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Original Research Article

Effect of sitagliptine and vildagliptine on carotid intima/media thickness in patients with type 2 diabetes mellitus

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ABSTRACT

Background: Atherosclerosis is a known macro-vascular complication of diabetes mellitus. Gliptins, as a drug class have non-glycemic beneficial action on blood vessels and in addition to their anti-diabetic effects. This study was carried out to find out the effects of sitagliptin and vildagliptin on common carotid intima-media thickness in patients with type 2 diabetes mellitus.
Methods: The observational longitudinal study was carried out on 100 patients with 80 patients with confirmed clinical diagnosis of type 2 diabetes mellitus. They were divided in 3 groups. Group A and Group B received drugs, either sitagliptine or vildagliptin and Group C control group did not receive any drug. High resolution B-mode ultrasonography was carried out for the measurement of intima-media thickness (IMT) of both the common carotid arteries (CCA). Data analysis was done using Microsoft excel spreadsheet and GraphPad Prism version 7.0 (free trial version) software package. A p value of ≤ 0.05 was considered as statistically significant.
Results: The baseline value for the control group was 0.812±0.0748 mm for both the right and left CCA. At 52 weeks the CCA IMT for the right and left CCA were 1.0185± 0.272 mm and 0.936±0.149 mm respectively. At 104 weeks the CCA IMT for the right and left CCA were 0.923±0.243 mm and 0.859±0.123 mm respectively.
Conclusions: There was a significant decrease in carotid intima-media thickness in patients of type-2 diabetes mellitus treated with sitagliptin and vildagliptin.

Keywords: Common carotid artery intima/media thickness, Dipeptidyl peptidase-4 inhibitors, Type -2 diabetes mellitus

INTRODUCTION

Dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins) are oral incretin-based glucose-lowering agents with proven efficacy and safety in the management of type 2 diabetes mellitus (T2DM). Preclinical data and mechanistic studies have suggested a possible additional non-glycemic beneficial action on blood vessels and the heart, via both glucagon-like peptide-1-dependent and glucagon-like peptide-1-independent effects.[1] Intima-media thickness of common carotid artery (CCA IMT) is a surrogate marker of atherosclerosis in coronary and cerebral vessels.[2] The common carotid artery is prone to diffuse atherosclerosis whereas the internal carotid artery usually has focal atherosclerotic plaques. The evaluation of intima-media thickness of common carotid artery is an option for vascular imaging evaluation of atherosclerosis.[3] Studies conducted on carotid intima-media thickness as an

independent marker for the assessment of macro-vascular risk in diabetic patients have also concluded that CCA IMT can be used as a preliminary non-invasive test to identify the early atherosclerosis in diabetic patients, so that, appropriate therapy can be targeted at an early stage.[4] Non-invasive imaging techniques have been used to identify pre-clinical atherosclerosis and to monitor the rate of atherosclerosis progression.[5] Thus, CCA IMT measurement using high resolution B-mode ultrasound scanning can be a routine check-up in the initial evaluation of diabetic subjects.[6] Though, meta-analyses have demonstrated that, DPP-4 inhibitors decrease the occurrence of cardiovascular events.[7] But, there is a there is scarcity of published literature to conclude the relative efficacy of gliptins in reducing CCA IMT and progression of artheroselerosis in type 2 diabetes mellitus. With this background, this study was carried out to find out the effects of two commonly used gliptins-sitagliptin and vildagliptin on common carotid intima-media thickness in patients with type 2 diabetes mellitus.

METHODS

The observational longitudinal study was carried out at the Department of Medicine and Department of Radiology, M.K.C.G Medical College and Hospital, Berhampur during the period from November 2015 to October 2017. The test arms constituted of consecutive patients of either gender with a confirmed clinical diagnosis of type 2 diabetes mellitus in the OPD and IPD in the Department of Medicine and Department of Endocrinology. The control arm include patients without diabetes mellitus.

Inclusion criteria

Cases in the study group were selected according to the American Diabetes Association (2015) criteria and included the newly diagnosed type 2 diabetic patients of either gender.

Exclusion criteria

Patients with type 1 diabetes, secondary forms of diabetes, any major illness with a life expectancy of <5 years, uncontrolled hypertension, hypersensitivity to gliptins, chronic or acute renal diseases, history of taking hepatotoxic drugs like INH, rifampicin, pyrazinamide, anabolic steroids, oral contraceptives, sodium valproate, dapsone or anti-cancer chemotherapeutic agents in the preceding two months were excluded.

After implementing the inclusion and exclusion criteria the eligible study participants were divided into three groups.

Study groups

Group A constituted 40 consecutive patients of type 1 diabetes mellitus and were on sitagliptin 100 mg once daily orally. Group B also constituted 40 consecutive patients of type 1 diabetes mellitus and were on vildagliptin at a dose of 50 mg twice daily orally. 20 normal patients (without diabetes mellitus) were taken as control in Group C and neither of the gliptins was administrated to them. Patients in the three groups were matched for other medications except for the test drugs.

Ethical issues

The study was approved by the Institutional Ethics Committee of MKCG Medical College, Berhampur (Approval No. 362). The participants were recruited only after obtaining written informed consent. They were explained about the implication of the study in the furtherance of the knowledge in management of diabetes mellitus by the investigators.

Study implementation

The history taking, general examination and the investigations were done as per standard protocol after obtaining the informed consent the eligible participants. High resolution B-mode ultrasonography was carried out for the measurement of intima-media thickness (IMT) of both the common carotid arteries (CCA) with a linear array transducer of 7.5 MHz or more attached to Toshiba diagnostic ultrasound system (Model-Nemio-30, SSA-550A). The 'B' mode ultrasound of common carotid arteries recorded the far-wall intima-media thickness at three different places (bulb, mid, proximal part) in each common carotid artery (right and left CCA). Finally the average of the six readings was calculated. The CCA IMT was recorded in all the participants at the initiation of the study (baseline), at 52 weeks and 104 weeks after treatment during the follow up visits. The data was recorded in pre-tested case record form by the investigators. The first part of the case record form recorded the clinic demographic characteristics of the participants like age, duration of diabetes, anti-diabetic treatment and complications of diabetes. The second part recorded the findings of the CCA IMT at baseline and during the subsequent visits.

Study definitions and measurement criteria

CCA IMT is defined as the area of tissue starting at the luminal-intimal interface and the media-adventitia interface of CCA. Since B-mode (bright-mode) ultrasonography is a safe, noninvasive, and cost-effective to measure CIMT, a recent study more precisely defined CIMT as the double-line pattern visualized by B-mode vascular ultrasound formed by two parallel echogenic lines representing junction of the vessel lumen with intima and media-adventitia interface.[8] The consensus statement on use of CIMT from ASE has recommended adhering to carotid ultrasound scanning technique and procedures to facilitate high-quality, reproducible images, and requires both sonographer and patient to be positioned properly to obtain high-quality images. CIMT testing is conducted in supine position on scan bed with head of the patient resting comfortably, and neck slightly hyper-extended and rotated

in direction opposite to the probe. A wedge pillow at an angle of 45° standardizes lateral rotation. Optimization of images is done by adjusting patient's neck position especially in anterior scanning planes, and rolled towels are given under neck and legs for comfort. With the use of external landmarks such as the Meijer arc or similar device, transducer angle is standardized. Height and location of ultrasound system keyboard and monitor, examination bed, and chair are adjusted accordingly to avoid any musculoskeletal injuries to patients.[9]

Statistical analysis plan

All the statistical calculations were done by using SPSS version 16. The continuous variables were expressed as mean±SD. The comparison of mean among the three groups of subjects was analyzed by Kruskal Wallis test. The significance of the difference in mean at baseline, at 52 weeks and 104 weeks were analysed by using the Wilcoxon matched pairs test. The categorical data was analyzed by Chi square test. A p value of <0.05 was considered as statistically significant.

RESULTS

The present study was carried out on 100 participants of which 80 were included in the test groups A and B and 20 were in the control group C. The median age of the patients in Group-A, Group-B and Group-C was 60.5, 60.0 and 62.0 years of age (p=0.514). Majority of patients were male in all the groups, that is, 75% (30/40), 67.5% (27/40) and 60% (12/20) in Group-A, Group-B and Group-C respectively. There is no statistical difference in the gender wise distribution of cases across the groups ($\chi 2$= 1.43; p=0.479). At baseline, 38 patients (95%) in Group-A and 35 patients (87.5%) in Group-B had more than 0.8 mm of CCA-IMT value. All the three (left, right and mean) CCA-IMT value were compared among the groups at baseline and found a similar result in the three measurements. In brief, there was a significant difference in the CCA-IMT value between the Group-A and Group-C (p<0.01) and between the Group-B and Group-C (p<0.01), however there was no differences (p>0.05) when compared between Group-A and Group-B (Figure 1).

To observe the effect of two drugs, that is, sitagliptin (Group-A patients) and vildagliptin (Group-B patients), we have compared the CCA-IMT value at baseline against at 52 weeks and another at 104 weeks. In both the groups of patients, there was a significant and progressive decrease in the CCA-IMT value at 52 weeks and at 104 weeks compared to baseline value in all the left, right and mean measurements respectively (Table 1).

However, this significant decrease was found to be irregular as represented in Figure 2. Few patients in both the groups showed either an increase in the CCA-IMT value or same as baseline value to respective therapy. In Group-A, 34.2% (13/38) were found to have either an increased or same CCA-IMT value after sitagliptin therapy compared to 20% (7/35) in Group-B patients after vildagliptin therapy (Figure 3).

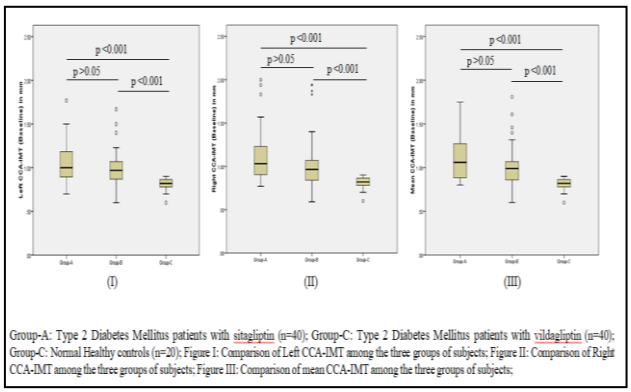

Figure 1: Comparison of baseline intima-media thickness of common carotid artery (CCA-IMT) value among the three groups of study subjects.

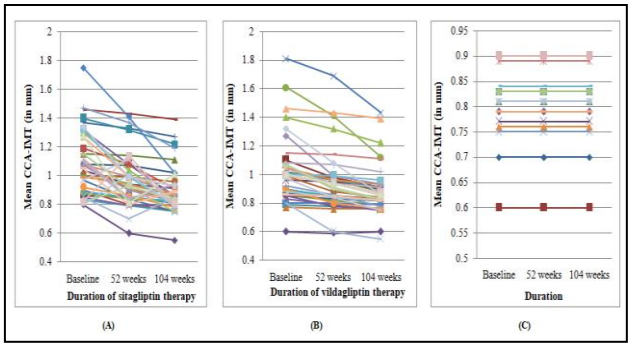

Figure 2: Changes in the mean CAA-IMT value at baseline (0 day), 52 weeks and 104 weeks of respective drugs. A: type 2 diabetes mellitus patients with sitagliptin (n=40); B: type 2 diabetes mellitus patients with vildagliptin (n=40); C: normal healthy controls (n=20).

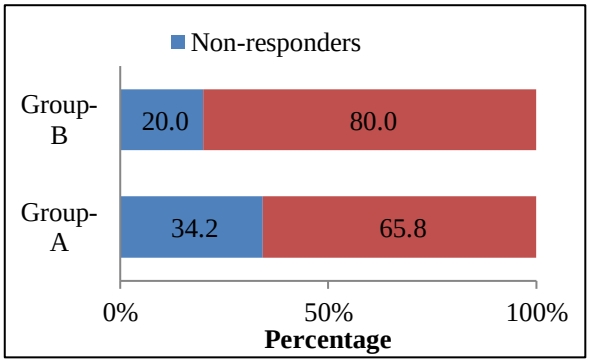

Figure 3: Group A, patients with sitagliptin and Group B, patients with vildagliptin. Non-responders are those with either an increase or same (left or right or mean) CCA-IMT value after respective therapy.

Table 1: Effects of sitagliptin and vildagliptin on CCA-IMT value.

	Duration of therapy (Mean±SD)			Wilcoxon matched pairs test (P value)		
Group-A (Sitagliptin)	**Baseline**	**52 weeks**	**104 weeks**	**Baseline vs 52 weeks**	**52 weeks vs 104 weeks**	**Baseline vs 104 weeks**
Left	1.06±0.23	0.94±0.15	0.86±0.12	<0.0001	<0.0001	<0.0001
Right	1.13±0.31	1.02± 0.27	0.92±0.24	<0.0001	<0.0001	<0.0001
Mean	1.08±0.23	0.98±0.19	0.89±0.16	<0.0001	<0.0001	<0.0001
Group-B (Vildagliptin)	**Baseline**	**52 weeks**	**104 weeks**	**Baseline vs 52 weeks**	**52 weeks vs 104 weeks**	**Baseline vs 104 weeks**
Left	0.98±0.2	0.91±0.17	0.85±0.13	<0.0001	<0.0001	<0.0001
Right	1.04±0.32	0.97± 0.29	0.91±0.25	<0.0001	<0.0001	<0.0001
Mean	1.02±0.24	0.94±0.21	0.88±0.17	<0.0001	<0.0001	<0.0001

DISCUSSION

Carotid artery intima-media thickness (IMT) is associated with cardiovascular risk factors and prevalent cardiovascular disease (CVD) and is predictive of cardiovascular events.[10] Increased carotid artery IMT is considered as a marker of early atherosclerotic changes. Studies have observed that the normal IMT of CCA as evaluated by B-mode ultrasound imaging to be 0.74±0.14 mm and a carotid IMT at or above 1 mm to be associated with atherosclerosis and significantly increased CVD risk in any age group.[11] In the present study about 76% participants had an increased CCA IMT (>8 mm) of which 55% are males and 21% are females.

But, other studies have observed that females showed average IMT for the CCA that was slightly higher than the average in males. In a study done in Sudan it has been observed that ethnically females from East of Sudan show the highest average of CCA-IMT while females from South of Sudan show the lowest IMT. The authors in the study have observed that most of the average common carotids' IMT measured was slightly greater in females rather than in males.[12] Thus, CCA IMT is subject to ethnic and geographical variations. In the present study, Group A, the baseline mean right and left CCA IMT (±SD) was 1.125±0.311 mm and 1.062±0.232 mm respectively. In Group B the baseline mean right and left CCA IMT (±SD) was 1.041±0.321mm and 0.982±0.205 mm respectively. The baseline value for the control group was 0.812±0.0748 mm for both the right and left CCA. In an Asian study done in Korea, it has been observed that the mean values of common carotids' IMT (in mm) for healthy reference sample aged 40-49, 50-59, and 60-70 years were 0.55, 0.59 and 0.66 for men and 0.48, 0.55 and 0.63 for women, respectively.13 The difference in the observations may be due to ethnic and geographical variations. It has been reported that age and gender contributed 23.5% to the variability of the CCA IMT and 22.5% to that of the ICA IMT, followed by the next most important influencing factor being systolic blood pressure (1.9%) for the CCA IMT and smoking (1.6%) for the ICA IMT.10 In healthy middle-aged adults, CCA IMT values between 0.6 and 0.7 mm have been considered normal, while CCA IMT of 1 mm or more has been associated with significant increased absolute risk of CHD.[14] Studies have observed that in healthy Indian adults, the average and maximum CCA IMT values reported were 0.67 and 0.70 mm, respectively.[15] The measurement of CCA IMT varies with age and values >1.0 mm are considered abnormal in younger population and confer increased absolute risk of CHD.[16,17] In a cross-sectional study, apparent age-related increase in common CCA IMT was observed in both the genders (approximately 0.010 mm/year in seemingly healthy men and ~0.014 mm/year in seemingly healthy women), whereas it is 0.010 mm for both genders in the ICA. Patients with known CAD had three times higher rate of CCA IMT progression than patients without known CAD (0.030 mm/year vs. 0.010 mm/year, respectively).[18]

CCA IMT testing as a marker of atherosclerotic vascular disease generated considerable interest among physicians globally including India because of its simplicity, safety, and reproducibility. India has a population with a high incidence of diabetes, a high prevalence of dyslipidemia, and with increasing urbanization, an ever increasing population with adverse lifestyle changes. Among the different tools for subclinical atherosclerosis assessment, CCA IMT offers distinct advantages such as CCA IMT is associated with CVD risk factors, with prevalent and incident CVD, and is an independent predictor of CV events in a variety of populations. Due to its ease of use and reproducibility, CCA IMT would be the ideal choice for assessing subclinical atherosclerosis in clinical practice. CCA IMT as a reliable marker of atherosclerosis and harbinger of CV risk appears to be feasible in low-risk Indian population where cost effectiveness is of paramount importance. Increased CCA-IMT and plaque score are associated with acute ischemic stroke in patients with type 2 diabetes. The higher CCA-IMT and plaque score found in ischemic stroke in patients with type 2 diabetes seem to be induced by cerebrovascular risk factors. Therefore, to prevent ischemic stroke in patients with type 2 diabetes, strict control of hyperglycemia, hypertension, smoking, and low HDL, together with monitoring of CCA-IMT and carotid plaque, may be important.[19] B-mode sonography is a noninvasive method for examining the walls of peripheral arteries and provides a measure of intima-media

thickness and the presence of stenosis and plaques. The IMT corresponds to the intima-media complex, which comprises endothelial cells, connective tissue, and smooth muscle and is the site of lipid deposition in plaque formation. The IMT of the carotid artery is an established sonographic marker for early atherosclerosis, and thickening of the intima-media complex reflects generalized atherosclerosis.[20] Increased CCA-IMT has been reported under various conditions, including hypertension, dyslipidemia, obesity, diabetes, smoking, and cardiovascular disease, including ischemic stroke. In patients with type 2 diabetes, aging, hypertension, duration of diabetes, hyperglycemia, dyslipidemia, and smoking have been identified as significant risk factors for stroke.[21,22]

In the present study an increased baseline CCA IMT was seen predominantly in males in the control arm as well as in the sitagliptin and vildagliptin administered participants. There was a significant and progressive decrease in the CCA IMT at 52 weeks and 104 weeks of treatment with sitagliptin and vildagliptin was significant. With respect to OHA, previous studies showed that pioglitazone treatment led to the regression of carotid IMT in patient with T2DM probably through a multitude of mechanisms, including improvement in several metabolic factors and insulin sensitivity, anti-inflammatory effect, and direct actions on the vascular cells.[23,24] A post hoc sub-analysis has suggested that the tissue characteristics of the carotid arterial wall were improved in the sitagliptin treatment group during the 104-week treatment period but not in the conventional treatment group.[25,26] Studies have reported that sitagliptin attenuated the progression of carotid IMT in insulin-treated patients with T2DM free of apparent cardiovascular disease compared with conventional treatment. Administration of both sitagliptin and vildagliptin treatment resulted in a significant decline in IMT. Reduction of glucose excursion due to DPP-IV inhibitors administration, may prevent atherosclerosis progression in patients with type 2 diabetes probably through the reduction of daily inflammation and oxidative stress.[27] Lack of head to head trial and small sample size becomes the limitation of this study to prove their efficacy in reducing CCAIMT, hence their role in preventing progression of atherosclerosis and thereto macrovascular complication.

CONCLUSION

There was a significant decrease in carotid intima-media thickness in patients of type-2 diabetes mellitus treated with sitagliptin and vildagliptin. Thus, use of gliptin in type-2 diabetes mellitus may decrease the progression of artherosclerosis in patients with type-2 diabetes mellitus. To prevent ischemic stroke in patients with type 2 diabetes, strict control of hyperglycemia, hypertension, smoking, and dyslipidemia, together with monitoring of CCA-IMT and carotid plaque, is an important option.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Scheen AJ. Cardiovascular effects of dipeptidyl peptidase-4 inhibitors: from risk factors to clinical outcomes. Postgrad Med. 2013;125(3):7-20.
2. Kokubo Y, Watanabe M, Higashiyama A, Nakao YM, Nakamura F, Miyamoto WY, et al. Impact of intima-media thickness progression in the common carotid arteries on the risk of incident cardiovascular disease in the suita study. J Am Heart Assoc. 2018;7(11):e007720.
3. Ravani A, Werba JP, Frigerio B, Sansaro D, Amato M, Tremoli E, et al. Assessment and relevance of carotid intima-media thickness (C-IMT) in primary and secondary cardiovascular prevention. Curr Pharm Des. 2015;21(9):1164-71.
4. Lorenz MW, Price JF, Robertson C, Bots ML, Polak JF, Poppert H, et al. Carotid intima-media thickness progression and risk of vascular events in people with diabetes: results from the PROG-IMT collaboration. Diabetes Care. 2015;38(10):1921-9.
5. Blum A, Nahir M. Future non-invasive imaging to detect vascular plaque instability and subclinical non-obstructive atherosclerosis. J Geriatr Cardiol. 2013;10(2):178-85.
6. Mahmoud MZ. Sonography of common carotid arteries' intima: media thickness in the normal adult population in Sudan. N Am J Med Sci. 2013;5(2):88-94.
7. Santamarina M, Carlson CJ. Review of the cardiovascular safety of dipeptidyl peptidase-4 inhibitors and the clinical relevance of the CAROLINA trial. BMC Cardiovasc Disord. 2019;19(1):60.
8. Liviakis L, Pogue B, Paramsothy P, Bourne A, Gill E. Carotid intima-media thickness for the practicing lipidologist. J Clin Lipidol. 2010;4:24-35.
9. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid intima-media thickness task force. endorsed by the society for vascular medicine. J Am Soc Echocardiogr. 2008;21:93-111.
10. Polak JF, Pencina MJ, Meisner A. Associations of carotid artery intima-media thickness (IMT) with risk factors and prevalent cardiovascular disease: comparison of mean common carotid artery IMT with maximum internal carotid artery IMT. J Ultrasound Med. 2010;29(12):1759-1768.
11. Paul J, Dasgupta S, Ghosh MK. Carotid artery intima media thickness as a surrogate marker of atherosclerosis in patient with chronic renal failure on hemodialysis. N Am J Med Sci. 2012;4:77-80.

12. Mahmoud MZ. Sonography of common carotid arteries' intima: media thickness in the normal adult population in Sudan. N Am J Med Sci. 2013;5(2):88-94.
13. Youn YJ, Lee NS, Kim JY, Lee JW, Sung JK, Ahn SG, et al. Normative values and correlates of mean common carotid intima-media thickness in the Korean rural middle-aged population: the atherosclerosis risk of rural areas in korea general population (ARIRANG) study. J Korean Med Sci. 2011;26:365-71.
14. Jacoby DS, Mohler IE, Rader DJ. Noninvasive atherosclerosis imaging for predicting cardiovascular events and assessing therapeutic interventions. Curr Atheroscler Rep. 2004;6:20-6.
15. Hansa G, Bhargava K, Bansal M, Tandon S, Kasliwal RR. Carotid intima-media thickness and coronary artery disease: An Indian perspective. Asian Cardiovasc Thorac Ann. 2003;11:217-21.
16. O'Leary DH, Bots ML. Imaging of atherosclerosis: Carotid intima-media thickness. Eur Heart J. 2010;31:1682-9.
17. Ballantyne CM. Clinical Lipidology: A companion to Braunwald's heart diseases. 1 st ed. Saunders Elsevier Publication; 2008:608.
18. Crouse JR, Tang R, Espeland MA, Terry JG, Morgan T, Mercuri M. Associations of extra-cranial carotid atherosclerosis progression with coronary status and risk factors in patients with and without coronary artery disease. Circulation. 2002;106:2061-6.
19. Lee EJ, Kim HJ, Bae JM, Kim JC, Han HJ, Park CE, et al. Relevance of common carotid intima-media thickness and carotid plaque as risk factors for ischemic stroke in patients with type 2 diabetes mellitus American J Neuroradiol. 2007;28(5):916-9.
20. Cupini LM, Pasqualetti P, Diomedi M. Carotid artery intima-media thickness and lacunar versus nonlacunar infarcts. Stroke. 2002;33:689-94.
21. Matsumoto K, Sera Y, Nakamura H. Correlation between common carotid arterial wall thickness and ischemic stroke in patients with type 2 diabetes mellitus. Metabolism. 2002;51:244-7.
22. Kawamori R, Yamasaki Y, Matsushima H. Prevalence of carotid atherosclerosis in diabetic patients. Diabetes Care. 1992;15:1290-4.
23. Langenfeld MR, Forst T, Hohberg C. Pioglitazone decreases carotid intima-media thickness independently of glycemic control in patients with type 2 diabetes mellitus: results from a controlled randomized study. Circulation. 2005;111(19):2525-31.
24. Yamasaki Y, Katakami N, Furukado S. Long-term effects of pioglitazone on carotid atherosclerosis in Japanese patients with type 2 diabetes without a recent history of macrovascular morbidity. J Atherosclerosis Thrombosis. 2010;17(11):1132-40.
25. Katakami N, Mita T, Irie Y. Effect of sitagliptin on tissue characteristics of the carotid wall in patients with type 2 diabetes: a post hoc sub-analysis of the sitagliptin preventive study of intima-media thickness evaluation (SPIKE). Cardiovasc Diabetol. 2018;17:24.
26. Lu Z, Ma G, Chen L. Sitagliptin on carotid intima-media thickness in type 2 diabetes mellitus patients and anemia: a subgroup analysis of the prologue study. Mediators Inflamm. 2020;2020:8143835.
27. Barbieri M, Rizzo MR, Marfella R, Boccardi V, Esposito A, Pansini A, et al. Decreased carotid atherosclerotic process by control of daily acute glucose fluctuations in diabetic patients treated by DPP-IV inhibitors. Ahterosclerosis. 2013;227(2):349-54.

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