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A Comparative Study of the Impact of Sevelamer and Calcium Carbonate on Lipid Profile and HbA1c in Diabetic Kidney Disease

Jais Kumar*, Naveed Sarwar, Muzaffar Shoaib, and Syed Ali Naqi

Department of Nephrology, Akbar Niazi Teaching Hospital, IMDC, Pakistan

Corresponding author:
Jais Kumar, Department of Nephrology, Akbar Niazi Teaching Hospital, IMDC, Pakistan. E-mail: jais_k115@gmail.com

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Abstract

Diabetic kidney disease, a formidable complication of diabetes, prompts exploration into drugs that can impede the intestinal absorption of advanced glycation end products (AGE), potentially enhancing glycemic control and lipid profiles. Sevelamer, a calcium-free phosphate binder, is hypothesized to play a role in AGE absorption prevention. This study aimed to compare the mean changes in HbA1c and lipid profiles in diabetic kidney disease patients treated with sevelamer versus calcium carbonate. The mean age of the patients was 58.53 years. Sevelamer exhibited a mean decrease in HbA1c and lipid profile compared to calcium carbonate (-0.57 ± 0.45, -8.35 ± 9.006, -1.40 ± 7.07, -4.20 ± 4.26, vs -0.08 ± 0.21, 0.10 ± 2.51, 0.62 ± 1.03, 1.00 ± 1.55). However, there was a mean increase in C-reactive protein. In conclusion, sevelamer induced a greater mean decrease in HbA1c and lipid profile compared to calcium carbonate but did not reduce C-reactive protein.

Keywords: Advanced Glycation End Products (AGE), Diabetic Nephropathy, Glomerular Filtration Rate (GFR), Hyperfiltration, Nephrotic Syndrome, End-Stage Renal Disease (ESRD), Chronic Kidney Disease (CKD), UK Prospective Diabetic Study (UKPDS), HbA1c, C-reactive protein (CRP), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), Chronic Renal Insufficiency.

Introduction

Diabetic nephropathy (DN) manifests as a clinical syndrome marked by persistent albuminuria (exceeding 300mg/dl or 200mg/dl) confirmed on at least two occasions spaced 3-6 months apart. It is characterized by a progressive decline in the glomerular filtration rate (GFR) and elevated arterial blood pressure [1]. This condition follows a protracted natural course in individuals with type 1 diabetes. Initially, patients exhibit hyperfiltration, progressing to occasional microalbuminuria. Subsequently, there is a gradual decline in GFR and sustained microalbuminuria, eventually leading to mild to moderate proteinuria. The disease's final stage involves severe proteinuria, with or without nephrotic syndrome, and chronic renal insufficiency that may progress to end-stage renal disease (ESRD) [2].

DN is a significant contributor to chronic kidney disease (CKD) and stands as the primary cause of end-stage renal disease globally. The prevalence of DN in individuals with type 1 diabetes ranges from 15-40%, peaking at 15-20 years of disease duration. In type 2 diabetes, the occurrence varies between 5-20%, with higher prevalence in individuals of Asian or African descent. The UK Prospective Diabetes Study (UKPDS) reported that 38% developed albuminuria, and 29% developed renal impairment within 15 days of follow-up [3,4].

Advanced glycation end products (AGEs) form through a non-enzymatic process known as glycation, where elevated glucose levels covalently bind with plasma proteins. The glycation process, leading to AGE formation, is considered a significant contributor to diabetic nephropathy [5,6]. This phenomenon results in an imbalance between extracellular matrix formation

and degradation, causing increased deposition of collagen, fibronectins, and laminin. The altered density of collagen due to glycation affects cell adhesion and growth, inhibiting the assembly of collagen and laminin [7].

Sevelamer, a non-absorbable, calcium-free, and albumin-free anion exchange resin, binds to dietary phosphate in the gastrointestinal tract [8]. Previous studies indicate that sevelamer reduces the absorption of AGEs present in our food [9,10]. The current study was conducted to evaluate the potential beneficial effects of sevelamer, particularly its impact on reducing HbA1c, serum lipids, and inflammatory markers in the Pakistani population.

Methods

This research was conducted at the Nephrology Department of Akbar Niazi Teaching Hospital in Islamabad, spanning from November 1, 2017, to April 30, 2018. The study included patients of both genders, aged between 30 and 70 years, with type 2 diabetes undergoing treatment with at least one medication and diagnosed with diabetic kidney disease according to the established protocol. Patients undergoing treatment for hyperphosphatemia, those with biopsy-proven kidney diseases other than diabetic kidney disease, and those experiencing hypophosphatemia and hypercalcemia were excluded from the study [10].

Enrolled patients meeting the inclusion and exclusion criteria provided informed consent before participating in the study. Demographic details such as name, age, gender, medical registration number, address, and contact number were recorded, along with the duration of diabetes. Baseline measurements of HbA1c, lipid profile, and C-reactive protein were documented for all participants.

Using a lottery method, patients were randomized into two groups. One group received Sevelamer at a dosage of 1600mg thrice daily, while the other group was administered calcium carbonate at 80mg thrice daily. After three months, HbA1c, lipid profile, and C-reactive protein were measured. Subsequently, a crossover technique was implemented after a one-week washout period: patients initially receiving Sevelamer were switched to calcium carbonate, and vice versa. After another three months, measurements of HbA1c, lipid profile, and C-reactive protein were taken again.

The mean change in HbA1c, fasting cholesterol, LDL, triglyceride, and C-reactive protein following the use of Sevelamer and calcium carbonate was calculated using the student t-test, with a p-value ≤ 0.05 considered significant. Data was further stratified for age, gender, and duration of diabetes. Post-stratification student t-test was applied, and a p-value ≤ 0.05 was deemed significant.

Results

The average age of the patients was 58.53 ± 8.90 years. Among them, 31.1% (n=87) fell within the age range of 30-49 years, while 68.9% (n=193) were aged between 50-70 years. Regarding gender distribution, 53.2% (n=149) were males, and 46.8% (n=131) were females. The average duration of diabetes among the participants was 10.45 years.

The mean changes in HbA1c, total cholesterol, HDL, LDL, triglyceride, and C-reactive protein after three months of using calcium carbonate were as follows: -0.08 ± 0.21, 0.10 ± 2.51, 0.6 ± 6.39, 0.62 ± 1.03, 1.00 ± 1.55, and 0.10 ± 0.07, respectively. Conversely, the mean changes in HbA1c, total cholesterol, HDL, LDL, triglyceride, and C-reactive protein after three months of using sevelamer were 0.57 ± 0.45, 8.35 ± 9.006, 1.79 ± 10.85, -1.04 ± 7.07, -4.20 ± 4.26, and 0.54 ± 0.42, respectively (Table. 1).

The results were further stratified based on age, with a p-value < 0.05 considered significant [10].

Discussion

This randomized control trial aimed to compare the mean changes in HbA1c, lipid profile, and C-reactive protein between sevelamer and calcium carbonate. Sevelamer is believed to possess an additional anti-inflammatory effect, aside from its role in preventing the absorption of advanced glycation end products (AGEs) from the gut, owing to its resin-like properties [10]. The avoidance of AGEs in food is known to play a role in improving glycemic control and preventing diabetic nephropathy [11].

Table 1: Gender Distribution.

	Calcium Carbonate			Sevelamer		
	Mean change	SD	P-value	Mean change	SD	P-value
HbA1C	-0.08	0.21	0.000	-0.575	0.45	0.000
Total cholesterol mg/dl	0.10	2.51	0.506	-8.35	9.006	0.000
HDL mg/dl	-0.6	6.39	0.71	1.79	10.85	0.15
LDL mg/dl	0.62	1.03	0.000	-1.40	7.072	0.001
Triglyceride mg/dl	1.00	1.55	0.000	-4.20	4.26	0.000
C reactive proteins mg/dl	0.10	0.07	0.000	0.54	0.427	0.000

In our study, the patient demographics were relatively balanced in terms of gender, with a majority (68.9%) falling within the age range of 50-70 years, highlighting the prevalence of diabetes in older age. The mean age of the participants was 58.3 years, and the mean duration of diabetes was 10.45 years, indicating a cohort with a prolonged history of diabetes.

The analysis of the mean changes after three months of using calcium carbonate revealed a statistically significant decrease in HbA1c (0.08%), accompanied by an increase in total cholesterol, HDL, LDL, triglyceride, and C-reactive protein. Conversely, sevelamer demonstrated a greater reduction in HbA1c (-0.57%), substantial decreases in total cholesterol and triglyceride, but no significant impact on C-reactive protein.

Upon stratification by age, a greater decrease in HbA1c was observed in patients aged 30-49 years compared to those aged 50-70 years when using sevelamer (-0.64 vs. 0.54). Similarly, a more substantial decrease in total cholesterol was noted in the younger age group. While our findings align with previous studies [9, 10], sevelamer did not exhibit a clear anti-inflammatory effect in our study, as indicated by a mean increase in C-reactive protein. Further investigations are warranted to evaluate the anti-inflammatory potential of sevelamer in our population.

Conclusion

Sevelamer resulted in a greater mean decrease in HbA1c, total cholesterol, HDL, LDL, and triglyceride compared to calcium carbonate. However, sevelamer did not demonstrate a reduction in C-reactive protein, suggesting the need for additional studies to explore its anti-inflammatory effects in our population.

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