Efficacy and Comparability of Thiazide-type Diuretics
Chlorthalidone vs. Hydrochlorthiazide (HCTZ)/ Triamterene in Hypertensives

Chlorthalidone (50 mg/day) was compared to HCTZ plus triamterene (25/50 and 50/100 mg/day) in 126 patients with DBP 90-115 mm Hg over an 8-week treatment period in a 3-arm double-blind, placebo-controlled randomized trial.

Chlorthalidone vs. Hydrochlorothiazide (HCTZ)/Triamterene in Hypertensives


All drugs produced a significant reduction in BP from placebo

* sig. lower than H25/T50
Chlorthalidone vs. Hydrochlorothiazide (HCTZ)/ Triamterene in Hypertensives

- All three regimens significantly reduced SBP and DBP at every week of therapy
- Significant BP differences between chlorthalidone and HCTZ/triamterene (25/50 mg) were found, but not for chlorthalidone compared to HCTZ/triamterene (50/100 mg) or between the two HCTZ formulations

Chlorthalidone vs. Hydrochlorothiazide (HCTZ)/ Triamterene in Hypertensives

- Once daily administration of HCTZ/triamterene was effective in patients with diastolic hypertension, although HCTZ/triamterene at the lower dose (25/50 mg) was less effective than 50 mg of chlorthalidone.

Dose-Response to Chlorthalidone in Patients with Stage 1 Hypertension

4 doses of chlorthalidone (12.5, 25, 50, 75 mg) were compared to placebo for 12 weeks of treatment in 100 patients with DBP of 90-109 mm Hg.

Success was defined as DBP <90 mm Hg and/or decrease of 10 mm Hg or more at the final visit.

Dose-Response to Chlorthalidone in Patients with Stage 1 Hypertension


[Graph showing blood pressure responses to various doses of chlorthalidone in supine and standing positions, with significant reductions compared to placebo marked with stars.]
Dose-Response to Chlorthalidone in Patients with Stage 1 Hypertension

- Although chlorthalidone 12.5 mg was superior to placebo in reducing supine and standing systolic BP, there were no differences in standing systolic BP for doses between 25 and 75 mg.
- Diastolic success rates were not significantly different among all active doses: 45% (12.5 mg), 35% (25 mg), 41% (50 mg), and 42% (75 mg)
- The decline in serum potassium was worse than placebo only with the 50 and 75 mg doses
- No changes in serum uric acid, serum glucose, or serum sodium were observed.

Dose-Response to Chlorthalidone in Patients with Stage 1 Hypertension

- 25 mg of chlorthalidone was as effective as 50 and 75 mg doses for treatment of hypertension, with fewer adverse effects.
- 12.5 mg of chlorthalidone was also effective, although the decline in blood pressure was smaller than that achieved by the larger doses.

Chlorthalidone vs. Hydrochlolethiazide (HCTZ) in Moderate Hypertensives

Chlorthalidone (50 mg once per day) was compared to hydrochlolethiazide (50 mg twice per day)

- 55 patients
- DBP 100-120 mm Hg
- 4 week treatment period

Chlorthalidone 50 mg vs. HCTZ 50 mg BID in Hypertensives with DBP 100-120 mm Hg

Chlorthalidone vs. HCTZ in Moderate Hypertensives

- Both treatment groups experienced a significant reduction in SBP and DBP during treatment, with no significant differences between groups.
- Near normotensive mean DBP levels were achieved by both groups within two weeks, and were sustained for the duration of the study.
- Serum potassium declined significantly only in the HCTZ group.
- No other significant changes were found in serum sodium, serum creatinine, serum cholesterol, or fasting glucose.

Chlorthalidone vs. HCTZ in Moderate Hypertensives

- Chlorthalidone 50 mg QD and HCTZ 50 mg BID were equally effective in reducing BP.
- Chlorthalidone was associated with fewer side-effects when given at ½ the HCTZ dose.

## Pharmacokinetic and Pharmacodynamic Comparisons of HCTZ and Chlorthalidone

<table>
<thead>
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<th>Drug</th>
<th>Onset, h</th>
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<th>Half-Life, h</th>
<th>Duration, h</th>
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<tr>
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<td>6-9 (Single dose)</td>
<td>12 (Single dose)</td>
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<td>8-15 (Long-term dose)</td>
<td>16-24 (Long-term</td>
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<td>dosing)</td>
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<tr>
<td>Chlorthalidone</td>
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<td>2-6</td>
<td>40 (Single dose)</td>
<td>24-48 (Single dose)</td>
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<td>45-60 (Long-term dosing)</td>
<td>48-72 (Long term</td>
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Conclusions (I)

1. In these studies chlorthalidone 25 mg/d or HCTZ 50 mg/d lowered BP as well as higher doses with fewer adverse effects.

2. Lower doses (chlorthalidone 12.5 mg or HCTZ 25 mg) were effective in lowering BP, but less so than chlorthalidone 25 mg or HCTZ 50 mg.

3. Chlorthalidone has a considerably longer duration of action than HCTZ.
Conclusions (II)

4. The ideal dose-comparison trial of HCTZ versus chlorthalidone has not yet been conducted.

5. Low-moderate dose diuretics are consistent in showing a reduction of events in morbidity and mortality trials.