

Lactobacilli vs Antibiotics to Prevent Urinary Tract Infections A Randomized, Double-blind, Noninferiority Trial in Postmenopausal Women

BACKGROUND:

- After menopause, there is a loss of lactobacilli in vaginal flora, making colonization with the potentially pathogenic *E.coli* more common.
- The increasing rate of antibiotic resistance is an area for concern, making the study of non-antibiotic treatments important.

OBJECTIVE

- The objective of the study was to determine if lactobacilli was non-inferior to antibiotic prophylaxis, specifically trimethoprim-sulfamethoxazole, for recurrent UTIs in postmenopausal women.

METHODS

- **Design:** Double-blind, double dummy, parallel, randomized non-inferiority trial; Duration 15 months
- **Inclusion criteria:** Postmenopausal status and a history of at least 3 self-reported symptomatic UTIs in the previous year.
- **Exclusion criteria:** Presence of UTI symptoms at inclusion, antibiotic use in the previous two weeks, interactions of the antibiotic with concurrent medications or a contraindication to the antibiotic, renal failure and renal transplant. In addition, no other types of prophylaxis could be used two weeks prior to or during the study.
- **Primary outcome measures:** Between group difference in mean number of clinical recurrences during prophylaxis; percentage of resistant *E.coli* isolates in asymptomatic women at 1 and 12 months of treatment.
- **Secondary outcome measures:** Mean number of microbiologically confirmed symptomatic UTIs, proportion of patients with at least one microbiologically confirmed recurrence, time to first confirmed recurrence, proportion of patients reporting serious adverse events, change in vaginal microflora as evidenced by Nugent score.
- **Treatments assigned:** Of 252 patients enrolled in the trial, 115 patients received the active control trimethoprim-sulfamethoxazole and 123 patients received *Lactobacilli* isolates.
 - Antibiotic arm: one 480mg trimethoprim-sulfamethoxazole tablet at bedtime with one placebo capsule twice daily.
 - Lactobacilli arm: one capsule with 10⁹ CFU of *Lactobacilli* strains twice daily with one placebo tablet at bedtime.
- Data handling method was intent-to-treat.

RESULTS

- A total of 167 patients completed the study, with 88 in the control arm and 79 in the treatment arm.
- **Primary outcome measures:**
 - The between group difference in mean number of clinical recurrences was 13.8% difference, which lies outside the predetermined 10% non-inferiority margin. Between group difference = 0.4 recurrences (95% CI, -0.4 to 1.5)
 - Resistance of *E.coli* isolates to trimethoprim, trimethoprim-sulfamethoxazole, and amoxicillin increased from 20-40% at baseline to 80-95% at 1 month, and 100% at 12 months in the antibiotic group. There was no change in resistance in the lactobacilli group.
- **Secondary outcome measures:**

- Mean number of microbiologically confirmed symptomatic UTIs was 1.2 (95% CI, 0.9 to 1.6) in the antibiotic group and 1.8 (95% CI, 1.4 to 2.3) in the lactobacilli group.
- The proportion of patients with at least one microbiologically confirmed recurrence at 12 months was 49.4% patients in the antibiotic group and 62.9% in the lactobacilli group.
- There was no significant change from baseline in vaginal microflora as evidenced by Nugent score in either group.
- **Author's conclusion:** Lactobacilli is not non-inferior to trimethoprim-sulfamethoxazole in the prophylaxis of UTIs in the general population of post-menopausal women, but does have some value in certain populations.

STRENGTHS

- Showed potential benefit of lactobacilli in women with complicated UTIs
- Studied non-antibiotic treatment in a time with high antibiotic resistance rates

LIMITATIONS

- Did not achieve target number of participants, also did not discuss power of the study
- Did not confirm number of self-reported UTIs in year before study
- Used antibiotic with high rates of resistance at baseline
- Lacked detailed information regarding patient education.

CONCLUSION

- The study showed that treatment with lactobacilli was inferior to trimethoprim-sulfamethoxazole in the prophylaxis of recurrent UTIs in postmenopausal women.
 - However, lactobacilli did show potential benefit in some populations, specifically women with complicated UTIs.
 - Prophylaxis with lactobacilli may have a place in prophylaxis in women who prefer not to take antibiotics or vaginal estrogens regularly.
- Future research:
 - Comparing lactobacilli's efficacy with another antibiotic that does not have high rates of resistance at baseline may give a better representation of the benefits of this therapy.
 - Further research regarding lactobacilli's use in postmenopausal women with complicated UTIs is necessary, as this study's findings has yet to be corroborated in that area.

Reference: Beerepoot AJ, ter Reit G, Nys S, van der Wal WM, de Borgie CAJM, de Reijke TM, et.al. Lactobacilli vs Antibiotics to Prevent Urinary Tract Infections. Arch Intern Med. 2012;172(9):704-12.

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