

Green tea as an adjunctive therapy for treatment of acute uncomplicated cystitis in women: A randomized clinical trial

BACKGROUND:

- Co-trimoxazole (sulfamethoxazole-trimethoprim) is commonly used to treat acute uncomplicated cystitis, however *E. coli* bacterial resistance has increased in recent years. In vitro studies have reported antimicrobial effects of green tea and synergistic effects of green tea with co-trimoxazole against *E. coli*.
- The components of green tea that hold antibacterial properties are polyphenolic catechins, specifically (-)-epigallocatechin-3-gallate (EGCG) and (-)-epigallocatechin (EGC). However, only EGC is excreted into the urine. Reygaert et al. showed that EGC concentrations in the urine equal about 3.5 mg after drinking one cup of green tea, and that the MICs (minimum inhibitory concentrations) for EGC are below 3.5 mg for several strains of *E. coli*.
- There are no studies to investigate the in vivo clinical efficacy of green tea in the treatment of urinary tract infections (UTI).

OBJECTIVE:

- To evaluate the efficacy of green tea as an adjuvant to co-trimoxazole in women with acute uncomplicated cystitis

METHODS

- This was a double-blind, randomized controlled trial conducted in at Besat Clinic in Kerman, Iran from August 2017 to October 2017
- Inclusion criteria: healthy, pre-menopausal, non-pregnant women aged 18-50 years old with acute uncomplicated cystitis
- Exclusion criteria: recurrent UTI's, vaginitis, irritation, or discharge, underlying conditions that increase the risk of infection, green tea hypersensitivity, regular green tea drinkers
- 70 patients were enrolled
- Patients were assigned to receive 500 mg x4 green tea capsules or placebo (starch – identical dosage forms) once daily for 3 days plus co-trimoxazole 480 mg x2 tablets twice daily
- Primary outcomes: presence of cystitis symptoms (dysuria, frequency, suprapubic pain, blood in urine, and back pain) at 1, 2, and 3 days and urinalysis results after 4 days
- Secondary outcomes: adverse effects
- Sample size of 35 patients per group was expected to yield a power of 80% and an alpha of 0.05, and P-values < 0.05 were considered statistically significant
 - Independent samples t-test was used to compare quantitative data (means between each group)
 - Generalized estimating equation was used to compare binary data (symptoms) over time
 - Chi-squared test was used to compare qualitative data (urinalysis)

RESULTS

- 70 patients were randomized and completed the trial. No patients were lost to follow up, and no patients discontinued treatment early.

Table 1
Prevalence of cystitis symptoms over the time in green tea and placebo groups.

Time point	Group	Presence of symptoms (%)	^a Exp (B)	95% ^b CI for Exp(B)	^c P-value
Baseline	Green tea	68%	0.71	0.48–1.07	0.099
	Placebo	75%	1		
After 1 day	Green tea	61%	0.55	0.38–0.78	0.001
	Placebo	74%	1		
After 2 days	Green tea	34%	0.26	0.17–0.39	0.0001
	Placebo	67%	1		
After 3 days	Green tea	2%	0.01	0.003–0.03	0.0001
	Placebo	63%	1		

^a Exponential beta.

^b Confidence interval.

^c Based on generalized estimating equation.

Table 2
The urinalysis data at baseline and on fourth day after receiving intervention in green tea and placebo groups.

Examination	Group					
	Baseline Number (Percent)			After 4 days Number (Percent)		
	Green tea	Placebo	^a P-value	Green tea	Placebo	^a P-value
^b Abnormal urine color	24 (68.6%)	27 (77.1%)	0.296	0 (0.0%)	13 (37.1%)	0.0001
^c Pyuria	35 (100%)	33 (94.3%)	0.246	0 (0.0%)	20 (57.1%)	0.0001
^d Hematuria	30 (85.7%)	31 (88.6%)	0.500	2 (5.7%)	6 (17.1%)	0.130
^e Bacteriuria	29 (82.9%)	32 (91.4%)	0.239	0 (0.0%)	13 (37.1%)	0.0001

^a Based on Chi-square test.

^b Normal: straw [4].

^c ≥ 5 white blood cells per high-power field of centrifuged urine [4,13].

^d ≥ 3 red blood cells per high-power field [13].

^e ≥ 5 bacteria per high-power field [13].

- There were no differences in adverse reactions between each group. (6 patients in the treatment and 7 patients in the placebo group reported nausea, likely due to co-trimoxazole)
- Authors stated conclusions
 - The treatment group showed a statistically significant reduction in cystitis symptoms at each time point and an improvement in the urinalysis results (except for hematuria) compared to placebo. There was not a significant difference between the two groups regarding hematuria at day 4, however pyuria and bacteriuria are more valuable laboratory values for diagnosing UTIs. Green tea was an effective adjuvant to co-trimoxazole to treat acute uncomplicated cystitis in women. Further studies are required to confirm these results.

STRENGTHS

- List pertinent study strengths
 - Power was met, no patients dropped out of the study
 - Excluded an appropriate patient population
 - Appropriate dosing was used for sulfamethoxazole-trimethoprim
- Weaknesses:
 - Urinalysis did not include nitrites
 - Placebo group had longer duration of symptoms at baseline
 - Potential un-blinding in treatment group due to increased urination due to green tea
 - Did not breakdown which symptoms were present at each time point for each group
 - Small sample size (however, did meet power)
 - Urine culture and susceptibility testing were not used
 - Adherence was not measured / documented
 - Did not specify the dose of trimethoprim
 - Baseline characteristics (past medical history, medications, etc.) were not specified

LIMITATIONS

- The authors generalized the results of this study to patients drinking green tea. However, these results cannot be extrapolated in this way since patients were treated with green tea tablets instead of cups of tea. Further studies will need to be performed in order to investigate patient administration with variable versus fixed doses of green tea extract.

CONCLUSIONS

- Green tea is a potentially beneficial, cost-effective adjuvant to co-trimoxazole for treatment of acute uncomplicated UTI's in women. Additional studies should also report nitrites in the urinalysis and collect urine cultures in order to exclude patients with infections not caused by E. coli or E. coli that has resistance to co-trimoxazole. Resistance varies on location (city, country, etc.) which may impact the clinical applicability to other regions. Future studies investigating the clinical efficacy of green tea should also utilize three treatment arms including patients taking green tea "tablets", cups of green tea of green tea, and placebo plus co-trimoxazole.

Reference:

Kheirabadi Z, Mehrabani M, Sarafzadeh F, et al. Green tea as an adjunctive therapy for treatment of acute uncomplicated cystitis in women: A randomized clinical trial. *Comp Ther in Clin Pract.* 2019;34:13-16.

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