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EFFICACY OF ANTI-DIABETIC DRUGS ON PREVENTION OF MYOCARDIAL INFARCTION IN DIABETIC SUBJECTS

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ABSTRACT

Background: Compared to subjects without diabetes mellitus, those with the disease are more likely to need repeated PCI (percutaneous coronary intervention).

Aim: The purpose of this study was to evaluate and compare the effectiveness of glucose-lowering medications on the secondary prevention of myocardial infarction in individuals with type 2 diabetes.

Methods: During the specified study period, 200 subjects who were over or equal to 30 years old and had percutaneous coronary intervention at the Institute were evaluated. Based on their anti-diabetic medication prescription records, the 200 participants were split up. The rate of coronary revascularization was the primary outcome evaluated in the research participants.

Results: Among the 200 participants in the study, those taking metformin had a significantly lower risk of needing percutaneous coronary intervention. Thiazolidinedione (TZD)-treated obese individuals with a BMI of ≥25 kg/m2 had a lower risk of repeated revascularization than non-TZD-treated individuals ($p<0.05$). Regardless of their BMI, subjects taking metformin had a lower risk of requiring revascularization. Meglitinide, insulin, and alpha-glucosidase inhibitors were associated with the need for repeated percutaneous coronary interventions.

Conclusion: Individuals with diabetes treated with metformin and obese individuals treated with thiazolidinedione had a significantly lower risk of requiring revascularization. According to these results, doctors should choose the right anti-diabetic medications for secondary prevention of coronary artery disease.

Keywords: Coronary artery disease, Diabetes mellitus, metformin, Percutaneous coronary intervention, Secondary prevention

INTRODUCTION

Cardiovascular disease and related morbidity in subjects with type 2 diabetes mellitus remains a worldwide clinical challenge, as individuals with type 2 diabetes mellitus are more likely than those without the disease to experience coronary artery disease and cardiovascular death. Percutaneous coronary intervention, or PCI, is an essential treatment option for patients with cardiovascular disease. Even though DESs (drug-eluting stents) are widely used to prevent vascular proliferation, subjects with type 2 diabetes mellitus who underwent PCI had higher rates of death and restenosis than people without the disease. Rosiglitazone users have a markedly higher risk of MI (myocardial infarction) or sudden death, according to a number of published studies.[1]

The Food and Drug Administration (FDA) has recommended a number of guidelines for the pharmaceutical industry that require evaluation of cardiovascular outcomes for all of the more recent anti-diabetic medications. Following FDA guidelines, a number of cardiovascular studies have been conducted in subjects with a high risk of cardiovascular disease and poor cardiovascular outcomes when a new glucose-lowering medication is added to standard treatment. In order to evaluate cardiovascular safety, the majority of these studies evaluated MACE (major adverse cardiovascular events), which include cardiovascular deaths, neonatal stroke, and/or neonatal MI.[2]

According to the findings of these studies, sodium-glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) are effective medications for secondary prevention and lowering cardiovascular events. Although more recent glucose-lowering medications like GLP-1Ras and SGLT-2 inhibitors have demonstrated cardioprotective effects, doctors are not persuaded to recommend these medications. Due to financial limitations and the requirement for subcutaneous injections for GLP-IRAs, a significant percentage of subjects still prefer older medications despite the introduction of newer ones.[3]

Dipeptidyl peptidase-4 inhibitors, or DPP-4is, have been shown to have no effect on major cardiovascular events in individuals with type 2 diabetes mellitus and pre-existing cardiovascular disease. Additionally, studies evaluating saxagliptin-treated patients with cardiac failure have indicated a high risk of hospitalization. Numerous studies have shown that TZD (thiazolidinedione) is beneficial for secondary prevention of MACE. Few studies, however, have questioned thiazolidinedione's dubious cardiovascular safety.[4]

The results of different anti-diabetic medications' cardioprotective effects are debatable. Additionally, there is a dearth of information in the literature regarding the effectiveness of each anti-diabetic medication in preventing repeat revascularization, especially in patients who had PCI.4 Therefore, the purpose of this study was to evaluate and compare the effectiveness of glucose-lowering medications on the secondary prevention of myocardial infarction in individuals with type 2 diabetes mellitus.

MATERIALS AND METHODS

The purpose of this retrospective clinical study was to evaluate and compare the effectiveness of glucose-lowering medications on the secondary prevention of myocardial infarction in individuals with type 2 diabetes mellitus. The Institute's Department of Cardiology provided the study participants. Prior to their involvement in the study, all participants provided written and verbal informed consent.

The study evaluated 200 participants who had undergone percutaneous coronary intervention at the Institute during the specified study period and were older than or equal to thirty. Based on their anti-diabetic medication prescription records, the 200 participants were split up. Age, gender, income, eligibility type, and other socioeconomic factors were evaluated for each subject, along with general assessment, lifestyle, and death data. Additionally, mortality and diagnosis data. Procedures and prescriptions were evaluated.

200 adult participants with reported PCI history who were at least 30 years old and had at least two general health evaluations were included in the study. Only participants who had a PCI assessment within a year were included in the study. Participants who died or underwent repeat revascularization within a year following a prior PCI were not included in the study.

The International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) or the use of at least one anti-diabetic medication or insulin at the time of study enrollment, as well as fasting glucose levels of ≥126 mg/dL, were the criteria used to define diabetes mellitus. Additionally, subjects with missing data were not included in the study. Every subject's data was evaluated either until death or for the duration of the study, whichever came first.

A pre-made self-reporting questionnaire proforma was used to gather data for laboratory assessment and anthropometric measurements, which were then followed by a physical examination and serum biochemical parameters. Body weight in kg and height in m2 was evaluated to evaluate the BMI. Following a 12-hour fast, the levels of total cholesterol, alanine aminotransferase, aspartate aminotransferase, and fasting blood glucose were measured.

Hypertension among comorbid conditions was defined as systolic and diastolic blood pressure of at least 140/90 mm Hg or at least one prescription for antihypertensive medications. Total cholesterol ≥240 mg/dL or at least one prescription for antihyperlipidemic medications were considered indicators of dyslipidemia.

Alpha-glucosidase inhibitors (AGI), DPP-4 inhibitors (DPP-4i), TZD, meglitinide, metformin, sulfonylurea (SU), and insulin were the seven classes of glucose-lowering agents. For individuals using multiple medications, combination therapy was taken into consideration. Three types of therapies were identified: monotherapy, dual therapy, and triple therapy. Revascularization with PCI during follow-up was the main outcome evaluated in research participants.

The chi-square test, Fisher's exact test, Mann Whitney U test, and SPSS (Statistical Package for the Social Sciences) software (IBM Corp., Armonk, NY, USA) were used to statistically analyze the collected data. ANOVA, chi-square test, and student's t-test were also used. A p-value of less than 0.05 was used as the significance level.

RESULTS

The purpose of this retrospective clinical study was to evaluate and compare the effectiveness of glucose-lowering medications on the secondary prevention of myocardial infarction in individuals with type 2 diabetes mellitus. The current study evaluated 200 participants who were over 30 years old and had percutaneous coronary intervention at the Institute during the specified study period. Based on their anti-diabetic medication prescription records, the 200 participants were split up.

70% (n=140) of the study participants were male, and their mean age was 64.4±9.50 years. PCI incidence was measured for a mean of 4.25±1.71 years. In the study, there were more men than women who had repeated PCI revascularization. Subjects who underwent repeat PCI had a higher rate of insulin treatment than those who did not ($P<0.001$). The individuals who had repeated PCI had high BMIs and were obese. Triglyceride and fasting blood glucose levels were lower in subjects who did not receive repeat PCI than in those who did (Table 1).

The risk of repeat revascularization with repeated PCI for different anti-diabetic medications was significantly lower in study participants taking DPP-4i. Subjects on DPP or metformin had a lower risk of repeat PCI ($p<0.001$) after confounding variables like insulin use and the number of drug agents used were adjusted. Except for individuals taking metformin, no statistical significance was observed after controlling for the length of diabetes and fasting blood glucose levels. When compared to individuals who were not taking glucose-lowering medications, AGI, meglitinide, SU, and insulin did not demonstrate any beneficial effects for secondary prevention of repeated PCI. These medication-treated subjects had a higher risk of PCI (Table 2).

The preventive effectiveness of different anti-diabetic medications was evaluated by stratifying subjects according to their BMI in order to analyze study subgroups based on BMI. With the exception of metformin, which was associated with a significantly lower risk of PCI ($p=0.02$), there was no significant association in repeat revascularization using PCI in subjects with a BMI of less than 25 kg/m2. With the exception of TZD, which showed a significantly lower risk of PCI with TZD use ($p=0.01$), no significant association was observed in repeat revascularization using PCI in subjects who were obese and had a BMI of ≥25 kg/m2 (Table 3).

Additionally, the beneficial effects of TZD were not observed in non-obese subjects, and there was no discernible decrease in the risk of repeated PCI revascularization. The risk of repeat revascularization was higher in non-obese individuals treated with multiple antidiabetic medications, although this difference was not statistically significant. The number of oral anti-diabetic medications and the risk of repeat PCI revascularization in obese individuals did not significantly correlate (Table 4).

DISCUSSION

The current study evaluated 200 participants who were over 30 years old and had percutaneous coronary intervention at the Institute during the specified study period. Based on their anti-diabetic medication prescription records, the 200 participants were split up. 70% (n=140) of the study participants were male, and their mean age was 64.4±9.50 years. PCI incidence was measured for a mean of 4.25±1.71 years.

In the study, there were more men than women who had repeated PCI revascularization. Subjects who underwent repeat PCI had a higher rate of insulin treatment than those who did not ($P<0.001$). The individuals who had repeated PCI had high BMIs and were obese. Triglyceride and fasting blood glucose levels were lower in those who did not receive repeat PCI than in those who did. These findings were similar to those of earlier research by Kim HY et al. (2018) and Schnell O et al. (2017), in which participants with diabetes mellitus were evaluated on anti-diabetic medications and underwent PCI, just like in this study.

The risk of repeat revascularization with repeated PCI for different anti-diabetic medications was observed to be significantly lower in study participants on DPP-4i. Subjects on DPP or metformin had a lower risk of repeat PCI ($p<0.001$) after confounding variables like insulin use and the number of drug agents used were adjusted. Except for individuals taking metformin, no statistical significance was observed after controlling for the length of diabetes and fasting blood glucose levels. When compared to individuals who were not taking glucose-lowering medications, AGI, meglitinide, SU, and insulin did not demonstrate any beneficial effects for secondary prevention of repeated PCI.

These medication-treated subjects had a higher risk of PCI. These findings were in line with those of Ko SH et al. (2018) and Hanefeld M. et al. (2016), who found that the risk of repeat revascularization with repeated PCI for different anti-diabetic medications was similar to that of the current study. The study's findings demonstrated that the preventive effectiveness of different anti-diabetic medications was evaluated by stratifying participants according to their BMI in order to analyze study subgroups based on BMI. With the exception of metformin, where there was a significantly lower risk of PCI with metformin use (p=0.02), no significant association was observed in repeat revascularization using PCI in subjects with BMI <25 kg/m2.

No significant correlation was found in repeat revascularization using PCI in subjects who were obese and had a BMI of ≥25 kg/m2, with the exception of TZD, which demonstrated a significantly lower risk of PCI with TZD use (p=0.01). Bell DS et al. (9) and Gamble JM et al. (10), whose authors reported similar findings regarding the preventive efficacy of various anti-diabetic agents based on BMI, were in agreement with these results. TZD did not significantly reduce the risk of repeated PCI revascularization and had no positive effect on the evaluation of non-obese subjects. Although this difference was not statistically significant, non-obese patients receiving multiple antidiabetic medications had a higher risk of repeat revascularization.

The number of oral anti-diabetic medications and the risk of repeat PCI revascularization in obese subjects did not significantly correlate. These findings were consistent with those of Curie CJ et al. (2013) and Roumie CL et al. (2014), who also found that TZD and metformin protected study participants from coronary artery disease. In conclusion

CONCLUSION

Within its limitations, the current study concludes that individuals with diabetes treated with metformin and obese individuals treated with thiazolidinedione had a significantly lower risk of requiring revascularization. According to these results, doctors should choose the right anti-diabetic medications for secondary prevention of coronary artery disease.

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S. No	Characteristics	Total	Repeat PCI	No repeat PCI	p-value
1.	**Number (n)**	200	21	174	
2.	**Mean age (years)**	64.4±9.50	63.8±9.20	64.5±9.54	**<0.0001**
3.	**Male gender**	136 (68)	15 (69)	121 (67)	**0.01**
4.	**Low income**	42 (21)	5 (22)	37 (21)	**0.02**
5.	**Alcohol drinking**				
a)	None	142 (71)	16 (72)	126 (71)	0.203
b)	Mild (<30 g/day)	48 (24)	5 (23)	43 (24.7)	
c)	Heavy (≥30g/day)	10 (5)	1 (5)	9 (5)	
6.	**Smoking status**				
a)	Never	100 (50)	11 (51)	89 (51.1)	0.208
b)	Former	54 (27)	6 (28)	48 (27)	
c)	Current	46 (23)	5 (23.8)	41 (23.56)	
7.	**Regular exercise**	42 (21)	1 (5)	40 (23)	0.116
8.	**Anti-diabetic agent used**				
a)	DPP4 inhibitor	70 (35)	7 (33.3)	63 (36)	0.09
b)	TZD	10 (5)	1 (5)	9 (5)	0.326
c)	Meglitinide	10 (5)	2 (6)	8 (4.5)	**<0.0001**
d)	Metformin	152 (76)	16 (75)	136 (76)	**0.01**
e)	Sulfonylurea	118 (59)	13 (62)	105 (59)	**0.0006**
f)	Insulin	82 (41)	9 (45)	73 (41.9)	**<0.0001**
9.	**Triglycerides (mg/dl)**	138.6	141	138.3	**0.02**
10	**LDL-C (mg/dl)**	97.4±43.77	98.4±43.62	97.2±43.79	0.09
11	**Weight (kg)**	65.5±10.85	66.0±10.5	65.5±10.87	**0.004**
12	**Wasit circumference (cm)**	86,5±8.04	87.0±8.05	86.4±8.03	**0.0008**
13	**FBG (mg/dl)**	138.5±45.84	141.148.72	138.1±45.40	**<0.0001**
14	**Total cholesterol (mg/dl)**	175.2±47.0	176.6±47.47	175±47.13	**0.04**
15	**DBP mm Hg**	77.2±10.41	77.0±10.51	77.2±10.40	0.210
16	**SBP mmHg**	129.3±16.57	130±16.81	129.2±16.54	**0.01**
17	**BMI kg/m2**	25±3.04	24.9±3.05	24.8±3.03	**0.03**
18	**CKD**	44 (22)	5 (21)	39 (25)	**<0.0001**
19	**Dyslipidemia**	180 (90)	19 (90)	161 (90)	**0.04**
20	**Hypertension**	178 (89)	19 (89)	159 (91)	**0.003**

Table 1: Baseline demographic and disease data in study subjects

S. No	Drug	Number	Repeat PCI	Duration	95% CI
1.	**AGI**	168	5	126.44	1.26 (1.17-1.36)
2.	**DPP4**	70	16	100.65	0.96 (0.90-1.03)
3.	**TZD**	10	2	143.47	0.92 (0.80-1.06)
4.	**Meglitinide**	10	2	6.71	1.38 (1.22-1.54)
5.	**Metformin**	152	18	115.57	0.88 (0.82-0.94)
6.	**Sulfonylurea**	118	16	90.27	1.09 (1.02-1.15)
7.	**Insulin**	82	12	59.72	1.23 (1.16-1.31)

Table 2: Repeat revascularization risk with repeated PCI for various anti-diabetic drugs in study subjects

S. No	Drug	Number	Repeat PCI	Duration	95% CI	p-value
1.	**BMI <25kg/m2**					
a)	AGI	18	2	14.48	1.27 (.15-1.40)	0.13
b)	DPP4	38	4	26.86	1.03 (0.91-1.08)	0.23
c)	TZD	4	2	36.21	1.09 (0.90-1.31)	0.42
d)	Meglitinide	6	2	39.52	1.39 (1.18-1.63)	0.85
e)	Metformin	80	8	60.74	0.91 (0.82-1.00)	**0.02**
f)	Sulfonylurea	64	10	47.92	1.12 (1.03-1.22)	0.43
g)	Insulin	46	6	33.10	1.17 (1.08-1.27)	0.77
2.	**BMI >25kg/m2**					
a)	AGI	12	2	101.65	1.24 (1.10-1.39)	0.75
b)	DPP4	32	4	23.55	0.94 (0.86-1.04)	0.49

c)	TZD	4	2	40.10	0.78 (0.63-0.96)	**0.01**
d)	Meglitinide	4	1	27.74	1.36 (1.12-1.65)	0.82
e)	Metformin	70	8	54.80	0.86 (0.78-0.95)	0.39
f)	Sulfonylurea	54	7	42.33	1.04 (0.95-1.14)	0.26
g)	Insulin	36	6	26.59	1.28 (1.17-1.39)	0.15

Table 3: Analysis of study subgroups based on the BMI

S. No	Number	Number	Repeat PCI	95% CI	p-value
1.	**BMI <25kg/m2**				
	No. of anti-diabetic drugs				
a)	0	14	1	1 (reference)	0.08
b)	1	20	2	1.01 (0.86-1.18)	
c)	2	34	4	1.11 (0.96-1.28)	
d)	≥3	38	4	1.17 (10.2-1.35)	
2.	**BMI <25kg/m2**				
3.	**No. of anti-diabetic drugs**				
4.	0	12	1	1 (reference)	0.07
5.	1	18	2	0.95 (0.81-1.10)	
6.	2	32	4	0.88 (0.76-1.01)	
7.	≥3	30	4	0.96 (0.83-1.10)	

Table 4: Analysis of study subgroups based on the BMI and number of anti-diabetic drugs