ГРНТИ 76.29.00
УДК 615.032.13-616.69-008.6 http://doi.org/10.47526/YJoHS-2025.3-14

ENDOLYMPHATIC ANTIBIOTIC THERAPY IN PATIENTS WITH RECURRENT UROGENITAL DISEASES RESISTANT TO TRADITIONAL ANTIBIOTIC THERAPY: A LITERATURE REVIEW

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Abstract. Endolymphatic and lymphotropic therapies have recently been applied across various medical fields, including acute surgical abdominal conditions, urology, gynecology, traumatology, phthisiology, and oncology. These therapies are used for both prevention and treatment of complications in urogenital diseases.

Objective: To review the literature on the efficacy of endolymphatic antibiotic therapy in men with recurrent urogenital diseases resistant to conventional antibiotic treatment.

Materials and methods: A comprehensive literature search was conducted using PubMed, Scopus, Web of Science, Medline, and Wiley Online Library for publications from 2015 to 2025. Fifty full-text, English-language articles were selected based on inclusion criteria: open access, high methodological quality, and relevance. Studies of low quality, conference abstracts, and articles without full-text access were excluded.

Results and Conclusions: Endolymphatic antibiotic administration is recommended as a primary treatment for men with acute inflammatory urogenital diseases. Literature analysis shows broad applications of endolymphatic and lymphotropic therapies in surgery, urology, gynecology, traumatology, phthisiology, oncology. Further research is needed to optimize drug selection, dosage, and administration schedules. Enhancing immune function through lymphological methods appears promising.

Keywords: anti-infective agents; drug resistance; endolymphatic infusion; urinary tract infections.

Дәстүрлі антибиотикотерапияға төзімді қайталама урогениталды аурулары бар науқастарда эндолимфатикалық антибиотикотерапия: әдебиеттерге шолу

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Аңдатпа. Эндолимфатикалық және лимфотроптық терапия жақында абдоминальды жедел хирургиялық аурулар, урология, гинекология, травматология, фтизиатрия және онкология сияқты бірнеше медициналық салаларда қолданыс табуда. Бұл терапиялар урогениталды аурулардың асқынуларының алдын алу және емдеуде пайдаланылады.

Received: 02.11.2025 / **Accepted:** 11.12.2025

Мақсаты: Дәстүрлі антибиотикотерапияға төзімді қайталама урогениталды аурулары бар ер адамдарда эндолимфатикалық антибиотикотерапияның тиімділігін зерттеу мақсатында әдебиеттерді шолу.

Әдістері: PubMed, Scopus, Web of Science, Medline және Wiley Online Library дерекқорларында 2015 жылдан 2025 жылға дейінгі мерзімде әдебиеттерді жан-жақты іздеу жүргізілді. Іріктелген 50 толық мәтінді ағылшын тіліндегі мақала қамтылды, енгізу критерийлері: ашық қолжетімділік, жоғары әдістемелік сапа және релеванттылық. Төмен сапалы зерттеулер, конференция баяндамалары және толық мәтіні жоқ мақалалар алынып тасталды.

Нәтижелері мен қорытындылары: Эндолимфатикалық антибиотик енгізу ерлерде жедел қабыну урогениталды ауруларды емдеуде негізгі әдіс ретінде ұсынылады. Әдебиеттер талдауы эндолимфатикалық және лимфотроптық терапияның хирургияда, урологияда, гинекологияда, травматологияда, фтизиатрияда, онкологияда және әскери дала хирургиясында кеңінен қолданылатынын көрсетеді. Дәрілерді таңдау, дозасы және енгізу режимдерін оңтайландыру үшін қосымша зерттеулер қажет. Иммундық жүйенің қызметін лимфологиялық әдістер арқылы ынталандыру емдеудің тиімділігін арттырудың перспективалы жолдарының бірі болып табылады.

Түйін сөздер: антимикробтық заттар; дәрі-дәрмекке төзімділік; эндолимфатикалық инфузия; зәр шығару жолдарының инфекциялары.

Эндолимфатическая антибиотикотерапия у пациентов с рецидивирующими урогенитальными заболеваниями, резистентными к традиционной антибиотикотерапии: обзор литературы

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Аннотация. Эндолимфатическая и лимфотропная терапия в последнее время применяется в различных медицинских областях, включая острые хирургические заболевания брюшной полости, урологию, гинекологию, травматологию, фтизиатрию и онкологию. Эти методы используются как для профилактики, так и для лечения осложнений урогенитальных заболеваний.

Цель исследования: Провести обзор литературы по эффективности эндолимфатической антибиотикотерапии у мужчин с рецидивирующими урогенитальными заболеваниями, резистентными к традиционной антибиотикотерапии.

Методы исследования: Проведен комплексный поиск литературы в базах данных PubMed, Scopus, Web of Science, Medline и Wiley Online Library за период с 2015 по 2025 годы. Отобрано 50 полнотекстовых статьи на английском языке, соответствующих критериям включения: открытый доступ, высокая методологическая качество и релевантность. Исключены исследования низкого качества, тезисы конференций и статьи без полного текста.

Результаты и выводы: Эндолимфатическое введение антибиотиков рекомендуется в качестве основного метода лечения мужчин с острыми воспалительными урогенитальными заболеваниями. Анализ литературы показывает широкое применение эндолимфатической и лимфотропной терапии в хирургии, урологии, гинекологии, травматологии, фтизиатрии, онкологии и военной полевой

Received: 02.11.2025 / **Accepted:** 11.12.2025

хирургии. Требуются дальнейшие исследования для оптимизации выбора препаратов, дозировок и режимов введения. Усиление иммунной функции с помощью лимфологических методов представляется перспективным.

Ключевые слова: противоинфекционные средства; лекарственная устойчивость; эндолимфатическая инфузия; инфекции мочевыводящих путей.

Introduction

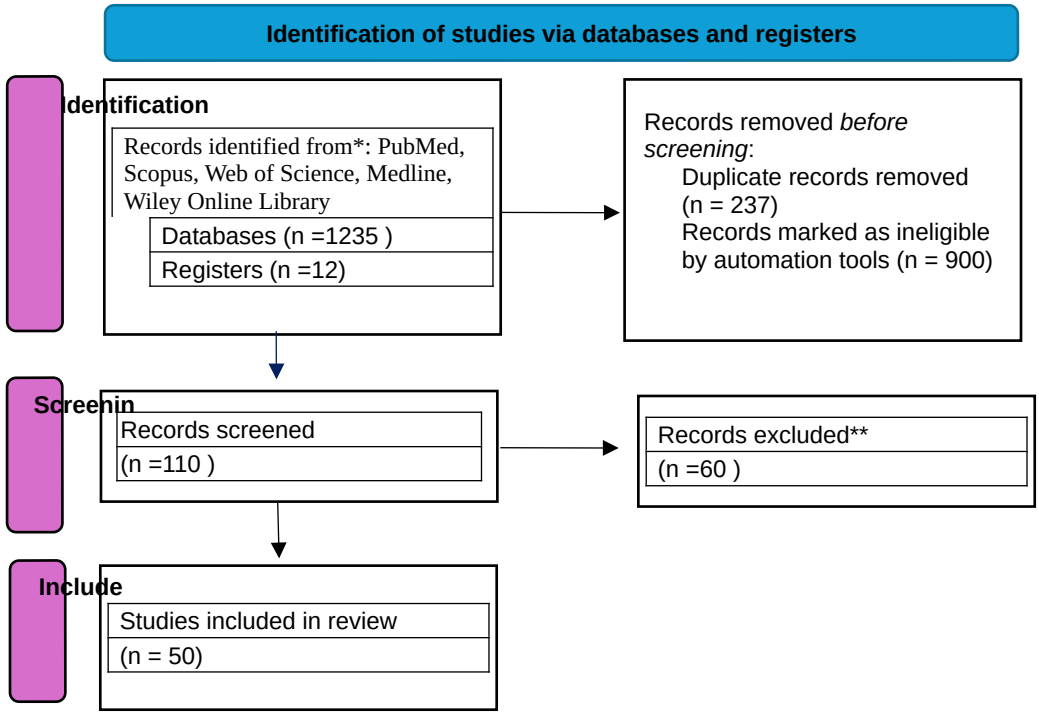
Endolymphatic and lymphotropic drug delivery strategies have emerged as promising alternatives to conventional systemic antibiotic therapies, particularly in disciplines such as abdominal surgery, urology, gynecology, and oncology, where optimizing pharmacokinetics and minimizing systemic toxicity are critical [1–3]. Their relevance is especially notable in the management of recurrent urogenital infections, where rising antimicrobial resistance significantly impairs the efficacy of traditional treatment regimens [4–6]. A key limitation of systemic antibiotic administration lies in its insufficient tissue penetration. For example, the prostate tissue-to-plasma ratio of piperacillin is only approximately 36%, underscoring the challenge of achieving adequate therapeutic concentrations in target organs [7]. In parallel, the emergence of multidrug-resistant uropathogens has contributed to persistent infections and high recurrence rates, particularly in chronic and recurrent urogenital conditions [8, 9]. In response to these challenges, alternative delivery routes such as endolymphatic and lymphotropic antibiotic administration have been increasingly explored. Endolymphatic antibiotic therapy (ELAT), which involves the direct administration of antimicrobial agents into the peripheral lymphatic system, enables targeted drug accumulation in regional lymph nodes and infected tissues. This not only improves local efficacy but also modulates immune responses through interactions with lymphatic immune cells [10]. Recent studies have revisited the clinical utility of ELAT in patients with urogenital infections refractory to standard systemic therapies, demonstrating prolonged local drug retention, enhanced therapeutic outcomes, and reduced systemic exposure [11, 12]. Moreover, lymphotropic antibiotic delivery has shown efficacy in the treatment of peritonitis of diverse etiologies and has been proposed as part of a novel therapeutic approach in conditions such as fibroplastic induration of the penis, particularly when combined with nitric oxide therapy [13]. Given the growing need for effective and targeted treatments in the era of antimicrobial resistance, this review aims to provide a comprehensive analysis of the current evidence on the efficacy, mechanisms, and clinical applications of endolymphatic antibiotic therapy in male patients with recurrent urogenital infections unresponsive to conventional antibiotic regimens.

Objective: To review the literature on the efficacy of endolymphatic antibiotic therapy in men with recurrent urogenital diseases resistant to conventional antibiotic treatment.

Materials and methods. A systematic search of literature from 2015 to 2025 was conducted using PubMed, Scopus, Web of Science, Medline, and Wiley Online Library. The inclusion criteria were English language, open access, and availability of full text; exclusion criteria included conference abstracts and low methodological quality studies. Fifty articles were selected for detailed analysis. The selection process followed PRISMA guidelines (Table 1).

Received: 02.11.2025 / **Accepted:** 11.12.2025

Table 1. PRISMA diagram



Risk of Bias Assessment. Since this review is based on published literature, a qualitative assessment of the risk of bias was performed for all included studies. Each article was evaluated according to key methodological criteria: clarity of study design, adequacy of sample size, presence of control groups, transparency of randomization (if applicable), completeness of outcome reporting, and potential conflicts of interest. For randomized controlled trials, the Cochrane Risk of Bias 2.0 (RoB 2) domains were considered. For non-randomized studies, relevant criteria from the ROBINS-I tool were applied. Each study was categorized as having a low, moderate, or high risk of bias based on the overall assessment of these domains. Discrepancies between reviewers were resolved by consensus. Because this work is a literature-based review, no formal statistical weighting or meta-analysis was performed, and the results of the bias assessment were used qualitatively to interpret the strength and reliability of the available evidence.

Results and Discussion. In urological practice, particularly among geriatric patients and individuals with immunosuppression, conventional systemic antibiotic therapy often fails to achieve sufficient drug concentrations in lymphatic structures involved in urogenital infections [14]. This pharmacokinetic limitation compromises the efficacy of treatment, contributing to persistent or recurrent infections. Recent studies have demonstrated that endolymphatic antibiotic therapy (ELAT) can lead to significant clinical improvement in patients with conditions such as prostatitis, epididymitis, and pyelonephritis, while utilizing lower antibiotic dosages compared to traditional systemic administration [15]. This reduction in dosage not only minimizes systemic toxicity but also potentially mitigates the emergence of antibiotic resistance. Furthermore, experimental and clinical data suggest that the sustained presence of antimicrobial agents within regional lymph nodes enhances local immune responses and helps contain the infection at the primary site [16]. Notably, the saturation of reticuloendothelial cells within lymphatic tissue appears to play a pivotal role in preventing

Received: 02.11.2025 / **Accepted:** 11.12.2025

microbial dissemination and the progression to systemic inflammatory responses or sepsis in the context of urogenital infections [17].

Application of Endolymphatic Antibiotic Therapy Across Various Medical Disciplines. Endolymphatic antibiotic therapy has demonstrated a significant reduction in the recurrence rate of erysipelatous inflammation, decreasing from 16.9% to 2.6%. This high efficacy is likely due to the early eradication of streptococcal infection reservoirs within the lymphatic system [18]. In a cohort of 160 patients with lung abscess, pneumonia, and chronic purulent bronchitis, treatment with gentamicin, brulamicin, pentrexyl, ketocef, and claforan via endolymphatic administration resulted in notable improvements in immune responsiveness. Delivering antibiotics directly into peripheral lymphatic vessels facilitates the saturation of reticuloendothelial components in lymph nodes, thereby enhancing their barrier function and preventing the dissemination of infection and multi-organ failure [19]. Furthermore, the efficacy of endolymphatic antibiotic therapy was assessed in pediatric patients suffering from chronic renal failure due to calculous etiology. The approach of short-course, lymphotropic antibiotic administration minimized systemic toxicity, particularly protecting structurally compromised renal tissue. Clinical data indicated that patients receiving regional endolymphatic antibiotics alongside conventional treatment exhibited earlier clinical improvement, with no incidence of acute exacerbation of calculous pyelonephritis or renal failure progression during the early postoperative phase [20]. Additionally, pharmacokinetic studies of ceftriaxone following endolymphatic infusion revealed sustained high drug concentrations in peritoneal exudate over a 24-hour period, supporting prolonged antimicrobial activity. The combination of antibacterial agents administered through both endovascular and endolymphatic routes was associated with accelerated recovery of organ function and improved outcomes in patients presenting with diffuse peritonitis complicated by intestinal failure syndrome [21]. The therapeutic effect of endolymphatic drug injection is based on three mechanisms: prolonged maintenance of therapeutic drug concentrations in biological fluids, lymph nodes, and the inflammation site due to antibiotic tropism to the lymphatic system; normalization of microcirculation in microvessels and interstitium; and an immunomodulatory effect through direct contact of the immunomodulator with immunocompetent lymph node cells [22]. Endolymphatic antibiotic therapy for peritonitis aims to provide anticoagulant, antibacterial, detoxifying, and immunostimulatory effects. Infusion via the lymphatic system enhances lymph transport into the bloodstream, promoting the restoration of normal microcirculatory function [23]. Endolymphatic antibiotic therapy has demonstrated high efficacy in managing erysipelas of the lower extremities. This effectiveness appears to result from targeted elimination of streptococcal infection within the lymphatic system, as confirmed by clinical and immunological assessments. A key measure of the therapy’s success is its pronounced ability to prevent disease recurrence [24]. The analysis of 34 female patients with locally advanced breast cancer allowed assessment of the outcomes of multimodal treatment and prognosis. Lymphatic duct drainage plays a key role in oncology, providing both cytological and immunological evaluation of lymph, as well as supporting therapeutic management of various malignancies, including locally advanced breast cancer [25]. Endolymphatic administration of sulodexide, selenase, and antibiotics promotes tissue repair, facilitating faster preoperative preparation. Although no statistically significant difference in ulcer healing was observed compared to controls, a trend toward improved healing of venous trophic ulcers suggests the need for further investigation [26]. Indirect endolymphatic therapy in patients with drug-resistant pulmonary tuberculosis promotes radiological stabilization, enhances microbiological clearance, and reduces the number of persistent bacilli excretors. It achieved a 95% reduction in bacilli carriers and closure of destruction cavities in 67.5% of cases

Received: 02.11.2025 / **Accepted:** 11.12.2025

[27]. Endolymphatic administration of anti-tuberculosis drugs improves treatment outcomes in patients with progressive tuberculosis [28]. Antimicrobial therapy remains the mainstay for chronic bacterial prostatitis. However, increasing antibiotic resistance and frequent treatment failures highlight the need for exploring novel therapeutic strategies [29]. A key challenge in medical research is developing therapeutic strategies targeting the lymphatic system, a critical contributor to the pathogenesis of acute and chronic conditions, including infections, atherosclerosis, diabetes, and autoimmune diseases [30]. Lymphatic drug delivery allows once-daily antibiotic administration, reducing total dosage, toxicity, allergenicity, and treatment costs. Compared to conventional methods, it can accelerate recovery, shorten hospital stays, and decrease complications and side effects [31]. The lymphatic system plays a key role in pathogen dissemination, including intra-abdominal infections. Pharmacology aims to develop targeted antibiotic delivery to lymphatic vessels and intestinal tissues, using agents that act as endolymphatic carriers to achieve high local drug concentrations [32]. The anatomical and physiological features of the lymphatic system make endolymphatic delivery of antibiotics and immunomodulators highly effective. Enhanced vessel permeability, slow lymph flow, and drug accumulation in lymph nodes contribute to improved outcomes in acute inflammatory and septic conditions of the thoracic and abdominal organs [33]. Microorganisms from the primary focus may spread via lymphatics to lymph nodes, causing obstruction and secondary infection. This supports the use of lymphotropic drug delivery, including antibiotics and therapeutic mixtures [34]. Antibiotic entry from the interstitial space into lymphatic capillaries is facilitated by increased local venous pressure (compression cuffs) and lymphotropic agents (lidase, trypsin, chymopsin), which enhance vessel permeability. This approach significantly improves drug delivery to pathological sites, including inflammation, wounds, and degenerative tissues [35]. Compared to conventional treatment, lymphotropic therapy accelerates healing of gunshot wounds, reduces edema, enhances resorption of necrotic tissue, foreign particles, and microbes, promotes early muscle fiber recovery, and limits pathological remodeling of the wound defect [36]. In lymphotropic therapy, drugs were administered subcutaneously in the submandibular region targeting the submandibular lymph nodes. Clinical recovery in patients with acute purulent maxillary sinusitis was 72.5% with conventional therapy and 94.4% following lymphotropic treatment [37]. In the treatment of facial furuncles and carbuncles, antibacterial lymphotropic therapy combined with phytotherapy improves microcirculation at the inflammation site and increases antibiotic concentration in biological fluids [38]. Lymphotropic antibiotic therapy reduced residual changes affecting lung function and promoted rapid subjective improvement in patients with tuberculous pleuritis [39]. During lymphotropic therapy, optimal drug concentration at the target site is maintained for 24 hours [40]. Analysis of endomesenteric lymphotropic therapy in postoperative abdominal surgery shows it accelerates gastrointestinal function recovery [41]. Regional lymphotropic administration delivers drugs directly to lymphatic capillaries, concentrating them in nearby lymph nodes and pathological sites, achieving higher local levels than conventional methods [42, 43]. Endolymphatic hydrops is an uncommon but recognized complication following cochlear implantation, and optimal management strategies are still being defined. Endolymphatic hydrops after cochlear implantation successfully managed with intratympanic gentamicin. This treatment effectively alleviated symptoms while maintaining implant performance. Intratympanic gentamicin may therefore serve as a less invasive alternative to labyrinthectomy [44, 45]. Endolymphatic shunt surgery achieved vertigo control comparable to that of intratympanic gentamicin injections, while demonstrating a lower rate of audiovestibular adverse effects [46, 47].

Using Endolymphatic Antibiotic Therapy in Urogenital Pathology. Inflammatory conditions of the genitourinary system in individuals aged over 70 frequently occur in the

Received: 02.11.2025 / **Accepted:** 11.12.2025

context of compromised lymphatic immunocompetence, often resulting in failure of the lymph nodes' barrier function and subsequent urosepsis. Conventional antibiotic administration methods inadequately target lymph node inflammation, leading to suboptimal therapeutic outcomes. In this context, endolymphatic antibiotic administration was employed in patients with acute inflammatory disorders, including pyelonephritis, prostatitis, and orchiepididymitis. Cannulation of the peripheral lymphatic vessel in the foot allowed administration of antibiotics such as gentamicin, tobramycin, amikacin, and ampiox at doses two to three times lower than those typically used in systemic therapy. This catheterization method maintained patient mobility, enabling concurrent prophylactic interventions against hypostatic complications. Clinical improvement was documented in 86% of cases, with 62.5% of patients receiving endolymphatic therapy following the failure of conventional antibiotic regimens. These findings suggest that endolymphatic antibiotic therapy represents a highly effective approach for managing purulent infections in elderly urological patients [48]. Moreover, endolymphatic antibiotic administration has been recommended as a frontline therapeutic strategy for acute inflammatory diseases of the scrotum [49]. In a separate investigation involving 21 patients with complicated urogenital tuberculosis, continuous endolymphatic antibiotic therapy using klaforan and gentamicin was administered over 3 to 13 days. The frequent occurrence of urinary tract lesions, chronic renal failure, and microbial resistance compromised the efficacy of standard treatment protocols. Utilizing a modified dosator device, continuous polycollector endolymphatic antibiotic delivery was combined with simultaneous lymphatic channel lavage, enhancing therapeutic outcomes [50].

Conclusion: Endolymphatic administration of antibiotics is recommended as a primary treatment method for male patients with acute inflammatory diseases of the urogenital system. The literature analysis demonstrates that endolymphatic and lymphotropic therapies have been successfully applied in acute surgical diseases of the abdominal cavity, urology, gynecology, traumatology, phthisiology, oncology, and military field surgery. However, further research is needed to determine the optimal drug selection, dosage, and duration of administration. Stimulating immune system mechanisms through lymphological therapy appears to be one of the most promising approaches to enhancing treatment effectiveness.

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Received: 02.11.2025 / **Accepted:** 11.12.2025