

Case Report: Tranexamic Acid-Induced Nausea After Bilateral Concha Reduction Surgery

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Abstract

Tranexamic acid (TXA) is an antifibrinolytic agent widely used to control perioperative bleeding, including in otolaryngologic procedures. Although generally well tolerated, gastrointestinal side effects such as nausea are occasionally reported but often overlooked in clinical practice. This case report presents a 32-year-old female who developed nausea following the administration of intravenous TXA after undergoing bilateral concha reduction surgery in a hospital in Bandung, June 2025. The nausea resolved after discontinuation of the drug but recurred with greater intensity upon re-administration the following day. A causality assessment was performed using the Naranjo Adverse Drug Reaction Probability Scale, resulting in a total score of 6, indicating a probable relationship between TXA and the onset of nausea. No alternative causes were identified, and symptoms subsided spontaneously without antiemetic intervention after TXA was discontinued. This clinical observation suggests that repeated administration of TXA may increase the risk or severity of nausea in susceptible patients. The use of a structured causality assessment provided objective support for the adverse drug reaction. This case emphasizes the importance of clinician awareness regarding the potential for TXA-induced nausea, especially in Ear, Nose, and Throat (ENT) surgery, where repeated doses may be required. Moreover, documentation of such cases contributes to strengthening ENT-specific pharmacovigilance and highlights the need for further research into adverse effects associated with TXA in this surgical population.

Keywords: adverse effect, case report, Naranjo algorithm, nausea, tranexamic acid

Laporan Kasus: Mual Akibat Asam Traneksamat Pasca Operasi Reduksi Konka Bilateral

Abstrak

Asam traneksamat (TXA) adalah agen antifibrinolitik yang banyak digunakan untuk mengendalikan perdarahan perioperatif, termasuk dalam prosedur otolaringologi. Meskipun umumnya ditoleransi dengan baik, efek samping gastrointestinal seperti mual terkadang dilaporkan tetapi sering terabaikan dalam praktik klinis. Laporan kasus ini menyajikan seorang wanita berusia 32 tahun yang mengalami mual setelah pemberian TXA intravena setelah menjalani operasi reduksi konka bilateral di rumah sakit di Bandung, Juni 2025. Mual tersebut mereda setelah penghentian obat tetapi kambuh dengan intensitas yang lebih besar setelah pemberian kembali keesokan harinya. Penilaian kausalitas dilakukan menggunakan Skala Probabilitas Reaksi Obat yang Merugikan Naranjo, menghasilkan skor total 6, yang menunjukkan kemungkinan hubungan antara TXA dan timbulnya mual. Tidak ada penyebab alternatif yang teridentifikasi, dan gejala mereda secara spontan tanpa intervensi antiemetik setelah TXA dihentikan. Observasi klinis ini menunjukkan bahwa pemberian TXA berulang dapat meningkatkan risiko atau keparahan mual pada pasien yang rentan. Penggunaan penilaian kausalitas terstruktur memberikan dukungan objektif terhadap reaksi obat yang merugikan. Kasus ini menekankan pentingnya kesadaran klinisi mengenai potensi mual akibat TXA, terutama pada operasi Telinga, Hidung, dan Tenggorokan (THT), yang mungkin memerlukan dosis berulang. Lebih lanjut, dokumentasi kasus-kasus tersebut berkontribusi pada penguatan farmakovigilans khusus THT dan menyoroti perlunya penelitian lebih lanjut mengenai efek samping yang terkait dengan TXA pada populasi bedah ini.

Kata kunci: algoritma Naranjo, asam traneksamat, efek samping, laporan kasus, mual

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Introduction

Tranexamic acid (TXA) is a synthetic lysine analog widely used in surgical practice to reduce perioperative hemorrhage through antifibrinolytic action by competitively inhibiting plasminogen binding to fibrin.¹ Its efficacy in minimizing intraoperative bleeding has been well documented across various surgical specialties, including neurosurgery, orthopedics, cardiac, and head-and-neck procedures. Moreover, TXA has been successfully employed in ear, nose, and throat (ENT) and endoscopic sinus surgeries, where it improves surgical field quality and reduces transfusion requirements.²

Although TXA is generally considered safe, its adverse effect profile particularly gastrointestinal symptoms such as nausea and vomiting warrants attention. Meta-analyses in obstetric and gynecological contexts consistently report an increased risk of nausea/vomiting with TXA use (e.g., incidence up to $RR \approx 2.3$ in hysterectomy and vaginal delivery settings).³⁻⁵ Additionally, a large randomized trial in cesarean delivery noted a significantly higher occurrence of postoperative nausea or vomiting (43.0% vs. 36.3%; adjusted risk ratio 1.19, $P < 0.001$) in the TXA group.⁶

In contrast, data on TXA-induced gastrointestinal side effects in ENT surgery, specifically following bilateral concha (inferior turbinate) reduction, are sparse. While endoscopic sinus surgery studies report no significant difference in postoperative emetic events,² these findings may not fully translate to concha reduction procedures. Post-concha reduction patients may exhibit different pathophysiological responses, and TXA-related adverse effects like nausea could substantially impact recovery and patient comfort.

Herein, we describe a case of TXA-

induced nausea after bilateral concha reduction surgery, highlighting an uncommon but clinically relevant adverse effect in head-and-neck surgery. This report underscores the importance of monitoring and managing TXA-related gastrointestinal symptoms in ENT practice.

Case Presentation

A 32-year-old Sundanese woman who works as a housewife presented to the ENT department with complaints of persistent nasal obstruction and a history of allergic rhinitis. The patient had no significant comorbidities, denied smoking or alcohol use, and reported a regular mixed diet without food intolerances. She was diagnosed with bilateral inferior turbinate hypertrophy and scheduled for bilateral concha reduction surgery on June 12, 2025 in a hospital in Bandung.

Her preoperative vital signs were stable (BP: 121/87 mmHg, HR: 84 bpm, RR: 20 bpm, T: 36°C, SpO₂: 100%). Preoperative medications included intravenous cefotaxime (1 g) and tranexamic acid (100 mg), administered before the procedure.

The surgery was performed under general anesthesia without intraoperative complications. Postoperatively, the patient received routine care including IV fluid therapy (Ringer's lactate 15 gtt), analgesics (paracetamol 1 g IV tid, tramadol 100 mg in Ringer Lactate), antibiotics (cefotaxime 1 g IV tid), corticosteroids (dexamethasone 5 mg IV bid), and antifibrinolytic therapy with tranexamic acid 500 mg IV three times daily (at 5 AM, 1 PM, and 9 PM) to manage surgical bleeding risk.

Approximately 15 minutes after taking the first dose tranexamic acid (afternoon of June 12), the patient began experiencing nausea. However, as time went on the nausea started to disappear. On the following day (afternoon

Table 1. Timeline of Tranexamic Acid Administration and Associated Nausea Events

Date	12 Jun				13 Jun	
Time	1:00 PM	1:15–2:00 PM	9:00 PM	5:00 AM	1:00 PM	1:15–6:00 PM
Event	TXA 1 st dose administered	Patient experienced nausea	TXA scheduled dose not administered	TXA scheduled dose not administered	TXA 2 nd dose administered	Recurrence of nausea, more severe and prolonged

of June 13), re-administration of tranexamic acid resulted in a recurrence of nausea, this time with a prolonged duration of over five hours without spontaneous resolution, further supporting the suspected causal relationship. The timeline can be seen in Table 1.

Causality was subsequently assessed using the Naranjo algorithm. Regarding the intervention, no antiemetic or placebo was administered because the patient's initial nausea episode resolved spontaneously without requiring pharmacologic treatment. The symptoms were mild, self-limiting, and did not progress to vomiting or hemodynamic instability; therefore, observation was considered clinically appropriate at that time. Additionally, placebo or drug-challenge interventions were not performed because they are not part of routine clinical care and would not be ethically justified outside a research setting.

Discussion

This case highlights an uncommon yet clinically meaningful occurrence of TXA-induced nausea in the context of bilateral concha reduction surgery, an ENT setting where such adverse effects are rarely documented. The clear temporal relationship, resolution after discontinuation, and recurrence upon re-administration strongly support TXA as the suspected cause, later confirmed as “probable” based on

the Naranjo algorithm. These findings underscore the importance of heightened clinician awareness regarding TXA-related gastrointestinal reactions in ENT procedures and demonstrate the value of structured causality assessment in improving the accuracy and robustness of adverse event reporting.

Nausea and vomiting are established but often under-reported adverse reactions of intravenous TXA. Clinical data reveal an increased incidence of postoperative nausea or vomiting (PONV) in patients receiving TXA. For example, a randomized trial in spinal surgery showed significantly higher PONV rates in the TXA group compared to placebo.⁷ Similar findings were observed in cesarean section trials, where nausea/vomiting occurred in approximately 43% of TXA patients versus 36% in controls (RR 1.19; $p = 0.001$).⁸ A randomized trial in postpartum hemorrhage showed TXA doubled the incidence of PONV.⁹ In acute gastrointestinal bleeding settings, mild GI side effects occur in approximately 7–14% of patients receiving TXA.¹⁰ These data validate the relevance of gastrointestinal side effects even among elective surgical populations, though such reactions are not consistently captured in ENT settings.

This case differs from previously reported TXA-related adverse reactions because it occurs in a surgical setting where such events are rarely documented, bilateral

Table 2. Naranjo Analysis Results in Nausea Due to Tranexamic Acid

No.	Question	Yes	No	Don't Know	Score
1	Are there previous conclusive reports on this reaction?	1	0	0	1
2	Did the adverse event appear after the suspected drug was administered?	2	-1	0	2
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	1	0	0	1
4	Did the adverse reaction reappear when the drug was readministered?	2	-1	0	2
5	Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	2	0	0
6	Did the reaction reappear when a placebo was given?	-1	1	0	0
7	Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	1	0	0	0
8	Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	1	0	0	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	1	0	0	0
10	Was the adverse event confirmed by any objective evidence?	1	0	0	0
Total					6

concha (inferior turbinate) reduction, an ENT procedure that has not been the focus of major TXA safety studies. Most evidence linking TXA to nausea and vomiting originates from obstetric, orthopedic, and major surgical populations, including large randomized trials by Shakur *et al.* (2017) and cesarean delivery trial by Sentilhes *et al.* (2021), both demonstrating increased gastrointestinal adverse effects with TXA.^{6,9}

TXA likely induces nausea by interacting with the chemoreceptor trigger zone (CTZ) located in the area postrema, a medullary structure sensitive to blood-

borne pharmacological agents.^{11–13} The CTZ contains multiple receptors implicated in emesis dopamine D₂, serotonin 5-HT₃, and neurokinin-1 (NK-1).¹⁴ Evidence from animal studies, notably in dogs, suggests that TXA-induced emesis is mediated via neurokinin-1 pathways rather than dopamine D₂.¹⁴ With a plasma half-life of 2–3 hours, TXA's pharmacokinetics align closely with the timeline of symptom onset and duration in our case.

We performed a causality analysis of the occurrence of nausea by tranexamic acid with the Naranjo algorithm. The Naranjo scale was

chosen because it is a validated, widely used, and pragmatic tool for structured causality assessment in single-case reports, enabling transparent evaluation of temporal relations, dechallenge/rechallenge, and alternative explanations. The results can be seen in Table 2. In Naranjo's analysis for question number 1 (*are there previous conclusive reports on this reaction?*), we found several references regarding the occurrence of nausea as an adverse effect of TXA in various clinical contexts. Shakur *et al.* (2017), through the WOMAN trial, conducted a randomized, double-blind, placebo-controlled trial involving over 20,000 women with postpartum hemorrhage.⁹ They reported that gastrointestinal symptoms, including nausea and vomiting, occurred more frequently in the TXA group than in the placebo group, although the difference was not the primary endpoint.⁹ Similarly, Sentilhes *et al.* (2021), in a study published in the New England Journal of Medicine, evaluated the prophylactic use of TXA during cesarean delivery.⁶ They found that 43.0% of women in the TXA group experienced postoperative nausea or vomiting compared to 36.3% in the placebo group, with a statistically significant adjusted risk ratio of 1.19 (95% CI, 1.10–1.28; $p < 0.001$).⁶

These studies, conducted across different surgical populations and published in high-quality journals, confirm that nausea is a recognized adverse effect of TXA, thereby justifying a “yes” answer and assigning a +1 score for question number 1 in the Naranjo algorithm. For the second question (*did the adverse event appear after the suspected drug was administered?*), the answer is “yes” because the patient experienced nausea several minutes after tranexamic acid was administered. Third question (*did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?*), the answer is “yes”

because after 15 minutes of the first dose, nausea disappeared. Question no. 4 (*did the adverse reaction reappear when the drug was readministered?*), the answer is “yes” because on the next day the patient experienced nausea again after the drug was administered. This rechallenge phenomenon where nausea reappeared more rapidly and was prolonged upon re-administration provides compelling evidence under the Naranjo framework. In fact, recurrence after rechallenge is one of the strongest indicators of drug causality, directly impacting the Naranjo weighting. Next question (*are there alternative causes (other than the drug) that could on their own have caused the reaction?*) we answered “don't know” because there is no data to support. We answered the question number 6 (*did the reaction reappear when a placebo was given?*) with “don't know” because the placebo wasn't given. We couldn't answer question number 7 (*was the drug detected in the blood (or other fluids) in concentrations known to be toxic?*) because they were not done, so we answered “don't know”. Also we didn't do any changes to the dosage so the answer is “don't know” for the question number 8. For question 9 (*did the patient have a similar reaction to the same or similar drugs in any previous exposure?*), we also answered “don't know” because the patient had never experienced something similar. For the last question (*was the adverse event confirmed by any objective evidence?*), the answer is “no” because nausea can't be measured by objective evidence.

The causal analysis using the Naranjo Adverse Drug Reaction Probability Scale yielded a total score of 6, indicating a “probable” relationship between the administration of tranexamic acid and the onset of nausea. This categorization suggests a strong temporal association and clinical consistency with known adverse effects of the drug, suggesting that TXA was likely

involved in triggering the patient's symptoms.

Although the temporal association and positive rechallenge strongly support the causal relationship, several ambiguities remain. Nausea in the postoperative setting is inherently multifactorial and may also be influenced by anesthetic agents, opioid analgesics such as tramadol, stress response, or the surgical procedure itself. The absence of objective biomarkers (e.g., serum TXA levels), lack of placebo control, and limited ENT-specific safety data introduce uncertainty regarding the exact contribution of TXA to the patient's symptoms.

Despite these uncertainties, this case has notable strengths, including a clear onset-offset pattern, reproducibility of symptoms upon readministration, both of which support a causal link. Additionally, the use of a structured causality assessment tool (Naranjo algorithm), adds methodological robustness to the evaluation.

Nevertheless, important limitations must be acknowledged. This report describes a single patient, limiting generalizability. Potential confounders could not be completely excluded, and the lack of pharmacokinetic data such as serum TXA levels were unavailable. Likewise, the absence of a placebo rechallenge limits the ability to confirm causality. To address these uncertainties, future investigations could incorporate more rigorous methodological approaches. Controlled trials using placebo comparators may be particularly valuable because this approach would allow investigators to clearly differentiate TXA-related nausea from postoperative or anesthesia-related factors, thereby strengthening causal inference. Additionally, dose response evaluations could be implemented as this allows researchers to determine whether adjusting the TXA dose, either reducing or incrementally modifying it may decrease the likelihood or severity of nausea, providing insight into

whether the adverse effect is dose dependent. These strategies would offer a more robust framework for characterizing the relationship between TXA administration and nausea in ENT settings.

This case report addresses an important yet underrecognized aspect of pharmacovigilance within the field of otolaryngology. While the efficacy of TXA in reducing intraoperative blood loss is well-established across various surgical disciplines, including ENT procedures, its potential to induce gastrointestinal side effects particularly nausea remains insufficiently explored in this specific context. The recurrence of nausea upon repeated administration, as observed in our patient, highlights a clinically relevant adverse reaction that may be underestimated in routine practice. By applying the Naranjo algorithm to systematically assess causality, this report contributes objective evidence supporting TXA as the probable cause, thereby strengthening the quality and credibility of adverse event documentation. Such structured assessment is rarely utilized in surgical case reporting, despite its potential to enhance clinical decision-making. This case therefore underscores the importance of heightened clinician awareness regarding TXA-related nausea in ENT procedures, encourages consideration of preventive strategies such as slow infusion rates and prophylactic antiemetics, and supports the need for further research. Prospective studies and targeted pharmacovigilance in ENT populations are warranted to better understand the incidence, risk factors, and optimal management approaches for TXA-induced nausea. Ultimately, the findings presented here advocate for a more nuanced and patient-centered approach to the perioperative use of antifibrinolytic. In this case, the patient reported that the nausea she experienced was unexpected and significantly affected her comfort during recovery, but she

felt relieved once the symptoms subsided after TXA discontinuation. Her perspective reinforces the importance of recognizing and addressing patient-reported outcomes when evaluating adverse drug reactions.

Conclusion

This case report highlights a probable causal relationship between TXA administration and nausea, supported by a Naranjo score of 6. The strength of this report lies in the clear temporal association, symptom resolution after drug discontinuation, and reproducibility upon rechallenge, elements that collectively provide strong clinical evidence for causality. However, important limitations remain, including the single-patient nature of the case, the inability to exclude all postoperative confounders, and the absence of objective biomarkers or placebo controlled assessment. Based on these limitations, further research is recommended, particularly controlled studies in ENT surgical populations and dose response evaluations. Such investigations are proposed to clarify the true incidence of TXA-induced nausea, differentiate drug related effects from other perioperative factors, and determine whether dosing strategies or prophylactic antiemetics can mitigate symptoms. These recommendations are justified by the need to improve patient safety, optimize perioperative management, and support the need for improved monitoring and reporting of TXA-related adverse effects in ENT practice.

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Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics Declaration

This case report was conducted in accordance with the principles of the Declaration of Helsinki. Verbal informed consent was obtained from the patient for the use of clinical information and publication of this case report. Patient anonymity was strictly maintained, and no identifying data were included in the manuscript.

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