Use of Aspirin and Statin as primary prevention for cardiovascular diseases
Bahaa Aba Alkhail¹, Rahila Iftikhar², Adnan Al Shaikh³

ABSTRACT
Objective: To ascertain whether recommendations for the use of Statins and Aspirin as primary prevention in diabetic patients are correctly implemented at our institution.
Methods: This cross-sectional study was conducted between February 2014 and April 2014 at the General Practice Department of King Abdulaziz University Hospital. Three hundred twelve patients were included in the study. Data were collected from the electronic patient medical records for the characteristics of the patients, existing co-morbidities, and results of laboratory investigations. Descriptive statistics were performed for all variables.
Results: Of 312 patients, aspirin was indicated for 17.0% but it was not prescribed. It was both indicated and prescribed in 36.2% of the cases. Statin treatment was indicated in 27.2% of the patients but it was not prescribed, while in 63.1% of cases it was indicated and prescribed.
Conclusion: The proportion of patients who achieved treatment targets at our institution is greater than that reported by other studies, albeit treatment targets are not being met in a significant number of cases.

KEY WORDS: Aspirin, Cardiovascular disease, Diabetes mellitus, Primary prevention, Statin.

INTRODUCTION
The burden of cardiovascular disease (CVD) is substantial in patients with diabetes mellitus, who have a two-to four-fold increase in the incidence of cardiovascular events compared with age- and sex-matched, non-diabetic persons.¹² The increased risk of cardiovascular events and mortality in diabetic patients has created a need for researchers to identify more efficient strategies for cardiovascular risk reduction.

During the past three decades, several trials have attempted to demonstrate the efficacy of aspirin and statins to decrease cardiovascular events in diabetic patients, albeit with conflicting evidence about the efficacy of aspirin for primary prevention of CVD in persons with diabetes. While the American Diabetes Association (ADA), American Heart Association (AHA), and the American College of Cardiology Foundation (ACCF) created updated recommendations, these guidelines are, in practice, difficult to implement.³

In practice, the implementation of guidelines is influenced by various factors and, depending on the circumstances, the target goal is often not easy to achieve. These factors may include physician knowledge and attitudes, patient behaviors, or
health system facilities. The ADA guidelines recommend a comprehensive care plan for diabetic patients. These guidelines comprise preventative medication use of aspirin and statins based on specific criteria.

According to previous research, aspirin and lipid-lowering agents are often not appropriately prescribed: in some practices aspirin is overprescribed, whereas statins are under prescribed. While it is crucial to understand current practices in diabetes care in order to improve outcomes in diabetic patients, there are few data that show to what extent these guidelines are followed.

We aimed to investigate whether recommendations for the use of statins and aspirin in diabetic patients are correctly employed at our institution. Therefore, this study was designed to assess the prescription of aspirin and statin therapy in diabetic patients to prevent CVD.

METHODS

This cross-sectional, study was conducted between February 2014 and April 2014 at the General Practice Department of King Abdulaziz University Hospital (KAUH) Jeddah, Saudi Arabia. All patients with ischemic heart disease, kidney disease and stroke were excluded.

Data were collected from the patients’ electronic medical records for demographic and clinical characteristics, including existing co-morbidities, and laboratory findings.

We followed the ADA 2014 recommendations, which recommends initiating statin therapy in individuals with diabetes and other cardiovascular risk factors target LDL cholesterol levels of <100 mg/dL are recommended in this group of patients. The ADA recommends aspirin for those who are ≥ 50 years old or who have additional risk factors (family history of CVD, high blood pressure [BP], smoking, dyslipidemia, or albuminuria). The ACCF recommends aspirin for high-risk diabetic patients at increased cardiovascular risk.

Similarly, we followed the ADA working definition for aspirin therapy:

a) Cardiovascular disease risk >10%,
b) Men aged 50 years or women aged 60 years who have at least one additional major risk factor (family history of CVD, hypertension, smoking, dyslipidemia, microalbuminuria), or
c) Diabetes mellitus with CVD.

Ethics: Permission to conduct this study was obtained from the Ethics Research Committee at King Abdulaziz University, Jeddah. All procedures followed were in accordance with the ethical standards of the Ethics Research Committee at King Abdulaziz University, Jeddah and with the latest (2008) version of Helsinki Declaration of 1975.

Statistical analysis: The data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS), version 16. Normal distribution of the data was checked by Shapiro-Wilk’s statistics and if the p-value was ≤ 0.05, the data were considered to be non-normally distributed. Normally distributed quantitative variables are presented as mean ± standard deviation (SD). Frequencies and percentages were calculated for qualitative variables.

RESULTS

The study included 312 patients who were aged 52 to 67 years (mean, 59.6±11.8 years). Patients aged ≥ 50 years comprised approximately four-fifths of the sample. Females accounted for approximately 72.6% of the sample. The majority of the patients (93.7%) were married. The sample was composed of patients of different ethnic and

| Variable                  | Frequency (Percent)* |
|---------------------------|----------------------|
| **Age Group**             |                      |
| ≤ 39 years                | 13 (4.2)             |
| 40-49 years               | 43 (13.8)            |
| 50-59 years               | 107 (34.3)           |
| 60-69 years               | 86 (27.6)            |
| 70-79 years               | 49 (15.7)            |
| 80+ years                 | 14 (4.5)             |
| **Gender**                |                      |
| Male                      | 86 (27.6)            |
| Female                    | 226 (72.4)           |
| **Marital Status**        |                      |
| Single                    | 10 (3.3)             |
| Married                   | 283 (93.7)           |
| Divorced / widowed        | 9 (3.0)              |
| **Nationality**           |                      |
| Saudi                     | 98 (31.6)            |
| Non-Saudi                 | 214 (68.4)           |
| **Educational Status**    |                      |
| Primary                   | 45 (19.5)            |
| Intermediate              | 67 (29)              |
| High school               | 66 (28.6)            |
| Graduate                  | 48 (20.8)            |
| Post graduate and above   | 5 (2.2)              |

*For some observations, the total is < 312 due to missing values.
racial origins, only one-third of which were Saudis. Approximately 77.1% had completed at least high school (Table-I).

Aspirin was indicated in 17.0% of the 312 patients but was not prescribed; it was indicated and prescribed in 36.2% of the cases. In more than half of the patients (63.1%) statin therapy was indicated and prescribed. However, statin treatment was indicated in 27.2% of the patients but it was not prescribed (Table-II).

**DISCUSSION**

Based on the recommendations of the ADA, AHA, and ACCF, most of the patients in our cohort were at high-risk for cardiovascular events: approximately four-fifths were aged ≥ 50 years and about 65% had at least two co-morbid conditions. However, 17.0% and 27.2% of patients at increased risk for cardiovascular events did not receive aspirin and statin treatments, respectively. This demonstrated gaps in cardiovascular risk management. Other researchers have reported similar gaps in the management of cardiovascular risk. While aspirin is frequently used by millions of patients worldwide, especially for primary prevention of CVD, many patients with established CVD are not using aspirin.\(^6\) In another report,\(^7\) it was found that statin treatment was not prescribed for 41% of diabetic patients at high risk for cardiovascular events.

In this study we specifically considered whether aspirin was indicated for primary prevention of CVD. Recent research demonstrates that its indication in the primary prevention of CVD is very limited. Nevertheless, many physicians tend to prescribe aspirin for primary prevention of CVD without quantifying CVD risk, and it might take some time for physicians to modify their practice in response to current recommended guidelines.\(^8\)

Recommendations for prescribing aspirin to diabetic patients need to be more emphasized, informed and explained to physicians. Physicians should be educated about comprehensive diabetes management and risk reduction strategies in these patients. Gaps between guideline recommendations and practice in managing BP and lipids are relatively high compared with gaps for controlling glucose.\(^9\)

Comprehensive treatment must include blood pressure lowering, tobacco cessation, reaching optimal weight and emphasizing on regular walks for primary atherosclerotic cardiovascular disease (ASCVD) prevention.

It has been shown that Diabetic care is not optimum. A recent report from Italy indicates that only 46.3% of high risk CVD patient used aspirin for prevention,\(^10\) while in another study 35% of clinicians indicated that patients were using it for primary prevention.\(^11\) Similarly, a survey showed a small proportion of patients were prescribed aspirin.\(^12\) Conversely, another study demonstrated overutilization of aspirin in patients for whom the drug was not recommended.\(^13\) In fact, aspirin should be prescribed appropriately,\(^14\) and given that the risk of gastrointestinal bleeding must be weighed against the potential benefit, physicians should make shared decisions.\(^15\) Aspirin utilization and statin prescription can be improved by using a heart scoring system.\(^16\) Furthermore; this scoring system can enhance appropriate targeting of high risk population.

We found that 63% of patients were prescribed statins appropriately. In another study that assessed statin prescribing patterns according to the ADA guidelines, only 35.1% of the patients were prescribed statins.\(^17\) The new ACC/AHA guidelines recommend primary prevention with moderate-intensity statin to individuals with diabetes aged 40-75 years and LDL-C 70-189 mg/d. This will definitely increase the number of patient eligible for statin treatment. Although statins carry a small risk for new onset DM, clinical guidelines recommend its use in high risk groups, as the benefits outweigh the risks.\(^18\)

**Limitations of the study:** First, this single-center study was conducted in a tertiary care setting. Hence, the results cannot be generalized to the local population. Second, the patients in our study had free health care, including dietician consultation, and medication, which might not be available to patients in other settings. Third, we did not perform inferential statistics to determine whether differences
between patients were significant. Finally, we did not discuss the complications of diabetes. We, therefore, suggest that future studies should investigate and discuss the effectiveness of aspirin and statins in the primary prevention of CVDs in patients with diabetes.

CONCLUSION

These findings reveal that our patients who had good glycemic control, the use of aspirin and statin for the prevention of CVD in diabetic patients can be improved. This suggests the need to investigate the reasons for this failure in order to develop strategies for awareness program and a better multidisciplinary approach to achieve treatment targets. We also suggest further investigations to better understand the basis for physicians’ estimates of how many of their patients with diabetes were reaching target values, as this will help to evaluate current practice trends and assist in formulating programs to enhance the appropriate use of primary prevention strategies in our setting.

ACKNOWLEDGEMENTS

The authors would like to thank the medical students Dr. Sarah Binmahfooz, Dr. Zainab Alsadeq, Dr. Sajeda Alsadah, Dr. Hanin Ayoub, and Dr. Maryam Alsadeh for their efforts in helping with data collection.

Source(s) of support: Self-financed.

Declaration of interest: None declared.

REFERENCES

1. Eliasson M, Talbäck M, Rosén M. Improved survival in both men and women with diabetes between 1980 and 2004—a cohort study in Sweden. Cardiovasc Diabetol. 2008;7:32.
2. Asegaonkar SB, Marathe A, Tekade ML, Chererek L, Bavi kar J, Bardapkurkar J, et al. High-sensitivity C-reactive protein: a novel cardiovascular risk predictor in type 2 diabetics with normal lipid profile. J Diabetes Complications. 2011;25:368–370.
3. Bryant W, Greenfield JR, Chisholm DJ, Campbell LV. Diabetes guidelines: Easier to preach than to practise? Med J Aust. 2006;185(6):305-309.
4. Bruckert E, Ferrières J. Evidence supporting primary prevention of cardiovascular diseases with statins: Gaps between updated clinical results and actual practice. Arch Cardiovasc Dis. 2014;107(3):188-200.
5. American Diabetes Association. Aspirin therapy in diabetes: position statement. Diabetes Care. 2014;24(Suppl.1):S62-S63.
6. Webster RJ, Heeley EL, Peiris DP, Bayram C, Cass A, Patel AA. Gaps in cardiovascular disease risk management in Australian general practice. Med J Aust. 2009;191(6):324-329.
7. Kolber MR, Korownyk C. An aspirin a day? Aspirin use across a spectrum of risk: cardiovascular disease, cancers and bleeds. Expert Opin Pharmacother. 2014;15(2):153-157.
8. Waldron S, Horsburgh M. Cardiovascular risk assessment: audit findings from a nurse clinic-a quality improvement initiative. J Prim Health Care. 2009(1):226-231.
9. Minder CM, Blumenthal RS, Blaha MJ. Statins for primary prevention of cardiovascular disease: the benefits outweigh the risks. Current opinion in cardiology. 2013;28(5):554-560.
10. Lugo A, Asciutto R, Bosetti C, Parazzini F, La Vecchia C, Gallus S. Regular use of aspirin for cardiovascular disease prevention in Italy. Prev Med. 2014;63:48-51.
11. VanWormer JJ, Miller AW, Rezkalla SH. Identifying opportunities to improve aspirin utilization for the primary prevention of cardiovascular disease in a regional healthcare system. WMJ. 2014;113(5):190.
12. Fiscella K, Winters PC, Mendoza M, Noronha GJ, Swanger CM, Bisognano JD, et al. Do clinicians recommend aspirin to patients for primary prevention of cardiovascular disease? J Gen Intern Med. 2015;30(2):155-160.
13. VanWormer JJ, Miller AW, Rezkalla SH. Aspirin overutilization for the primary prevention of cardiovascular disease. Clin Epidemiol. 2014;6:433-440.
14. VanWormer JJ, Greenlee RT, McBride PE, Peppard PE, Malecki KC, Che J, et al. Aspirin for primary prevention of CVD: are the right people using it? J Fam Pract. 2012;61(9):525-532.
15. Mora S, Ames JM, Manson JE. Low-Dose aspirin in the primary prevention of cardiovascular disease: shared decision making in clinical practice. JAMA. 2016;316(7):709-710.
16. Romero SC, Dela Rosa KM, Linz PE. Aspirin for primary prevention of coronary heart disease: using the Framingham Risk Score to improve utilization in a primary care clinic. South Med J. 2008;101(7):725-729.
17. Pauff BR, Jiroutek MR, Holland MA, Sutton BS. Statin Prescribing Patterns: An Analysis of Data From Patients With Diabetes in the National Hospital Ambulatory Medical Care Survey Outpatient Department and National Ambulatory Medical Care Survey Databases, 2005-2010. Clin Ther. 2015;37(6):1329-1339.
18. Parker K, Dohr K, Neher JO, Kelsberg G, Kelsberg G, St Anna L. Clinical Inquiry: Do statins increase the risk of developing diabetes? J Fam Pract. 2016;64(4):245-246.

Author’s Contribution:

BAK conceived and designed the study, supervised data collection and wrote initial draft of manuscript. RI wrote the manuscript, analyzed and interpreted the data.

AS participated in writing the manuscript and supervised data collection. All authors reviewed and approved the final version of the manuscript.