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Original Research Article

FROM TRANEXAMIC ACID TO RESCUE THERAPY OF ETAMSYLATE IN THE MANAGEMENT OF PERSISTENT HEMATURIA IN LASSA FEVER IN ONDO STATE, NIGERIA: A CASE SERIES SURVEY

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ABSTRACT
Lassa fever is an acute viral hemorrhagic illness endemic to West Africa and remains a major public health challenge in Nigeria, particularly in Ondo State where annual outbreaks occur. Hematuria is a recognized complication linked to endothelial dysfunction, capillary fragility, and platelet impairment. Tranexamic acid (TXA) is frequently used as an adjunct hemostatic agent, but evidence supporting its effectiveness in Lassa-related bleeding is limited. Etamsylate, a capillary-stabilizing agent that enhances primary hemostasis, has shown potential benefits in various bleeding conditions, yet its role in viral hemorrhagic illnesses remains largely undocumented. These case series report three adults who were PCR-confirmed cases of Lassa fever presenting with gross hematuria. Patients were admitted and received standard ribavirin therapy and tranexamic acid for five days, but the hematuria persisted without improvement. After switching to etamsylate (dicynone), the three patients showed rapid clinical response, with significant reduction in hematuria within 24–48 hours of switching to the therapy and complete resolution by days 4–6. No adverse reaction was recorded for the three patients. The findings suggest that tranexamic acid may be inadequate for Lassa fever–associated hematuria, whereas etamsylate appears more effective. Further studies are recommended to clarify its therapeutic role.

Keywords: Lassa fever, haematuria, tranexamic acid, etamsylate

INTRODUCTION

Lassa fever is a viral hemorrhagic illness endemic to West Africa, associated with multi-system involvement and variable bleeding tendencies, most commonly mucosal bleeding and hematuria.(Okoro *et al.,* 2020)(Duvignaud *et al.,* 2021) According to (Asogun *et al.,* 2025), the annual infection rate of Lassa virus across West Africa is from 100,000 to 300,000 cases, out of which approximately 5000 deaths results, with the majority of these cases occurring in Ondo, Bauchi, and Edo States. Ondo State consistently ranks among the top most affected states annually, reflecting ongoing intense transmission, environmental risk factors, and sustained reservoir–human contact.(Asogun *et al.,* 2025) Clinically, Lassa fever is characterized by non-specific symptoms such as fever, sore throat, chest pain, and gastrointestinal disturbances, but can progress to severe disease involving renal dysfunction, hepatic injury, shock, and bleeding tendencies. Hemorrhage in Lassa fever is related to microvascular injury, platelet dysfunction, and impaired coagulation. (WHO, 2023)(Okokhere *et al.,* 2018)(Duvignaud *et al.,* 2021), in the LASCOPE prospective cohort study involving over 500 patients, demonstrated that bleeding manifestations though less frequent compared to other viral hemorrhagic fevers are strong predictors of poor outcomes, with hematuria among the notable presentations associated with increased disease severity and higher mortality risk. Their findings also highlighted that abnormal liver enzymes, thrombocytopenia, high viral load, and delayed presentation were key prognostic markers.

Bleeding in Lassa fever arises from complex mechanisms including microvascular damage, endothelial dysfunction, increased vascular permeability, platelet dysfunction, and impaired coagulation rather than classical disseminated intravascular coagulation.(Horton *et al.,* 2020) This pathophysiologic pattern explains why tranexamic acid may offer limited benefit. It's worth mentioning that Tranexamic acid (TXA) is an antifibrinolytic agent sometimes used as adjunctive therapy in viral hemorrhagic fevers, although evidence is limited, and outcomes are inconsistent.(NCDC, 2018)(Rajapakse *et al.,* 2017)(Kiiza *et al.,* 2020) Tranexamic acid is a synthetic lysine analogue that prevents premature clot breakdown by blocking plasminogen's lysine-binding sites, thereby inhibiting its attachment to fibrin and reducing its activation to plasmin.(Lam *et al.,* 2023) Etamsylate (dicynone) has been shown to reduce bleeding by enhancing platelet adhesion to damaged endothelium and strengthening capillary walls, thereby promoting the early platelet plug formation and reducing capillary permeability without significantly affecting the coagulation cascade or fibrinolysis and has been used in menorrhagia, abnormal uterine bleed, post-operative and surgical bleeding control.(HU *et al.,* 2023) However, evidence on the use of etamsylate in viral hemorrhagic illnesses remains limited. (Ramos-Sánchez *et al.,* 2019)(Fraile *et al.,* 2019) Nonetheless, its use alongside tranexamic acid as adjunctive therapy has been reported in a pregnant woman with Lassa fever.(Adewole *et al.,* 2022).

Lassa fever in pregnancy is associated with extremely poor outcomes, with high maternal and fetal mortality rates. In the report by Adewole et al. (2022), two pregnant women with confirmed Lassa fever died despite receiving standard ribavirin therapy and supportive management. The study highlighted that bleeding manifestations including postpartum hemorrhage were prominent complications, contributing significantly to clinical deterioration. Because of the severity of bleeding in one of the cases, both tranexamic acid and etamsylate were used as adjunctive hemostatic agents, suggesting a potential role for etamsylate in controlling Lassa-associated hemorrhage. Given the persistent burden of Lassa fever in West Africa, Nigeria and especially in Ondo State; the need for effective adjunctive therapies for bleeding complications, and documentation of clinical responses to alternatives such as etamsylate is very crucial. This case series presents three adults with PCR-confirmed Lassa fever who developed persistent hematuria unresponsive to tranexamic acid but showed rapid improvement following etamsylate therapy.

Study Design: This was a retrospective case series describing adult patients with laboratory-confirmed Lassa fever managed at the Federal Medical Centre (FMC), Owo Isolation Centre, Ondo State, Nigeria. The study reviewed existing inpatient records, laboratory results, and treatment data to explore the relationship between tranexamic acid and improved nature of etamsylate therapy in the clinical outcomes in adults.

Ethical Considerations: This study was conducted as a retrospective review of routinely collected clinical data. The hospital management and infection control unit approved data use for research purposes, and all patient information was anonymized and all identifiers were removed. Formal ethical approval was waived in line with institutional and national guidelines for retrospective descriptive studies.

Case 1

History

A 32-year-old male farmer presented with 6 days of fever, malaise, chest pain, sore throat, and progressive dark-colored urine. He reported no comorbidities.

Examination

On admission, he was febrile (38.9°C), tachycardic (112 bpm), mildly hypotensive (98/60 mmHg), and moderately dehydrated with mild epigastric tenderness.

Investigation

Lassa virus RT-PCR was positive (CT values 27.84 and 29.66 for G and L genes respectively). Baseline Laboratory investigation revealed anaemia (PCV-25%), thrombocytopenia (PLT-98,000/uL), elevated liver enzymes (alkaline phosphatase-503IU/L, aspartate transaminase-471IU/L, alanine transaminase-497IU/L, hypoalbuminemia-28g/L) and gross hematuria on urinalysis.

Treatment

He received ribavirin per protocol, IV fluids, 2 units of whole blood, antibiotics, proton pump inhibitor and tranexamic acid 500mg every 8 hours for 5 days. Despite TXA, the hematuria persisted. Due to non-response, TXA was discontinued. Intravenous Etamsylate 500 mg 12 hourly was commenced. By day 2 of etamsylate therapy, urine color lightened, and by day 4, hematuria resolved completely and the patient was discharged on day 14.
The table below shows the clinical and laboratory timeline.

Table 1: Clinical and investigation timeline of case 1

Day	Clinical & Lab. Findings	Intervention/Treatment	Outcome
Day 1	Fever, malaise, chest pain, sore throat, progressive dark-coloured urine; Febrile-38.9°C; pale; tachycardia-112 bpm; BP 98/60 mmHg; moderate dehydration; mild epigastric tenderness; Lassa RT-PCR positive (CT 27.84 & 29.66); Anaemia (PCV 25%); Thrombocytopenia (98000/uL); Elevated liver enzymes (ALP-503 IU/L, AST-471 IU/L, ALT-497 IU/L); Hypoalbuminemia-28 g/L; Gross hematuria on urinalysis	Ribavirin protocol started; IV fluids; antibiotics; PPI; 1-unit whole blood; TXA 500 mg q8h, Vit K 10mg daily for 3 days (supportive medication in lieu of thrombocytopenia, ongoing bleeding, and elevated liver enzymes depicting some level of liver affectation)	Stabilisation initiated
Day 2	Persistent hematuria, malaise, febrile (38.0°C), pale, tachycardic 108b/m	1-unit whole blood transfused Continue care	Improved haemodynamics
Day 3	Hematuria persisted, malaise, febrile (37.4°C), PCV 31%, PLT 115000/uL,	Sustained ongoing care, stopped Vit k(improved platelet count)	In status quo
Day 4-5	Hematuria persisted, malaise, fever resolved	Discontinued TXA	In status quo

		Commenced IV Etamsylate 500 mg q12h	
Day 6-7	Urine started lightening, malaise, PCV 30%, PLT 113000/uL	Continued care	Improving clinical status
Day 8-9	Urine colour returned to normal, malaise, vitals stable	Sustained ongoing care	Marked improvement
Day 10-13	Malaise, Stable vitals	Discontinued Etamsylate, extended ribavirin	Stable
Day 14	General condition stable, PCV 28%, PLT 120000/uL, improved liver function (ALP-112 IU/L, AST-105 IU/L, ALT-98 IU/L), repeated PCR was negative	Discharged home	Good recovery

Case 2

History

A 45-year-old female trader presented with a week history of fever with associated headache, generalized body weakness and poor appetite, abdominal pain, and sudden onset of hematuria.

Examination

Examination findings revealed an acutely ill-looking woman, in obvious respiratory distress evidenced by flaring of the ala nasi, febrile (39.2°C), tachypneic (32c/m), tachycardic (113b/m), SpO2 90% and mild upper abdominal tenderness.

Investigation

Lassa virus RT-PCR was positive (CT values 27.84 and 26.66 for G and L genes respectively). Routine investigations revealed mild PCV of 35%, thrombocytopenia (PLT-110,000/uL), elevated liver enzymes (alkaline phosphatase-309IU/L, aspartate transaminase-571IU/L, alanine transaminase-397IU/L) and gross hematuria on urinalysis

Treatment

She was commenced on intravenous ribavirin and other supportive care including intravenous fluid, antibiotics, dexamethasone, and oxygen therapy. She also had tranexamic acid 500mg 8 hourly for 5 days. However, her hematuria remained unchanged, and on day 5 she developed worsening fatigue due to ongoing blood loss and PCV dropped to 28%. She received a unit of whole blood, TXA was discontinued, and intravenous etamsylate 500 mg 12 hourly was initiated. Hematuria began to decline within 36 hours and cleared by day 5 of etamsylate therapy. She improved progressively and was discharged after 15 days on admission.

The table below shows the clinical and laboratory timeline.

Table 2: Clinical and investigation timeline of case 2

Day	**Clinical & Lab. Findings**	**Intervention/Treatment**	**Outcome**
Day 1	Fever, headache, weakness, poor appetite, abdominal pain; sudden onset hematuria; Acutely ill; respiratory distress (ala nasi flaring); fever 39.2°C; RR 32c/min; SpO2-90% HR-113 bpm; upper abdominal tenderness; Lassa RT-PCR positive (CT 27.84 & 26.66); PCV 35%; Thrombocytopenia 110000/uL; Elevated	IV ribavirin started; IV fluids; IV antibiotics; IV dexamethasone; IV omeprazole, oxygen therapy @ 4L/min; TXA 500 mg q8h, IV	Stabilization of patient initiated

	liver enzymes (ALP-309 IU/L, AST-571 IU/L, ALT-397 IU/L); Gross hematuria	vit K, IV vit B complex	
Day 2-5	Persistent hematuria; worsening fatigue and appetite; Restless, acutely ill-looking, febrile 38.5^{o}C, tachypneic 34c/m, tachycardic 120b/m, SpO2-93% on intranasal oxygen (INO2) @ 4L/min; PCV 28% (ongoing hematuria), PLT 108000/uL	1-unit whole blood transfused, INO2 increased to 6L/min Discontinued TXA Commenced IV Etamsylate 500 mg q12h	Stabilization and rescue therapy started
Day 6-9	Improvement of hematuria, fatigue, and poor appetite; Febrile-(37.4°C), dyspneic-32c/m, SpO2-98% on intranasal oxygen therapy @ 6L/min; PCV 32%, PLT 120000/uL,	Reduced oxygen flow rate to 4L/min, Sustained ongoing care	Fair clinical state
Day 10	Hematuria and fever resolved, fatigue and poor appetite subsiding; Still dyspneic 28c/m, SpO2-99% on intranasal oxygen therapy @ 4L/min	Reduced oxygen flow rate to 2L/min Ribavirin extension	Improving clinical status
Day 11-14	Fatigue and poor appetite resolved, No longer dyspneic 22c/m, SpO2 100% @ 1L/min	Weaned off oxygen Discontinued Etamsylate	Significant improvement in clinical status
Day 15	Clinically stable, PCV 29%, PLT 125000/uL, improved liver function (ALP-102 IU/L, AST-115 IU/L, ALT-111 IU/L), repeated PCR was negative	Discharged home	Stable

Case 3

History

A 29-year-old male mechanic presented with 2-week fever, myalgia, chest pain, and passage of dark-coloured urine of 2-day duration.

Examination

Physical examination showed temperature of 38.7°C, pulse of 108b/m, and moderate dehydration.

Investigation

Lassa virus RT-PCR was positive (CT values 30.24 and 32.66 for G and L genes respectively). Baseline laboratory evaluations showed mild thrombocytopenia (132,000/uL), elevated liver enzymes (alkaline phosphatase-180IU/L, aspartate transaminase-166IU/L, alanine transaminase-173IU/L) and significant hematuria on urinalysis.

Treatment

He received ribavirin and other supportive therapies, including tranexamic acid 500mg 8-hourly. Nevertheless, hematuria failed to improve after 5 days on TXA and urine remained dark-coloured. He was commenced on intravenous etamsylate therapy at 500 mg 12 hourly while TXA was discontinued. Within 48 hours, there was a marked reduction in hematuria, and complete resolution occurred by day 6. He recovered fully and was discharged on day 12. The table below shows the clinical and laboratory timelines.

Table 3: Clinical and investigation timeline of case 3

Day	Clinical & Lab. Findings	Intervention/Treatment	Outcome
Day 1	Persistent fever, myalgia, chest pain; onset of dark-coloured urine; Temp 38.7°C; pulse 108 bpm; moderate dehydration, gross hematuria Lassa RT-PCR positive (CT 30.24 & 32.66); PCV 40%; Thrombocytopenia 132000/uL; Elevated liver enzymes (ALP-180 IU/L, AST-166 IU/L, ALT-173 IU/L	IV ribavirin started; IV fluids; IV omeprazole, antibiotics; TXA 500 mg q8h, IV Vit K 10mg daily for 3 days	Stabilization initiated
Day 2-5	Persistent gross hematuria; urine remained dark-coloured. Chest pain persisted; Febrile 37.8°C; PCV 28% (ongoing hematuria), PLT 108000/Ul	Discontinued TXA Commenced IV Etamsylate 500 mg q12h	Stabilization and rescue therapy started
Day 6-10	Significant improvement of hematuria; fever resolved PCV 36%, PLT 114000/uL,	Sustained ongoing care	Improving clinical status
Day 11	Hematuria resolved; Stable vitals	Completed treatment	Stable
Day 12	Clinically stable, PCV 34%, PLT 145000/uL, normalized liver function (ALP 42 IU/L, AST 50 IU/L, ALT 44 IU/L)	Discharged home	Full recovery

DISCUSSION

These three confirmed cases of Lassa fever were complicated by persistent hematuria that failed to resolve with tranexamic acid but improved within days of initiating etamsylate. Tranexamic acid exerts its haemostatic effect by inhibiting fibrinolysis, a mechanism that may be inadequate in Lassa fever where bleeding is not primarily driven by hyperfibrinolysis. Rather, hemorrhagic manifestations in Lassa fever are largely attributed to endothelial dysfunction, capillary fragility, and platelet impairment, as documented in both clinical and pathological studies.(Duvignaud *et al.,* 2021)WHO, 2023). The limited response to tranexamic acid observed in our patients therefore highlights a potential mismatch between the drug's mechanism of action and the underlying pathophysiology of Lassa fever–associated bleeding.

Lassa fever remains a major public health challenge in Nigeria, with recurrent outbreaks and significant morbidity and mortality particularly in endemic states such as Ondo, Edo, Bauchi, and Ebonyi. (Asogun *et al.,* 2025) Although hemorrhage is not a universal feature of Lassa fever, its presence is widely recognized as a marker of severe disease, reflecting extensive endothelial injury, capillary leakage, and multi-organ involvement.(Horton *et al.,* 2020) Hematuria, while often less dramatic than mucosal or gastrointestinal bleeding, is increasingly acknowledged as a clinically significant manifestation of severe infection that warrants close monitoring and timely intervention.(Horton *et al.,* 2020) The persistence of hematuria in our cases underscores the severity of disease and the need for effective supportive haemostatic strategies. The bleeding tendency in Lassa fever is more closely linked to capillary fragility, thrombocytopenia, and impaired platelet function than to classical coagulation failure or disseminated intravascular coagulation.(Horton *et al.,* 2020) This pathophysiological framework provides a plausible explanation for the observed therapeutic response to etamsylate in our case series. Etamsylate enhances capillary resistance, reduces microvascular permeability, and improves platelet adhesion, thereby promoting primary hemostasis without directly activating the coagulation cascade.(HU *et al.,* 2023)(Ramos-Sánchez *et al.,* 2019)(Fraile *et al.,* 2019) Its mechanism of action therefore appears better aligned with the vascular and platelet-driven bleeding seen in Lassa fever. Both the World Health Organization and the Nigeria Centre for Disease Control emphasize the importance of strengthening supportive care

measures, including early recognition and management of bleeding complications.(NCDC, 2018,WHO, 2023). Our findings support this recommendation, suggesting that early transition to an alternative haemostatic agent such as etamsylate may prevent progression to severe anemia, hemodynamic instability, and prolonged hospitalization.

All three patients in this series demonstrated rapid clinical improvement following etamsylate initiation, suggesting that it may offer greater benefit in the management of Lassa fever–associated hematuria. A similar use of etamsylate in combination with tranexamic acid has been reported in a case of postpartum hemorrhage complicating Lassa fever, although the clinical outcome was unfavorable.(Adewole *et al.,* 2022). While this underscores the severity and unpredictability of hemorrhagic Lassa fever, it also highlights the need for further systematic evaluation of etamsylate, including its optimal timing, dosing, and role as adjunctive therapy. Larger case series and prospective studies are required to better define its safety and efficacy in this setting.

CONCLUSION

Etamsylate showed a possible benefit in resolving persistent hematuria in all three Lassa fever patients after using tranexamic acid for some days without significant outcome, suggesting it may offer a more suitable hemostatic option for Lassa-related bleeding. Its rapid response and favorable safety profile highlight its potential clinical value in managing hemorrhagic complications, particularly in resource-limited and high-burden settings. This case series highlights that tranexamic acid may not adequately control Lassa fever–associated hematuria, whereas etamsylate demonstrated consistent success in the three adults described; suggesting a more beneficial therapy for use in complex hemorrhagic presentations. Emerging clinical experience suggests that etamsylate may serve as a valuable rescue therapy, targeting platelet function and capillary integrity where traditional antifibrinolytic therapy falls short. This documented case series not only contribute to the sparse evidence base, but also has the potential to reshape therapeutic strategies as well as improve patient outcomes. Further controlled research to establish evidence-based guidance and optimal use are needed to evaluate etamsylate's role in managing Lassa-related bleeding, as well as the optimal dosing and timing strategies.

RECOMMENDATIONS

1. Consider Etamsylate as Rescue Therapy**:** Etamsylate should be considered as an alternative hemostatic agent in Lassa fever patients who do not respond to tranexamic acid, especially when hematuria persists despite adequate TXA dosing.

2. Review Current Hemorrhage Management Protocols: Treatment guidelines for Lassa fever should be updated to acknowledge the potential role of etamsylate, particularly in bleeding patterns driven by capillary fragility and endothelial dysfunction.

3. Strengthen Early Monitoring of Bleeding Complications: Clinicians should conduct close monitoring of urine output, urine color changes, platelet levels, and liver function to detect hemorrhagic complications early and guide timely therapeutic adjustments.

4. Conduct Larger Controlled Studies: Well-designed clinical trials or prospective cohort studies are needed to evaluate the efficacy, optimal dosage, and safety profile of etamsylate in viral hemorrhagic fevers, including Lassa fever.

5. Improve Awareness among Frontline Clinicians: Healthcare workers in endemic regions should receive training on recognizing TXA-refractory bleeding and understanding alternative therapies such as etamsylate.

6. Enhance Supportive Care Infrastructure: Facilities in Lassa fever endemic areas should ensure the availability of essential hemostatic agents, blood transfusion support, and point-of-care diagnostics to optimize outcomes in severe cases

Limitations: This study is a small descriptive series, limiting the generalizability of our findings. There is also no control group used, as well as no pharmacologic monitoring done. Additionally, as a descriptive study, it does not allow for statistical inference. The last limitation is the subjective assessment of the haematuria resolution.

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