TJVS Turkish Journal of Vascular Surgery

Turk J Vasc Surg 2026;35(2):186-93
DOI: 10.9739/tjvs.2026.02.08

Available online at www.turkishjournalofvascularsurgery.org

Review Article

Hidden risk of antibiotic usage and tumescent local anesthesia: A clinical review

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Received: February 07, 2026 Accepted: April 09, 2026 Published online: June 09, 2026

Abstract

To analyze the pharmacokinetic interactions between high-volume tumescent local anesthesia (TA) and concurrent antimicrobial therapy in endovenous thermal ablation, and to propose a standardized safety protocol. A narrative review with a systematic literature search was conducted (1993–2026) using MEDLINE, Google Scholar, and Cochrane databases. Studies were selected based on clinical relevance to lidocaine pharmacokinetics, CYP450 enzyme inhibition, and documented adverse events in tumescent anesthesia settings. Three distinct risk categories for antibiotics were identified based on their inhibitory effects on lidocaine clearance. Analysis of case reports revealed that Local Anesthetic Systemic Toxicity (LAST) frequently manifests with delayed onset (8–18 hours post-operatively) in TA. Furthermore, 74% of recent LAST-related fatalities have been attributed to lidocaine, often in outpatient settings where early central nervous system (CNS) prodromes (agitation, trembling) are misidentified as benign sympathomimetic responses to epinephrine. Standardizing a 7–14 day antibiotic washout and integrating a medication-specific "Surgical Timeout" are essential. Clinicians must distinguish the neuro-excitatory signs of toxicity from adrenaline-induced reactions to prevent avoidable cardiovascular collapse.

Keywords: Endovenous ablation, lidocaine toxicity, Cytochrome P450, surgical safety, drug interactions

INTRODUCTION

Endovenous thermal ablation (ETA) relies on tumescent anesthesia (TA) for thermal protection and analgesia. While the dilute lidocaine technique (DLT) allows for higher dosages (up to 28 mg/kg), its safety is dependent on the hepatic cytochrome P450 system [1].

The Cytochrome P450 (CYP) system is a superfamily of membrane-bound hemoprotein isoenzymes located primarily within the smooth endoplasmic reticulum of hepatocytes. This system serves as the principal mediator of Phase I drug metabolism, utilizing oxidation, reduction, and hydrolysis to transform lipophilic medications such as lidocaine into polar, water-soluble metabolites (e.g., MEGX) suitable for biliary or renal excretion [2,3]. Understanding this enzymatic machinery is critical, as its inhibition or induction by common antibiotics directly determines the safety margin of tumescent anesthesia.

Lidocaine metabolism is predominantly mediated by two specific hepatic isoenzymes: CYP1A2 and CYP3A4. The primary metabolic route involves oxidative N-deethylation, converting the parent drug into its first pharmacologically active metabolite, monoethylglycinexylidide (MEGX), which subsequently undergoes further de-ethylation to glycinexylidide (GX) [4,5].

Recent pharmacokinetic data suggest that the contribution of these enzymes is concentration dependent. At systemic plasma concentrations typically seen during standard endovenous tumescent anesthesia, CYP1A2 (high-affinity, low-capacity) is the predominant driver of lidocaine clearance [4,5]. The historical focus on CYP3A4-mediated interactions led to an

CITATION
Toonder I, Doganci S. Hidden risk of antibiotic usage and tumescent local anesthesia: A clinical review. Turk J Vasc Surg. 2026;35(2):186-93.

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underestimation of the risk posed by CYP1A2 inhibitors. Consequently, the co-administration of Ciprofloxacin reduces lidocaine clearance by approximately 22%, significantly increasing the risk of delayed systemic toxicity in high-dose protocols [6]. CYP3A4 (low-affinity, high-capacity) becomes more active as lidocaine concentrations rise; while it is the most abundant CYP enzthreshold. [liver, its role in lidocaine metabolism is secondary until plasma levels approach the toxic threshold [3,4,7].

Because these enzymes have a finite processing capacity, introduction of an antibiotic that functions as a competitive or irreversible inhibitor (e.g., Clarithromycin for CYP3A4 or Ciprofloxacin for CYP1A2) creates a metabolic bottleneck. This results in an exponential increase in lidocaine elimination half-life (T1/2), which can extend the typical 90-minute half-life to over 4–6 hours, leading to delayed-onset LAST [1,6,8].

Many patients present for surgery while taking antibiotics for unrelated conditions. This review categorizes these risks and defines avoidable systemic complications arising from metabolic interference.

This review does not constitute a systematic review as defined by PRISMA guidelines. No formal meta-analysis or risk-of-bias scoring was performed. Study selection prioritized pharmacokinetic trials, pharmacovigilance analyses, and case reports directly relevant to lidocaine-antibiotic interactions in high-volume infiltration settings. Findings should be interpreted within the context of a narrative synthesis and expert clinical extrapolation.

A comprehensive narrative review with a systematic literature search was performed to identify pharmacokinetic interactions between lidocaine and antimicrobial agents. We searched electronic databases including PubMed/MEDLINE, Google Scholar, and Cochrane Library for English and Turkish language articles published between 1993 and 2026.

The following Boolean search strings were employed:

- "Tumescent anesthesia" OR "Lidocaine" AND "Antibiotics" OR "CYP3A4" OR "CYP1A2"
- "Endovenous ablation" AND "Drug interactions"
- "Local Anesthetic Systemic Toxicity" AND "Case Report"

Study selection articles were screened for clinical relevance to vascular surgery and endovenous thermal ablation. Priority was given to:

1. Studies detailing hepatic metabolic pathways of lidocaine.
2. Pharmacokinetic trials observing enzyme inhibition by fluoroquinolones and macrolides.
3. Documented case reports of LAST involving drug-drug interactions.

The clinical decision tree and washout periods were synthesized by cross-referencing established pharmacokinetic half-life data for potent enzyme inhibitors with Klein-style dosing standards for tumescent anesthesia.

Our analysis identified specific antimicrobial agents that significantly impair lidocaine clearance by inhibiting hepatic Cytochrome P450 isoenzymes.

Table 1 categorizes these agents, highlighting the risk of Category B (Potent Inhibitors) such as Ciprofloxacin and Clarithromycin. These inhibitors can reduce lidocaine clearance by up to 22–31%, significantly narrowing the safety margin during high-volume tumescent infiltration.

Pharmacokinetic modelling and intravenous lidocaine interaction studies suggest that concurrent Ciprofloxacin use may increase lidocaine Cmax by approximately 22–50%; however, these estimates derive from intravenous lidocaine studies, and their magnitude may differ in tumescent depot-absorption models [6].

Unlike inhibitors (Category B), Rifampin acts as an inducer (Category C). The induction of hepatic enzymes by Rifamycins is not an immediate process, nor is its resolution. Our protocol's 14-day washout requirement is supported by physiologically based pharmacokinetic (PBPK) modelling demonstrating that the disappearance of CYP3A4 induction requires precisely 14 days to return to baseline abundance [8]. An earlier surgical intervention would occur while the patient still possesses an artificially high enzyme load, leading to unpredictable and potentially toxic metabolic spikes of lidocaine derivatives [9].

Recommended washout durations are extrapolated from established pharmacokinetic half-life data for CYP enzyme inhibitors and inducers and PBPK modelling, and represent the authors' clinical synthesis rather than prospectively validated vascular surgery protocols [8,9].

The incidence of LAST in peripheral nerve blocks is estimated at 0.87 to 1 per 1.000 cases [10,11]. However, in high-volume tumescent anesthesia, data are less centralized. Large-scale surveys in related fields suggest a serious adverse event rate of approximately 19.1 per 100.000 [12]. There is a substantial likelihood that systemic complications from TA are significantly underreported due to three primary factors:

- **Delayed Onset:** Unlike traditional local anesthesia, where toxicity occurs within minutes, TA-related LAST often peaks 8–18 hours post-operatively due to depot absorption of subcutaneous lidocaine [1,13,14].
- **Atypical Presentation:** Approximately 40% of LAST cases present atypically, manifesting as isolated cardiac symptoms (bradycardia, hypotension) without the classic CNS prodrome (seizures) [7,15].
- **Diagnostic Misattribution:** Post-operative CNS or cardiac events in elderly or comorbid patients are often mislabelled

as primary strokes or myocardial infarctions, rather than recognizing the underlying metabolic bottleneck caused by an antibiotic interaction [16,17].

The literature search identified a persistent and increasing trend in lidocaine-related poisonings despite an overall decline in other local anesthetic toxicities [18,19]. In the context of outpatient vascular procedures, morbidity often arises when therapeutic dosages of lidocaine are rendered toxic by metabolic blockade (Table 2).

Analysis of these cases highlights a critical diagnostic trap. Early signs of toxicity, such as agitation and muscle trembling, are often misattributed to the adrenaline component during the procedure, facilitating progression from manageable CNS excitation to irreversible cardiac arrest [15,20,21].

While systemic inhibitors pose a clear risk, our analysis confirms a broad spectrum of Category A alternatives. As summarized in Table 3, the safety of an agent is dictated not only by its chemical class but also by its route of administration. Topical and ophthalmic formulations of known inhibitors (e.g., Ofloxacin) were found to be clinically neutral due to negligible systemic bioavailability [22,23].

Analysis of recent pharmacovigilance data reveals a critical shift in the landscape of LAST. While overall fatalities from long-acting anesthetics have declined due to ultrasound guidance and lipid rescue, lidocaine-related mortality has increased, now accounting for 74% of all published LAST fatalities [24].

This figure is derived from a 2025 pharmacovigilance analysis of the US National Poison Data System and reflects reporting trends across all clinical contexts of lidocaine use, not exclusively tumescent anesthesia populations. Caution is warranted in direct extrapolation to endovenous ablation settings [18,19,24].

Furthermore, fatalities in controlled operating rooms have decreased from 47% to 15%, while those in pre-hospital and outpatient settings have increased to 31%. In these settings, early CNS prodromes, specifically agitation and trembling are frequently misidentified as sympathetic responses to epinephrine rather than early-stage toxicity [19].

A common clinical counterargument suggests that for short-segment treatments (e.g., small saphenous vein or segmental perforators), the low total volume of TA renders these interactions negligible. In such cases, a surgeon might use only 150–200 mL of 0.1% lidocaine (150–200 mg), which is well within the 7 mg/kg traditional safety limit [1].

However, the risk of toxicity is not merely about total dose, but about peak plasma concentration (Cmax) and area under the curve (AUC). In the presence of a potent inhibitor like Ciprofloxacin, the Cmax of lidocaine can increase by nearly 50%, and its half-life can be significantly prolonged [6]. The risk of LAST correlates more closely with Cmax and AUC, both of which depend on the balance between systemic absorption and hepatic metabolism [25]. In tumescent local anesthesia (TLA), slow systemic uptake and delayed Cmax generally enhance safety in healthy individuals, but conditions that reduce hepatic metabolism, such as advanced age or subclinical hepatic congestion common in chronic venous insufficiency, narrow the metabolic buffer and increase susceptibility to toxicity [26].

Lidocaine toxicity in tumescent anesthesia is not purely dose dependent. Body composition is clinically relevant: because lidocaine is highly lipophilic, dosing referenced to total body weight (TBW) in obese patients may underestimate effective plasma concentration relative to hepatic metabolic capacity. Lean body weight (LBW)-based dosing is preferable in patients with elevated body mass index (BMI), and the total lidocaine dose should be calculated conservatively in the context of body composition, hepatic function, and concurrent medications.

Clinical and pharmacokinetic studies demonstrate prolonged lidocaine elimination in the elderly, and consensus reviews of TLA emphasize dose modification and vigilance when hepatic clearance is impaired, as elevated systemic concentrations (Cmax/AUC) are directly linked to neurologic and cardiovascular manifestations of LAST [27].

Elderly patients (>65 years) and those with clinically significant comorbidities,including hepatic impairment, congestive heart failure, and advanced chronic venous insufficiency with hepatic congestion, represent a distinct high-risk subgroup for LAST. In these patients, reduced hepatic blood flow and diminished CYP enzyme activity narrow the metabolic buffer even in the absence of drug interactions. We recommend that preoperative screening explicitly stratify these patients, with consideration given to dose reduction (≤15 mg/kg), extended post-operative observation beyond 18 hours, and avoidance of concurrent hepatically-metabolized medications where possible. In cases where lidocaine carries an unacceptable risk, prilocaine (Citanest) may warrant consideration as an alternative local anesthetic for the tumescent solution, given its substantially greater extrahepatic metabolism and reduced dependence on hepatic CYP pathways. However, clinicians should be aware that prilocaine carries a dose-dependent risk of methaemoglobinaemia via its metabolite o-toluidine, which is of relevance in high-volume tumescent infiltration; specialist guidance and further prospective evaluation in this setting are advised before routine adoption [26,27].

LAST typically presents with early central nervous system symptoms (metallic taste, perioral numbness, tinnitus, agitation) that may progress to slurred speech, muscle twitching, and generalized seizures. As plasma concentrations rise, cardiovascular manifestations including bradycardia, conduction abnormalities (PR/QRS prolongation), ventricular arrhythmias, and refractory cardiac arrest may occur. Prompt recognition is essential for early diagnosis and management [28].

Management of LAST follows established ASRA guidelines [7,20]. At the first sign of CNS excitation (agitation, tinnitus, perioral numbness), infiltration must be immediately halted and the patient assessed. Airway, breathing, and circulation should be secured. Benzodiazepines (e.g., midazolam) are first-line agents for seizure suppression. The cornerstone of pharmacological management is 20% Intravenous Lipid Emulsion (ILE) therapy: an initial bolus of 1.5 mL/kg followed by an infusion of 0.25 mL/kg/min, which acts as a lipid sink, sequestering free lidocaine from plasma and cardiac tissue. Epinephrine, if required for cardiovascular support, should be used at low doses (<1 mcg/kg). Prolonged resuscitation should be maintained, as lidocaine toxicity is potentially reversible with sustained lipid rescue. All facilities performing tumescent anesthesia should maintain a dedicated LAST rescue kit containing 20% lipid emulsion with clearly posted dosing protocols [7,20,28].

To ensure predictability, we recommend a standard Klein-style dilute solution: 445 mL of 0.9% NaCl, 50 mL of 1% lidocaine (500 mg), and 5 mL of 8.4% sodium bicarbonate, resulting in a 0.1% lidocaine concentration. This allows for high-volume infiltration (5–10 mL per cm of vein) required for effective thermal protection while staying within safe metabolic thresholds. In cases where perioperative infection prophylaxis is required, clinicians should consider tumescent anesthesia antibiotic delivery (TAAD). Adding antibiotics like Cefazolin directly to tumescent solution ensures massive, localized tissue concentrations and prevents surgical site infections without interfering with systemic lidocaine metabolism [29]. TAAD is particularly indicated in combined procedures, such as endovenous laser ablation (EVLA) plus extensive ambulatory phlebectomy, where the risk of skin flora contamination is higher [30].

In patients receiving neuraxial (spinal) or general anesthesia for whom tumescent anesthesia is still required for thermal protection, the lidocaine component may be reduced or omitted from the tumescent solution. Saline-based tumescent fluid (without lidocaine) can fulfill the perivenous thermal buffering function while eliminating systemic local anesthetic exposure. This approach is particularly valuable in high-risk patients — including the elderly, those with hepatic impairment, or patients on Category B/C antibiotics for whom procedural delay is clinically unacceptable. The decision to use lidocaine-free tumescent solution should be individualized and documented [1,25].

A key diagnostic challenge during the infiltration phase is the sudden onset of anxiety, tachycardia, and lower extremity trembling. While epinephrine commonly causes transient palpitations, focal muscle tremor and pronounced anxiety are characteristic of CNS excitation rather than adrenergic stimulation alone. In the presence of a metabolic bottleneck (e.g., concurrent Ciprofloxacin use), these findings should prompt immediate reassessment of rising lidocaine plasma levels rather than attribution to benign adrenergic effects. Continued infiltration under these circumstances risks progression to cardiovascular collapse, underscoring the necessity of the 'Stop and Assess' step embedded in our proposed protocol [15,31-33].

Because tumescent lidocaine is absorbed gradually from the subcutaneous depot, peak plasma concentrations occur 8–18 hours after infiltration — typically after ambulatory discharge. This depot-driven pharmacokinetic profile means that mild early symptoms — perioral numbness, tinnitus, or transient agitation — are frequently dismissed as post-procedural fatigue, and reporting fails unless the clinical picture escalates to seizure or cardiac arrest. Underreporting therefore represents a systematic bias that obscures the true incidence of lidocaine-related morbidity in outpatient vascular practice [27,32,33].

In our institutional experience, clinically significant lidocaine toxicity attributable to drug-drug interaction has been rare but not absent. The principal value of this review lies in recognizing that subclinical toxicity, manifesting as transient agitation, trembling, or mild tinnitus, may be significantly underreported due to misattribution to epinephrine effects or post-procedural fatigue. Prospective multi-centre registries are needed to establish true incidence rates in endovenous ablation populations.

Clinicians must differentiate systemic from topical antimicrobial therapy. Oral fluoroquinolones (Category B) require a mandatory 10-day washout, whereas topical ophthalmic ofloxacin (0.3%) generally does not achieve systemic concentrations sufficient to impair lidocaine metabolism and may be considered Category A (safe), except in patients receiving intensive fortified regimens for severe ocular pathology.

Although the tumescent technique relies on subcutaneous sequestration to achieve slow, depot-like absorption, inadvertent intravascular injection during perivascular procedures such as endovenous ablation remains a recognized risk. This bypasses the pharmacokinetic buffering of adipose tissue and may convert a therapeutic dose into a rapid intravenous bolus capable of precipitating acute LAST and cardiovascular collapse within minutes [1,7,13,32].

To mitigate this, strict use of real-time duplex ultrasound guidance is paramount. Continuous ultrasound monitoring not only ensures the necessary thermal jacket for the vein but also acts as the primary defence against systemic toxicity. In the presence of a metabolic bottleneck (e.g., Category B/C antibiotic use), an intravascular accident is significantly more lethal; therefore, visualization of needle-tip placement must be considered a non-negotiable standard of care.

Proposed Standardized Protocol and Best Practice Recommendations

To facilitate the practical application of these metabolic safety principles, we propose a standardized clinical algorithm (Figure 1), which should be utilized during both the initial preoperative assessment and the surgical timeout.

DOI: 10.9739/tjvs.2026.02.08

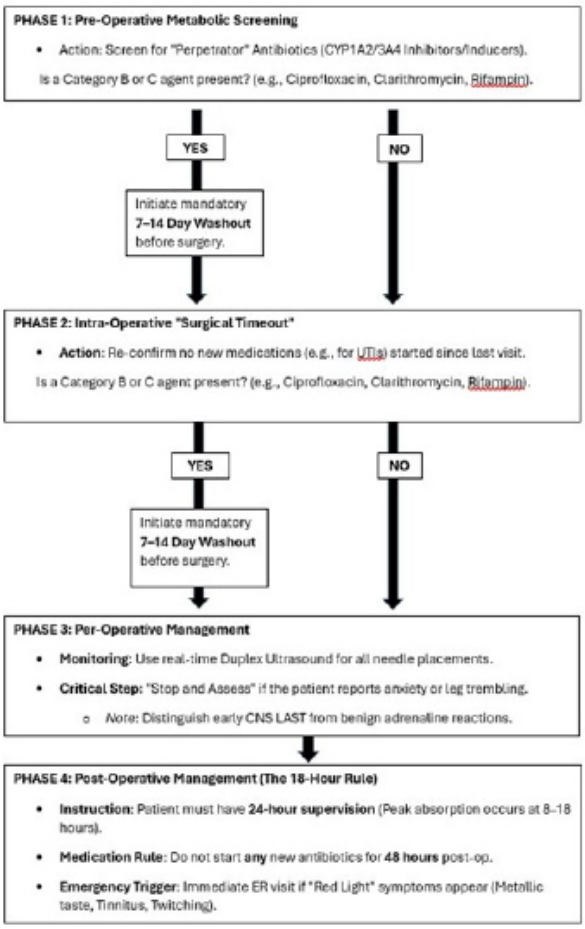

Figure 1. Clinical Algorithm for Metabolic Risk Stratification and Management of Tumescent Local Anesthesia. The algorithm details the pre-operative screening process, intra-operative monitoring, and post-operative safety rules based on hepatic CYP450 interactions. CYP: Cytochrome P450; LAST: Local Anesthetic Systemic Toxicity; TLA: Tumescent Local Anesthesia; ER: Emergency Room. Note: Mandatory washout periods are based on the pharmacokinetic half-life of Category B and C antimicrobial agents

In accordance with the WHO Surgical Safety Checklist, we recommend that a specific verbal check for "Recent Antibiotic Use" be added to the timeout procedure immediately prior to skin incision or catheter insertion [34]. Even if a patient was cleared during initial consultation, they may have started a Category B antibiotic (e.g., Ciprofloxacin for a urinary tract infection) in the intervening period. The surgical team must confirm that no enzyme-inhibiting agents have been ingested within the last 10 days. Impaired lidocaine clearance leads to LAST and, because TA is absorbed slowly, toxicity can manifest 12–24 hours post-operatively [32,35].

It must be acknowledged that the proposed 7–14 day antibiotic washout protocol represents a pharmacokinetically informed expert recommendation rather than a prospectively validated clinical guideline. No randomized controlled trial or large observational study has directly evaluated washout periods in tumescent anesthesia for endovenous ablation. Clinicians must weigh the metabolic risk reduction against the infectious risk of premature antibiotic discontinuation on an individualized basis. In patients with active or incompletely treated infections, a multidisciplinary approach involving the prescribing physician is strongly advised before enforcing elective surgical delay. Future prospective studies in vascular surgery populations are needed to validate these pharmacokinetic extrapolations.

By stratifying patients according to their current antimicrobial therapy and hepatic clearance status, clinicians can determine whether to proceed with the planned tumescent volume, implement a mandatory washout period, or select a metabolically neutral anesthetic alternative.

To maintain a precise 0.1% lidocaine concentration, clinicians must account for the pharmaceutical 10% rule and manufacturer overfill [36]. Standard 500 mL saline bags typically contain a 5–10% overage (approx. 25–50 mL). When adding 55 mL of medication (50 mL lidocaine + 5 mL bicarbonate) to a non-aspirated bag, the actual solvent volume can reach 605 mL, resulting in a final concentration of 0.082%, a nearly 18% deviation from the 0.1% target. This rigorous approach is necessitated by high reported rates of undetected compounding errors in manual drug preparation [37].

Patients should be reassured that the following symptoms are typical signs of the vein-closure process:

- **Ecchymosis (Bruising):** Common around the access site and along the treated vein segment.
- **Pulling/Tightness:** Occurs 5–10 days post-op as the treated vein undergoes fibrotic contraction.
- **Tenderness and Pigmentation:** Mild redness or a cord-like sensation along the vein (superficial thrombophlebitis) is a sign of successful ablation and typically resolves with walking and NSAIDs.

The central theme of this review, delayed lidocaine toxicity, must be distinguished from Deep Vein Thrombosis (DVT) and Endothermal Heat-Induced Thrombosis (EHIT). Both can present 12–24 hours post-operatively, but their signatures differ:

- **DVT/EHIT:** Presents as unilateral leg swelling, localized heaviness in the calf, or pain that worsens with dorsiflexion.
- **Lidocaine Toxicity (LAST):** Presents as systemic neurological or cardiac distress.

Because lidocaine has a known anti-thrombotic effect (inhibiting platelet activation), a patient with a metabolic bottleneck (on Ciprofloxacin) may have a lower risk of early DVT but a much higher risk of late-onset toxicity [33]. The agitation and trembling from toxicity can mimic the restlessness of early pulmonary embolism (PE), underscoring the need for a clear written discharge guide for patients (Supplementary 1).

Table 1. High-risk (Category B/C) inhibitors and inducers

Source reference	Antibiotic class	Specific agents	Interaction mechanism	Required washout	Category
Isohanni (2005) [6] Martin (2024) [38]	Fluoroquinolones	Ciprofloxacin	Potent CYP1A2 Inhibitor; reduces lidocaine clearance by 22-31%	7–10 Days	B (Inhibitor)
Bolhuis (2011) [39] Quellet (1998) [40]	Macrolides	Clarithromycin, Erythromycin	Strong CYP3A4 Inhibitors; elevates lidocaine AUC by up to 70% in oral/systemic models	7–10 Days	B (Inhibitor)
Niwa (2014) [41] Yamaguchi (2021) [42]	Antifungals	Ketoconazole, Itraconazole	Potent CYP3A4 inhibition; leads to rapid accumulation of lidocaine parent drug.	7–10 Days	B (Inhibitor)
Niemi (2003) [9] Bettonte (2023) [43]	Rifamycins	Rifampin, Rifampicin	Potent CYP3A4 Inducer; accelerates lidocaine to toxic metabolite MEGX spikes with unpredictable clearance	14 Days	C (Inducer)
Bolhuis (2011) [39]	Rifamycins	Rifabutin	Moderate CYP3A4 Inducer; similar to Rifampin but with ≈50% less potency in enzyme regulation	10-14 Days	C (Inducer)

Abbreviations: CYP: Cytochrome P450; AUC: Area Under the Curve; MEGX: Monoethylglycinexylidide

Table 2. Summary of documented adverse events and fatalities

Case source	Primary interaction/error	Peak plasma level	Clinical outcome	Key complication
Klein (1997) [35]	Sertraline & Flurazepam (CYP3A4 Inhibition)	6.1 – 6.3 mg/L	Morbidity	Delayed toxicity (10-23h post-op); dysarthria & memory loss
Mehra (1998) [44]	Lidocaine (Oropharyngeal Topicalization)	8–12 m g/L	Morbidity	Tonic-clonic seizure (CNS Toxicity)
Martin (2024) [39]	Therapeutic dose (Medial Branch Block)	<1.0 mg/L	Morbidity	Seizures despite "safe" levels; resolved with Lipid Emulsion (ILE)
Zuberi (2000) [45]	Lidocaine (Oropharyngeal Topicalization)	Not measured	Fatality	High-dose absorption leading to sudden asystole

Abbreviations: CNS: Central Nervous System; ILE: Intravenous Lipid Emulsion

Table 3. Antibiotics not influenced by tumescent anesthesia (Category A: Safe)

Antibiotic class	Recommended agents	Route & context	Clinical rationale
Cephalosporins	Cefazolin, Cefadroxil	IV / TAAD	Gold Standard. No CYP450 inhibition. Compatible with Tumescent Antibiotic Delivery [46,47,29]
Penicillins	Amoxicillin	Oral	Metabolically neutral. Safe for concurrent treatment of minor infections [39]
Tetracyclines	Doxycycline	Oral	No interaction with lidocaine clearance pathways [39]
Safe macrolide	Azithromycin	Oral	The only safe macrolide; does not inhibit CYP3A4 [39]
Fluoroquinolones	Ofloxacin	Topical (Ophthalmic)	Route Exception: Systemic absorption is <0.1% of oral dose; safe for concurrent use [22]
Dermatologicals	Erythromycin	Topical (Skin)	Route Exception: Topical application does not reach hepatic inhibitory thresholds [23]

Abbreviations: CYP: Cytochrome P450; TAAD: Tumescent Aesthesia Antibiotic Delivery; IV: Intravenous

CONCLUSION

Pharmacokinetic vigilance is a prerequisite for the modern vascular surgeon. By screening for non-related antibiotic therapy and enforcing 7–14-day washout periods based on specific drug class, we can effectively eliminate avoidable systemic complications. This structured approach ensures that the heat sink of tumescent anesthesia remains a safety feature rather than a metabolic liability.

The recommendations proposed in this review represent pharmacokinetically informed expert consensus synthesized from available pharmacokinetic, pharmacovigilance, and case-based evidence. Prospective validation in dedicated vascular surgery cohorts remains an important priority for the field.

Acknowledgments: During the preparation of this work, the authors used Gemini (Google) to assist in the structural organization and language refinement of the clinical review. The author reviewed and edited the content as needed and takes full responsibility for the clinical accuracy, literature synthesis, and final conclusions of the publication.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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