Refills

Your dose of drug information in between sessions

Switching to chlorthalidone compared to continuing hydrochlorothiazide: A new trial

Conclusion: Switching patients already taking hydrochlorothiazide for hypertension to chlorthalidone did not reduce their risk of adverse cardiovascular outcomes or risk of death after 2.4 years of follow-up.

The BC Provincial Academic Detailing (PAD) service began delivering the topic Hypertension in Primary Care in 2017. We noted an absence of completed trials directly comparing thiazides for cardiovascular and mortality outcomes, but we referred to an ongoing trial.[1] The trial was published in December 2022 (Diuretic Comparison Project trial) and compared people switched from hydrochlorothiazide to chlorthalidone for hypertension to those who stayed on hydrochlorothiazide.[2]

There were no differences in the primary outcome (non-fatal cardiovascular event or non-cancer death) between switching to an equipotent dose of chlorthalidone and continuing hydrochlorothiazide. Switching to chlorthalidone did result in an increase in allergic or adverse reactions and hypokalemia. However, in this trial's unblinded design, patients who switched to chlorthalidone underwent more laboratory monitoring, which may have resulted in the capture of more hypokalemia events. There were no significant differences between the two groups in all-cause mortality, serious adverse events, all-cause hospitalization, acute gout episodes, new onset diabetes, renal failure or hyponatremia.

In B.C., both chlorthalidone and hydrochlorothiazide are regular benefit drugs on the BC PharmaCare formulary.

Diuretic Comparison Project trial summary: chlorthalidone compared to hydrochlorothiazide[2]		
Participants	▪ 13,523 people ▪ age ≥ 65 (mean age: 72), 97% male, 77% White ▪ hypertension defined as SBP ≥ 120 mmHg (mean SBP: 139 mmHg) ▪ with an active prescription for hydrochlorothiazide ▪ 87% taking additional antihypertensives	
Intervention	switch to chlorthalidone 12.5 mg or 25 mg once a day (median dose: 12.3 mg)	
Comparator	continue hydrochlorothiazide 25 mg or 50 mg once a day (median dose: 23 mg)	
Outcomes	non-fatal cardiovascular event or non-cancer death	HR 1.04 (95%CI 0.94 to 1.16)
	death from any cause	HR 1.00 (95%CI 0.87 to 1.13)
	new allergic or adverse reaction to diuretic	HR 5.23 (95%CI 3.28 to 8.35) absolute risk increase: 1.3%
	hypokalemia	HR 1.38 (95%CI 1.19 to 1.60) absolute risk increase: 1.6%
Study Design	▪ pragmatic open-label trial design, median follow-up 2.4 years ▪ primary care electronic health records in the Veterans Affairs Healthcare System (United States)	

[1]BC Provincial Academic Detailing service: Hypertension in Primary Care (November 2017)
[2]Ishani A et al Diuretic Comparison Project Working Group N Engl J Med 2022;387:2401-2410 (PMID: 36516076)

BC Provincial Academic Detailing Service
Email: PAD@gov.bc.ca
Web: www.bcpad.ca