

Bizarre bleeps-a case report of propofol-induced urine discoloration following a single dose

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ABSTRACT

Background: Green discoloration of urine following propofol use is a rare yet benign side effect. While rare with propofol infusions, it is even less recognized following single doses of propofol and can cause anxiety for both patients and healthcare professionals.

Case Presentation: This paper presents the case of a patient with alcohol-induced liver cirrhosis who transiently produced green urine following a single dose of propofol at the induction of anesthesia. The exact incidence and mechanism are not known; however, it is thought to be due to the extrahepatic pharmacokinetics associated with propofol metabolism and clearance. Due to its rarity, it can propagate anxiety and lead to unnecessary investigations.

Conclusion: Propofol is a very commonly used anesthetic drug. The case highlights that the prompt recognition of this rare adverse effect can prevent unnecessary investigations and provide reassurance to the patient and healthcare providers.

Keywords: Propofol, anesthesia, case report, pharmacokinetics, adverse effects, hepatic dysfunction.

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Background

Urinary discoloration is a sign which often causes anxiety to patients and caregivers alike. Green urine is commonly described on intensive care units; however, it is rarely encountered on general wards. It may be caused by medications, infections, dietary changes, and genetic diseases (for example, Hartnup Disease, pseudomonas infections, biliverdin, methylene blue, and other phenol and nonphenol-based medications) [1]. While possibly pathological, there are some rarer benign causes which should be considered if appropriate to dissipate anxiety and prevent unnecessary investigations. Here, we present the case of a 59-year-old gentleman who began producing green urine (Figure 1) postoperatively, which prompted the nurses to bleep the night on-call junior doctor.

Case Presentation

The patient had been admitted for an elective esophago-gastroduodenoscopy with endoscopic submucosal dissection of a T1b N0 M0 esophageal adenocarcinoma. His past medical history included Barrett's esophagus, alcohol-induced liver cirrhosis (Child-Pugh A), portal hypertension, and epilepsy. He reported being abstinent from alcohol for the past 4 years. His prehospital medications included levetiracetam, omeprazole, and propranolol. On review 8 hours post-operatively, the patient was unperturbed by his urinary discoloration, but the nursing



Figure 1. Urine sample from the patient highlighting green discoloration.

staff were concerned. His observations were normal, but he appeared dehydrated having been made nil-by-mouth post-procedure without concurrent intravenous fluid administration. He denied all urinary symptoms, including dysuria, frequency, and abdominal and flank pain. The

patient reported a history of a green tinge to his urine in the past, but it had resolved, and no cause was identified. The previous episode of urinary discoloration did not appear to be associated with general anesthesia.

The review of the patient's anesthetic chart showed that he received 200 mg propofol IV at induction, in addition to 2 mg midazolam, 60 mg rocuronium, 150 mcg fentanyl, and 4 mg ondansetron. During the procedure his anesthesia was maintained on sevoflurane. His procedure and anesthesia progressed without concern, and he was well post-operatively. He was admitted overnight for monitoring and was due to be discharged the following day.

Urinalysis revealed a normal pH (7) and was negative for glucose, ketones, nitrites, and leucocytes. Blood tests were equally unremarkable (C-reactive protein: 6.6, sodium: 141, potassium: 4.9, creatinine: 64, bilirubin: 13, alkaline phosphatase: 78, aspartate transaminase: 26, albumin: 42, corrected calcium: 2.42, phosphate: 1.17, platelets: 145, hemoglobin: 152, lymphocytes: 2.03, monocytes: 0.8, and eosinophils: 0.0) except for a mild neutrophilia (white cell count: 12.63 and neutrophils: 9.78) which was felt to be reactive post-operatively. He was prescribed a liter of Hartmann's solution overnight, and by the morning his urine color had begun to normalize. The patient and nursing staff were reassured appropriately since this side effect is felt to be completely benign and non-nephrotoxic [2].

Discussion

The working diagnosis was that this urine discoloration was related to the single dose of propofol given at induction and was made darker in color due to ongoing dehydration. The majority of propofol (70%) is directly metabolized in the liver by phase II conjugation to propofol glucuronide. This metabolite is subsequently excreted in the urine unchanged. Around 29% of propofol is metabolized in the liver by phase I modification with cytochrome P450 catalyzed hydroxylation. This produces 2,6-diisopropyl-1,4-quinol, which then undergoes phase II metabolism by conjugation with glucuronic acid which may occur in the liver or extra-hepatic sites. The resulting product of this conjugation is 1 or 4-(2,6-diisopropyl-1,4-quinol)-glucuronide. These phenolic metabolic products are excreted in the urine with the potential, rarely, to cause green urine [3]; however, it is unclear if this is dose dependent.

We propose that this patient's history of alcohol excess and liver cirrhosis impaired his ability to conjugate propofol in the liver, hence reducing direct metabolism to propofol glucuronide. This would then increase metabolism down the cytochrome P450 hydroxylation route followed by extra-hepatic conjugation to glucuronic acid as previously described. The kidneys are the main site of extra-hepatic conjugation and are known to have glucuronosyltransferase isoforms (UGT1A8/9) with a predilection

for propofol [4]. This would lead to the increased levels of 1 or 4-(2,6-diisopropyl-1,4-quinol)-glucuronide which likely potentiated the green urine in this case.

A literature review highlighted 16 previous reports of green urine discoloration secondary to propofol use [5]. The exact incidence is unknown but is thought to be less than 1% [2]. The discoloration of urine is usually secondary to propofol infusion but can be seen very rarely after single doses as in this case [6–10].

Conclusion

Urinary discoloration is a frightening occurrence for both patients and caregivers. Medications should always be considered in any patient, and this case report provides an important learning point for junior doctors covering general wards, particularly those who have not worked previously in anesthesia or intensive care medicine. Propofol is an especially, pertinent cause in post-operative patients with transient green discoloration of their urine, and therefore the anesthetic record should be reviewed. The case also highlights that although this effect of propofol is rare, patients with pre-existing hepatic impairment may be at increased risk. Prompt recognition of this rare yet benign adverse effect can reduce anxiety, prevent unnecessary investigations, and help facilitate a prompt and timely discharge. The authors recommend urinalysis and blood work as the maximal necessary investigations in a well patient with urinary discoloration and a temporal relationship to propofol administration. Furthermore, the administration of intravenous fluids is an appropriate intervention to normalize urine color, particularly in patients who have reduced oral fluid intake.

What is new?

This case report of propofol-induced urine discoloration highlights and attempts to provide an explanation for a known adverse effect of propofol which is rare but may cause anxiety. The authors provide several learning points for junior doctors who may encounter urine discoloration in their out-of-hours practice.

List of Abbreviations

TNM Tumour, Nodes, Metastasis

Consent for publication

Written informed consent was taken from the patient.

Ethical approval

Ethical approval is not required at the institution for publishing an anonymous case report.

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Summary of the case

1	Patient (gender, age)	A 59-year-old male.
2	Final diagnosis	Propofol-induced urinary discoloration
3	Symptoms	8 hours post-operatively, the patient began producing green urine, and he was otherwise well with a normal physical examination and did not report any other symptoms
4	Medications	The patient received 200 mg propofol IV at induction of anesthesia
5	Clinical procedure	The patient received a liter of Hartmann's solution for rehydration which prompted the urine color to begin normalizing
6	Specialty	Anesthetics and clinical pharmacology