



Green urine appearance in a patient with refractory status epilepticus due to propofol infusion

Green urine due to propofol

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Abstract

The color change in urine may result from various factors such as drugs, stains, foods, infections, metabolic diseases and structural abnormalities. When Status Epilepticus can not be controlled with the benzodiazepine and at least one antiepileptic drug treatments, it is defined as refractory status epilepticus. Propofol, which is a drug that may be used for the treatment of refractory status epilepticus. We present a 28-year-old male with refractory status epilepticus who experienced a color change in urine to green due to propofol infusion. Green urine discoloration is a benign and very rare side effect of propofol.

Keywords

Propofol; Green Urine; Status Epilepticus

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Introduction

Status Epilepticus (SE) is a neurological emergency with the incidence of 10-40/100.000 which has high morbidity and mortality [1]. When SE can not be controlled with the benzodiazepine and at least one antiepileptic drug treatments, it is defined as refractory status epilepticus (RSE).

The color change in urine may result from various factors such as drugs, stains, foods, infections, metabolic diseases and structural abnormalities [2]. Propofol, which is a drug that may be used for general anesthesia induction, sedation or treatment of RSE, may also turn the color of urine green. Here, we present a case with RSE who experienced a color change in urine to green due to propofol infusion.

Case Report

A 28-year-old male, who did not have any diseases except chronic epilepsy, admitted to the emergency room with recurrent epileptic seizures. He was taken to neurological intensive care unit with the diagnosis of SE. He was taking triple antiepileptic drugs (Valproic acid 1000mg/d (Depakin; Sanofi, Paris, France) Levetiracetam 2000mg/d (Keppra; UCB S.A., Brussels, Belgium), and oxcarbazepine 600 mg/d (Trileptal; Novartis, Basel, Switzerland)) before admitting to the emergency room. Physical examination revealed that heartbeat was 112 bpm, blood pressure was 140/80 mmHg, respiratory rate was 22/min, and body temperature was 36.9°C. A confusion state was revealed after neurological examination. On the first day of admission, the laboratory findings were as follows: aspartate transaminase (AST): 45 U/L (15-41); alanine transaminase (ALT): 86 U/L (17-63); total bilirubin: 0,5 mg/dl (0,4-2); direct bilirubin: 0,1 mg/dl (0,1-0,5); blood urea nitrogen (BUN): 10,0 mg/dl (8-20); creatinine: 0,61 mg/dl (0,7-1,2); serum level of valproic acid: 61,50 microgram/ml (50-100); glucose, HbA1c (5.0%), the total protein, albumin, gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), prothrombin time (PTT), activated partial thromboplastin time (aPTT), the international normalization ratio (INR), erythrocyte sedimentation rate, whole blood count, the urine microscopy were normal, and urinary bilirubin was negative. HbsAg and anti-HCV were negative, abdominal ultrasonography (USG) was normal, and the mildly elevated liver enzyme levels were associated with the medications he was taking.

Diazepam (Diazem; Deva, Istanbul, Turkey) 20 mg was administered to the patient via the intravenous (iv) route and phenytoin (Epanutin; Pfizer Inc, NY, USA) 20 mg/kg at loading dose was administered via the intravenous route as a consequence of recurrent complex partial seizures. Levetiracetam (Keppra; UCB S.A., Brussels, Belgium) loading via the iv route was administered since the seizures continued. He was diagnosed with RSE, and as the seizures continued, 10 mg midazolam (Dormicum; Deva, Istanbul, Turkey) loading was administered after intubating the patient, and mechanical ventilation was started, and the infusion was started at the dose of 0.2 mg/kg/h. Propofol (Diprivan; Astra Zeneca, Cambridge, UK) infusion at the dose of 50 mcg/kg/min was started for general anesthesia induction as the seizures could not be controlled with the previous treatments.

The color of urine turned to green at the 8th hour of propofol infusion (Figure 1A). We considered that the patient should be

examined in detail for porphyria due to the color difference between the urine that was not exposed to light after the urinary bag was clamped, and the urine that was waited in the urine bag (Figure 1B). Consequently, patient's relative was questioned for the possible symptoms of porphyria episode, namely abdominal pain, mental symptoms, autonomic dysfunction, peripheral neuropathy, and encephalopathy; however, suggestive findings for porphyria could not be detected. The patient did not have a family history of porphyria. The levels of Delta-aminolevulinic acid, coproporphyrin and porphobilinogen were within normal limits.

Examinations were performed for vesico-enteral fistula and urinary tract infection; however, no pathologies were detected. The laboratory examinations were performed when the urine was green revealed total bilirubin: 1,66 mg/dl (0,4-2); direct bilirubin: 0,15 mg/dl (0,1-0,5); AST: 33 U/L (15-41); ALT: 43 U/L (17-63), renal function tests, whole blood count, urine examination, urine microscopy were all normal, and the urinary bilirubin was negative. The dose of Propofol was increased upon observation of seizures at the 24th hour when the dose was decreased. The urine color was green during the 72 hours of propofol infusion. The urine color returned to yellow at the 10th hour after infusion (Figure 1C). Antiepileptic treatment was revised during this

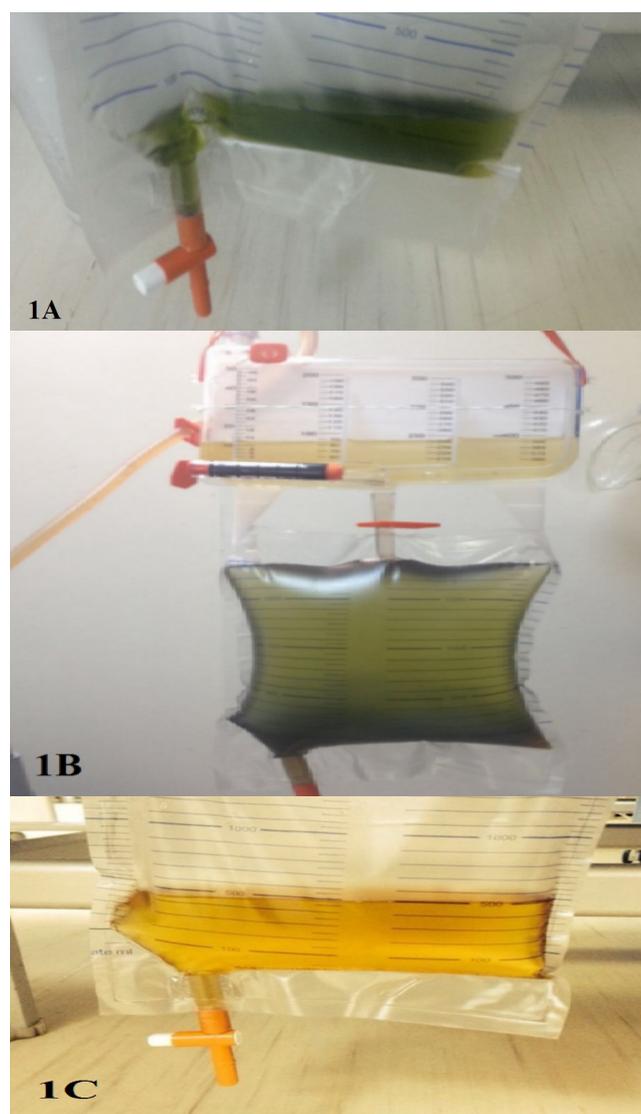


Figure 1. Urine color at the 8th hour of propofol infusion (A). The color difference between the urine not exposed to light after urinary bag is clamped and the urine having been awaited in the urine bag (B). Urine color 10 hours after discontinuation of infusion (C).

process. The seizures were able to be controlled with valproic acid 2000 mg/d, levetiracetam 1000 mg/d, carbamazepine 800 mg/d (Tegretol; Novartis, Basel, Switzerland) and gabapentin 1200 mg/d (Neurontin; Pfizer Inc, NY, USA).

Discussion

The urine color may become dark yellow in hyperbilirubinemia, dehydration and multi-vitamin drug use (B complex vitamins); the color may change to orange with rifampicin, red in hemoglobinuria, myoglobinuria, after beetroot or blackberry ingestion, brown with metronidazole, phenytoin, nitrofurantoin use, and dark pink in porphyria [3].

The causes of green urine development, which is quite rare, is not exactly known. The main causes of green urine include phenol-containing compounds such as promethazine, propofol and thymol, stains such as indigo blue, indigo carmine, carbolic acid and flavin derivatives, presence of urinary biliverdin due to longstanding obstructive jaundice, amitriptyline, pseudomonas infection, cimetidine, indomethacin and methylene blue, Hartnup disease, and vesico-enteral fistula [3,4]. Pseudomonas-related urinary tract infection should be considered when green urine develops, particularly in diabetic patients. Our patient was not diabetic, and there were no infection findings in his urine microscopy and urinary culture.

Propofol is a short-acting hypnotic agent and third line drug in the SE treatment. Presence of the green urine, particularly triggered with light exposure, suggests porphyria in a patient who is unconscious and receives SE treatment. Abdominal pain, mental symptoms, autonomic dysfunction, peripheral neuropathy and encephalopathy indications may be seen in porphyria. A porphyria episode may be triggered with porphyrinogenic anti-epileptics such as valproic acid, lamotrigine, carbamazepine, phenytoin and topiramate through microsomal enzymes [5]. However, non-porphyrinogenic drugs (anti-epileptics other than valproic acid, lamotrigine, carbamazepine, phenytoin, and topiramate) should be used in a patient who has known porphyria. Porphyria, which has a high mortality, should certainly be excluded as our patient was using valproic acid, and his seizures could not be controlled on the second day of admission.

The pathophysiology of green urine discoloration has not been clearly explained yet. Propofol is metabolized, not only by the liver and small intestine but also by the kidneys. The urine color may turn to green due to constipation, impaired peristalsis and related impaired entero-hepatic circulation, use of albumin and erythrocytes as carrier proteins, extra-hepatic glucuronidation mainly occurring in the kidneys in patients receiving continuous propofol infusion. Green urine development is explained by phenolic metabolite formation in the liver and their urinary excretion [6].

Propofol infusion-related green urine is a benign condition and rarely encountered. The urine color returned to yellow 10 hours after discontinuation of propofol infusion. In the literature, urine has been reported to return to yellow 2 hours - 2 days after discontinuation of propofol infusion [7].

Conclusion

In conclusion, it should be kept in mind that green urine may develop due to propofol, that this is a benign condition in a patient

who is receiving propofol infusion, and that it is reversible once the drug is discontinued.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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