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Anti-platelet therapy in diabetic hypertensive patients with and without cardiovascular diseases in Palestine, from 2003 to 2008

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KEYWORDS
Aspirin;
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Summary
Objective: To determine the current frequency of anti-platelet use as indicated in medical charts of diabetic hypertensive patients with and without cardiovascular disease (CVD) using American Diabetes Association (ADA) guidelines compared with use in 2003.
Methodology: Data from both years were collected retrospectively from diabetic hypertensive patients attending government clinics in Nablus district, Palestine. Demographic details and medications were obtained from medical files. Diabetes mellitus and hypertension were confirmed based on documentation of the diagnosis and on listed anti-diabetic and anti-hypertensive medications. Eligibility for anti-platelet therapy was determined with reference to ADA guidelines.
Results: There were 358 patients included in the 2008 study with a mean age of 64.4 years. The mean age of the 342 patients included in the 2003 study was 64.4 ± 8.7 years. Aspirin was the only anti-platelet drug documented in the files in both years. The overall frequency of aspirin listed in 2008 was 66.5% compared to 31.5% in 2003. Among patients with CVD, aspirin therapy for secondary prevention (SP) was found in 77.9% of cases in 2008 compared to 82.4% in 2003 ($P = 0.23$). Among patients without CVD for whom anti-platelet therapy was indicated, aspirin was listed for primary prevention (PP) in 56.9% of cases in 2008 compared to 17.5% in 2003 ($P = 0.001$). In 2008, the frequency of aspirin use was independent of gender or age. However, in 2003, the frequency of aspirin use was significantly higher in men and younger patients than in women and elderly patients.

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Conclusion: There has been an improvement in anti-platelet therapy using aspirin for primary prevention among high risk patients. No significant change was observed for secondary prevention over the five years. Efforts are needed to enhance the use of aspirin particularly for cardiovascular patients requiring secondary prevention.

Introduction

It is well known that the risk of cardiovascular diseases (CVD) and the resultant mortality are higher among diabetic than non-diabetic patients [1,2]. Furthermore, the CV complications among diabetic patients are augmented by the co-existence of hypertension [3]. The American Diabetes Association (ADA) recommends 75—162 mg/day of Aspirin as a SP strategy in diabetic patients with CVD defined as a history of myocardial infarction, stroke or transient ischemic attack, peripheral vascular disease, claudication and/or angina [4]. Aspirin therapy is recommended for PP in diabetic patients without CVD, who are at increased risk of developing CVD. Such risk factors include hypertension. Therefore, aspirin is indicated in diabetic hypertensive patients for SP as well as PP with or without CVD. Despite accumulating evidence to support the effectiveness of antiplatelet prophylaxis among high risk patients, for example in those with diabetes mellitus, previously published studies have demonstrated its under-utilization, particularly in women [5—10].

In Palestine, the Ministry of Health is the major provider of medical services for a total population of 4,151,668 inhabitants. In the northern part of Palestine, Nablus district is a well-defined area with a total population of 362,159 native Palestinian inhabitants. Therefore, patients attending government clinics in Nablus district are considered representative of those living in north Palestine. In a representative sample of adults with diabetes and hypertension who were eligible for aspirin therapy, we wanted to (1) determine the frequency of aspirin use among such individuals in north Palestine, and (2) examine aspirin use in diabetic hypertensive patients with and without CVD, comparing current data with those obtained in 2003.

Methodology

The medical files of patients who attended Al-Watani in and out-patient clinics during the 12-months of 2008 and who had a documented diagnosis of diabetes mellitus and hypertension were examined. Permission from health authorities and medical ethics committee was obtained before the start of the study. Confirmation of the diagnosis of diabetes mellitus and hypertension was based on medical history and laboratory results. We did not distinguish between Type 1 and Type 2 diabetes because this distinction is not clinically important when recommending anti-platelet therapy. Patient demographic details and lists of medications including the use of anti-platelets were obtained from medical files. Medication use was defined as documentation in a list of medications prescribed and/or mentioned by the patient. We did not assess actual use, i.e. compliance. Patients with CVD were defined as those having at least one or more of the following conditions: history of myocardial infarction, stroke or transient ischemic attack, peripheral vascular disease, claudication and/or angina. Such conditions were identified based on a documented history of such conditions in patient's medical files. For stroke attacks, definitive computerized tomography scans were used as a confirmation of diagnosis. For myocardial infarction, history of laboratory data and electrocardiograms were used for confirmation. Other conditions including possible angina or claudication were confirmed based on a documented diagnosis and self-reports of the clinical symptoms of the disease.

Data from the study conducted in 2003, which were also collected from patients attending government medical clinics in Nablus district, north Palestine were analyzed and compared with the current data. The 2003 data were previously published by the author [11]. Data collection in 2003 was similar to the current method and was obtained from patients' medical files.

In this study, secondary prevention is defined as the long term treatment to prevent recurrent cardiac morbidity and mortality and to improve quality of life in people who either had a prior acute myocardial infarction or severe coronary artery disease or stroke. Primary prevention or prophylaxis is defined as the long term treatment to prevent occurrence of a cardiac event in people who are at high risk of developing CVD. Based on this definition, diabetic patients without CVD were consid-

ered for ''primary prevention" while diabetic patients with CVD were considered for secondary prevention.

We investigated the overall frequency of anti-platelet use in 2008 and 2003 stratified by the presence and absence of CVD as well as gender and age. Overall use was defined as the total number of patients using anti-platelet drugs regardless of age, gender or category (i.e. for primary or secondary prevention) divided by the total number of included patients. Statistical comparison regarding use of aspirin in 2008 and 2003 was made using the chi-square test. Statistical testing and graphics were made using SPSS version 16.

Results

In 2008, approximately 3600 patients attended the clinics during the study period and 358 (9.9%) patients met the inclusion criteria of having both diabetes mellitus and hypertension. The mean age was 64.4 ± 10.8 years (range = 22—97 years). Half of the patients (50.3%) were above 65 years of age. There were 201 (56.1%) women and 157 (43.9%) men. One hundred and sixty three patients (45.5%) had a history of at least one type of CVD. The remaining patients (195, 54.5%) did not have any documented CVD, but had hypertension as a risk factor for CVD. Therefore all patients in the study were eligible for either SP or PP with aspirin therapy according to the ADA recommendations.

Aspirin (80—325 mg) was the only anti-platelet used. The total number of patients using aspirin was 238 (66.5%). Of those, the majority (88%) were using a dose of 100 mg/day while 8% were using 80 mg/day and the remaining patients (4%) were using a dose of 325 mg/day. The use of aspirin was significantly associated with the presence of CVD (OR = 2.7, $P < 0.001$) but not with either gender (OR = 1.1, $P = 0.7$) or older age (OR = 1, $P = 0.7$).

Aspirin was used for SP in 77.9% of diabetic patients with CVD and for PP in 56.9% of diabetic patients without CVD. The frequency of aspirin use in 2008 was the same in women and men (66.7% vs 66.2%, P = NS) (Fig. 1). Similarly, no significant differences were seen in the frequency of aspirin use among senior ($\geqslant$65 years) and younger (<65 years) patients in 2008 (66.1% vs 66.9%, P = NS) (Fig. 2). The lowest rates (54.1%) of aspirin use were among elderly women ($\geqslant$65 years) without CVD, and the highest rates (81.4%) were among elderly women with CVD.

In 2003, 344 out of approximately 2000 patients met the inclusion criteria. The average age of the included patients was 64.4 ± 8.7 years. There were slightly more men 174 (50.9%) than women 168 (49.1%). Seventy-four patients (21.6%) had a history of CVD. The remainder were diabetic patients without CVD but with hypertension as a risk factor. All the patients in the study were eligible for either SP or PP with aspirin therapy according to the ADA recommendations.

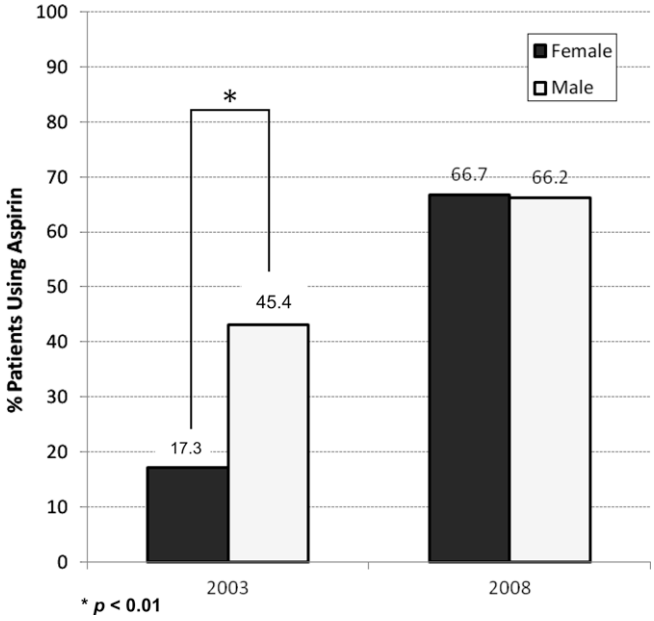

Figure 1 Aspirin use in diabetics with hypertension by sex.

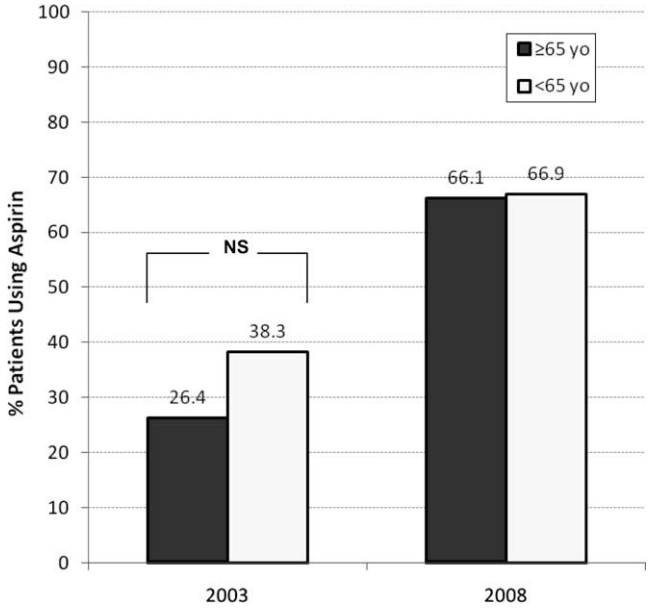

Figure 2 Aspirin use in diabetics with hypertension by age.

In 2003, aspirin was the only documented antiplatelet. Aspirin was used by 108 patients giving an overall frequency of 31.6%. Aspirin was used for SP in 82.4% of the patients with CVD and for PP in 17.5% of diabetic patients without CVD. In 2003, men showed a significantly higher frequency of aspirin use than women (45.4% vs 17.3%, $P < 0.01$). Similarly, younger patients (<65 years) had a significantly higher frequency of aspirin use than elderly patients ($\geqslant$65 years) in 2003 (38% vs 26.4%, $P = 0.031$) (Fig. 2).

The general use of aspirin among diabetic hypertensive patients in 2008 was significantly higher ($P = 0.0001$) than that in 2003 (Fig. 3). There was more than a 2-fold increase in the overall use of aspirin in 2008 compared to 2003. The use of aspi-

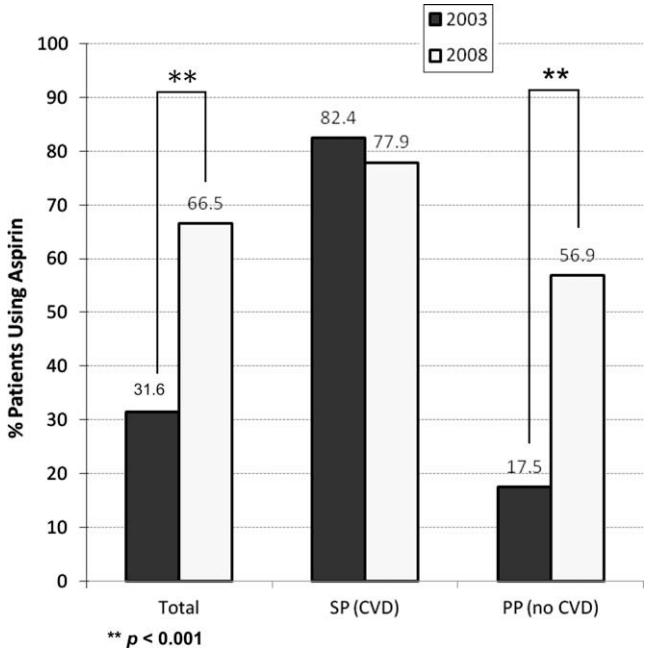

Figure 3 Aspirin use in diabetics as primary (PP) and secondary (SP) prevention.

rin for SP was comparable in 2008 and 2003. In fact, there was no significant difference ($P = 0.23$) between the use of aspirin for secondary prevention in 2008 compared with 2003. However the use of aspirin for PP in diabetic patients without CVD was significantly higher in 2008 compared with 2003. The use of aspirin for PP in 2008 was three times greater compared to 2003.

Discussion

The results obtained in 2008 showed an encouraging increase in aspirin use among adults with diabetes mellitus and hypertension over the preceding five years. This increase was observed for primary prevention but not for secondary prevention. Furthermore, the results of this study showed that differences in aspirin use based on gender or age decreased in 2008. Elderly patients are known to have multiple co-morbid diseases and thus are at higher risk of developing CVD than younger patients. Nevertheless, data showed that aspirin use in 2008 was less than ideal for patients with and without CVD. Approximately 20% of individuals known to have CVD such as myocardial infarction, angina or stroke were not using aspirin for secondary prevention. Moreover, more than one-third (43%) of adults with diabetes and without diagnosed CVD did not use this widely available, inexpensive and proven effective therapy for prophylaxis (primary prevention).

The increase in the overall use of aspirin in 2008 compared to 2003 may be attributed to increased awareness by the public as well as to the extensive medical educational program carried out by health authorities as well as the non-governmental organization to promote primary prevention among high risk patients. Another explanation is the inclusion of many patients with chronic diseases in the free government health insurance program. It has been shown that health insurance has a positive correlation with the likelihood that an individual will receive appropriate preventive care.

In 2008, the frequency of aspirin use as secondary prevention was 56.9% which is lower than that reported in some studies from USA (78%), Spain (91.7%) and India (100%) [12—14]. However, the frequency of aspirin use for PP in this study (77.9%) is higher than that reported in the same studies: USA (45%), Spain (25.9%) and India (11%). The use of aspirin in diabetic patients is increasing. Studies from the USA and Europe reported that in 1988—1994, aspirin was used regularly only by 37% of diabetic patients with coronary artery disease and by 13% of those with cardiovascular risk factors without CVD [6]. The frequency of aspirin use increased to 17% and 48.7% in 2000 and 2001, respectively [8,9]. In the most recent US study, only 54% of diabetic patients eligible for anti-platelets were prescribed such therapy [10].

Less than optimal use of aspirin may be attributed to physicians' concerns about toxic effects of chronic aspirin use, which is known to increase the risk of nonfatal bleeding in all users by a factor of 1.5—2.0 [15,16]. However, randomized trials that have included many patients with diabetes have not shown aspirin to be particularly dangerous in this group [17—19]. A second possible reason for less than optimal use of aspirin is that patients and physicians may underappreciate the CVD risk associated with diabetes. A study has shown that physicians and many diabetic patients do not appreciate their risk of CVD, and that physicians place greater importance on glucose control than on blood pressure management, cholesterol lowering, or aspirin use as a means of reducing CVD risk [20].

In the current study, no difference was observed in the overall use of aspirin between women and men. This is an improvement since 2003 when men were more likely to use aspirin than women. A study from 1988 to 1994 found that there was no significant difference in aspirin usage between men and women [21]. Previous research has demonstrated less frequent use of invasive cardiovascular procedures and effective medications for acute myocardial infarction, including thrombolytics, b-blockers, and aspirin, in women compared with men [22—28]. A similar disparity now exists for the use of aspirin for primary and secondary CVD prevention in diabetes. There are several possible explanations for low use of aspirin among women. Physicians may not counsel women with diabetes to use aspirin if they underestimate a women's risk of CVD. Although women are at a lower risk of new-onset CVD than men, diabetes greatly reduces this female advantage [29—32].

While not nationally representative, this study showed that application of ADA clinical practice guidelines regarding aspirin use in primary prevention among the high risk group of diabetic hypertensive patients has improved positively in the past five years. However, the use of aspirin for secondary prevention remained unchanged. Further investigations are required at the national level to assess the adherence to international guidelines regarding the use of aspirin and other anti-platelet agents in high risk patients.

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