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Prevalence of Aspirin Prescriptions among Type 2 Diabetic Patients in Songklanagarind Hospital

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Abstract:

Objective: The American Diabetes Association (ADA) and the American Heart Association (AHA) recommend aspirin use for primary and secondary prevention of cardiovascular disease in patients with diabetes. There are, however, some doubts regarding the prescription of aspirin therapy to prevent cardiovascular events in diabetic patients, aspects of its safety, and contraindications of the drug administration. This study was conducted in order to evaluate the amount of prescribed aspirin for diabetic patients who received the treatment at Songklanagarind Hospital.

Material and Method: A cross-sectional study was conducted to review the medical records of diabetic patients who received the treatment at outpatient departments from 1st-31st December 2013.

Results: A total of 1,342 diabetic patients are included in this study: 80.3% from the primary prevention group and 19.7% from the secondary prevention group. Mean age was 64.3 years old. Of the patients, 44.7% were male. The study revealed that prescribed aspirin accounted for one-third of total prescriptions (31.7%). The primary prevention group was 19.0% (95% confidence interval (CI)=12.0-21.3) and the secondary prevention group was 83.7% (95% CI=78.6-87.9). The departments that frequently prescribed aspirin for the primary prevention group was endocrinology (21.2%) and for the secondary prevention group it was the Primary Care Unit (87.5%). Aspirin side effects were gastrointestinal 1.0% and tinnitus 0.1%. Aspirin contraindications were active peptic ulcer (0.1%), history of gastrointestinal bleeding (0.4%), bleeding disorders (0.2%), history of recent intracranial bleeding (0.2%) and severe liver disease (0.9%). There was a positive correlation between age, hemoglobin A1c (HbA1c) and the dose of prescribed aspirin (p-value<0.001, 0.003 respectively). These patients were more likely to have the dose of aspirin increased as age and HbA1c increased.

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Conclusion: Despite aspirin being a safe, inexpensive and readily available therapy that is effective in preventing cardiovascular disease in diabetic patients and likely to provide benefits rather than side effects and contraindications. The author found significant underuse of aspirin therapy, especially in the primary prevention of cardiovascular disease in diabetic patients.

Keywords: aspirin, contraindications, diabetes mellitus, diabetes mellitus type 2, side effects

Introduction

Diabetes mellitus (DM) has been a chronic disease affecting the health of people in Thailand and globally for a long time. Moreover, DM has globally increased morbidities, the mortality rate and economic losses such as costs of medical treatment, absences from work, etc. Cardiovascular disease (CVD) and chronic complications are the most common causes of death in patients with diabetes mellitus.[1,2] Patients with diabetes have a 2-4 fold increased risk of cardiovascular events compared with age and sex matched individuals without diabetes.[3]

Aspirin is a salicylate nonsteroidal anti-inflammatory drugs (NSAIDs). Although originally used as a pain reliever and fever reducer, many studies have shown that aspirin can reduce the risks of cardiovascular diseases, such as atherosclerotic coronary heart disease, cerebrovascular disease and peripheral arterial disease. One of the effects of aspirin is to inhibit enzyme cyclo-oxygenase resulting in the direct inhibition of the biosynthesis of prostaglandins and thromboxanes from arachidonic acid. Thus inhibiting platelet aggregation can reduce the causes of cardiovascular disease.

Research has shown that aspirin therapy is effective for primary prevention in diabetic patients (preventing a first heart attack, stroke or peripheral arterial disease).[4,5] The Fremantle Diabetes Study[4] observed that the administration of aspirin (≥75 mg/day) with a total follow-up period of 7,537 patient-years in patients with type 2 diabetes and no prior history of CVD association led to a reduction of CVD and all-cause mortality of at least 50.0%. For secondary prevention,[6,7] aspirin has also been reported to significantly decrease the risks of future events in diabetic patients with previous myocardial infarction, stroke, transient cerebral ischemia or peripheral vascular disease.

The American Diabetes Association (ADA)[8] and the American Heart Association (AHA)[9] recommend aspirin for both primary and secondary prevention. Aspirin is recommended for primary prevention in adults with diabetes who have an increased risk of cardiovascular disease (10-year risk ≥10%) (75–162 mg/day) including men aged over 50 years and women over 60 who possess at least one additional risk factor (family history of CVD, hypertension, smoking, dyslipidemia or albuminuria). Aspirin therapy (75–162 mg/day) is recommended as a secondary prevention strategy in patients with diabetes and a history of CVD.

Although there is a guideline recommendation for the use of aspirin in patients with diabetes, several studies have found that the prevalence of aspirin prescription is considerably low,[10,11] for example the BMC[10] Family Practice Journal 2007 found that 20.8% of aspirin was prescribed routinely in the primary prevention group and 60.8% in the secondary prevention group.

Despite the benefits of aspirin, its side effects[12-16] are also frequently found such as gastrointestinal (GI)

bleeding, tinnitus, hypersensitivities including bronchospasm, rhinitis, urticaria, angioedema and anaphylaxis or hepatic side effects including hepatotoxicity and cholestatic hepatitis.

Furthermore, there are also the contraindications of aspirin use such as active peptic ulcer, history of previous GI or intracranial bleeding, aspirin allergy or intolerance and bleeding disorders: hemophilia, Von Willebrand disease (VWD), thrombocytopenia or severe liver disease.

However, there have been very few studies on aspirin prescriptions in diabetic patients conducted in Thailand. Therefore, the rationale for the study was developed to investigate the prevalence of aspirin prescriptions, the frequency of adverse effects and contraindications of aspirin in diabetic patients who received the treatment at the outpatient departments of Songklanagarind Hospital, to measure the size of problems, to see whether the practice guidelines for diabetes treatment follow the standard guidelines provided, and lastly to develop future medical treatment for these patients.

Material and Method

Research methodology

This study is a cross-sectional study with retrospective medical review.

Study population

The population was type 2 diabetic patients who were followed up regularly at outpatient clinics at Songklanagarind Hospital. The sample in this study was type 2 diabetic patients who were followed up regularly and received diabetes treatment at the primary care unit, internal medicine clinic, endocrinology clinic, cardiovascular clinic, general practice clinic and surgery clinic from 1st–31st December 2013. Retrospective analysis of diabetes records was performed consecutively. Exclusion criteria werepatients diagnosed with others types of diabetes mellitus (type 1, gestational diabetes mellitus (GDM) and other specific types); consequently routine diabetes care visits would not be performed.

Study variables

The variables included in this study are demographic data: age, sex, bodyweight, body mass index (BMI), systolic blood pressure, diastolic blood pressure and health insurance. Laboratory investigations consisted of serum fasting blood glucose (FBS), serum glycosyated hemoglobin (HbA1c), serum lipid levels, albuminuria (microalbuminuria, macroalbuminuria), diabetes with/without CVD complications (primary and secondary groups), cardiovascular risk factors (hypertension, hyperlipidemia, albuminuria, current smoking, family history of CVD), and aspirin usage.

Data collection

Data for this study were collected and recorded in data extraction form using Microsoft Excel® 2013. Medical records of patients who were diagnosed with non-insulin-dependent diabetes mellitus (ICD-10 code with E11 computerized from outpatient hospital data) were reviewed since 2013. Retrospective analysis was conducted on medical history, aspirin prescription, side effects and contraindications. Lab investigation results were recorded based on recent blood tests.

Data analysis

Statistical analyses were performed using Stata Corp 2013. Demographic and baseline characteristics of all participants as discrete data are represented in percentage values and continuous data are represented in arithmetic mean with standard deviation (S.D.) and corresponding 95% confidence interval (CI). Subgroup differences were evaluated using on Likelihood-ratio,

chi-squared tests, Pearson's chi-squared test or Fisher's exact test. Statistical significance was p-value<0.05. Prevalence of aspirin use in both primary and secondary groups was calculated with corresponding 95% CI.

Ethical considerations

The study protocol was approved by the Ethics Committee, Faculty of Medicine, Prince of Songklanagarind University.

Results

Baseline characteristics of diabetic patients

The number of diabetic patients who were followed up at outpatient clinics at Songklanagarind Hospital from 1st-31st December 2013 was 1,342 patients. Diabetes was more commonly found in female patients (55.3%) than in male patients (44.7%). Mean age was 64.3 years old. Most patients hadgovernment health insurance coverage (62.3%). Nearly half of the patients received treatment at the internal medicine clinic (52.5%). The mean bodyweight and BMI were 66.9 kg and 26.3 kg/m^2 respectively. Most patients fell in the obese group (50.5%). Mean blood pressure was 139.6/76.4 mmHg. Two-thirds of patients took anti-diabetic medications (77.9%). The other drugs that most diabetic patients used were NSAIDs (15.7%). Mean lipid profile, FBS, and HbA1c are shown in Table 1.

Types of diabetic patients (prevention group)

Types of prevention groups consisted of the primary prevention group (diabetic patients without a history of coronary heart disease, cerebrovascular disease or peripheral vascular disease) comprising 1,078 patients (80.3%), (95% CI=78.1-82.4) and the secondary prevention group (diabetic patients with history of coronary heart disease, cerebrovascular disease or peripheral vascular disease) which had 264 patients (19.7%), (95% CI=17.5-21.8).

Table 1 Baseline characteristics of diabetic patients

Characteristics	Mean or percentage (n=1,342) (%)	Standard deviation	95% confidence interval
Age (year)	64.3	11.5	63.7-64.9
Sex			
Men	44.7	-	42.0-47.4
Women	55.3	-	52.5-57.9
Health insurance			
Social insurance	3.9	-	2.9-5.1
Universal health coverage service	15.1	-	13.1-17.0
Government	62.3	-	59.6-64.8
No insurance	12.2	-	10.4-14.0
Government enterprise	2.7	-	1.8-3.6
Local government	3.8	-	2.9-5.0

Table 1 (continued)

Characteristics	Mean or percentage (n=1,342) (%)	Standard deviation	95% confidence interval
Population per clinic			
Internal med	52.5	–	49.7–55.1
Endocrine med	25.2	–	22.9–27.6
Cardio med	3.4	–	2.4–4.4
GP	0.6	–	0.2–1.1
Surgery	0.1	–	0.0–0.4
PCU	18.3	–	16.2– 20.4
Bodyweight (kg)	66.9	12.8	66.1–67.5
Body height (cm)	159.4	8.6	158.9–159.9
BMI (kg/m^2)	26.3	4.2	26.0–26.5
BMI group			
Underweight	0.9	–	0.6–1.9
Normal	17.4	–	18.1–22.9
Overweight	16.2	–	16.8–21.4
Obesity	50.5	–	56.4–62.1
Blood pressure			
Systolic BP (mmHg)	139.6	18.9	138.5–140.6
Diastolic BP (mmHg)	76.4	12.8	75.7–77.1
Lipid profile			
Total cholesterol (mmol/L)	177.6	42.4	175.3–179.8
Low density lipoprotein cholesterol (mmol/L)	108.8	36.7	106.7–110.7
Triglyceride (mmol/L)	147.5	87.2	142.8–152.2
High density lipoprotein cholesterol (mmol/L)	50.9	13.5	50.2–51.7
Fasting blood sugar (mmol/L)	155.3	54.8	152.3–158.1
HbA1c	8.0	1.8	7.9–8.1
Treatment			
Life style	4.6	–	3.4–5.8
Oral med	77.9	–	75.5–80.0
Oral med+Insulin	10.9	–	9.3–12.7
Insulin	6.6	–	5.3–08.0
Others drug			
Antiplatelet	4.4	–	3.3–5.6
Anticoagulant	1.4	–	0.8–2.2
NSAIDs	15.7	–	13.7–17.7
Steroids	3.4	–	2.5–4.5

GP=general practice, PCU=primary care unit, BMI=body mass index, BP=blood pressure, HbA1c=hemoglobin A1c, NSAIDs=nonsteroidal anti-inflammatory drugs

In the primary prevention group dyslipidemia was a more common risk factor for cardiovascular disease than hypertension, albuminuria, current smoking and family history of CVD. According to the risks of cardiovascular disease in the primary prevention group, we found that the high risk group (10-year risk ≥10.0%) contained most patients in this group (71.5%). In the secondary group, we found that diabetic patients with a history of cardiovascular disease were the most common type. Results shown in Table 2.

Prevalence of aspirin prescription in diabetic patients

The prevalence of aspirin prescribed for type 2 diabetic patients in Songklanagarind Hospital was 425 patients (31.7%) which could be categorized as the primary prevention group: prevalence of aspirin prescription was 19.0% (n=205), (95 % CI=12.0-21.3). The department that most frequently prescribed aspirin for the primary prevention group was the endocrinology clinic (21.2%) and cardiology was the clinic that prescribed aspirin the least (15.4%). The highest risk factor for cardiovascular disease in diabetic patients who were prescribed aspirin was albuminuria (39.6%) and the lowest risk factor was family history of CVD (17.6%). When risk factors were subdivided into high, moderate and low according to the ten-year risk of cardiovascular disease in diabetic patients, we found that the high risk group (recommend low-dose aspirin) had the highest aspirin prescription rate (22.6%), the moderate risk group (prescribed aspirin according to clinical judgment) was 9.9% and the low risk group (aspirin should not be recommended for CVD prevention) was not prescribed aspirin. Results shown in Table 3. The secondary prevention group: Prevalence of aspirin prescription was 83.7% (n=220), (95% CI=78.6-87.9). The diabetic patients with a history of coronary

Table 2 Baseline characteristic of diabetic patients categorized by patient prevention group

Characteristics	Mean of percentage (n=1,342) (%)	95% confidence interval
Primary prevention group variables (n=1,078)		
Diagnosis of hypertension	73.9	71.5-76.3
Diagnosis of dyslipidemia	85.6	83.6-87.4
Diagnosis of albuminuria	23.9	21.4-26.5
Current smoking	11.2	8.1-14.9
Family history of cardiovascular diseases	88.2	63.5-98.5
Risk of CVD in primary prevention group		
High risk	71.5	68.6-74.1
Moderate risk	27.1	24.4-29.8
Low risk	1.5	0.8-2.4
Secondary prevention group variables (n=264)		
History of cardiovascular diseases	11.8	10.0-13.6
History of cerebrovascular disease	8.5	7.0-10.1
History of peripheral arterial disease	0.4	0.1-0.9

heart disease were prescribed aspirin the most (89.8%), patients with cerebrovascular disease were prescribed aspirin 80.7% of the time, and patients with a history of PAD were prescribed aspirin at a rate of 66.0%. According to the clinics in this group, we found that the Primary Care Unit prescribed aspirin more than the other clinics (87.5%) and the Endocrinology Clinic had the lowest aspirin prescription rate (80.4%). Results shown in Table 3.

Table 3 Aspirin prescription among type 2 diabetic patients categorized by patient characteristics

Patient characteristics	Percentage	P-value
Primary prevention group		
Risk factor of cardiovascular disease		
Diagnosis of hypertension		0.000[A]
Yes	37.9	
No	62.1	
Diagnosis of dyslipidemia		0.000[A]
Yes	34.6	
No	65.4	
Diagnosis of albuminuria		0.002[A]
Yes	39.6	
No	60.4	
Current smoking		0.015[B]
Yes	35.0	
No	65.0	
Family history of cardiovascular diseases		0.875[B]
Yes	17.6	
No	82.4	
Ten-year cardiovascular risk		0.000[B]
Low		
Yes	0	
No	100	
Moderate		
Yes	9.9	
No	90.1	
High		
Yes	22.6	
No	77.4	
Secondary prevention group		
History of coronary heart diseases		0.000[A]
Yes	89.9	
No	10.1	
History of peripheral arterial disease		0.070[B]
Yes	80.7	
No	19.3	
History of cerebrovascular disease		0.855[B]
Yes	66.7	
No	33.3	

A=Pearson chi-squared test, B=Fisher's exact test

Prevalence of contraindications and side effects

The contraindications of aspirin prescription in this study were severe liver disease (0.9%), history of resent GI bleeding (0.4%), history of recent intracranial bleeding (0.2%), bleeding disorders (0.2%) and active peptic ulcer 0.1%). Results shown in Table 4.

Table 4 Contraindications of aspirin prescription

Contraindication	Percentage (n=1,342) %	95% confidence interval
Active peptic ulcer	0.1	0.0-0.4
History of recent gastrointestinal bleeding	0.4	0.1-0.9
History of recent intracranial bleeding	0.2	0.0-0.5
Bleeding disorders (such as thrombocytopenia, hemophilia, Von Willebrand disease)	0.2	0.0-0.5
Severe liver disease	0.9	0.5-1.6

The most common side effects of aspirin prescription found in this study were gastrointestinal such as gastro-intestinal bleeding, GI upset, dyspepsia or gastritis (1.0%), followed by tinnitus (0.1%). Results shown in Table 5.

There was a positive correlation between age, HbA1c and the dose of prescribed aspirin (p-value< 0.001, 0.003 respectively). These patients were more likely to have their dose of aspirin increased as age and HbA1c increased. Results shown in Figure 1-2.

Table 5 Side effect in case prescribed aspirin

Side effect	Percentage (n=425) (%)	95% confidence interval
Not reported	96.5	95.4-99.1
Gastrointestinal	1.0	0.8-2.4
Neurological (tinnitus)	0.1	0.0-0.6

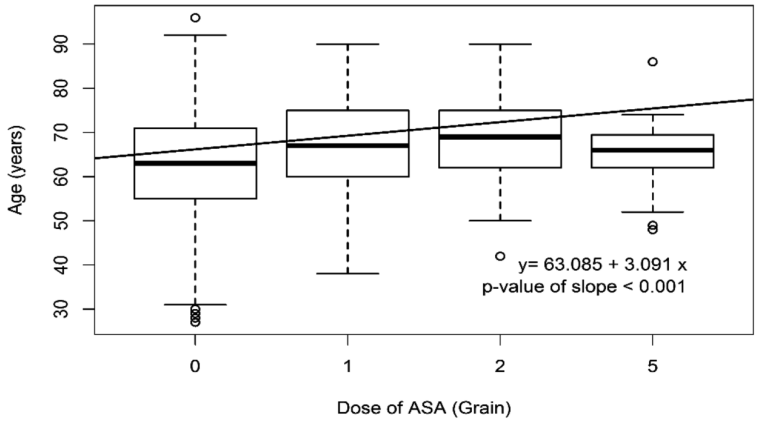

Figure 1 Box plot shows correlation between age and dose of aspirin prescription

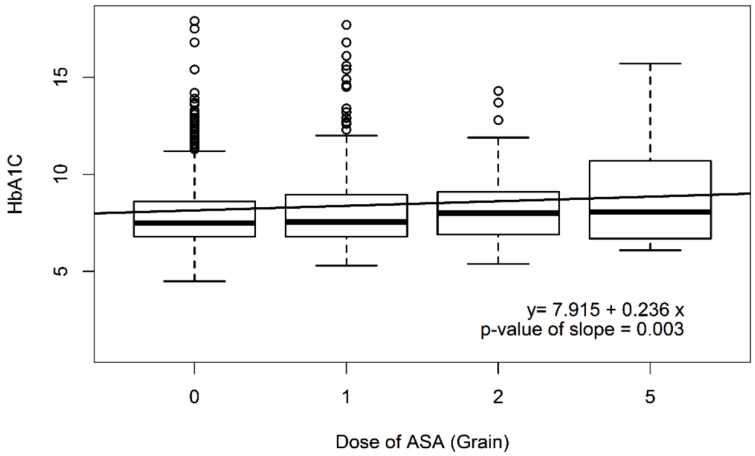

Figure 2 Box plot shows correlation between HbA1c and dose of aspirin prescription

Discussion

This study is cross-sectional aimed at investigating the prevalence of aspirin prescriptions among type 2 diabetic patients who were followed up at outpatient clinics at Songklanagarind Hospital. The author was motivated to conduct the study because in Thailand there have been few studies on the topic. In this study, 31.7% of diabetic patients were prescribed aspirin. Although prescribing regular low-dose aspirin might reduce all-cause CVD and mortality in the primary prevention of type 2 diabetes, only 19.0% of patients in this study had total aspirin prescriptions. In the secondary prevention group, in which aspirin is reported to significantly decrease the risks of recurrent cardiovascular events the rate of aspirin prescription was found to be 83.7%. Both results of aspirin prescription are as low as studies conducted in Spain, Canada, Taiwan and the United Kingdom.[10,17-19] where retrospective and observational data were collected in diabetic patients using the same techniques as this study. However these results are inconsistent with studies from the USA.[11] It could be due to the fact that in the USA aspirin prescriptions for diabetic patients are recommended by ADA and AHA guidelines.[8,9] Aspirin (75–162 mg/day) is recommended for primary prevention in adults with diabetes who have a high risk of cardiovascular disease (10-year risk≥10%), but this study found that only 22.6% of total aspirin recommendations were prescribed. Therefore, physicians are recommended to consider the risks of developing cardiovascular complications in all diabetic patients: if there is a high risk for a cardiovascular event and no limitation to receiving aspirin, aspirin should be prescribed based on the guidelines.

Aspirin has many side effects such as the increased risk of GI bleeding, intracranial bleeding, tinnitus, hepatic transminitis and hypersensitivity[12-16] but this study found a very low rate of side effects, consistent with the contraindications too.

Data for this study were collected by computerizing the outpatient hospital data where some histories were insufficient causing a lack of accuracy in, for example, history of smoking, height, family history of CVD or side effects of aspirin and etc.

Conclusion

Despite the fact aspirin is a safe, inexpensive and readily available therapy that is effective in preventing cardiovascular disease in diabetic patients and likely to provide benefits rather than side effects and contraindications, the author found significant underuse of aspirin therapy, especially in the primary prevention of cardiovascular disease in diabetic patients. Aspirin should be prescribed more frequently by physicians in order to reduce the risk of cardiovascular disease in these patients.

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