Prevalence of Aspirin Use among Type 2 Diabetic Patients in Iran

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Abstract

Objective: Patients with type 2 diabetes mellitus (DM) have a markedly increased risk of cardiovascular morbidity and mortality. There are some recommendations for prescription of aspirin in these patients. Our purpose was to determine aspirin usage rate in diabetic patients and to compare it in different ages and based upon cardiovascular disease (CVD) risk factors.

Materials and Methods: In this study we collected data from 1256 self-reported diabetes mellitus patients referred to Yazd Diabetes Research Center during 2010-2011. This data included age, sex, history of diabetes mellitus, drug history, antiplatelet therapy duration, smoking, hypertension, dyslipidemia, family history of premature CVD and albuminuria.

Results: 48.5% of patients were male (609 patients) and 51.5% were female (647 patients). From female patients ≤60 years old, 52.7% used antiplatelet drug; however, this percent for patients over 60 years was 58.9% and for male patients ≤50 and >50 was 47.7% and 81%, respectively. From antiplatelet drug users, 43.1% of males aged ≤50 and 29.2% of females aged ≤60 years old had no or one risk factor that is unnecessary to take it.

Conclusion: Physician must encourage diabetic patients to use aspirin when the potential benefit of a reduction in cardiovascular disease outweighs the potential harms. So, clinical judgment is required for prescription of aspirin in men aged ≤ 50 years and women aged ≤ 60 years without multiple risk factors.

Keywords: Diabetes mellitus, aspirin, CVD primary prevention, ADA recommendation.

Introduction

Macrovascular events, such as myocardial infarction or stroke, are the most common cause of morbidity and mortality in type 2 diabetes mellitus (1,2). People with diabetes are two to four times as likely to develop CVD as people without diabetes (3). It may be because of increased tendency toward intracoronary thrombus formation (4), increased platelet reactivity (5), and worsened endothelial dysfunction (6). Aspirin has been shown an effective and relatively safe treatment for people with diabetes. Trials have demonstrated that aspirin therapy can prevent the first heart attack, stroke, or other indication of CVD (primary prevention) (7-9) and also subsequent cardiovascular events (secondary prevention) (6-8) without any significant increase in retinal

or vitreous hemorrhage, gastrointestinal bleeding, or hemorrhagic stroke (8). But recently some studies have raised questions about this (10,11), and its safety is now controversial (12). Based upon these, in 2010, American Diabetes Association (ADA), American Heart Association (AHA) and the American College of Cardiology Foundation (ACCF) revised their recommendations about prescription of aspirin in type 2 diabetes mellitus. Updated recommendations are as follows:

Low-dose (75-162 mg/d) aspirin use for prevention is reasonable for adults with diabetes and no previous history of vascular disease who are at increased CVD risk (10 year risk of CVD events over 10%) and who are not at increased risk for bleeding (based on a history of previous gastrointestinal bleeding or peptic ulcer disease or concurrent use of other medications that increase bleeding risk, such as non-steroidal anti-inflammatory drugs (NSAIDS) or warfarin). Those adults with diabetes who are at increased CVD risk include most men over age 50 years and women over age 60 years having one or more of the following additional major risk factors: smoking, hypertension, dyslipidemia, family history of premature CVD, and albuminuria. So, patients below this age must not use aspirin except for very high risk patients (with multiple other risk factors) according to physician judgment, since the potential adverse effects from bleeding likely offset the potential benefits (13).

We decided to evaluate and compare the rate of aspirin prescription in men before and after 50 years old and women before and after 60 years old based upon last recommendation. The aim of study was to encourage patients to use aspirin when the potential benefit of a reduction in cardiovascular disease outweighs the potential harm of an increase in gastrointestinal hemorrhage. So, it is a mandatory emphasis for physicians not overuse or underuse prescription of aspirin for patients.

Materials and Methods

In this descriptive cross sectional study we collected data from 1256 self-reported diabetes mellitus patients referred to Yazd Diabetes Research Center, a tertiary healthcare referral center for diabetes in Yazd (central province, Iran) during 2010-2011. This center is both self-referral and referral from other medical practitioners for specialized care. Written informed consent was taken from all the participants. Demographic data including age, sex, history of diabetes mellitus, drug history, duration of antiplatelet therapy, smoking, hypertension, dyslipidemia, family history of premature CVD, and albuminuria was collected by a questionnaire. Patients with the history of CVD were excluded from the study. Participants were classified as regular aspirin users if they reported taking aspirin ≥15 times in the month before the interview. This definition was designed to take into account the alternate-day as well as daily use, both of which have been found effective for preventing CVD (8). We classified the patients into two groups: male patients that are equal or more than 50 years old and female patients equal or more than 60 years old; the remaining patients were classified as another group. According to the last ADA/AHA (2010) recommendation (13), diabetic patients below 60 in women and 50 in men should not use antiplatelet drug except some patients that have more than one risk factor. Chi-square and Student t tests, as appropriate, were used to determine differences in demographic and clinical variables between the groups. We compared the aspirin usage rate in these two groups based on the risk factors. Analysis was done using SPSS software (ver. 21). Statistical significance was set at $P \leq 0.05$.

Results

From 1256 patients aged 18-84 years that included in this study, 48.5% were male (609 patients) and 51.5% were female (647 patients). The Majority of these patients were treated with oral anti-diabetic agents (88.5%). Others were using insulin (7.6%) and

combination of insulin and tablets (3.2%). Seven percent were not under any treatments (Table 1).

Overall, 57.8% of patients used 80-100mg aspirin at every other day in a previous month and 5.5% of patients used dipyridamole. 36.7% (461 patients) did not use any antiplatelet drug (Table 2).

Among the patients there were 458 men over the 50 years old (36.4%) and 180 women over the 60 years old (14.3%). In male patients ≤50 years old, 47.7% used antiplatelet drug; however, for patients over 50 years, this was 81% (Table 3) and for female patients ≤60 and >60 was 52.7% and 58.9%, respectively (Table 4).

From 72 males with age ≤50 who used antiplatelet drugs, 15.3%, 27.8% and 56.9% had no, one and multiple risk factor(s), respectively. Also, in female group aged ≤ 60, these values were 8.1%, 21.1% and 70.8%, respectively.

Discussion

Studies have shown that aspirin therapy is effective for both primary and secondary prevention of cardiovascular and cerebrovascular events (8,14,15), but we must not ignore its side effects (12). ADA recommendation for primary prevention of CVD with aspirin in diabetic patients in 2000, allowed prescription of aspirin in all diabetic patients with age over 30 years old (16); But in updated recommendation in 2007, this allowance limited to patients over 40 years old or with additional risk factors (family history of CVD, heart disease, dyslipidemia, proteinuria, hypertension and smoking) (17). In 2010 recommendation it is limited more ever (13). It was because of two recent randomized controlled trials of aspirin performed specifically in patients with diabetes that raised questions about the efficacy of aspirin for primary prevention in diabetes (10,11). In the last recommendation, aspirin can be prescribed for diabetic patient with at least one risk factor and age over 50 in male and over 60 in female. So, the patients without these conditions must not use aspirin except for very high risk ones (i.e. with multiple other risk factors) according to physician judgment. Also, aspirin should not be recommended for CVD prevention for adults with diabetes at low CVD risk, such as in men aged less than 50 years and women aged less than 60 years with no major additional CVD risk factors, since the potential adverse effects from bleeding likely offset the potential benefits (13).

In this study, we found that many diabetic patients below this age range that have ≤1 CVD risk factor was using antiplatelet drugs, usually aspirin (43.1% in male vs. 29.2% in female). It can cause morbidity and mortality due to aspirin side effects. The Women's Health Study showed higher rate of events such as gastrointestinal bleeding, peptic ulcers, self-reported hematuria (blood in the urine), easy bruising, and epistaxis in the primary prevention of cardiovascular events in patients used aspirin than placebo (18).

The Third National Health and Nutrition Examination Survey showed that aspirin was used regularly by 37% of those with CVD and by 13% of those with risk factors only, despite guideline recommendation in 2000 (19) that in the absence of specific contraindications, aspirin should be considered for primary prevention in adults who have one or more risk factors for CVD (family history of coronary heart disease, smoking, hypertension, obesity, albuminuria, or lipid abnormalities) or

Table 1. Frequency of taking anti-diabetic drugs among type 2 diabetic patients

Anti-diabetic drugs	Frequency	Percent
Tablet	1112	88.5
Insulin	95	7.6
Tablet + Insulin	40	3.2
None	9	0.7
Total	1256	100.0

Table 2. Frequency of taking antiplatelet drugs among type 2 diabetic patients

Antiplatelet drugs	Frequency	Percent
Aspirin	726	57.8
Dipyridamole	69	5.5
None	461	36.7
Total	1256	100.0

Table 3. Frequency of antiplatelet drugs in male diabetic patients

Antiplatelet treatment	Age≤50		Age>50	
	Frequency	Percent	Frequency	Percent
Aspirin	55	36.4	349	76.2
Dipyridamole	17	11.3	22	4.80
None	79	52.3	87	19.0
Total	151	100	458	100

Table 4. Frequency of antiplatelet drugs in female diabetic patients

Antiplatelet treatment	Age≤60		Age>60	
	Frequency	Percent	Frequency	Percent
Aspirin	225	48.2	97	53.9
Dipyridamole	21	4.5	9	5.0
None	221	47.3	74	41.1
Total	467	100	180	100

who are ≥30 years of age. Nearly every adult with diabetes in the United States has at least one risk factor for CVD and thus may be considered a potential candidate for aspirin therapy upon ADA recommendation in 2000. This study emphasized major efforts are needed to increase aspirin use.

In another study that performed in rural Alberta, Canada from April through October 2000, only 23% of patients were using an antiplatelet agent, usually aspirin (20). A systematic review that concluded 33 studies showed average rate of aspirin use of 41%. Among those with an indication for primary or secondary prevention, aspirin was used by 27% and 73%, respectively (21).

The reason for high rate of aspirin taking in our study may be previous recommendation that allow to prescribe aspirin for >40 years old or every diabetic patient with one risk factor. Aspirin is a safe, inexpensive, and readily available therapy that is effective for preventing cardiovascular disease, and patients with T2DM are particularly likely to benefit from such preventive therapy. However, we must use it in a correct and reasonable manner.

Conclusion

We found significant overuse of aspirin therapy among our study population. Physician must encourage patients to use aspirin when the potential benefit of a reduction in cardiovascular disease outweighs the potential harm of an increase in gastrointestinal hemorrhage. So it is a mandatory emphasis for physicians not overuse aspirin especially in men aged ≤ 50 years and women aged ≤ 60 years without multiple other risk factors.

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