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ORIGINAL ARTICLE

The Role of Hormonal changes in Recurrent Urinary Tract Infections among Postmenopausal Women. A Clinical Perspective Study

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ABSTRACT

Aims and Objectives: The objectives of the study were to understand the urinary tract infections (UTIs) and their importance in postmenopausal women, associated with estrogen deficiency, alterations in vaginal microbiota and urogenital susceptibility.

Methodology: The role of hormonal and non-hormonal interventions in reducing UTI recurrence was tested in a prospective multicenter cohort. Six hundred postmenopausal women were stratified into three groups: hormone replacement therapy (HRT), non-hormonal interventions (e.g., probiotics, D-mannose), and a control group. Demographic, clinical history, biomarkers and outcomes were analyzed.

Results: Results showed a 45% and 38% reduction in UTI recurrence rates for HRT and non-hormonal groups compared to controls. Intervention groups showed improved lactobacillus abundance and vaginal pH, improved quality of life. These findings highlight how these interventions are effective in management of recurrent UTIs without adverse effects on antimicrobial resistance. Given this, further research is recommended to investigate long term efficacy and to integrate behavioral factors to promote comprehensive prevention strategies.

Conclusion: Interventions, both hormonal and non-hormonal, including hormone replacement therapy, probiotics, and D-mannose, substantially decrease recurrent UTIs in postmenopausal women and address concerns about antimicrobial resistance. These findings underscore the need for individualized, preventive strategies to promote clinical outcomes and quality of life.

Keywords: Hormone, Urinary tract infection, Postmenopausal, Antimicrobial, Probiotics.

INTRODUCTION

A recurrent health problem consistent with UTI is seen in the postmenopausal woman. However, these infections have a large impact on patient morbidity, healthcare costs and quality of life. Of clinical interest is the interaction between hormonal changes associated with menopause and the increased risk of recurrent UTIs[1]. In postmenopausal women, estrogen deficiency changes the urogenital environment resulting in alterations in vaginal microbiota, reduced urothelial integrity, and increased uropathogen colonization including Escherichia coli. Postmenopausal women are more physiologically susceptible to UTIs than their premenopausal counterparts. Health of the urogenital tract is dependent on the vaginal ecosystem[2]. Until menopause, estrogen promotes Lactobacillus species' dominance in the vaginal microbiota to maintain an acidic vaginal pH and protect from uropathogenic bacteria. But postmenopausal estrogen deficiency disrupts this balance by raising vaginal pH and reducing the numbers of Lactobacillus. As a result, this shift fosters the development of pathogenic bacteria and their ascent into the urinary tract[3,4].

Evidence exists for a strong association between menopause and increased UTI susceptibility, but the mechanisms by which this occurs are poorly understood. Antimicrobial resistance is currently the leading cause for failing to cure patients with bacterial infections, and current treatment approaches are based on antibiotics[5]. The potential interventions include hormone replacement therapy (HRT) and other non-antibiotic preventive measures such as probiotics, D-mannose and intravaginal estrogens, but efficacy and safety of these measures are still under debate[6]. The objective of this study is to present a comprehensive clinical view of the part played by hormonal changes in recurrent UTIs among postmenopausal women. We examine the impact of estrogen deficiency and other risk factors with the aim of advancing pathophysiological mechanisms, assessing the potential of hormonal and non-hormonal interventions, and providing evidence based clinical management strategies. The results of this study are expected to enhance prevention and treatment protocols for this at risk population[7, 8].

The purpose of this study is to present a thorough clinical viewpoint on how hormonal alterations contribute to postmenopausal women's recurring UTIs. We want to improve our understanding of pathophysiological mechanisms, assess the effectiveness of hormonal and non-hormonal therapies, and provide evidence-based therapeutic care methods by looking at the impact of estrogen insufficiency and other risk factors[9]. It is expected that this study's conclusions will help develop better preventative and treatment strategies for this susceptible group. This study also emphasizes how important it is to fill up knowledge gaps and look into new treatment alternatives in order to lessen the burden of recurrent UTIs in postmenopausal women[10].

MATERIALS AND METHODS

Study Design and Setting: A multicenter prospective cohort design was employed in this study from May 2019 till November, 2022 across five principal centers with expertise in urology and women's health. The research followed Declaration of Helsinki guidelines and was approved by institutional review boards at all participating centers. The recruitment spanned 24 months and included urban as well as rural healthcare facilities with a demographic diversity.

Study Population: Women 45–79 years old who had a history of recurrent UTIs (two or more episodes in six months, or three or more episodes in twelve months and documented history) were included. Exclusion included participants with active malignancies, chronic immunosuppressive conditions, or indwelling urinary catheters. Accurate eligibility assessment was ensured with a comprehensive screening process including medical history, physical examination and laboratory testing. Data measurements and collection.

At baseline and during follow up visits, 3 month intervals over a 12 month study period data were collected. Key variables included:

1. **Demographic Data:** Ethnicity, age, body mass index (BMI) and socioeconomic status.

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2. **Clinical History:** Menopause history, duration of menopause, history of UTIs, use of hormone replacement therapy (HRT), comorbidities (e.g., diabetes, hypertension).
3. **Behavioral Factors:** Sexual activity, hydration habits, personal hygiene practices, and dietary intake.
4. **Biomarkers:** Vaginal pH, serum estrogen levels and urinary microbiota profiles, using 16S r- RNA sequencing.
5. **Outcomes:** Incidence and recurrence of UTIs, symptom severity as measured using validated scales and patient reported quality of life.

Interventions: Participants were stratified into three groups based on their chosen preventive strategy: This is randomized, (1) HRT users, (2) users of non-hormonal interventions (e.g., probiotics, D-mannose) and (3) control group (no intervention).

Microbiological Analysis: Urine and vaginal swab samples were obtained at each visit. Uropathogens were identified by microbiological cultures and antimicrobial susceptibility testing was performed to determine resistances patterns.

Assess resistance patterns. High-throughput sequencing methods were employed to characterize the microbiome and evaluate shifts in microbial diversity associated with interventions.

Statistical Analysis: Baseline parameters were summarized using descriptive statistics, and time-to-recurrence rates were evaluated using Kaplan-Meier analysis. Independent risk variables for recurrent UTIs were found using Cox proportional hazard models. To assess the effectiveness of hormonal and non-hormonal therapies, subgroup analyses were performed. R and SPSS software were used for the analyses, and the threshold for statistical significance was established at significance level i.e. ($p < 0.05$).

Ethical Considerations: Prior to enrollment, all participants provided written informed consent. No personally identifiable information was shared, and participant data was kept confidential. Participants experiencing UTI recurrences during the study were promptly treated following established clinical guidelines.

RESULTS

In total, 600 postmenopausal women were enrolled in the study and 200 women in each group (HRT, non-hormonal interventions, and control). Participants were aged 63.4 years (±7.2) with a mean of 13.5 years (±6.1) duration of menopause. Baseline characteristics of BMI, comorbidities and previous UTI history were similar between the groups (Table- 1).

The HRT and the non-hormonal intervention groups had significantly lower incidence of recurrent UTIs than the control group during the 12 month follow up. Kaplan-Meier analysis demonstrated that participants in the HRT group experienced a 45% reduction in recurrence risk (HR: 0.In the non-hormonal group there was a 38% reduction (HR: 0.62; 95% CI: 0.48–0.80; $p < 0.001$) and in the hormonal group a 55% reduction (HR: 0.45; 95% CI: 0.42–0.71; $p < 0.001$) compared to controls.

The abundance of Lactobacillus was significantly different across groups. In regards to Lactobacillus dominance, the HRT group had a 3.2 fold increase, and the non-hormonal group had a 2.8 fold. In the control group, some had a decline in Lactobacillus levels. In both the HRT and non-hormonal groups, quality of life (measured by a validated UTI-specific questionnaire) improved significantly after treatment. Symptom reduction (dysuria, urgency and frequency) was reported by participants.

Table 1: Participant Demographics

Variable	HRT Group (n=200)	Non-Hormonal Group (n=200)	Control Group (n=200)	p-value
Mean Age (years)	63.7 (±7.0)	63.2 (±7.3)	63.3 (±7.2)	0.89
BMI (kg/m²)	27.5 (±3.2)	27.8 (±3.4)	27.7 (±3.1)	0.78
Diabetes (%)	24.0	23.5	25.0	0.85
Previous UTI Episodes	3.5 (±1.2)	3.6 (±1.3)	3.4 (±1.2)	0.67

In conclusion, the results highlight the efficacy of both hormonal and non-hormonal interventions in reducing recurrent UTIs and improving urogenital health among postmenopausal women. Further studies are warranted to confirm these findings and explore long-term outcomes.

Table 2: Incidence of UTI Recurrence

Group	Recurrence Rate (%)	Hazard Ratio (95% CI)	p-value
HRT Group	25.0	0.55 (0.42–0.71)	<0.001
Non-Hormonal Group	29.5	0.62 (0.48–0.80)	<0.001
Control Group	45.0	Reference	-

Table 3: Microbiome Analysis

Microbiome Metric	HRT Group	Non-Hormonal Group	Control Group	p-value
Lactobacillus Abundance (%)	72.5 (±12.4)	68.3 (±14.1)	55.0 (±15.3)	<0.001
Vaginal pH	4.2 (±0.5)	4.4 (±0.6)	5.5 (±0.8)	<0.001

DISCUSSION

These findings offer robust support to the use of hormonal and non-hormonal interventions in the reduction of recurrent UTIs in postmenopausal women. The observed reduction in recurrence rates in both the HRT and non-hormonal groups underscores the need for preventive approaches to managing UTIs in patients with a uterus[11]. The rise in Lactobacillus abundance and accompanying decrease in vaginal pH among HRT users mirrors previous work that indicates that estrogen can protect against vaginal dysbiosis and maintain an acidic environment. It is plausible that these changes limit colonization and growth of uropathogens, and may be the mechanism by which the reduction in UTI recurrences occurs[12]. Substantial benefits were found for non-hormonal interventions, including probiotics and D-mannose, which suggest that such alternatives will be effective for women who are not or do not wish to use HRT[13].

Results support that recurrent UTIs in postmenopausal women are also multifactorial in nature. While not measured in this study, behavioral factors such as hydration, sexual activity and hygiene practices are all important. These variables should be included in future studies in order to achieve a more comprehensive approach to UTI prevention[14, 15]. There was one finding of note: the effect on recurrence rates in the control group was minimal, indicating that proactive interventions are needed. The persistence of high recurrence rates in this group highlights the limitations of a purely conventional antibiotic therapy that, because of the increasing prevalence of antimicrobial resistance, is becoming increasingly compromised. This further emphasizes the multifactorial nature of recurrent UTIs in postmenopausal women[16]. However, behavioral factors such as hydration, sexual activity and hygiene practices are important, although they are not measured in this study. These variables should be integrated in future studies in order to gain a more complete picture of UTI Prevention[17]. Among other things, we found that the control group, while receiving no active intervention, had a minimal impact on recurrence rates, indicating that proactive interventions are necessary. The high recurrence rates in this group illustrate the shortcomings of standard antibiotic treatments, which are rapidly eroded by antimicrobial resistance[18].

The strengths of this study are the large sample size, diverse population, utilization of advanced microbiome analysis techniques to describe microbial changes associated with different interventions. However, some limitations warrant consideration[19]. However, the short follow up period may not capture long term outcome and the data on some behaviorally are self-reported. Furthermore, no effects of specific non hormonal interventions, such as probiotics and D-mannose, were studied separately, and further study is needed. This research has clinical implications. The findings are important for healthcare providers to consider both hormonal and non-hormonal strategies when counseling postmenopausal women with recurrent UTIs[20]. These results highlight for policymakers the importance of research and funding to develop non-antibiotic approaches to UTI prevention where antimicrobial resistance is on the rise. Finally, this study presents

strong evidence of both hormonal and non-hormonal interventions that reduce recurrent UTIs in postmenopausal women. Future research should focus on long term efficacy, how the combined interventions work, and the integration of behavioral factors to optimize prevention strategies. Filling these gaps will help us to extend the quality of life and health outcomes for this vulnerable population[21, 22].

CONCLUSION

Current study showed hormonal and non-hormonal interventions are a major way to reduce the burden of recurrent UTIs among postmenopausal women. The results highlight the importance of preventing recurrence through individualized and preventive approaches. Promising alternative to conventional antibiotic treatment are non-antibiotic strategies, including hormone replacement therapy and probiotics as well as D-mannose. Not only do these interventions restore urogenital health, but they also respond to the growing fear of antimicrobial resistance. These findings should be validated over longer follow up periods, the synergistic effects of combined interventions should be evaluated, and behavioral factors should be included in developing comprehensive prevention strategies. Doing so will allow us to improve clinical outcomes as well as improve the quality of life of postmenopausal women at risk of recurrent UTIs.

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