Case Report / Olgu Sunumu

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Green Urine: A Rare Adverse Effect of Propofol in Critically Ill Children

Yeşil İdrar: Kritik Hastalığı Olan Çocukta Propofolün Nadir Bir Yan Etkisi

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Abstract

Propofol is an intravenous agent commonly used for anesthesia induction, procedural interventions, and sedation in intensive care units due to its rapid onset and relatively safe profile. In this report, we present the case of a 12-year-old male patient with traumatic brain injury who developed green urine following propofol infusion for sedation. After excluding other potential causes of urine discoloration, the propofol infusion was discontinued at the 50th hour, and the urine color returned to normal within 5 hours. We aimed to highlight that green urine, which may be alarming for clinicians, is a benign side effect of propofol and does not impact renal function.

Keywords: Craniocerebral trauma, critical care, hypertonic solutions, phenols

Öz

Propofol, hızlı başlangıç ve nispeten güvenli profili nedeniyle anestezi indüksiyonu, prosedürel müdahaleler ve yoğun bakım ünitelerinde sedasyon için intravenöz olarak kullanılan bir ajandır. Bu yazıda, sedasyon için propofol infüzyonunu takiben yeşil idrar gelişen travmatik beyin hasarı olan 12 yaşında bir erkek hasta sunuldu. İdrar rengindeki değişimi yapabilecek diğer nedenler dışlandıktan sonra, propofol infüzyonu 50. saatinde propofol infuzyonu kesildi ve 5 saat sonra idrar rengi normale döndü. Klinisyenler için endişe verici olabilecek yeşil renkli idrarın aslında propofolün iyi huylu bir yan etkisi olduğunu ve böbrek fonksiyonlarını etkilemediğini vurgulamak istedik.

Anahtar Kelimeler: Kraniyoserebral travma, kritik bakım, hipertonik solüsyonlar, fenoller

Introduction

Propofol (2,6-diisopropylphenol) is an oil at room temperature with minimal solubility in water.[1] It is an intravenous agent widely used for induction of anesthesia, procedural sedation, and sedation in intensive care units (ICUs) due to its rapid onset and relatively safe profile.[2] The pharmacodynamics of propofol are characterized by its ability to enhance the inhibitory effects of the neurotransmitter gamma-aminobutyric acid (GABA) through GABA-A receptors.[3]

In adult ICUs, propofol infusions are favored for their ability to reduce cerebral blood flow, cerebral metabolism, and intracranial pressure.[4] Given its frequent use for sedation in adults, a rare side effect has been observed: green discoloration of urine.[5] The primary site of propofol metabolism is the liver, where a portion undergoes glucuronidation, rendering it water-soluble and allowing renal excretion. The remainder is metabolized via hepatic cytochrome P450 enzymes through oxidation, followed by sulfation, making it water-soluble.[6] The green discoloration of urine is thought to result from phenolic metabolites of propofol and is considered benign, with no adverse effects on renal function.[7] A meta-analysis identified 53 cases of propofol-induced green urine in the literature, of which only seven cases occurred in pediatric patients.[2]

With this case report, we aim to raise awareness of this rare and benign side effect of propofol infusion.

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Case Report

A 12-year-old male patient was admitted to our pediatric ICU (PICU) with a diagnosis of traumatic brain injury following a motor vehicle accident as a pedestrian. Computed tomography revealed a subdural effusion and cerebral edema in the right frontal region. As the patient did not meet surgical drainage criteria, we decided to proceed with medical management. No intra-abdominal solid organ injuries or extremity fractures were identified.

On physical examination, the patient's general condition was poor. Prior to endotracheal intubation, his Glasgow Coma scale (GCS) score was evaluated as 8, and his pupils were bilaterally reactive to light. Due to his response to painful stimuli only, irregular breathing, and a GCS score of 8, we administered intravenous remifentanil (1 mg/kg) and ketamine (1 mg/kg) for intubation. Skin examination revealed ecchymosis and abrasions consistent with friction injuries, while other system examinations were unremarkable.

For sedation and analgesia, continuous infusions of propofol (1 mg/kg/hour) and fentanyl (1 mcg/kg/hour) were initiated. The propofol infusion was later increased to 2 mg/kg/hour for ongoing management. Hyperosmolar therapy with 3% NaCl was started to manage cerebral edema. Body temperature was maintained between 35 and 37 °C, and prophylactic levetiracetam was initiated. At the 16th hour of the propofol infusion, the patient's urine turned dark green. Comprehensive evaluations, including complete blood count, liver function tests, urine microscopy, and culture, were performed, but no findings explained the urine discoloration. The only notable laboratory result was alkaline urine with a pH of 8 (Table 1, Figure 1).

As there were no signs of systemic inflammation during the PICU stay, antibiotic therapy was not initiated. Blood culture samples were collected within the first 24 hours of admission. Early enteral nutrition was deferred, and intravenous isotonic sodium-containing dextrose solutions were administered.

Given that no other cause for the urine discoloration was identified, the propofol infusion was discontinued at the 50th hour, and ketamine was initiated at 1 mg/kg/hour. Within 5 hours of stopping the propofol infusion, the urine color returned to normal (Figure 2).

On the fourth day of monitoring, sedation infusions were gradually tapered off, and the patient was extubated and transitioned to oxygen therapy via nasal cannula. The patient's urine color remained normal throughout the remainder of the PICU stay, and blood and urine cultures showed no growth. Informed consent was obtained from the patient's parents.

Discussion

Green urine is a rare yet concerning finding associated with propofol administration.[8] In the literature, the exact incidence of propofol-induced green urine has not been clearly defined.[9] Other causes of green urine include urinary tract infections caused by *Pseudomonas* species, Hartnup disease, methylene blue administration, and the use of medications such as amitriptyline, cimetidine, metoclopramide, and promethazine.[10-12]

Propofol is primarily metabolized in the liver, and its metabolites are subsequently excreted via the kidneys. Water-soluble quinol derivatives of propofol metabolites are thought to be the main cause of urine discoloration.[8] Although propofol-induced

Table 1. Laboratory findings at PICU admission, at the time of green urine discoloration, and prior to discharge

Parameter	At PICU admission	At the time of green urine discoloration	Prior to discharge
Urea (mg/dL)	22.3	12.2	21
Creatinine (mg/dL)	0.46	0.72	0.4
Alanine aminotransferase (U/L)	20	17	38
Aspartate aminotransferase (U/L)	47	39	45
Alkaline phosphatase (U/L)	220	205	133
Gamma-glutamyl transferase (U/L)	32	37	32
Creatine kinase (U/L)	300	500	425
Glucose (mg/dL)	80	116	92
Sodium (mmol/L)	136	148	138
Potassium (mmol/L)	4	3.8	3.6
Chloride (mmol/L)	102	113	108
Calcium (mg/dL)	9.8	9.2	10.4
Phosphorus (mg/dL)	5	5.3	4.6
Magnesium (mg/dL)	2.4	2.32	2.15
Total bilirubin (mg/dL)	0.31	0.3	0.33
Direct bilirubin (mg/dL)	0.21	0.2	0.1

Table 1. Continued

Parameter	At PICU admission	At the time of green urine discoloration	Prior to discharge
Uric acid (mg/dL)	3.9	2.2	2.4
Albumin (g/dL)	4.2	3.3	3.2
Venous blood gas			
pH	7.48	7.41	7.45
CO_2 (mmHg)	35	37.6	32
HCO_3 (mmol/L)	24	24.1	23
Lactate (mmol/L)	0.3	1	1.5
Hemoglobin (g/dL)	13.1	10.1	10
Urinalysis (microscopy and biochemistry)			
pH	–	8	–
Density	–	1.019	–
Leukocyte and erythrocyte (strip)	–	Negative	–
Bilirubin, urobilinogen	–	Absent	–
Ketone, protein, nitrite	–	Absent	–
Bacteria and yeast cells	–	Absent	–
Pathological casts and crystals	–	Absent	–

PICU: Pediatric intensive care units

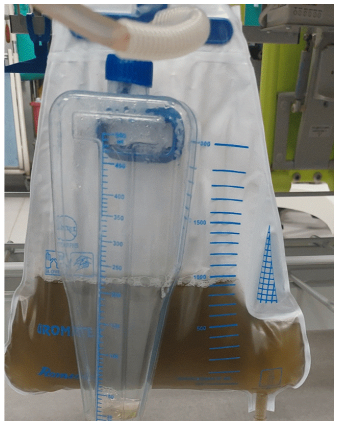

Figure 1. Dark green urine observed after propofol infusion green urine

Figure 2. Normal urine color restored 5 hours after discontinuation of the propofol infusion

may raise suspicion for serious conditions such as propofol-related infusion syndrome (PRIS), it is generally considered a benign side effect.[13] PRIS, associated with prolonged propofol infusions, is a rare but potentially fatal condition characterized by multiorgan failure. Its primary manifestations include cardiovascular dysfunction, metabolic acidosis, lactic acidosis, rhabdomyolysis, hyperkalemia, hyperlipidemia, hepatomegaly, and acute kidney injury.[14] In our case, the appearance of green urine was not accompanied by clinical deterioration or abnormalities in hematological and biochemical parameters. After ruling out other potential causes, we discontinued the propofol infusion, and the urine color returned to normal within a few hours.

According to a meta-analysis summarizing cases of urine discoloration associated with propofol infusion, only seven pediatric cases have been reported.[2] This is the first reported case of green urine discoloration linked to propofol infusion in a pediatric patient with traumatic brain injury. However, we identified a single similar case in the adult population. That case involved a 77-year-old patient who developed green urine during a propofol infusion while receiving hypothermia and hyperosmolar therapy in the ICU due to intracerebral hemorrhage. The authors of that report speculated that the observed condition might be associated with tubulopathy, a potential consequence of hypothermia treatment. However, they stated that no such association could be established in their patient.[15] Furthermore, it was emphasized that hypothermia treatment might increase the risk of tubular dysfunction and electrolyte imbalances, which could potentially combine with the effects of osmotic therapy to

exacerbate renal side effects. However, in the reported case, the patient's renal function remained normal, with stable levels of creatinine, urea, and arterial blood gas parameters. Similarly, in our case, renal function was within normal limits for the patient's age, and no evidence of tubulopathy was observed. The absence of renal dysfunction in both our case and the previously reported case challenges the explanation for this side effect of propofol.

The mechanism of propofol-induced urine discoloration described in the literature is thought to involve extrahepatic propofol glucuronidation because impaired hepatic enzyme function or decreased gastrointestinal motility leads to reduced hepatic glucuronidation.[6,12,16] However, in our case, there were no signs of decreased gastrointestinal motility (e.g., ileus, constipation, vomiting), and the patient's liver enzyme and bilirubin levels remained within normal ranges from admission to discharge.

There is currently no biomarker to predict which patients might develop green urine during propofol infusion. However, it has been suggested that the excretion of phenolic metabolites is enhanced in alkaline urine.[8,17] In our case, the absence of other findings to explain this side effect supports the hypothesis that alkaline urine facilitated the excretion of these metabolites, resulting in green urine.

Conclusion

We believe that propofol metabolites are responsible for the development of green urine and that alkaline urine, which can influence propofol metabolism, facilitate the emergence of this side effect. We aimed to emphasize that green urine, which may initially be alarming for clinicians, is actually a benign side effect of propofol and does not adversely affect renal function.

Ethics

Informed Consent: Informed consent was obtained from the patient's parents.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Ö., N.O.K., Concept: A.Ö., N.O.K., Ö.B., Design: A.Ö., N.O.K., Data Collection or Processing: A.Ö., Ö.B., S.M.I., M.E., Analysis or Interpretation: A.Ö., Ö.B., S.M.I., Literature Search: A.Ö., N.O.K., S.Y., M.E., Writing: A.Ö., N.O.K., S.Y.

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