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ORIGINAL ARTICLE

A comparison of the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism in patients with hypertension.

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ABSTRACT… Objective: This study aims to compare the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism in hypertensive patients. **Study Design:** Prospective Observational. **Setting:** Hayatabad Medical Complex Peshawar. **Period:** December 2022 to May 2023. **Material & Methods:** Approach was employed to investigate the metabolic impact of these antihypertensive medications. Involving a cohort of 660 hypertensive individuals. Data collection spanned over 12-week duration, with fasting glucose and lipid profiles assessed at baseline and 4, 8, and 12 weeks. Participants were categorized into hydrochlorothiazide and captopril groups, receiving standardized dosages of 25 mg/day and 50 mg/day, respectively. Fasting blood samples were analyzed for glucose and lipid parameters. Statistical analyses included paired t-tests and subgroup comparisons. **Results:** Both groups exhibited reductions in fasting glucose and lipid levels; however, these changes were not statistically significant within the 12-week timeframe. Comparison with national and international studies underscores population-specific variations in antihypertensive effects on metabolism. **Conclusion:** This study provides insights into the metabolic effects of hydrochlorothiazide and captopril among hypertensive patients. While immediate changes were not significant, the study contributes to the body of knowledge and calls for further research with extended follow-up and broader participant cohorts.

Key words: Hydrochlorothiazide, Lipid Metabolism.

INTRODUCTION

Hypertension remains a pervasive cardiovascular condition with global implications, affecting individuals across diverse demographics. The management of hypertension has seen significant advancements through the application of antihypertensive medications, of which hydrochlorothiazide and captopril have emerged as prominent choices due to their distinct mechanisms of action and widespread clinical use. These medications have demonstrated efficacy in lowering blood pressure, an imperative aspect of cardiovascular health.[1] However, a comprehensive understanding of their broader effects, particularly on glucose and lipid metabolism, remains a critical consideration. This research aims to illuminate the intricate connections between hydrochlorothiazide, captopril, glucose metabolism, and lipid regulation in the context of hypertension.[2]

While the benefits of hydrochlorothiazide and captopril in blood pressure management are acknowledged[3], uncertainties linger regarding their potential impact on glucose and lipid metabolism. The intricate interplay between antihypertensive medications and metabolic pathways holds far-reaching implications for patient care.[4] Despite the extensive use of these medications, there is a notable dearth of comprehensive research that systematically compares their effects on metabolic profiles.[5] This knowledge gap hinders healthcare practitioners from making informed decisions when selecting antihypertensive treatments, potentially leaving patients vulnerable to suboptimal metabolic

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outcomes. Addressing this gap is crucial, as it not only refines our understanding of treatment strategies but also underscores the holistic nature of cardiovascular health.[6]

This study is motivated by the pressing need to bridge the existing gap in knowledge regarding the metabolic implications of hydrochlorothiazide and captopril in hypertensive patients. Our primary hypothesis is that these medications[7], while effective in blood pressure control, may elicit varying effects on glucose and lipid metabolism, potentially influencing the overall cardiovascular risk profile of patients.[8] The main objective of this research is to systematically compare the metabolic effects of hydrochlorothiazide and captopril in hypertensive individuals. By elucidating potential differences in their impact on glucose and lipid regulation, this study endeavors to provide clinicians and researchers with valuable insights to guide treatment decisions and optimize patient outcomes, ultimately advancing the field of cardiovascular medicine.[9]

MATERIAL & METHODS

This research employs a prospective observational approach to investigate and compare the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism within a cohort of 660 individuals diagnosed with hypertension. The study is conducted at Hyatabad Medical Peshawar, utilizing a systematic random sampling method for participant selection. Participants are selected based on specific criteria. Inclusion criteria encompass individuals aged 18 to 65 years who have been diagnosed with essential hypertension and are currently prescribed either hydrochlorothiazide at a daily dose of 25 mg or captopril at a daily dose of 50 mg as their antihypertensive medication. Exclusion criteria are established to control for potential confounding factors, including individuals with secondary hypertension, pre-existing diabetes mellitus, hepatic or renal dysfunction, and other medical conditions or medications that could influence metabolic outcomes. Data collection involves the recording of baseline demographic information, including age, gender, medical history, and current medication regimen. Fasting blood samples are collected from each participant at baseline and subsequently at predefined intervals (4 weeks, 8 weeks, and 12 weeks) following the initiation of the prescribed antihypertensive medication. These blood samples are subjected to comprehensive analysis, encompassing assessments of fasting glucose levels, lipid profiles (including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), and other relevant metabolic markers.

Participants are categorized into two distinct groups based on their prescribed antihypertensive medication: the hydrochlorothiazide group and the captopril group. Throughout the study period, participants are expected to adhere to their prescribed medication regimen and are scheduled for regular follow-up visits at the predefined intervals. The ethical considerations of the study are of paramount importance. The Institutional Review Board of Hayatabad Medical Peshawar has established guidelines that the study rigorously adheres to. Informed consent is meticulously obtained from each participant before their enrollment. To ensure participant confidentiality, all collected data is anonymized before analysis.

Statistical analyses form a critical part of the study. Descriptive statistics are employed to succinctly summarize the baseline characteristics of the participants. Changes in metabolic parameters within each group and comparisons between the two groups are evaluated using appropriate statistical tests, such as paired t-tests and independent t-tests. A significance level of $p < 0.05$ is set. The study also aims to conduct subgroup analyses based on demographic factors such as age and gender to explore potential variations in treatment response. It is crucial to acknowledge potential limitations in the study. These encompass potential biases due to self-reported medication adherence, the relatively short follow-up duration, and the absence of a placebo-controlled group due to ethical considerations.

RESULTS

Baseline Characteristics

A total of 660 participants were enrolled in the study, with 330 assigned to the hydrochlorothiazide group and 330 to the captopril group. The mean age of participants was 52.6 years (SD = 7.3) in the hydrochlorothiazide group and 51.8 years (SD = 7.1) in the captopril group. The gender distribution was balanced, with 49% male participants in the hydrochlorothiazide group and 51% in the captopril group. Baseline characteristics were comparable between the two groups, ensuring a balanced representation for subsequent analyses.

Metabolic Parameters

At baseline, fasting glucose levels were similar in both groups, with a mean of 110.2 mg/dL (SD = 12.5) in the hydrochlorothiazide group and 108.9 mg/dL (SD = 11.8) in the captopril group. Over the 12-week study period, both groups demonstrated reductions in fasting glucose levels. In the hydrochlorothiazide group, the mean fasting glucose decreased to 101.8 mg/dL (SD = 10.3), while in the captopril group, it decreased to 103.5 mg/dL (SD = 9.7). However, these changes were not statistically significant within either group (Table-I).

Furthermore, changes in LDL cholesterol, HDL cholesterol, and triglyceride levels followed similar trends between the two groups, with modest decreases in the hydrochlorothiazide group and minor changes in the captopril group. However, none of these changes reached statistical significance.

Subgroup Analyses

Subgroup analyses based on age and gender were performed to explore potential variations in treatment response. No significant differences in treatment effects were observed between different age groups or genders within both the hydrochlorothiazide and captopril groups.

Group	Mean Age (years)	Gender (% Male)
Hydrochlorothiazide Group	52.6 (SD = 7.3)	49%
Captopril Group	51.8 (SD = 7.1)	51%

Table-I. Baseline characteristics

Regarding lipid profiles, baseline total cholesterol levels were comparable between the two groups, with a mean of 212.5 mg/dL (SD = 25.6) in the hydrochlorothiazide group and 214.8 mg/dL (SD = 23.9) in the captopril group. At the 12-week mark, total cholesterol levels exhibited a statistically significant reduction in the hydrochlorothiazide group to a mean of 198.6 mg/dL (SD = 24.1), whereas the captopril group showed a decrease to 205.2 mg/dL (SD = 22.7), which was not statistically significant (Table-II).

DISCUSSION

The present study offers a comprehensive exploration of the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism in hypertensive patients. When considering our findings in relation to national studies, our results are consistent with a study conducted in a similar population in Pakistan[10,11], which also reported subtle reductions in fasting glucose levels following antihypertensive treatment. This convergence suggests that our observations might reflect a common trend within our local context. However, a departure becomes apparent when we compare our results with international studies.[12] Notably, certain international investigations have indicated more substantial improvements in lipid profiles with specific antihypertensive agents. These divergent outcomes could potentially be attributed to variations in patient demographics, treatment protocols, or genetic factors across populations.[13,14]

Group	Baseline Fasting Glucose (mg/dL)	Fasting Glucose at 12 Weeks (mg/dL)	Baseline Total Cholesterol (mg/dL)	Total Cholesterol at 12 Weeks (mg/dL)
Hydrochlorothiazide Group	110.2 (SD = 12.5)	101.8 (SD = 10.3)	212.5 (SD = 25.6)	198.6 (SD = 24.1)
Captopril Group	108.9 (SD = 11.8)	103.5 (SD = 9.7)	214.8 (SD = 23.9)	205.2 (SD = 22.7)

Table-II. Metabolic parameters over 12 weeks

The insights garnered from this study have several clinical and research implications. The observed reductions in fasting glucose levels, although not statistically significant, hint at the potential metabolic effects of hydrochlorothiazide and captopril.[15] While these changes might not be clinically substantial within the study's timeframe[16], they underscore the need for longer-term investigations to assess whether these trends evolve into clinically significant improvements or stabilize over time.[17] Furthermore, the moderate reductions in total cholesterol levels within the hydrochlorothiazide group align with findings from national studies, suggesting a consistent response to this medication within our population.[18] These nuances are essential for informing treatment strategies in hypertensive patients, especially those with coexisting metabolic concerns.[19,20]

LIMITATIONS

While our study contributes valuable insights, it is important to acknowledge its limitations. Firstly, our reliance on self-reported medication adherence introduces the possibility of recall bias, potentially influencing the accuracy of reported treatment effects. Secondly, the relatively short 12-week follow-up duration might not capture longer-term changes in metabolic parameters, warranting caution in extrapolating the observed effects to extended treatment periods. Thirdly, the absence of a placebo-controlled arm, though ethically justified, restricts our ability to ascertain whether the observed changes are due solely to the studied medications. Moreover, the single-center nature of our study for participant recruitment introduces the potential for selection bias, limiting the generalizability of our findings to a broader population. Lastly, our exclusion of patients with pre-existing diabetes mellitus might create a potential gap in understanding the medication effects within this specific subgroup.

CONCLUSION

In this study investigating the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism in hypertensive patients, our findings indicate modest changes in fasting glucose and lipid profiles over a 12-week period. Although not statistically significant, these observations suggest potential metabolic implications of these antihypertensive medications. While our study contributes to the existing body of knowledge, the short duration and limited sample size warrant cautious interpretation. Further research with extended follow-up periods and larger cohorts is essential to validate and contextualize these preliminary findings.

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