Frequency of aspirin use in patients with type 2 diabetes: Is there any effect of concomitant diseases?

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Abstract

Aim: Current guidelines recommend the use of low-dose aspirin in diabetic patients with increased cardiovascular disease risk with no risk of bleeding to prevent cardiovascular events. The aim of this study was to investigate the frequency of aspirin use in Type 2 Diabetes Mellitus and the effects of concomitant diseases.

Material and Methods: Our retrospective and cross-sectional study was planned of data for rate of aspirin use in Type 2 Diabetes mellitus patients. In our study, the socio - demographic characteristics of the participants, their concomitant diseases with Type 2 DM and the drugs they used were questioned. Chi-square test was used for the analysis of categorical variables. P<0.05 was considered statistically significant.

Results: The mean age of the 910 participants was 57.27±10,00. 64.2% of the participants were female and 35.8% were male. Hypertension was the most common concomitant disease in type 2 DM. The prevalence of aspirin use was found to be %38.6. There is a statistically significant difference between aspirin use rates according to genders (p <0.05). Aspirin use was significantly higher in those who quit smoking and those with concomitant disease with type 2 DM. (p<0.05).

Conclusion: The rate of aspirin use in our diabetic group was insufficient. In order to increase the use and awareness of aspirin, the factors affecting the use of aspirin should be investigated.

Keywords: Aspirin; type 2 diabetes mellitus; risk factors; cardiovascular disease

INTRODUCTION

Diabetes is a widely known risk factor for cardiovascular (CV) events and has been demonstrated to predispose to both first and recurrent atherothrombotic events (1). The overall risk of cardiovascular death is 2 to 4 times higher and the incidence of cardiovascular disease is 2 to 3 times greater in patients with type 2 DM than in those without the disease (2-4). A pivotal role of increased risk of CV events in DM is played by an exaggerated platelet activation and aggregation (5). In diabetic patients it was observed that platelets were larger and fibrinogen levels were higher (6). In light of this, early 2000s guidelines recommended to start low-dose aspirin (75-162 mg/day) for primary prevention in patients with diabetes when other CV risk factors were present (7,8).

Many studies have shown the benefit of aspirin in both primary and secondary prevention. In the Physicians' Health Study with 20000 patients, aspirin has been reported to reduce MI risk from 10% to 4% (9). In the ETDRS study, 3711 DM patients were examined and aspirin use was reported to reduce MI risk by 28% and major KV event risk by 18% (10). One of the most comprehensive research on the effect of aspirin on primary prevention in patients with diabetes is JPAD. In this study, the efficacy of low dose aspirin in primary protection was investigated in 2539 type 2 diabetic patients. A total of 86 atherosclerotic events were observed in 1277 patients who were not aspirin versus 68 atherosclerotic events in 1262 patients who received low-dose aspirin after a mean follow-up of 4.4 years. This difference was not found to be statistically significant but fatal risk of coronary and cerebrovascular events in the aspirin group lower than non-aspirin group (11).

Current Diabetes guidelines recommend the use of aspirin in primary and secondary prevention.The American College of Cardiology/American Heart Association and American Diabetes Association guidelines advocate the use of low dose aspirin in diabetes patients tailored to the individual risk of CVD and bleeding, whereas the 2016 European Society of Cardiology (ESC) guidelines give the use of aspirin for primary prevention in DM a class III recommendation (evidence or general agreement that given treatment is not effective and might be harmful in some cases; therefore its use is not recommended) (12). Turkey Diabetes Foundation recommends the use of low-dose aspirin in diabetes with increased cardiovascular disease risk (13).

In the literature, it is recommended to use aspirin in increased CV risk with diabetic patients without bleeding risk. In this context, when we investigate at the frequency of aspirin use; Miller et al. reported the frequency of aspirin use as 47.3% in diabetic patients (14). Khalil et al. reported that 55.2% of patients with diabetes used aspirin (15). Despite current recommendations, only half of the diabetic patients used aspirin.

In the literature review, there was no data on the frequency of aspirin use in the diabetic patients in Turkey. The aim of this study was to investigate the frequency of aspirin use in diabetic patients in our country. Therewital we were investigated the effect of concomitant disease on aspirin use because aspirin is especially recommended in case of increased cardiovascular risk.

MATERIAL and METHODS

Our retrospective and cross-sectional study was planned of data for rate of aspirin use in Tip 2 Diabetes mellitus patients who applied to the our Training and Research Hospital outpatient clinics between January 2012 and November 2012. The study population consisted of all patients who were admitted to internal medicine outpatient clinic and diagnosed with type 2 diabetes.

The data obtained from the study were collected under 3 headings. The sociodemographic characteristics of the participants (age, gender, blood pressure, weight, height, smoking and alcohol use), presence of concomitant disease and the drugs used by the participants were obtained by scanning the patient files. Body mass indexes of all participants calculated by the researcher and included in the study. (BMI= kg/ m2)

The inclusion criteria; presence of   type 2 diabetes and fully recorded in the patient file of the research data. Below 18 years old and patients for whom data were missing were excluded.

In our study, all patient files were screened between January and November 2012 and no sample selection was made. We aimed to reach the all universe in our study. We included 910 patients who providing the study criteria.

Ethical procedure

The study was conducted by taking the necessary permission from the Haydarpaşa Numune Training and Research Hospital Ethics Committee. (April 17, 2012 Issue: 4915) Data were anonymized and it was unnecessary to obtain consent.

Statiscal analysis

For the statistical analyzes, SPSS (Statistical Package for Social Sciences) for Windows 15.0 program was used. Continuous variables showing normal distribution in the patients' data were given as mean ± standard deviation and categorical variables as number and percentage. Chi-square test was used for the analysis of categorical variables. $P<0.05$ was considered statistically significant.

RESULTS

The mean age of the 910 participants was 57.27±10.00. 64.2% of the participants were female and 35.8% were male. Mean systolic blood pressure was 143.50±21.76 mmHg and mean diastolic blood pressure was 80.40±13.25 mmHg. 13.8% of the participants were smoking and 7.6% were using alcohol. (Table 1)

Table 1. Sociodemographic characteristics of participants		
Characteristic	Min-Max	Mean and Std.
Age (years)	25-87	57.27±10.00
Systolic Pressure (mmHg)	80-233	143.50±21.76
Diastolic Pressure (mmHg)	38-141	80.40±13.25
Weight (kg)	47-161	82.45±14.56
Length (cm)	113-187	161.56±8.78
Body mass index (kg/m2)	17-64	31.72±5.90
Gender	Number (n)	Percent (%)
Men	326	35.8
Women	584	64.2
Smoking		
Never used	510	56.0
Quit	274	30.1
Still in use	126	13.8
Alcohol use		
Does not use	841	92.4
use	69	7.6

Hypertension was the most common concomitant disease in diabetes mellitus. Concominat diseases with diabetes mellitus are given in Figure 1.

The prevalence of aspirin use was found to be %38.6 in our study. Oral antidiabetic drug (OAD) use rate was 78.7% and antihypertensive drug use rate was 60.5%. (Figure 2)

Table 2. Evaluation of aspirin use rates according to demographic characteristics of patients			
	Aspirin		**Statistics value**
Characteristic	**Aspirin-free 559 n (%)**	**Using aspirin 351 n (%)**	
Gender			
Men	185 (56.7%)	141 (43.3%)	**0,030**
Women	374 (64.0%)	210 (36.0%)	
Smoking			
Never used	322 (63.1%)	188 (36.9%)	**0,001**
Quit	141 (51.5%)	133 (48.5%)	
Still in use	96 (76.2%)	30 (23.8%)	
Alcohol Consumption			
Does not use	517 (61.5%)	324 (38.5%)	0,921
use	42 (60.9%)	27 (39.1%)	
Coronary artery disease			
Have	84 (34.4%)	160 (65.6%)	**0,001**
Have not	475 (71.3%)	191 (28.7%)	
Hypertension			
Have	286 (50.4%)	281 (49.6%)	**0,001**
Have not	273 (79.6%)	70 (20.4%)	
Dyslipidemia			
Have	559 (61.4%)	351 (38.6%)	
Have not	0 (0%)	0 (0%)	
Chronic renal failure			
Have	41 (43.2%)	54 (56.8%)	**0,001**
Have not	518 (63.6%)	297 (36.4%)	
Cerebrovasculer events			
Have	16 (34.0%)	31 (66.0%)	**0,001**
Have not	543 (62.9%)	320 (37.1%)	
Retinopathy			
Have	67 (50.4%)	66(49.6%)	**0,005**
Have not	492 (63.3%)	285(36.7%)	
Thyroid disease			
Have	26 (46.4%)	30 (53.6%)	**0,017**
Have not	533 (62.4%)	321 (37.6%)	

There is a statistically significant difference between aspirin use rates according to genders (p <0.05).At present, the rates of men's use of aspirin (43.3%) are significantly higher than women (36%). Aspirin use was significantly higher in smokers and those with concomitant disease with diyabetes mellitus. (p<0.05) The factors affecting the use of aspirin are given in Table 2.
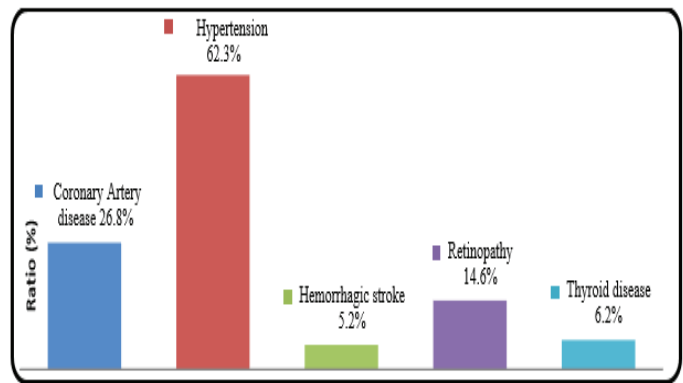

Figure 1. Distribution of concominant diseases in Diabetes Mellitus
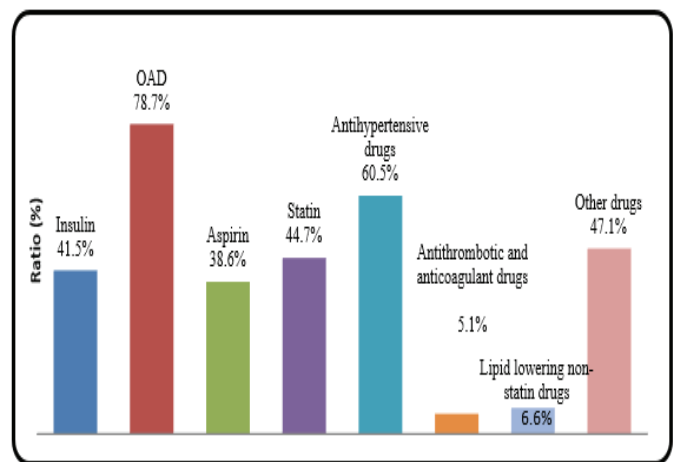

Figure 2. Distribution of drugs used

DISCUSSION

In general, literature data and current guidelines recommend the use of aspirin in patients with diabetes as a result of increased risk of cardiovascular disease. In this context, we investigated the frequency of aspirin use in our type 2 diabetic patients. The frequency of aspirin use was found to be 38.6% in our population of 910 people. In the literature, persel et al 48.7%, miler et al. 53.6% and Grimes et al. 53.6%, respectively, reported rates of aspirin use (14,16,17). The results of this study suggest that the use of aspirin in type 2 DM patients is insufficient compared to the literature. Compared to the literature, it was thought that the awareness of aspirin use did not develop in our country. In our country, the lack of data on the frequency of use of aspirin in our opinion may be the reason why there is not enough awareness about this issue.

Considering the factors affecting the use of aspirin, it was seen that the rate of aspirin use was significantly higher in men. In the literature, Miller et al. and Klinke et al. similarly, the rates of aspirin use in men have been reported to be high (14,18). The data we obtained were similar to the literature. This may be due to the fact that

the male gender is a risk factor for cardiovascular disease and that physicians encourage more aspirin use as the risk increases. There is no data to explain the effect of sex on aspirin use in literature data. It is thought that new studies are needed to clarify the hypothesis that the use of aspirin may be high due to the fact that male sex is a risk factor.

In our study, the effect of alcohol use status on aspirin use was not found. Another factor, smoking status, was found to have the highest rate of aspirin use in the quit smoking group. It was observed that smokers used less aspirin than those who did never smoke and quit smoking. There is no statistically significant relationship between smoking and aspirin use in the literature (14-18). Considering that smoking increased the risk of cardiovascular disease, it could be expected that aspirin usage rate would be higher in cigarette users. The literature data and our findings are thought to be insufficient to illuminate the relationship between smoking and aspirin use. In spite of the recommendations of the guidelines, the rate of aspirin use was found to be insufficient in diabetic patients with smoking. It is thought that studies should be done to increase the awareness of aspirin use in the DM and cigarette group who are at risk for cardiovascular disease.

Another aim of our study was to investigate the effect of concomitant diseases with diabetes on the rate of aspirin use. In our study, it was found that the rate of aspirin use in the case of concomitant disease with diabet was statistically higher. Considering that the physicians will recommend the use of aspirin more strongly to patients with high risk of cardiovascular disease, our findings may be expected. In literature, Miller et al. reported that the use of aspirin increased in diabetic patients with cardiovascular disease, cerebrovascular disease and peripheral arterial disease (14). In the study conducted by Persell et al, it has been reported that the rates of aspirin use increased diabetic patients with HT, Hiperlipidemi and CVD (16). The data we obtained were consistent with the literature. As the literature data and the data we have obtained increase the risk factor, the awareness and frequency of aspirin use increase in diabetic patients. In our study, it was not clear whether physicians or patients played a role in the increase of this difference. The effect of increased risk factors on the prescribing in physicians and use of aspirin in patients can be investigated in future studies. Increased use of aspirin in the case of concomitant disease suggests that more importance is given to tertiary protection than primary and secondary protection. In diabetic patients, increasing the use of aspirin before cerebrovascular disease, MI and CVD may be more useful. As mentioned in the study of Onalan et al. glycemic targets must certainly be individualized. Also they mentioned more flexible glycemic targets must be set in cases of low life expectancy, long diabetes duration, recurrent episodes of severe hypoglycemia, concomitant micro and macrovascular complications or other comorbid conditions (19). Similarly, we think that aspirin use should be individualized according to the risk factors of individuals.

CONCLUSION

In conclusion , it was seen that the recommended use of aspirin in primary and secondary prevention was insufficient in our study group. It was found that people with diabetes mostly used aspirin in the case of concomitant disease. It was thought that the efficacy of aspirin to reduce the risk of cardiovascular disease could not be used sufficiently in diabetic patients. Future research should contribute to clarifying the reasons for inadequate use of aspirin. we recommend that physicians give more importance to preventive health care based on current guidelines.

LIMITATIONS

The retrospective nature of our research can be reported as our first limitation. The data obtained from the study were taken from the patient files and restricted access to other data other than the recorded data. The use of aspirin was determined by questioning the presence of aspirin among the drugs used by the patient. The duration, frequency and usage reasons of aspirin in the patients were not questioned. We recommend planning prospective studies to investigate the frequency and the factors affecting aspirin use in diabetic patients.

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REFERENCES

1. American Diabetes Association. 9. Cardiovascular disease and risk management standards of medical care in diabetes-2018. Diabetes Care 2018;41:86-104.
2. Koskinen SV, Reunanen AR, Martelin TP, et al. Mortality in a large population-based cohort of patients with drug-treated diabetes mellitus. Am J Public Health 1998;88:765-70.
3. Bowman L, Mafham M, Wallendszus K, et al. Effects of aspirin for primary prevention in persons with diabetes mellitus. N Engl J Med 2018;379:1529-39.
4. Kannel WB, McGee DL: Diabetes and cardiovascular disease. The Framingham study. Jama 1979; 241:2035-38.
5. Ferreiro JL, Angiolillo DJ. Diabetes and antiplatelet therapy in acute coronary syndrome. Circulation. 2011;123:798-813.
6. Second International Study of Infarct Survival Collaborative Group. Randomised trial of intra-venous streptokinase, oral aspirin, both, or neither among 17, 187 cases of suspected acute myocardial infarction: ISIS−2. Lancet 1988;2:349-60.
7. Colwell JA, American Diabetes Association. Aspirin therapy in diabetes. Diabetes Care 2003;26(1):87-8.

8. Buse JB, Ginsberg HN, Bakris GL, et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation 2007;115:114-26.

9. Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group. N Engl J Med 1989;321:129-35.

10. Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study report 14. ETDRS Investigators. JAMA. 1992;268:1292-300.

11. Ogawa H, Nakayama M, Morimoto T, et all. Low-dose aspirin for primary prevention of atherosclerotic events in patients with type 2 diabetes: a randomized controlled trial. Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes (JPAD) Trial Investigators. JAMA 2008;300:2134-41.

12. Pignone M, Alberts MJ, Colwell JA, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: a position statement of the American Diabetes Association, a scientific statement of the American Heart Association, and an expert consensus document of the American College of Cardiology Foundation. Circulation 2010;121:2694-701.

13. TÜRKDİAB Diyabet Tanı ve Tedavi Rehberi 2018, Diyabet ve Kardiyovasküler hastalıklar. İstanbul: Türkiye Diyabet Vakfı; 2018;75-8.

14. Miller S.R, Littenberg B, Maclean C.D. Prevalence of antiplatelet therapy in patients with diabetes. Cardiovascular Diabetology 2005;4:18.

15. Khalil C.A, Omar O.M, Suwaidi J.A, et al. Aspirin Use and Cardiovascular Outcome in Patients With Type 2 Diabetes Mellitus and Heart Failure: A Population-Based Cohort Study. J Am Heart Assoc 2018;7:010033.

16. 16. Persell SD, Baker DW. Aspirin use among adults with diabetes: recent trends and emerging sex disparities. Arch Intern Med. 2004;164(22):2492-99. (pubmed)

17. 17. Grimes R.T, Bennett K, Tilson L, et al. Initial therapy, persistence and regimen change in a cohort of newly treated type 2 diabetes patients. Br. J. Clin. Pharmacol. 2015;79:1000–1009.(pubmed)

18. Kline J.A, Jonhson J.A, Guirguis L.M, et al. Underuse of Aspirin in Type 2 Diabetes Mellitus: Prevalence and Correlates of Therapy in Rural Canada. Clinical Therapeutics 2004;26:439-46.

19. Onalan E, Gozel N, Yakar B. An evaluation of type 2 diabetes mellitus patients on different oral antidiabetic medications with regard to glycemic control and diabetic complications. Medical Science and Discovery 2019; 6(9):180-5. Doi: 10.17546/msd.