

Chlorthalidone reduces cardiovascular events compared with hydrochlorothiazide
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Background:

- JNC7:
 - Without compelling indications: thiazide type diuretics +/- ACEI/ARB/BB/CCB if stage 2
 - If not initiated should be considered when additional therapy warranted
- Thiazide type diuretics: HCTZ, chlorthalidone (CTD), chlorothiazide, metolazone, indapamide
- CTD vs HCTZ: studies have shown that both are efficacious in treating HTN
 - CTD may have superior 24 hour BP control
- Multiple risk factor intervention trial (MRFIT)
 - Sponsored by national heart, lung and blood institute
 - 7 years; 12,866 men; 35-57 years old
 - Randomized cardiovascular primary prevention trial
 - Tested whether a multifaceted intervention program could reduce mortality from coronary heart disease (CHD)
 - Pt received HTN treatment, smoking cessation counseling and dietary guidance versus usual care
 - HTN treatment: HCTZ or CTD with weight and sodium reduction

Trial

- Objectives:
 - Primary: evaluate cardiovascular endpoint between patients who took CTD and HCTZ
 - Secondary: change in SBP, TC, LDL, HDL, TG, K, glucose, uric acid in two groups
- Methods
 - Retrospective observational cohort
 - Used MRFIT trial data
 - Drug exposure was defined as use of CTD or HCTZ
- Outcomes
 - Primary: cardiovascular events
 - Non-fatal: MI (clinical or via EKG), stroke, CABG, EKG, defined left ventricular hypertrophy, heart failure, angina, PAD
 - Secondary: change in SBP, TC, LDL, HDL, TG, K, glucose, uric acid
- Results
 - N=6441 (2392 CTD; 4049 HCTZ)
 - Baseline differences
 - More patients in CTD group received the MRFIT intervention
 - Number of HTN medications, other diuretics used and concomitant use of methyldopa (greater in HCTZ group)

- Cardiovascular events (CVE)
 - Versus no thiazide-type intervention: significantly lower in CTD group and HCTZ group : adjusted hazard ratios: 0.51, 0.65 respectively
 - CTD had fewer events than HCTZ: adjust hazard ratio: 0.79
 - In the patients that received MRFIT intervention:
 - Efficacy of CTD and HCTZ were enhanced compared to group that did not receive MRFIT intervention
 - CTD had fewer events than HCTZ—but not statistically significant
 - Specific CVE
 - CTD significantly better at preventing: clinical MI, EKG MI, CABG, angina, PAD
 - No difference: CV death, stroke, LVH, CHF
- Secondary outcomes
 - CTD significantly difference compared to HCTZ:
 - Lower: SBP, TC, LDL, K
 - Higher: uric acid
- Author's conclusions
 - CTD significantly reduced CVE compared to HCTZ
 - Author's thoughts on why:
 - CTD more potent antihypertensive at study doses
 - CTD lowered SBP more than HCTZ
 - LDL and glucose were lower in CTD group during treatment
- Limitations
 - Retrospective
 - Dated material (1973)
- Conclusion
 - Patients should receive a thiazide-type diuretic
 - CTD may be better at preventing CVE than HCTZ