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Case Report

Internal Medicine Section

Rare Presentation of Organophosphorus Poisoning Induced Diabetes Insipidus: A Case Report

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ABSTRACT

Organophosphorus Compounds (OPC) are widely used insecticides that pose significant health risks following intentional or accidental consumption. The effects of organophosphates on the central nervous system include irritability, restlessness, disorientation and confusion, which can progress to generalised seizures, status epilepticus and brain damage. Diabetes insipidus is a rare and unusual complication of organophosphorus poisoning. In this case study, a patient with organophosphate poisoning who was admitted to the Emergency Department (ED) with an alleged history of exposure to the OPC Chlorpyrifos 1.5% is presented. Upon admission, her Glasgow Coma Scale (GCS) score was 7/15 and she exhibited anisocoria (right pupil 4 mm and left pupil 2 mm) with sluggishly reacting pupils to light. She was immediately started on an atropine infusion, but later developed tachycardia and seizures, which were treated appropriately. Her electrolytes were abnormal, revealing hypernatremia (serum Na+ 182 mEq/L) and she was treated to reduce this condition. Additionally, the patient was monitored for urine output, which measured 250-350 mL/hr, with a serum osmolality of 379 mOsm/kg and a urine spot sodium of 243 mEq/L. Based on these findings, she was diagnosed with diabetes insipidus and started on desmopressin. However, her GCS showed no improvement and eventually decreased to 2T/15, indicating a poor prognosis. In conclusion, this case study suggests that diabetes insipidus is a rare transient complication of OPC poisoning. This idiosyncratic effect is uncommon and physicians should be aware of such complications and treat them accordingly.

Keywords: Atropine, Chlorpyrifos, Desmopressin, Hypernatremia, Organophosphorus compounds

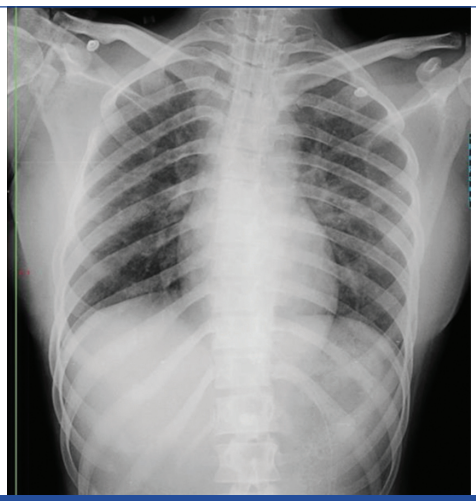
CASE REPORT

A 25-year-old female with a history of self-consumption of OPC (Chlorpyrifos 1.5%) at her residence, allegedly to commit suicide, was brought in an altered sensorium state by her parents to the ED within 24 hours. Initially, she was taken to a nearby hospital immediately after consumption, where she was treated with gastric lavage and activated charcoal. Therefore, the cardinal signs of increased urination or sweating were not present at the time of her arrival at the ED. An injection of atropine was given as a stat dose and she was then brought to our ED for further management. No significant family history or co-morbidities were elicited. There were no signs or symptoms of salivation, lacrimation, loose stools, vomiting, chest pain, palpitations, or breathlessness.

At the time of arrival, the patient was severely dehydrated, with a Blood Pressure (BP) of 110/70 mmHg, a pulse rate of 120 beats per minute, a respiratory rate of 43 cycles per minute and an oxygen saturation of 90% on room air. The GCS was 7/15 (GCS - E2V1M4) and her random blood sugar was 207 mg/dL. Consequently, two pints of Normal Saline (NS) were administered as a bolus to correct the dehydration.

On examination, anisocoria was present (right pupil 4 mm and left pupil 2 mm) and both pupils were sluggishly reacting to light. Hypotonia was observed in all four limbs, with a bilateral mute plantar reflex and power could not be assessed. Chest movements were normal and the Chest X-Ray (CXR) was clear [Table/Fig-1]. Cardiovascular and abdominal examinations showed no abnormalities.

Furthermore, the patient had an episode of involuntary movements in all four limbs, associated with up-rolling of the eyes. Baseline investigations [Table/Fig-2] revealed hypernatremia (serum Na+ 182 mEq/L) and due to severe dehydration, she was resuscitated with fluid bolus therapy. She received 5% dextrose at 150 mL/hr and half of NS at 150 mL/hr to reduce the sodium level and correct the dehydration. Urine osmolality was not performed due to the unavailability of the test.



[Table/Fig-1]: Chest X-Ray (CXR) of the patient- AP view of the CXR shows normal and clear fields.

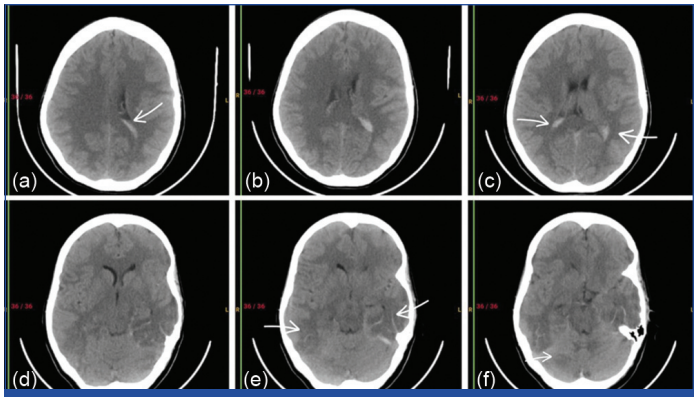
Test	Results (Day 1)	Normal range
Arterial blood gases (ABG)		
pH (mmHg)	7.02	7.38 to 7.42
pCO_2 (mmHg)	44	35-45
pO_2 (mmHg)	139	75-100
HCO_3 (mEq/L)	11.4	22-26
SO_2 (mmHg)	98	95-100
Complete blood profile		
Total counts (WBC) (cells/mm^3)	21300	4000-11000
Neutrophils (%)	80.3	40-75
Lymphocytes (%)	9.8	20-45
Eosinophils (%)	1.9	<6
Basophils (%)	0.8	<2
Monocytes (%)	7.2	2-10

Total RBC count (cells/mm^3)	5.63	3.8-4.8
PCV (%)	35.8	35.5 to 44.9
MCV (fL)	64.0	80-100
MCH (pg)	18.7	27-31
MCHC (%)	29.5	32-36
Haemoglobin (Hb) (g/dL)	10.6	12-16
RDW -CV (%)	21.3	11.5-14.5
Platelets (mm^3)	303000	150000-450000
Renal function test		
Blood urea (mg/dL)	21	6-24
Serum creatinine (mg/dL)	0.94	0.59 to 1.04
Liver function test		
Total protein (g/dL)	7.5	6-8.3
Albumin (A) (g/dL)	4.5	3.4 to 5.4
Globulin (G) (g/dL)	3.0	2.0 to 3.5
A/G ratio	1.5:1	1-2
Total bilirubin (mg/dL)	0.4	0.1 to 1.2
Direct bilirubin (mg/dL)	0.2	<0.3
Indirect bilirubin (mg/dL)	0.2	0.2 to 0.8
AST (SGOT) (U/L)	33	8 to 33
ALT (SGPT) (U/L)	17	4 to 36
Alkaline phosphatase (U/L)	56	44 to 147
Urine routine		
Reaction	Acidic	-
pH	6.0	-
Albumin and sugar	Nil and trace	-
Pus cells	3 – 5	-
Epithelial cells	2 – 4	-
RBC, casts, crystals,	Nil	-
Electrolytes		
Sodium (Na+) (mEq/L)	182	135 to 145
Potassium (K+) (mEq/L)	4.0	3.6 to 5.5
Chloride (Cl-) (mEq/L)	148	97 to 105
Calcium (mg/dL)	10.7	8.8 to 10.7
Magnesium (mg/dL)	2.9	1.5-3
Phosphorus (mg/dL)	1.5	1.8-2.3

[Table/Fig-2]: Laboratory investigations on admission day.
pH: Acid-base balance; pCO_2: Partial pressure of carbon dioxide; pO_2: Partial pressure of oxygen; HCO_3: Bicarbonate; SO_2: Sulfur dioxide; RBC: Red blood cells; PCV: Packed cell volume; MCV: Mean corpuscular volume; MCH: Mean corpuscular haemoglobin; MCHC: Mean corpuscular haemoglobin concentration; RDW-CV: Red blood cell distribution width; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase

After a few minutes, the patient experienced a seizure and was treated with intravenous lorazepam (2 mL stat). Following this, she was given intravenous Pralidoxime (PAM) (1 g in 250 mL NS over 20 min), atropine (0.6 mg i.v.), levetiracetam (500 mg BD i.v.) and pantoprazole (40 mg i.v. OD). Since there was no improvement in GCS (7/15) after fluid resuscitation, the patient underwent emergency intubation with a 7 mm endotracheal tube and was mechanically ventilated.

Her Arterial Blood Gases (ABG) were abnormal and are presented in [Table/Fig-2] along with other investigations. The ABG showed an HCO_3 level of 11.4 mEq/L and she received intravenous bicarbonate (100 mEq i.v. TDS). Following this, she underwent a Computed Tomography (CT) scan of the brain, which revealed Intraventricular Haemorrhage (IVH) in the bilateral occipital horns of the lateral ventricles and the body of the left lateral ventricle, as well as Subarachnoid Haemorrhage (SAH) in the sulcus spaces of the bilateral basi-temporal cortices. Ill-defined hypodensities were observed in the right cerebellum [Table/Fig-3].



[Table/Fig-3]: Computed tomography (CT) brain of the patient. Intraventricular haemorrhage in the bilateral occipital horn of lateral ventricle (white arrow in a) and body of left lateral ventricle (White arrow in c), SAH in the sulcus spaces of bilateral basi-temporal cortices. (White arrow in e).

A neurosurgical opinion was sought and an infusion of sodium bicarbonate at 20 mL/hr was prescribed, along with intravenous mannitol (100 mg i.v. stat). No other active neurosurgical interventions were performed. Due to her poor prognosis, she was shifted to the Intensive Care Unit (ICU).

On day 2, she experienced an episode of tachycardia (heart rate >182/min) along with hypotension. She also had severe metabolic acidosis with elevated lactate levels [Table/Fig-4]. Her SpO_2 was 99% while receiving 30% oxygen.

Test	Results (Day 2)
Arterial blood gases (ABG)	
pH (mmHg)	7.14
pCO_2 (mmHg)	49
pO_2 (mmHg)	102
HCO_3 (mEq/L)	16.7
SO_2 (mmHg)	96
Lactate (mmol/L)	4.4
Electrolytes – serial 1	
Sodium (Na+) (mEq/L)	159
Potassium (K+) (mEq/L)	3.6
Chloride (Cl-) (mEq/L)	132
Electrolytes – serial 2	
Sodium (Na+) (mEq/L)	157
Potassium (K+) (mEq/L)	4.3
Electrolytes – serial 3	
Sodium (Na+) (mEq/L)	158
Potassium (K+) (mEq/L)	4.2
Urine spot sodium (mEq/L)	243

[Table/Fig-4]: ABG and serial electrolytes on day 2.
pH: Acid-base balance; pCO_2: Partial pressure of carbon dioxide; pO_2: Partial pressure of oxygen; HCO_3: Bicarbonate; SO_2: Sulfur dioxide

Fluid resuscitation with half Normal Saline (NS) at 100 mL/hr, increased to 125 mL/hr, was initiated and 200 mL of free water was administered through a Ryle's tube. In light of her tachycardia, the administration of inj. Atropine was stopped and inj. Propofol 60 mg i.v. stat was given before taking her for an Electrocardiogram (ECG), which showed sinus tachycardia with a short PR interval and ST and T-wave abnormalities. A urine spot sodium test was sent. Her blood pressure dropped to 40/28 mmHg and she was started on inj. Noradrenaline at a rate of 0.5 µg/kg/min and inj. Vasopressin infusion at 2.4 mL/hr. Her blood pressure gradually improved and inj. Adrenaline infusion at 7.5 mL/hr was initiated. The patient was started on empirical antibiotics and cultures were sent, but no growth was found. Serial serum electrolytes were sent, showing a decrease in serum sodium. A repeat sodium measurement revealed a level of 176 mEq/L. A blood sample was sent to check the

cholinesterase level. Consequently, the patient was started on triple inotropic agents due to persistent hypotension. After resuscitation, her heart rate stabilised and the vasopressors were tapered down to a single agent.

Meanwhile, the patient was monitored for urine output, which ranged from 250-350 mL/hr, with a serum osmolality of 379 mOsm/kg and urine spot sodium of 243 mEq/L. Based on these findings, she was diagnosed with Diabetes Insipidus (DI) and treated with inj. Desmopressin. Subsequently, her urine output decreased to 100 mL and later to 75 mL/hr, after which the injection was stopped. Unfortunately, the patient succumbed despite the administration of triple inotropes, showing a poor prognosis with a reduced GCS score of 2T/15 (E1VTM1) and complications from an intracranial bleed. Due to her poor prognosis, the patient's family was counselled about the situation and they expressed their unwillingness to pursue further management due to financial constraints. Therefore, the patient was discharged Against Medical Advice (AMA).

DISCUSSION

In a country where agriculture is the predominant occupation, OPC, widely used as pesticides and insecticides, are commonly employed for suicidal purposes [1]. These substances present major health problems following intentional or accidental ingestion, inhalation, or skin absorption [1,2]. The incidence of OPC suicidal poisoning ranged from 10.3 to 43.8% in a survival study [3]. OPC is formed by the esterification of phosphoric acid and alcohol and is easily available as an over-the-counter poison [4]. OPC poisoning leads to various neurological manifestations.

When introduced into the body, OPC inhibits Acetylcholinesterase (AChE), resulting in an excess of the neurotransmitter Acetylcholine (ACh), which manifests as cholinergic toxidrome [2]. Its effects are observed on nicotinic and muscarinic receptors, as well as in the Central Nervous System (CNS), where symptom onset varies based on the specific compound, occurring within minutes and taking many weeks to resolve [2,5]. The level of toxicity depends on the amount ingested, the route of absorption and its toxicokinetics [6]. Neurological manifestations of OPC poisoning include confusion, agitation, coma and seizures, along with symptoms from nicotinic and muscarinic receptor actions such as weakness, fasciculations, cramps, paralysis, salivation, defecation, lacrimation, urination, emesis, hypotension and miosis, which occur within 24 hours [4,6]. Unfortunately, the neurological symptoms of OPC poisoning, as well as those of DI, can be similar [2,4,6,7], which may lead to misdiagnosis, as it is known that DI due to OPC poisoning is rare and not discussed in textbooks.

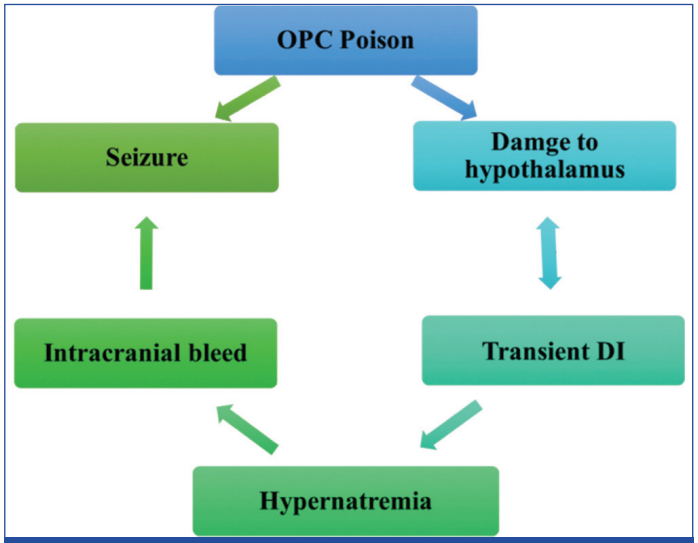
DI is rare, affecting roughly 0.004% of the global population [8]. It can be central, due to problems with the production of Antidiuretic Hormone (ADH or vasopressin) in the pituitary gland, or nephrogenic, due to a deficiency in or unresponsiveness to ADH, a main determinant of water homeostasis within the body [7,9]. This condition causes polyuria and polydipsia, along with hyposthenuria. ADH is released in response to plasma osmolality and circulating blood volume to maintain homeostasis by promoting water absorption at the collecting tubules [4]. To date, DI in OPC poisoning is a rare and unusual complication, with only a few reported cases in Nepal [4] resulting from diethyl compound ingestion and in Kuwait [10] due to malathion poisoning, a variant of OPC. Similarly, OPC poisoning resulting in diabetic ketoacidosis has been reported, but not DI [11]. However, this is the first case report of transient DI in India associated with Chlorpyrifos.

ADH is released in response to plasma osmolality and circulating blood volume to maintain homeostasis by absorbing water at the collecting tubules [4]. Most cases of central DI are idiopathic, but it may also occur due to tumours, infections, inflammatory disorders, granulomatous disorders, vascular issues, or toxins [7-9,12]. The sensation of intense thirst, which safeguards against severe hypernatremia in healthy individuals, may be absent or reduced in patients with altered mental status or hypothalamic lesions [7-9]. It has been shown that central DI can appear within 24 hours (acute) and may present for more than three weeks [6,9,12]. This condition can be diagnosed and confirmed by measuring urine and plasma osmolality, as well as urine output and serum sodium levels [9].

Furthermore, in present study, high urine spot sodium was observed, although this seems counterintuitive, as DI typically presents with normal or low urine sodium levels due to the body's inability to concentrate urine effectively [8,9,11]. In present case, the patient's high urine sodium can be explained by the unique pathophysiological effects of OPC poisoning, specifically with chlorpyrifos, which disrupts hypothalamic and pituitary functions. This disruption likely caused the unusual presentation of DI, influenced by severe hypernatremia (182 mEq/L) and dehydration, which affected the sodium levels in urine compared to typical DI cases [4,13].

In present case, the diagnosis of DI was confirmed primarily by high urine output, increased urine spot sodium and the fluctuation in serum sodium levels. Additionally, this case underscores the importance of recognising that OPC poisoning can lead to rare and complex presentations like transient DI, accompanied by unusual electrolyte patterns.

The mechanism of DI in OPC poisoning is still unclear. According to Keyal NK and Bhujel A, the possible mechanism involves damage to the hypothalamus and pituitary due to hypernatremia caused by OPC poisoning, leading to a transient decrease or absence of ADH production, which results in DI [4]. Furthermore, hypernatremia due to central DI can cause acute brain shrinkage, resulting in vascular rupture, cerebral bleeding and SAH, which can lead to neurological damage or death [7,8]. Moreover, the peak plasma concentration of chlorpyrifos occurs approximately six hours after oral ingestion, leading to the prominent symptoms that cause brain damage [1,2,14]. In present case, the predominant symptoms of seizures, tachycardia, electrolyte changes and altered urine osmolality began to appear approximately six hours after ingestion, with earlier neurological manifestations, which might explain the occurrence of DI. This damage to the hypothalamus coincided with the peak concentration of the toxin. The potential mechanism proposed in present study is illustrated in [Table/Fig-5].



[Table/Fig-5]: Proposed mechanism of OPC poisoning causing transient diabetes insipidus.

Additionally, OPC poisoning can lead to sinus tachycardia with abnormal ECG findings, including ST-T changes, prolonged PR interval and prolonged QT interval, along with hypotension [2,6]. Similarly, present case patient exhibited abnormal ECG findings with prominent tachycardia and hypotension and was managed with

a vasodilator injection of propofol. Despite the potential to cause hypotension, propofol is often used for intubation in hypotensive patients due to its rapid onset and quick recovery, which can be advantageous because it provides sedation and facilitates airway management with minimal haemodynamic disruption in some cases [15,16]. Moreover, it allows for a balanced approach to sedation and airway control when used alongside other medications that support blood pressure, although careful monitoring is warranted to mitigate the risks [15-18].

The primary treatment for OPC poisoning is atropine, which competes with acetylcholine at the muscarinic receptors [1-3,6]. In present case, atropine was administered and the patient responded with reduced symptoms; however, it failed to address other symptoms such as hypotension and CNS manifestations due to increased toxicity. The management of DI with desmopressin [7,12] also had minimal effect in this patient due to increased volume depletion. Thus, it is crucial to identify the cause of the symptoms and the appropriate management.

CONCLUSION(S)

OPC poisoning presenting with central DI is very rare. The diagnosis of DI is challenging because it relies on laboratory values, urine output and physical examination. Therefore, treating the toxicity and DI must be done simultaneously. It is crucial to suspect this idiosyncratic effect of DI in cases of OPC poisoning, as it is a rare complication. Clinicians should be aware of this and implement therapy as early as possible to prevent electrolyte disturbances and the associated mortality and morbidity. Additionally, undiagnosed hypernatremia might lead to intracranial bleeds, as seen in this patient; hence, a rigorous diagnosis must be conducted by clinicians.

REFERENCES

[1] Pandit V, Seshadri S, Rao SN, Samarasinghe C, Kumar A, Valsalan R. A case of organophosphate poisoning presenting with seizure and unavailable history of parenteral suicide attempt. J Emerg Trauma Shock. 2011;4:132-34. Doi: 10.4103/0974-2700.76825.

[2] Robb EL, Regina AC, Baker MB. Organophosphate Toxicity. StatPearls, Treasure Island (FL): StatPearls Publishing; 2023.

[3] Ahmed SM, Das B, Nadeem A, Samal RK. Survival pattern in patients with acute organophosphate poisoning on mechanical ventilation: A retrospective intensive care unit-based study in a tertiary care teaching hospital. Indian J Anaesth. 2014;58:11-17. Doi: 10.4103/0019-5049.126780.

[4] Keyal NK, Bhujel A. Transient diabetes insipidus following organophosphorus poisoning. J Crit Care Med. 2019;5:145-48. Doi: 10.2478/jccm-2019-0023.

[5] Dagg K, Irish S, Wiegand RE, Shililu J, Yewhalaw D, Messenger LA. Evaluation oftoxicity of clothianidin (neonicotinoid) and chlorfenapyr (pyrrole) insecticides and cross-resistance to other public health insecticides in Anopheles arabiensis from Ethiopia. Malar J. 2019;18:49. Doi: 10.1186/s12936-019-2685-2.

[6] Peter JV, Sudarsan T, Moran J. Clinical features of organophosphate poisoning: A review of different classification systems and approaches. Indian J Crit Care Med. 2014;18:735-45. Doi: 10.4103/0972-5229.144017.

[7] Hui C, Khan M, Khan Suheb MZ, Radbel JM. Diabetes Insipidus. StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.

[8] Christ-Crain M, Bichet DG, Fenske WK, Goldman MB, Rittig S, Verbalis JG, et al. Diabetes insipidus. Nat Rev Dis Primer. 2019;5:54. Doi: 10.1038/s41572-019-0103-2.

[9] Mutter CM, Smith T, Menze O, Zakharia M, Nguyen H. Diabetes insipidus: Pathogenesis, diagnosis, and clinical management. Cureus. 2021;13:e13523. Doi: 10.7759/cureus.13523.

[10] Abdul-Ghaffar NU. Transient diabetes insipidus complicating severe suicidal malathion poisoning. J Toxicol Clin Toxicol. 1997;35:221-23. Doi: 10.3109/15563659709001200.

[11] Swaminathan K, Sundaram M, Prakash P, Subbiah S. Diabetic ketoacidosis: An uncommon manifestation of pesticide poisoning. Diab Care. 2012;36(1):e4. Doi: 10.2337/dc12-1251.

[12] Saifan C, Nasr R, Mehta S, Sharma Acharya P, Perrera I, Faddoul G, et al. Diabetes insipidus: A challenging diagnosis with new drug therapies. ISRN Nephrol. 2013;2013:797620. Doi: 10.5402/2013/797620.

[13] Priya G, Kalra S, Dasgupta A, Grewal E. Diabetes insipidus: A pragmatic approach to management. Cureus. 2021;13:e12498. Doi: 10.7759/cureus.12498.

[14] Nolan RJ, Rick DL, Freshour NL, Saunders JH. Chlorpyrifos: Pharmacokinetics in human volunteers. Toxicol Appl Pharmacol. 1984;73:08-15. Doi: 10.1016/0041-008x(84)90046-2.

[15] Saugel B, Bebert EJ, Briesenick L, Hoppe P, Greiwe G, Yang D, et al. Mechanisms contributing to hypotension after anesthetic induction with sufentanil, propofol, and rocuronium: A prospective observational study. J Clin Monit Comput. 2021;36:341. Doi: 10.1007/s10877-021-00653-9.

[16] Folino TB, Muco E, Safadi AO, et al. Propofol. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430884/.

[17] Marler J, Howland R, Kimmons LA, Mohrien K, Vandigo JE, Jones GM. Safety of propofol when used for rapid sequence intubation in septic patients: A multicenter cohort study. Hosp Pharm. 2021;57:287. Doi: 10.1177/00185787211029547.

[18] Kakazu CZ, Lippmann M. Playing with fire: Debate about propofol-induced hypotension. BJA Br J Anaesth. 2015;114:164-65. Doi: 10.1093/bja/aeu425.

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