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A Multidisciplinary Approach to Managing Recurrent Urinary Tract Infections: The Integral Roles of Infectious Diseases and Urology in Enhancing Patient Outcomes

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Abstract

Background: Urinary tract infections (UTIs) are a prevalent health issue, particularly among non-pregnant women. Recurrent UTIs (rUTIs) pose significant clinical challenges, leading to increased healthcare utilization, antibiotic prescriptions, and potential antimicrobial resistance. Understanding the multidisciplinary approach involving infectious diseases and urology is crucial for effective management.

Methods: This review synthesizes recent literature on the management of recurrent UTIs, focusing on the roles of infectious disease specialists and urologists. A comprehensive search was conducted using databases such as PubMed, Scopus, and MEDLINE, with keywords including "recurrent urinary tract infections," "infectious diseases," "urology," and "multidisciplinary approach." The analysis included guidelines, clinical studies, and expert opinions published from 2010to 2023.

Results: The findings indicate that a multidisciplinary approach can significantly enhance the management of rUTIs. Collaboration between urologists and infectious disease specialists improves diagnostic accuracy and treatment efficacy, particularly in identifying resistant uropathogens. Current treatment strategies emphasize personalized antibiotic regimens, preventive measures, and the exploration of non-antibiotic options, including herbal therapies and vaccine development.

Conclusion: The integration of infectious diseases and urology in managing recurrent UTIs is essential in addressing the complexities of this common condition. A collaborative framework can optimize patient outcomes, reduce the incidence of antibiotic resistance, and improve overall healthcare delivery. Future research should focus on developing standardized protocols that incorporate multidisciplinary teamwork in the management of rUTIs.

Keywords: Recurrent urinary tract infections, multidisciplinary approach, infectious diseases, urology, antibiotic resistance.

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1. Introduction

Bladder infections in non-pregnant women without documented operational or anatomical defects or concurrent illnesses are often referred to as unsophisticated urinary tract illnesses (uUTIs) [1]. These are distinct from severe pyelonephritis and complex urinary tract infections (cUTIs). The latter constitutes a diverse array of illnesses, including those affecting male patients and females with specific co-morbidities and anomalies that influence urological function, as well as healthcare-associated and systemic infections [2].

Urinary tract infections (uUTIs) are prevalent among female patients across all age groups, with a yearly frequency of around 11%, and occur more often than complicated urinary tract infections (cUTIs) [2,3]. As many as 80% of females may encounter at least one uncomplicated urinary tract infection (uUTI) throughout their lifetime, with around 45% experiencing recurring uUTIs [4-6]. Due to their commonality, uUTIs constitute a significant burden; without timely and efficient intervention, symptoms may be incapacitating for many days, affecting professional and everyday activities [8-10].

The essential requirements of patients with uUTIs include precise and prompt diagnosis, followed by quick alleviation of symptoms. Current recommendations advocate for the empirical prescription of specific antibiotic medicines, which continues to be a useful strategy for acute episodes [11-13]. In young women presenting with their first episode of uUTI signs, urine culture is not advised when a definitive diagnosis can be established by patient history and the exclusion of alternative symptomatology, which is crucial to reduce overdiagnosis and unnecessary therapy [14-16]. Urinary tract infections (uUTIs) are prevalent illnesses linked to antimicrobial prescriptions, and prior antibiotic exposure correlates with a heightened risk of antimicrobial resistance (AMR), potentially posing a public health concern [17,18]. Specifically, antimicrobial resistance (AMR) of prevalent uropathogens, such as *Escherichia coli*. The prevalence of *E. coli* resistance to commonly used medications for the treatment of uncomplicated urinary tract infections, such as fluoroquinolones, is rising in several countries [19,20]. Fluoroquinolones temporarily inhibit commensal intestinal Enterobacteriaceae, linked to the development of antimicrobial resistance (AMR), and resistant strains may subsequently disseminate to unexposed household contacts of patients undergoing fluoroquinolone treatment for urinary tract infections (UTIs) [21]. Therefore, there is a need for innovative oral medicines effective against resistant varieties of uropathogens, particularly extended-spectrum β-lactamase (ESBL)-producing E. Coli strains that are becoming widespread globally [22-26].

The appropriateness of antimicrobial treatment remains a significant issue. Recently, the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have issued cautions about the use of fluoroquinolones for infections including uncomplicated urinary tract infections (uUTIs) [27-29]. Specifically, the potential for significant detrimental effects on many organ systems, cognitive function, and glycemic regulation has led to recommendations against using these medications for uncomplicated urinary tract infections unless no other options are available [1,11].

Recurrent urinary tract infections (uUTIs) pose a significant problem for several women, leading to multiple consultations with different healthcare providers and frequent antibiotic prescriptions, which heightens the risk of adverse consequences [30-32]. Consequently, several women may elect to forgo many doses of antibiotics and pursue other therapeutic modalities [33-35]. The current study aims to address existing difficulties and enhance the care of females with uUTIs. comprising urologists, obstetricians/gynecologists, infectious disease specialists, emergency medicine doctors, clinical microbiologists, and primary care physicians.

2. Diagnosis of simple urinary tract infections

Symptoms are the fundamental basis for the diagnosis of uUTI [1,11-15]. It was concurred that the symptoms of uUTIs are non-specific and may coincide with those of other conditions, including pyelonephritis, cUTIs, sexually transmitted infections (STIs), overactive bladder (OAB), urethral pain syndrome, interstitial cystitis/painful bladder symptoms, and menopausal symptoms in older women [1,36-39]. Symptoms highly indicative of a urinary tract infection (uUTI) include dysuria, urgency, and frequency; an increased number of symptoms correlates with a heightened probability of uUTI [40,41]. Prior reported instances of uUTI elevate the likelihood of recurrent infection. It was noted that symptoms alone may be inadequate to definitively establish a diagnosis of uUTI and might result in overdiagnosis. The length and intensity of symptoms may inform diagnostic and treatment recommendations. Validated scoring instruments for diagnosing uncomplicated urinary tract infections (uUTI), such as the Acute Cystitis Symptom Score (ACSS) and the Urinary Tract Infection Symptom Assessment (UTISA) questionnaire, may assist in treatment decision-making.

Excluding illnesses other than uUTIs is crucial, since they may need more study and other treatment strategies. Distinguishing between pyelonephritis and cUTI is essential, since symptoms including fever, flank discomfort, nausea, and vomiting may indicate these more severe infections [1]. Excluding diagnoses other than urinary tract infections (UTIs) is crucial, as these generally do not necessitate antimicrobial treatment. Such conditions include interstitial cystitis, overactive bladder (OAB), urethral pain disorder, and genitourinary signs in older women associated with menopause [42-45]. In sexually active women, contemporaneous vaginal discharge may signify a sexually transmitted infection (STI) or vaginitis and decrease the likelihood of an uncomplicated urinary tract infection (uUTI); nevertheless, more evaluation may be required, including STI testing, pelvic examination, and urine culture. Other diagnostic markers other from uUTI include defective emptying and neurogenic bladder.

Dipsticks are readily accessible, cost-effective, and provide prompt findings; in some areas, they are commonly used in conjunction with symptom assessment. Nevertheless, these tests are generally not definitive for uUTIs when considered alone—a negative result does not rule out infection—but may serve as adjunctive evidence when the symptomatology is inadequate for an accurate identification (nitrite examination for bacteriuria as well as leukocyte esterase for pyuria) [40,41,45,46]. Whenever any of the symptoms align with the findings of an uUTI and an individual has a history of UTIs, a dipstick test is often deemed unnecessary. The panel concluded that the detection of bacteriuria/pyuria with dipsticks may result in unwarranted reflex urine cultures and/or excessive therapy if the findings are not accurately interpreted alongside clinical signs.

Substantial bacteriuria in a urine culture, accompanied by indicative signs and symptoms, is the definitive criterion for diagnosing a urinary tract infection (UTI). The panel concurred that urine culture, as well as antimicrobial susceptibility tests, should be performed solely under the following conditions: during an initial or recurrent episode with belief of a resistant uropathogen; if symptoms persist or deteriorate during treatment; if infection recurs within four weeks of the initial episode; or when the diagnosis of uUTI is ambiguous (atypical symptoms). No agreement exists on a threshold for severe bacteriuria as outlined in guidelines—data indicate the presence of *E. coliform* bacteria in concentrations as low as 102 CFU/mL in urine is indicative of *E. coli* colonization in the bladder when coupled with characteristic symptoms, may still signify an ongoing infection [47].

3. Management of acute recurrent urinary tract infections

To achieve quick symptom relief, it was agreed that if taking history yields a definitive diagnosis of uUTI and rules out other illnesses, empirical antibiotic therapy should be administered without the need of a urine culture [48]. If the conclusion of therapy does not attain symptom recovery or if a patient encounters a recurring uUTI during the subsequent 3 months, urine culture and antibiotic susceptibility testing should be contemplated at this juncture [1,49-51]. Treatment adjustments may be necessary

based on these data, which might suggest that treatment failure is associated with improper addressing of uropathogens or the existence of a resistant uropathogen.

Existing treatments, including fosfomycin, pivmecillinam, andnitrofurantoin, are well recognized as helpful for treating acute uncomplicated urinary tract infections in many people. At present, there are no explicit guidelines for the selection of antimicrobial therapy for individuals with ESBL- and carbapenemase-producing organisms; nonetheless, in vitro studies indicate significant susceptibility to nitrofurantoin, fosfomycin, and pivmecillinam. The tolerability of these three medicines is typically favorable, and historically, resistance has been minimal, albeit not insignificant, according to recent findings. Trimethoprim/sulfamethoxazole (TMP-SMX) is recognized for its efficacy; nevertheless, its use may be constrained by elevated resistance rates globally [18,52-56].

Antimicrobial as well as non-antimicrobial (indicative) therapies are not mutually exclusive and may be administered together, although some patients may choose the latter. Nonetheless, the function of these therapies remains ambiguous; yet the increasing prevalence of antimicrobial resistance may make their use more attractive.Ibuprofen has been evaluated against antibiotics in two distinct randomized controlled trials (RCTs). In the first randomized controlled trial, 39% of patients in the ibuprofen cohort were asymptomatic by Day 4, in contrast to 56% of patients in the fosfomycin cohort [57]. The median duration of uUTI symptoms was one day higher in the ibuprofen cohort, with 31% of patients later requiring antibiotics. Pyelonephritis was documented in five women administered ibuprofen and one woman administered fosfomycin. The second non-inferiority research evaluated ibuprofen against pivmecillinam in premenopausal women [58]. By Day 4, symptoms had abated in 39% of individuals assigned to ibuprofen and 74% of those assigned to pivmecillinam, respectively. The median duration of symptoms was 6 days for ibuprofen and 3 days for pivmecillinam, with 41% of patients in the ibuprofen group receiving antibiotics within 14 days. Seven women in the ibuprofen cohort had pyelonephritis, but none in the pivmecillinam cohort did.

The effectiveness of diclofenac in women with uncomplicated urinary tract infections has been compared to norfloxacin. A much higher proportion of patients in the norfloxacin group achieved symptom remission by Day 3 compared to the diclofenac group, with 41% of women assigned to diclofenac requiring rescue antibiotics at this timepoint. Six instances of pyelonephritis were seen in women administered diclofenac, but none were reported in those receiving norfloxacin ($P = 0.03$) [59].

Some panel members believe that individuals with moderate to mild symptoms may initially receive analgesics after consultation, should they wish to forgo antimicrobial therapies [1,60]. However, a medical recommendation for antimicrobial medication should be provided if symptoms do not improve within 2–3 days. Patients must be informed of the possibility of pyelonephritis, analgesic usage should be restricted to a maximum of three days [60], and they should be instructed to quickly contact their healthcare practitioner if symptoms intensify.

A recent phase 3 randomized controlled trial evaluated the benefits of 7 days of therapy with either an herbal product (BNO 1045) or one administration of fosfomycin in 659 women with severe uncomplicated urinary tract infections. From Days 1 to 38, eighty-four percent of the individuals in the BNO 1045 category refrained from taking further antibiotics, compared to 90% in the fosfomycin group, with the difference remaining within the predetermined non-inferiority margin. The intensity of symptoms was equivalent at baseline and significantly diminished in both groups throughout time to a comparable degree. In the BNO 1045 group, there were five instances of pyelonephritis, whereas the fosfomycin group reported one occurrence [61].

A uva ursi extract formulation was compared to fosfomycin in a randomized controlled trial done in Germany, which included 398 women with uncomplicated urinary tract infections (uUTI) [62]. While the uva ursi extract correlated with decreased antibiotic use, symptom relief was shown for markedly fewer women in this cohort compared to those receiving fosfomycin. Significantly, there were eight instances of pyelonephritis in the uva ursi extract group and two in the fosfomycin group [62].

A recent randomized controlled trial involving 122 women with recurrent uncomplicated urinary tract infections compared Bazheng powder (administered for 4 weeks) to either levofloxacin or amoxicillin/clavulanic acid (1 week of therapy followed by 3 weeks of placebo) [63]. Within four weeks, clinical resolution of the acute episode was attained by 90.2% of women administered the herbal mixture, in contrast to 82.0% of women treated with antibiotics, a difference that was not statistically significant.

It was concurred that the limited quantity of high-quality randomized controlled trials (and therefore the absence of systematic reviews) to substantiate most non-antimicrobial strategies for the acute management of uncomplicated urinary tract infections (uUTIs) permits discussion of these treatments alongside antimicrobial therapy, although no conclusive recommendations can be established. Postponing antibiotic treatment in women with only minor symptoms is feasible, if the patient consents, however vigilant monitoring is essential.

4. Prevention of recurring simple urinary tract infections

In evaluating patients with recurrent uUTIs, it is crucial to gauge their comprehension of symptoms, since some may normalize them and delay seeking treatment. Furthermore, postmenopausal women may exhibit distinct characteristics and need an alternative diagnostic and therapeutic strategy compared to younger women. Symptoms may be misattributed to other illnesses, such as menopause or overactive bladder [36,37]. Recognizing possible risk factors for relapse is essential for initiating discussions on therapeutic solutions.

Nonetheless, the outcomes of cultures from prior events (because historical resistance forecasts present resistance) and regional resistance trends need to inform empirical therapy [64]. Continuous or intermittent antibiotic prophylaxis is a viable choice for women experiencing recurrent and troublesome recurrences, however, the potential for adverse effects and antimicrobial resistance must be taken into account [31,51,65,66]. Self-initiated antimicrobial treatment may be deemed appropriate for individuals with a history of recurrent urinary tract infections (uUTIs), presenting analogous symptoms, and who can be trusted to consult their healthcare professional if there is no symptom improvement. The length of antimicrobial treatment should be minimized. Prolonged preventive therapy should not exceed 12 months; for women with recurring infections linked to sexual activity, a single-dose prophylaxis administered before or after intercourse may be helpful [67,68]. In elderly individuals, the hazards associated with long-term antibiotic prophylaxis surpass the benefits. The effects of prolonged antibiotic exposure on the microbiome, referred to as 'collateral damage', remain mostly unexplored for many frequently used antimicrobial drugs, except fluoroquinolones; further study is required.

Several factors warrant the consideration of non-antimicrobial strategies for the prevention of recurrent uncomplicated urinary tract infections (uUTIs), including tolerance, safety, concerns around antimicrobial resistance (AMR), and patient preference. Women with recurrent uncomplicated urinary tract infections (uUTIs) may elect to forgo several courses of antimicrobials due to concerns about side effects, the potential for more infections, and the apprehension that prolonged usage may reduce their efficacy, hence limiting treatment alternatives in cases of severe infections [69,70]. Consequently, some women have sought various alternative therapies to avert further occurrences [3]. The panel concurred that these treatments warrant discussion; nevertheless, no conclusive recommendations were established due to the insufficient supporting data. Counseling should include a discussion of risk factors, such as sexual intercourse and the use of spermicides. Nonetheless, limiting sexual intercourse may be undesirable or impractical for some individuals. In discussions on personal cleanliness, it is crucial to inform the patient about the possible effects of excessive cleansing of the vaginal area on the local microbiota.

5. Managing simple urinary tract infections under rising antibiotic resistance

All experts agreed on the need for local monitoring data primarily pertaining to community-acquired uUTIs. Nevertheless, considering the therapeutic efficacy of existing antimicrobial medicines, such information is unlikely to significantly enhance patient outcomes at present. A significant problem ahead is the effectiveness of antimicrobials against the rising incidence of ESBL-producing uropathogens in

community environments. Presently, levels are comparatively low in North America and some regions of Europe, but they are significantly elevated in Latin America and Asia [22,24-26]. Carbapenemase-producing uropathogens are increasing in prevalence and pose an escalating danger to successful antibiotic treatment.

The collection of resistance data within the community is challenging due to: the low percentage of patients with uncomplicated urinary tract infections (uUTIs) undergoing urine culture and susceptibility testing, resulting in a highly selective patient subgroup, biased culture results, and hindering extrapolation to the broader population; and the necessity for primary care provider involvement to amass adequate data, which would increase workloads and expenses. An alternative metric to inform empirical prescription for uUTIs, in the absence of surveillance data, is the recognition of individual patient risk factors for antimicrobial resistance (AMR). Factors include advanced age, chronic medical disorders, recent antibiotic exposure, travel to regions with high antimicrobial resistance (AMR), and prior urine cultures indicating AMR [19,64,71-75].

6. Conclusions

The diagnosis procedure may be streamlined and standardized across healthcare organizations. Antimicrobial medications are fundamental for the treatment and prevention of several instances, necessitating more study into the effectiveness and safety of non-antimicrobial methods. Minimizing fluoroquinolone usage is essential to mitigate toxicity risks, decrease resistance selection pressure, and conserve these medicines for patients with severe illnesses. Enhanced use of international norms within the framework of local monitoring data is required. In the absence of this, enhanced recognition of risk factors for AMR might enable suitable empirical oral therapy in a context where AMR in uUTIs is expected to rise. The ramifications of COVID-19 have altered the manner in which doctors engage with patients throughout several nations, presenting both benefits and drawbacks. Advancements in virtual consultations may facilitate the enhancement of patient care over the long run.

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نهج متعدد التخصصات لإدارة التهابات المسالك البولية المتكررة: الأدوار الأساسية للأمراض المعدية وأمراض المسالك البولية في تحسين نتائج المرضى

الملخص

الخلفية :تُعد التهابات المسالك البولية (UTIs) مشكلة صحية شائعة، خاصة بين النساء غير الحوامل. تشكل التهابات المسالك البولية المتكررة (rUTIs)تحديات إكلينيكية كبيرة، مما يؤدي إلى زيادة استخدام خدمات الرعاية الصحية، ووصفات المضادات الحيوية، واحتمال مقاومة الميكروبات للمضادات الحيوية. يُعد فهم النهج متعدد التخصصات الذي يشمل متخصصي الأمراض المعدية وأطباء المسالك البولية أمرًا ضروريًا للإدارة الفعالة لهذه الحالة.

الطرق :تجمع هذه المراجعة بين الأدبيات الحديثة حول إدارة التهابات المسالك البولية المتكررة، مع التركيز على أدوار متخصصي الأمراض المعدية وأطباء المسالك البولية. تم إجراء بحث شامل باستخدام قواعد بيانات مثل PubMed و ScopusوMEDLINE، باستخدام كلمات مفتاحية مثل "التهابات المسالك البولية المتكررة"، "الأمراض المعدية"، "أمراض المسالك البولية"، و"النهج متعدد التخصصات". وشملت التحليلات الإرشادات والدراسات السريرية وآراء الخبراء المنشورة من عام 2010الى2023.

النتائج :تشير النتائج إلى أن النهج متعدد التخصصات يمكن أن يعزز بشكل كبير إدارة التهابات المسالك البولية المتكررة. يساهم التعاون بين أطباء المسالك البولية ومتخصصي الأمراض المعدية في تحسين دقة التشخيص وفعالية العلاج، خاصة في تحديد مسببات الأمراض المقاومة. تركز استراتيجيات العلاج الحالية على أنظمة المضادات الحيوية المخصصة، والتدابير الوقائية، واستكشاف الخيارات غير المعتمدة على المضادات الحيوية، بما في ذلك العلاجات العشبية وتطوير اللقاحات.

الخلاصة :يُعد دمج تخصصي الأمراض المعدية وأمراض المسالك البولية في إدارة التهابات المسالك البولية المتكررة أمرًا أساسيًا للتعامل مع تعقيدات هذه الحالة الشائعة. يمكن للإطار التعاوني أن يُحسّن نتائج المرضى، ويقلل من معدلات مقاومة المضادات الحيوية، ويُعزز تقديم الرعاية الصحية بشكل عام. ينبغي أن تركز الأبحاث المستقبلية على تطوير بروتوكولات موحدة تعتمد على العمل الجماعي متعدد التخصصات لإدارة التهابات المسالك البولية المتكررة.

الكلمات المفتاحية :التهابات المسالك البولية المتكررة، النهج متعدد التخصصات، الأمراض المعدية، أمراض المسالك البولية، مقاومة المضادات الحيوية.