIS, propofol infusion was discontinued at day 7 after sedation had started been administered, and hemodialysis was initiated from day 10 of hospital stay.

Computed tomography scans and radiographs of the thorax showed extensive ground-glass pattern opacities with foci of consolidation. An ultrasound scan of the abdomen showed a hyperdistended gallbladder, with mild wall edema, and contents corresponding to biliary sludge.

The patient progressed with clinical improvement and without the need for vasoactive drugs, in addition to a gradual reduction in potassium and CPK levels. On day 10 of hospitalization, 3 days after discontinuation of propofol, the patient presented with sustained tachycardia at 170 beats per minute and signs of hypoflux, requiring administration of adenosine and electrical cardioversion, with resolution of the condition. On day 15 of hospital stay, he suddenly had bradycardia and cardiorespiratory arrest with PEA, progressing to death despite the measures taken (Figure 1 and Table 1).

The study was approved by the Institutional Ethics Committees (CAAE: 55028521.0.0000.5479) of Irmandade da Santa Casa de Misericordia de São Paulo. Written informed consent was obtained from each subject following the principles of the Declaration of Helsinki.

DISCUSSION

PIS is a rare and very serious condition, with a frequency of 1.1% and a mortality rate of 48% in adults[2]. Its diagnosis is challenging due to the lack of guidelines on the syndrome and, in addition to that, patients commonly present with other severe illness-related conditions in an intensive care setting. Therefore, it is extremely important to evaluate preexisting clinical conditions and changes in laboratory parameters in patients receiving continuous propofol infusion, in order to allow for an early diagnosis and treatment of PIS effects[2].

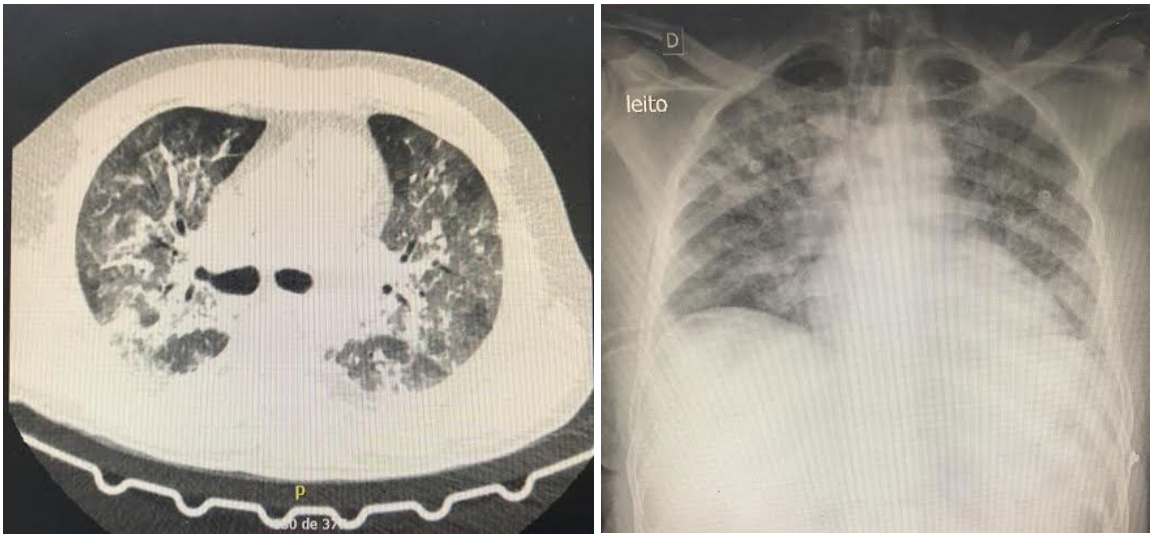

Figure 1 – Computed tomography scan and radiograph of the thorax indicating damage by SARS-CoV-2 infection. Brazil, 2021.

Table 1 – Daily evolution of laboratory tests values – patient. Brazil, 2021.

Tests	Admission	2	3	4	5	7	8*	9	11	13	14	15
Total bilirubin				1.9			6.8	6.4	7.3	4.2	3.1	5
AST					49		146	111	111	121	100	196
ALT					52		68	70	64	80	64	67
Gamma-GT					146		392	388				
Triglycerides							589			403		
Lactate	11.5	3.1	1.5	3	2.3	1.8	1.9	2	1.8	2.1	2.6	3.9
Potassium	4.5	3.8	7.1	7.4	6.4	6.8	6.5	6.8	5.1	5.6	5.7	5
pH	7.24	7.35	7.29	7.31	7.35	7.38	7.27	7.28	7.36	7.33	7.26	7.4
Amylase							140	219				
Creatine kinase							2,597	3,015	1,275	1,157	1,154	1,358
Creatinine	2.6	1.4	2.4	1.7	1.8	0.37	1.3	1.6	5.4	8.6	2.4	3.2
Urea	54	68	79	82	121	186	231	242	304	333	306	224
C-reactive protein	39.4		25.7	21.3	8.5	4.8	4.9	6.1	28.8	8.9	7.2	7.3

*Discontinuation of propofol.

In our report, the patient had severe pulmonary involvement due to confirmed SARS-CoV-2 infection, requiring orotracheal intubation and sedation. Sedation was performed with a continuous propofol infusion at 2,857 mg kg^{-1} h^{-1} and a CD of 480 mg kg^{-1}. Hemphill et al.[2], in their review of a number of cases, showed that doses greater than 5.1 mg kg^{-1} h^{-1} and/or with a CD > 240 mg kg^{-1} are predisposing factors for PIS in adults.

The safe propofol infusion dose for sedation of intensive care patients ranges from 1 to 4 mg kg^{-1} h^{-1}. However, fatal cases of PIS have been reported after infusion doses as low as 1.9–2.6 mg kg^{-1} h^{-1}, thereby giving rise to the hypothesis that genetic factors may play a key role in the etiology of this condition[4].

Bray et al.[1], in 1998, described the syndrome with the presence of bradycardia with progression to asystole, hyperlipidemia, hepatic alterations, metabolic acidosis, rhabdomyolysis, or myoglobinuria. In 2006, Schroeppel et al.[5] expanded its definition by adding acute kidney injury and dysrhythmias, data similar to the findings of this case report, in which the patient progressed with changes in renal and hepatobiliary function, increased CPK, dysrhythmia, hypertriglyceridemia, and metabolic acidosis, eventually dying due to bradycardia progressing to asystole.

Hemphill et al.[2] suggest that critically ill patients admitted to the ICU, especially those with brain comorbidities, are at a higher risk of developing the syndrome. In addition, accumulated dose of propofol is one of the main factors for developing PIS.

The use of corticosteroids has also been considered one of the main predisposing factors for developing PIS. Furthermore, the relationship between the use of vasopressors and the syndrome has been reported in the literature[2]. The patient in this report was receiving dexamethasone (0.14 mg kg^{-1}) and noradrenaline (1.8–25.6 µg kg^{-1}), thus confirming data previously published in the literature.

In the current context of the COVID-19 pandemic, in which the need for mechanical ventilation is imperative in some cases of acute respiratory failure, deeper sedation is used for better coupling, as well as minimizing ventilation-related lung injuries. Accordingly, PIS should be considered a possible complication in prolonged hospitalizations for SARS-CoV-2. Prevention is the best way to avoid the syndrome, and new sedation strategies should be considered alternatives.

ACKNOWLEDGMENT

The authors would like to thank the Service of Anesthesiology and Pain at Irmandade da Santa Casa de Misericórdia de São Paulo.

Funding: None.

Conflicts of interest: None.

Authors' contribution: Affonso Jonathan Moro: study design, patient recruitment, data collection, data analysis, interpretation of data, and writing the first draft of the article. **Mauro Prado da Silva, Ana Lígia Bittencourt Yamamura**: interpretation of data and revision of the article. **Thiago Ramos Grigio**: study design, data collection, data analysis, interpretation of data, and revision of the article.

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