Green discoloration of the urine after propofol administration is a rare clinical phenomenon. Although the exact incidence of propofol-induced green urine is not known, the reported incidence is thought to be less than 1%. In most reported cases of propofol-induced green urine, the clinical effects were benign and reversible. However, many clinicians are unfamiliar with this rare side effect of propofol. Here, we present the case of a patient who showed green urine following two-staged repair of a thoraco-abdominal aortic aneurysm with propofol infusion. His urine had a normal yellowish color after the first operation, but appeared green immediately after the second surgery. Because propofol is a commonly used sedative agent, knowing that green urine can be attributed to propofol administration and that its clinical effect is mostly benign will help clinicians with patient management, as such knowledge will also reduce unnecessary concerns and laboratory tests.

CASE REPORT

A 27-year-old, 173 cm, 73.4 kg man with Marfan syndrome was admitted in our hospital for a repair of the thoracoabdominal aortic aneurysm. He had an annulo-aortic ectasia (76 mm) with severe aortic regurgitation due to a coaptation failure, and a 50 mm sized infra-renal abdominal aortic aneurysm. He had no other underlying disease besides the Marfan syndrome. Preoperatively, he was only on oral beta-blocker (carvedilol) treatment aimed at reducing the rate of aortic root dilatation. Two-staged operation comprised a modified Bentall operation in the first stage, followed by an open abdominal aortic aneurysm repair after 7 days. The results of his preoperative laboratory tests were unremarkable.

Modified Bentall operation, which included 105 minutes of cardiopulmonary bypass, was done under 6 hours of total intravenous anesthesia (TIVA) with continuous infusion of propofol and remifentanil. During the Bentall operation, the infusion rate of propofol was 4.8–7.2 mg/kg/h and a total dosage of propofol was 2,400 mg. The estimated blood loss was 800 ml. No allogenic red blood cells or albumin was infused to the patient, except for 200 ml of albumin mixed in the pump priming volume, which is the standard of care in our hospital. He was extubated at 4 hours postoperatively in
the ICU and transferred to the general ward on postoperative day 2. During the time interval between the first and second operations, his systolic blood pressure and heart rate were controlled at 90 to 100 mmHg and around 90 bpm, respectively, with intermittent infusion of intravenous esmolol (50 μg/kg/min) and/or nicardipine (1 μg/kg/min). Intravenous famotidine, codein, and warfarin were also used occasionally. He was on oral carvedilol and losartan. During this time, the intraoperative and postoperative urine was normal yellowish.

Seven days later, open repair of an abdominal aortic aneurysm was performed under the same TIVA technique. The intraoperative and postoperative urine was normal yellowish. Four sequential tests performed at that time (from 1 hour to 5 hours postoperatively). All blood laboratory test results were within the normal range except for the slightly elevated C-reactive protein and white blood cell counts. The laboratory findings were as follows: albumin, 2.8 g/dl; total bilirubin, 0.9 mg/dl; aspartate aminotransferase, 11 U/L; alanine aminotransferase, 19 U/L; blood urea nitrogen, 15.1 mg/dl; creatinine, 0.59 mg/dl; C-reactive protein, 1.93 mg/dl; and white blood cell count, 13,940 /mm³. During the entire hospitalization period, the patient had no gastrointestinal problem, not even constipation. The urine color returned to normal yellowish spontaneously within a few hours. The patient was extubated 3 hours postoperatively in the ICU, transferred to the general ward on postoperative day 1, and discharged on postoperative day 7 after the second operation without specific complications.

**DISCUSSION**

Green discoloration of urine after propofol infusion is a rare clinical phenomenon. Although a propofol is a commonly used sedative drug, many physicians are still unfamiliar with the propofol-induced green urine because of its rare incidence. The clinical features of the previous reports of propofol-induced green urine were variable including propofol infusion rate, total infused dose, duration, and patient characteristics [1-11]. However, most cases reported the benign and reversible nature of propofol-induced green urine.

Green urine can be associated with certain medications, dyes, or urinary tract infections. Medications containing phenol groups, such as promethazine, thymol, cimetidine and propofol, and some non-phenol drugs such as metoclopramide, amitriptyline, and indomethacin are known to produce green urine [12]. Methylene blue and indigo blue dyes could also make green discoloration of the urine. Noteworthy is the fact that the green discoloration of urine caused by these drugs is mostly benign and self-limiting and thus, does not need further work-up or treatment if the results of urinalysis are normal.

However, because urinary tract infection by *Pseudomonas aeruginosa* related green urine is harmful, it is important to discriminate this condition from the benign green urine conditions. To rule out a urinary tract infection, the patient’s clinical history and physical examination should focus on the infectious signs, and the results of urine and blood cultures are needed to confirm the diagnosis [7,12]. In our patient, the urinalysis and urine culture revealed no signs of infection.
In the review of our case, the transient green urine seemed related to propofol infusion because of the absence of other related factors. As described above, there could be an endogenous or exogenous etiology for the green urine. In the management of our patient, first, the possibility of harmful endogenous causes of green urine, such as *Pseudomonas* urinary tract infection or chronic obstructive jaundice, were ruled out because there was no relevant clinical symptom or sign. Exogenous causes were also eliminated as there was no history indicating use of green urine-causing medication or dyes other than propofol during the perioperative period.

Propofol is metabolized in the liver and excreted in urine predominantly as the 1-glucuronide, 4-glucuronide, and 4-sulfate conjugates of 2,6-diisopropyl-1,4 quinol. Green discoloration of urine may attribute to the green chromophore of these phenolic metabolites of propofol. However, these metabolites are biologically inactive, and thus, they do not affect renal function [8]. It was assumed that green urine was associated with the failure of an enterohepatic circulation due to constipation and impaired peristalsis, an abundance of albumin or red blood cells as carrier proteins, and predominant extrahepatic glucuronidation in the kidneys [6]. Other than urine discoloration, propofol-related green pigmentation of the liver and hair has also been reported [11]. During the whole hospitalization, the patient in this case did not have any gastrointestinal symptoms, not even constipation, or allogetic red blood cell transfusion, or abundance of albumin. The amount of cell-saver collected self-blood transfused intraoperatively was only 230 ml.

Moreover, urine color changes other than green after propofol administration have been reported. Propofol-related pink urine may be associated with precipitation of uric acid [13] and a white urine after propofol administration is probably due to the high plasma concentration of the propofol and its vehicle [14]. All of those reports of discolorations of urine secondary to the use of propofol were reversible with a discontinuation of the propofol administration.

In our patient, the postoperative urinary pH after the second

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**Table 1.** Reported Cases of Green Urine Discoloration after Propofol Infusion

| Case No. | Ref. | Age | Sex | Operation or reason for ICU admission | Clinical situation | Propofol administration | Time until urine color normalization |
|----------|------|-----|-----|--------------------------------------|-------------------|-------------------------|--------------------------------------|
| 1*       | [7]  | 27  | M   | open abdominal aorta aneurysm repair  | ICU Seizure       | 4.8–7.2 mg/kg/h 2,100 mg | Within several hours from propofol stop |
| 2        | [7]  | 31  | M   | ICU Seizure                         | ICU Seizure       | 5.5 mg/kg/h 12,600 mg   | Normalized gradually                 |
| 3        | [2]  | 24  | M   | ICU Trauma                          | ICU Trauma        | 0.8–4.4 mg/kg/h 7 days  | Within a few hours                   |
| 4        | [2]  | 77  | F   | ICU Intracranial hemorrhage         | ICU Intracranial hemorrhage | 3.2 mg/kg/h 14,000 mg | Within a few hours                   |
| 5        | [3]  | 55  | M   | Pelvic mass wide excision           | Postoperative Mandible osteotomy | 4 mg/kg/h 235,000 mg | After 3 hours of propofol stop       |
| 6        | [3]  | 28  | F   | Mandible osteotomy                  | ICU Seizure, Central pontine myelolysis | 3 mg/kg/h 2,720 mg | After 6 hours of propofol stop       |
| 7        | [4]  | 49  | F   | Status epilepticus                  | Status epilepticus | 3.5 mg/kg/h 4,720 mg | After 3 hours of propofol stop       |
| 8        | [4]  | 19  | M   | ICU Status epilepticus              | Status epilepticus | 3.5 mg/kg/h 4,720 mg | After 6 hours of propofol stop       |
| 9        | [4]  | 32  | F   | Splenectomy after a traffic accident | Splenectomy after a traffic accident | 3 mg/kg/h 2,720 mg | After 6 hours of propofol stop       |
| 10       | [5]  | 54  | F   | Decompressive laminectomy           | Decompressive laminectomy | 200 mg Bolus | 1 h 30 min                            |
| 11       | [6]  | 19  | M   | Postoperative Angioectomy           | Postoperative Angioectomy | 2–3 mg/kg/h 39 h | After 6 days of propofol discontinuity |
| 12       | [8]  | 55  | F   | ICU Hematemesis                     | ICU Hematemesis    | 3 mg/kg/h 3 days | After 6 days of propofol discontinuity |
| 13       | [9]  | 40  | M   | Traumatic extradural hematoma       | ICU Traumatic extradural hematoma | 4 days | After 24 hours of propofol discontinuity |
| 14       | [10] | 52  | M   | ICU Esophageal variceal bleeding    | ICU Esophageal variceal bleeding | 100 mg Bolus | After 1 hour                            |
| 15       | [11] | 75  | M   | Postoperative Total knee replacement | ICU Sepsis         | 3 mg/kg/h 3 days | After 2 days                            |
| 16       | [11] | 40  | M   | ICU Sepsis                          | ICU Sepsis         | 3 mg/kg/h 3 days | After 2 days                            |

*The patient presented in this case report. ICU: intensive care unit.
surgery was slightly alkaline (pH 8.0). Although abnormally high urinary pH can indicate some pathological conditions such as autoimmune disorder, hyperparathyroidism, Marfan syndrome, or kidney disease including urinary tract infection [15], urinary pH is influenced by various factors such as diet, timing of the test during the day, and used medications [15], and can range from 4.5 to 8 in healthy condition. In our case, various electrolytes mixed in the fluids infused intraoperatively or various medications could affect the postoperative urinary pH. Although a previous report has commented that urine alkalization could favor the formation of the phenolic metabolites [5], urinary pH values in the previous reported cases of propofol induced green urine were variable ranging from 5.5 to 8.5 [2,4-6,8,10,11]. Thus, the relationship between the occurrence of propofol-induced green urine and the urinary pH could not be clarified.

Clinicians may wonder a possible association between this propofol-induced green urine and a propofol infusion syndrome (PRIS) because PRIS is the most severe and concerned side effects of propofol infusion. However, all the reported cases of propofol-induced green urine had not shown any significant clinical effects and had not increased the risk of PRIS. The clinical features of PRIS include acute refractory bradycardia leading to asystole in the presence of one or more of the following: metabolic acidosis (base deficit greater than 10 mmol/L), rhabdomyolysis, hyperlipidemia and an enlarged or fatty liver. It is known that high-dose propofol infusion (greater than 4 mg/kg/h) longer than 48 hours can be the cause of PRIS. In our case, any clinical feature of PRIS had not observed.

Clinical features in several previous reports of propofol-induced green urine were variable (Table 1). Different from PRIS, the relationship between the total dose or infused duration of propofol administration and the occurrence of green discoloration of urine seemed to be controversial. One case report has proposed the dose-dependent color intensity of propofol-induced green urine [7]. In their report, dark green urine color became light green with reducing a propofol infusion rate from 5.5 to 3.5 mg/kg/h and finally normalized after discontinue of propofol infusion. However, the dose dependency could not be clarified in the other several other cases. In three cases, propofol induced green urine was detected even after a single bolus use with induction dose of propofol [5,10,11]. The durations of green urine were also variable (Table 1).

In addition, in our case, the same patient showed different responses to propofol infusion. There was no green discoloration of urine after the first 2,400 mg of propofol infusion but green urine was noted after the second surgery with 2,100 mg propofol infusion. A review of medical records shows that there were no significant differences in the pre- and intra-operative management protocol between the two procedures except for the surgical procedure itself: the first was open cardiac surgery involving 105 minutes of cardiopulmonary bypass and the other was infrarenal aortic aneurysm repair without cardiopulmonary bypass. The intra-operative anesthetic and hemodynamic managements were similar in both stages. Considering the nonspecific clinical features documented in the previous reports, the exact mechanism for the different responses to propofol in our patient remains unveiled.

Our patient, a young man with a Marfan syndrome who underwent two sequential operations, showed different responses to intraoperative propofol infusions. As a rare clinical phenomenon, green discoloration of urine caused by propofol infusion may confuse the clinicians and patient. It is worth knowing that this rare phenomenon is, in most cases, a benign and reversible side effect of propofol administration. Sequential differential diagnosis and early recognition of the propofol effect would help in managing the patient, as well as reduce unnecessary concerns and laboratory tests.

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