NOSTONE TRIAL

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INTRODUCTION

- Full Title: Hydrochlorothiazide for the Prevention of Kidney-Stone Recurrence.
- Published In: The New England Journal of Medicine (NEJM), 2023.
- Location: Conducted in Switzerland.
- Duration: Median follow-up ~3 years.

- Objective:- To assess whether low- or moderate-dose hydrochlorothiazide reduces the risk of recurrent calcium kidney stones compared with placebo.

STUDY DESIGN

- Design**:** Multicenter, double-blind, randomized, placebo-controlled trial.
- Population : - Patients: 416 adults.

- Inclusion criteria:
  - History of recurrent calcium-containing kidney stones (≥2 episodes in the last 10 years).
  - Age: 18–75 years.
- Exclusion criteria:
  - Non-calcium stones
  - Secondary causes of stones (e.g., hyperparathyroidism).

STUDY GROUPS

- INTERVENTION GROUPS:-
- Participants were randomized into four groups:

  1. Placebo
  2. HCTZ 12.5 mg/day
  3. HCTZ 25 mg/day
  4. HCTZ 50 mg/day

- All participants received standard dietary counselling for stone prevention.
- PRIMARY OUTCOME:-
- Composite of symptomatic or radiologic recurrence of kidney stones.

RESULTS

- **No** significant difference in stone recurrence among the placebo and HCTZ groups.
- Recurrence rates over ~3 years:
  - Placebo: ~59%
  - HCTZ 12.5 mg: ~59%
  - HCTZ 25 mg: ~60%
  - HCTZ 50 mg: ~49%
- Trend toward benefit with the highest dose, but not statistically significant.
- Adverse Events :- More common with higher doses of HCTZ:
  - Hypokalemia , Hyperuricemia , Gout , New-onset diabetes.

CONCLUSION

- Hydrochlorothiazide did not significantly reduce the risk of recurrent calcium kidney stones compared to placebo, even at higher doses.

NOSTONE Trial: Limitations and Implications

Limitation	Description	Clinical Implication
Short Follow-up	Median ~3 years	May miss long-term benefits of HCTZ in stone prevention
Composite Outcome	Includes asymptomatic radiologic recurrence	Could overestimate clinical recurrence; less meaningful for patients
Unconfirmed Stone Composition	Not all patients had recent confirmed calcium stones	Potential misclassification; thiazides may not work on non-Ca stones
Medication Adherence	Dropouts, dose changes, and side effects affected drug exposure	Could dilute true effect of HCTZ
Low Baseline Risk	General dietary counseling provided; patients not selected for hypercalciuria	Reduced ability to detect incremental benefit of HCTZ
Generalizability	Swiss cohort, mostly White	May not apply to diverse populations or settings
Adverse Effects at Higher Doses	Increased risk of hypokalemia, gout, hyperglycemia	Challenges the risk-benefit ratio of HCTZ for primary prevention

NOSTONE: Is Hydrochlorothiazide (HCT) Beneficial in Recurrent Kidney Stone Prevention?

#NephJC

METHODS

- Randomized Control Trial (1:1:1:1)
- Double Blind
- 12 Centers in Switzerland
- Age>18 + ≥ 2 episodes of kidney stones
  n = 416
- 2.9 year median follow-up

- Placebo
- HCT 12.5 mg
- HCT 25 mg
- HCT 50 mg

RESULTS

Primary Outcome

Stone Recurrence
(Symptomatic or Radiologic)

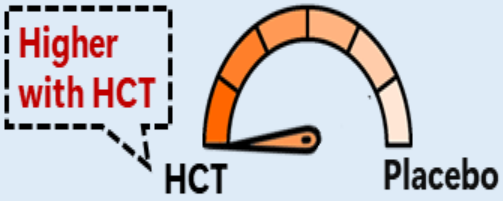
HCTZ vs Placebo

No Difference

(Rate ratio 0.98
95% CI, 0.87 to 1.09)

Safety Outcomes

Adverse Events
New-onset Diabetes, Hypokalemia, gout, skin allergy, plasma creatinine elevation



Serious Adverse Events
Cardiac, GI, Kidney, CNS, Kidney, Malignancy

CONCLUSION: Among patients with recurrent kidney stones, the incidence of recurrence did not appear to differ substantially between HCT or placebo.

Dhayat NA, Bonny O, Roth B, et al. Hydrochlorothiazide and Prevention of Kidney-Stone Recurrence. *N Engl J Med.* 2023; 388(9):781-791

Visual Abstract by: Renz Pasilan @RenzPasilan