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CASE REPORT

Ophthalmology

# Color vision disturbances secondary to oral tranexamic acid

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## Abstract

Tranexamic acid (TXA) is an antifibrinolytic commonly used to reduce blood loss due to surgical procedures, heavy menstruation, trauma, bleeding disorders, among other uses. Possible adverse reactions associated with TXA include abdominal pain, headache, fatigue, cerebral thrombosis, dizziness, retinal artery occlusion, chromatopsia, and more. We present a case of acute color vision disturbance developed soon after initiation of oral TXA for epistaxis prophylaxis in the setting of factor VII deficiency. To our knowledge we report the only case of color vision disturbance in a pediatric patient and the only case after receiving oral TXA. Soon after discontinuing oral TXA the patient's altered perception of color vision resolved. The patient was subsequently discharged home with a prescription for an alternative antifibrinolytic (aminocaproic acid) and follow-up with neuro-ophthalmology.

KEYWORDS

antifibrinolytic, factor VII deficiency, ocular pathology, pediatric, tranexamic acid

## 1 | INTRODUCTION

Tranexamic acid (TXA) is an antifibrinolytic medication that competitively inhibits the activation of plasminogen to plasmin. As a synthetic lysine analog, TXA adheres to the lysine binding sites on plasminogen and subsequently blocks the breakdown of fibrin clots by plasmin.[1] At high concentrations, TXA also directly inhibits the activity of plasmin.[2]

TXA is commonly used to reduce perioperative blood loss during various surgical procedures (eg, coronary artery bypass grafting and aortic valve replacement) and has been shown to decrease transfusion requirements when used during surgical procedures.[3] Additionally, TXA is often used to decrease blood loss during trauma, heavy menstrual bleeding, hyphema, and various bleeding disorders (eg, factor VII deficiency).[3] TXA is available as an intravenous and oral formulation and can be delivered via a variety of routes (eg, nebulized, oral, intravenous, and topical).

One subset of patients that TXA often is used in is those with factor VII deficiency. Factor VII is a coagulation factor integral for adequate clot formation. Therefore, a deficiency often leads to a greater propensity to bleed.[4] In this patient population, TXA is used to mitigate bleeding episodes, most commonly being used for menorrhagia.[4,5]

Although serious adverse reactions to TXA are uncommon, several incidents of ophthalmologic aberrations have been reported in the literature. Package inserts for both the intravenous and oral formulations include warnings for visual and ocular effects, and acquired defective color vision is listed as a contraindication for the use of intravenous TXA.[6,7] We present a novel case of color vision disturbance without identifiable ocular pathology in a pediatric patient with factor VII deficiency following treatment with oral TXA for prevention of further epistaxis.

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## 2 | CASE REPORT

A 7-year-old female presented to the emergency department (ED) for evaluation of acute onset altered color perception. The patient reported changes in her color vision (chromatopsia), specifically noting that objects appeared oddly colored. She mentions that her mother was transitioning from purple to white and vice versa. Based on how the patient describes the altered color perception it seems both eyes were affected. However, she was not distressed regarding the current events but more surprised and confused. Past medical history included factor VII deficiency, portal hypertension with esophageal varices, aortic stenosis with hyperplasia of the aortic arch, hypertension, sickle cell trait, and a splenorenal shunt. The patient's mother reached out to her hematologist regarding the constellation of ophthalmologic symptoms. She was instructed to take the patient to the ED for further evaluation. At that time, the mother had already discontinued TXA.

The patient was evaluated in the same ED 3 days before owing to an episode of epistaxis that developed spontaneously. During this visit she was hemodynamically stable with no fever, well appearing, and the nosebleed had resolved before arriving in the ED. The nosebleed was stopped with application of direct pressure alone by mother and patient. The patient's vital signs upon arrival were as follows: non-invasive blood pressure—151/85 mmHg, heart rate—91 beats/min, respiratory rate—20 breaths/min, temperature—98.4°F, oxygen saturation—100%. Labs were collected per pediatric hematology/oncology request, and notable results were as follows: serum creatinine—0.56 mg/dL (0.3–0.6 mg/dL), hemoglobin—10.8 g/dL (10.6–13.4 g/dL), platelets—188 k/$\mu$L (200–369 k/$\mu$L), elevated international normalized ratio—1.6 (0.9–1.1), and elevated activated partial thromboplastin time—38 seconds (25–36 seconds). Per pediatric hematology/oncology, the patient was discharged home with a prescription for oral tranexamic acid 10 mg/kg 3 times daily for 10 days for prevention of further epistaxis.

The patient began taking TXA 1 day after being discharged from the ED. On day 2, midmorning the patient described color vision disturbances. Pediatric hematology/oncology followed up with the mother on day 3. They recommended she bring the patient back to the ED for further evaluation. The mother had already discontinued administration of TXA. In total, the patient received 4 doses of TXA (2600 mg) before stopping therapy. Upon arrival for her second ED visit the patient's vital signs were as follows: non-invasive blood pressure—127/69 mmHg, heart rate—86 beats/min, respiratory rate—19 breaths/min, temperature—98.5°F, oxygen saturation—98%. The ED team consulted the ED pharmacist to determine if this adverse event may have been caused by TXA. Through a literature search, the pharmacist noted several cases of color vision defects and retinal venous and arterial occlusion associated with use of TXA. Based on this information we felt it was possible that vision disturbances were due to TXA. Pharmacy recommended discontinuation of therapy and consultation of ophthalmology for further evaluation of possible ocular pathology.

Ophthalmology reported to the ED and note that the patient's eyes were normal with healthy-appearing optic nerves, no relative afferent pupillary defect, and no pertinent findings on the dilated fundus exam. There was no evidence of a focal neurological symptom upon examination, so further imaging was not ordered. Ophthalmology could provide no potential etiology for the color vision disturbances and the patient's hematologist recommended no further testing. Hematology recommended permanent discontinuation of TXA and cleared the patient to begin taking aminocaproic acid, an alternative antifibrinolytic agent, and to follow up with the patient's hematologist. Ophthalmology instructed the patient's mother to keep a symptom journal and to follow up with neuro-ophthalmology in 3 to 4 weeks. Currently, the patient has not followed up because of the COVID-19 pandemic but does plan to follow up in the near future. The ED pharmacist followed up with the patient's mother 4 months after the second ED visit. The mother notes no additional issues with color vision disturbances since stopping TXA and starting aminocaproic acid.

## 3 | DISCUSSION

We have reported a case of transient color vision disturbance in a pediatric patient after taking oral TXA for prevention of epistaxis, which has not been previously reported in the medical literature.

In review of previously literature, multiple instances of non-color vision disturbances after TXA administration have been reported. A 1998 case report discusses an incidence of branch retinal artery occlusion in a 57-year-old female cancer patient who received IV TXA 750 mg twice daily for 5 days for treatment of hemorrhagic cystitis.[8] The thrombotic effect of TXA was the suspected cause of this blurred vision and the patient had no further issues after discontinuation. Two cases of central venous stasis retinopathy were reported in a case report in 1990 in women treated with TXA for menorrhagia.[9] A 38-year-old female and 40-year-old female both experienced blurred vision and loss of vision in the left eye approximately 1 week after starting TXA 2000 mg IV daily. TXA was discontinued in each patient and a treatment regimen consisting of prednisone and dipyridamole was given, and vision returned to normal in both patients within 8–10 weeks.

In 2003, it was reported that a 56-year-old male hemodialysis patient lost his sight after receiving IV TXA 2000 mg injections daily for 27 days while being hospitalized for a gastrointestinal tract bleed.[10] The TXA injections were discontinued and the patient's vision was restored within a few days. This patient had experienced a similar instance of visual impairment 4 months prior when he also received TXA to treat a bleeding ulcer, which strengthened the authors' conclusion that the TXA was the cause of his vision loss. It was hypothesized that the patient received a TXA overdose because of a failure to adjust the dose based on his renal function.

Regarding color vision disturbances specifically, to our knowledge, only 1 case has been reported. A 58-year-old male experienced color vision disturbances after receiving IV TXA in 2006.[11] This patient underwent en bloc vertebral resection for a thoracic chordoma and received TXA in order to minimize transfusion requirements and blood loss during a 2-part surgery performed with a 38-hour gap in-between

(TXA 1360 and 1840 mg administered intravenously, respectively). While recovering in the ICU after extubation, the patient reported that all objects appeared green. The extent of this color vision disturbance gradually diminished until the patient's vision returned to normal on the second postoperative day. As with the patient case that we have reported, this patient underwent an ophthalmologic exam that found no abnormalities. After ruling out other potential causes, the authors of this case report hypothesized that the vision changes resulted from a pharmacodynamic effect of TXA on retinal cone cells.

Although evidence of similar adverse ophthalmologic effects related to the use of TXA exists in the literature, we have detailed a unique case in which a pediatric patient experienced a considerable color vision disturbance after taking oral TXA. Additionally, our patient did not exhibit any identifiable ocular pathology and because of her hematologic disorder she represents a subpopulation of patients more likely to receive oral TXA.

## 4 | CONCLUSION

To our knowledge this is the first case of color vision disturbance in a pediatric patient treated with oral tranexamic acid. Current literature supports the assertation that TXA has the potential to cause ophthalmologic adverse effects with the intravenous and oral formulations. However, our case is unique in that the patient developed ocular manifestations secondary to the oral formulation of TXA and the patient is pediatric. Further investigation is needed to better elucidate why TXA may cause color vision disturbances. At this time physician and non-physician healthcare practitioners should be aware of this uncommon but possible adverse event.

### AUTHOR CONTRIBUTIONS

All authors contributed equally to this work.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### REFERENCES

1. Ng W, Jerath A, Wąsowicz M. Tranexamic acid: a clinical review. *Anaesthesiol Intensive Ther*. 2015;47(4):339-350.
2. Hunt BJ. The current place of tranexamic acid in the management of bleeding. *Anaesthesia*. 2015;70(Suppl 1):50-53.e18.
3. McCormack PL. Tranexamic acid: a review of its use in the treatment of hyperfibrinolysis. *Drugs*. 2012;72(5):585-617.
4. Sevenet PO, Kaczor DA, Depasse F. Factor VII deficiency: from basics to clinical laboratory diagnosis and patient management. *Clin Appl Thromb Hemost*. 2017;23(7):703-710.
5. Napolitano M, Siragusa S, Mariani G. Factor VII deficiency: clinical phenotype, genotype and therapy. *J Clin Med*. 2017;6(4).
6. *Tranexamic Acid Injection [package insert]*. Deerfield, IL: Baxter Healthcare Corporation; 2019.
7. *Tranexamic Acid Tablet [package insert]*. Weston, FL: Apotex Corp; 2019.
8. Parsons MR, Merritt DR, Ramsay RC. Retinal artery occlusion associated with tranexamic acid therapy. *Am J Ophthalmol*. 1988;105(6):688-689.
9. M S, Axer-Siegel R, Buckman G, Yassur Y. Central venous stasis retinopathy following the use of tranexamic acid. *Retina*. 1990;10(3):181-184.
10. Kitamura H, Matsui I, Itoh N, et al. Tranexamic acid-induced visual impairment in a hemodialysis patient. *Clin Exp Nephrol*. 2003;7(4):311-314.
11. Cravens GT, Brown MJ, Brown DR, Wass CT. Antifibrinolytic therapy use to mitigate blood loss during staged complex major spine surgery: postoperative visual color changes after tranexamic acid administration. *Anesthesiology*. 2006;105(6):1274-1276.

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