COMPARISON OF HYPERURICEMIA IN TYPE 2 DIABETICS ON LOW DOSE ASPIRIN AND NOT ON LOW DOSE ASPIRIN

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ABSTRACT

Objective: To compare the frequency of hyperuricemia in type 2 diabetes patients who are taking low dose aspirin with those patients who are not taking low dose aspirin.

Study design: Quasi experimental study.

Place and duration of study: This study was carried out at Military Hospital Rawalpindi for a period of two years (June 2006-May 2008).

Patients and Methods: Sixty diabetic patients were selected who were taking low dose aspirin comparing group A and sixty diabetic patients who were not taking aspirin were placed in group B. These patients were selected from the OPD through non probability convenience sampling**.** All these patients were being followed up in medical outpatient quite regularly on fort-nightly basis. Data had been collected through a carefully designed questionnaire.

Results: In group A, 90% of the patients had uric acid less than 445umol/l and 10% of the patients had uric acid more than 445umol/l. whereas in group B 100% of the patients had uric acid less than 445umol/l, there was a statistically significant difference between the two groups ($p< 0.05$).

Conclusion: Aspirin in low doses cause hyperuricemia and regular monitoring of uric acid is mandatory to prevent its adverse effects.

Keywords: Type 2 Diabetes Mellitus, Aspirin, Hyperuricemia, Cardiovascular risk.

INTRODUCTION

The incidence of diabetes mellitus (DM) has reached epidemic proportions across the world[1]. Most cases are diagnosed after 40 years of age and 20% of the people over 60 years of age have type 2 diabetes[2]. Type 2 diabetes is by far the most common type of diabetes and is characterized by variable degrees of insulin deficiency and resistance[3]. In patients with diabetes, there is a two to four times increased risk of developing coronary artery disease (CAD). Diabetes seems to eliminate the protective benefits of hormones in women. Not only is the incidence of CAD higher in diabetes, the mortality of the diabetic patients after a cardiac event is significantly increased as compared to non-diabetics, including sudden death[3]. Atherosclerosis and vascular thrombosis are major contributors in the development of CAD and it is generally accepted that platelets are contributory. A major mechanism is the increased production of thromboxane which is a potent vasoconstrictor and platelet aggregant, thus leading to platelet aggregation and thrombus formation. Aspirin blocks thromboxane synthesis by acetylating platelet cyclooxygenase and has been used as a primary and secondary strategy to prevent cardiovascular events in non-diabetic and diabetic individuals. Substantial evidence suggests that low-dose aspirin therapy should also be used as a primary prevention strategy in men and women with diabetes who are at high risk (over age 40 or with other cardiovascular disease risk factors) for cardiovascular events[4-6]. Primary prevention can play an important role in decreasing the incidence of CAD in diabetic patients[7,8]. Apart from this useful effect aspirin is also known to have a bimodal effect on the renal handling of uric acid (UA). High doses (>3 gm /day) are uricosuric, while low doses cause UA retention and hyperuricemia. The independent risk relationship between hyperuricemia and acute MI is confirmed[9,10]. Hyperuricemia is associated with an excess risk of acute MI, and this is not explained by its well-known links with renal function, metabolic syndrome, diuretic use, and

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traditional cardiovascular risk factors[11-14].

The purported significance of the study is to find out the frequency of hyperuricemia in these patients and to see the magnitude of the problem in our set up and our environment. At one end aspirin is being used to decrease the cardiovascular complications and at the other end it is itself causing hyperuricemia which is a cardiovascular risk. If the problem appears to be significant then future studies can be carried out to formulate treatment strategies to reduce or eliminate a potential preventable risk. The objective of this study is to compare the frequency of hyperuricemia in type 2 diabetic patients who are taking low dose aspirin with those patients who are not taking low dose aspirin.

MATERIALS AND METHODS

This Quasi experimental study was carried out at Department of Medicine, Military Hospital Rawalpindi for a period of 2 years (June 2006- May 2008).

Type 2 diabetics' patients between 40 to 65 years of age were included in the study, while there who had deranged serum urea and creatinine levels, drugs use like diuretic, warfarin, cytotoxic drugs, ethambutol, pyrazinamide, levodopa, laxative abuse, dyslipidemias, obesity, blood Pressure more than 140/90 mmHg, alcohol use, any history of co-morbid conditions like malignancies, myeloproliferative or lymphoproliferative disorders, psoriasis, Down's syndrome, chronic heart failure, hypothyroidism, and sarcoidosis were not included in the study.

Sixty patients were selected who were taking low dose aspirin and sixty patients who were not. These patients were selected from the OPD through non probability convenience sampling

Group A: Taking low dose Aspirin

Group B: Not taking low dose Aspirin

These patients were being followed up in medical outpatient quite regularly on fort nightly basis. All the treatment was given in outdoor. Each patient was thoroughly examined. Patients fulfilling the required criteria were informed about the study work and after taking consent from them were enrolled in the study.

Confounding variables were controlled by taking detailed history and asking them specifically about any other previously diagnosed disease, which included past history of gout, renal disease, malignancies, myeloproliferative disorders, lymphoproliferative disorders, psoriasis, Down's syndrome, chronic heart failure, hypothyroidism and sarcoidosis. Detailed drug history was taken to exclude specifically drug intake of diuretics, warfarin, cytotoxic drugs, ethambutol, pyrazinamide, levodopa and laxatives abuse.

Detailed physical examination was carried out. Vital signs were recorded and only those patients were included whose blood pressures were less than or equal to 140/90mmHg. Height and weight of the patient was recorded and body mass index (BMI) of all these patients was calculated by using the formula, body weight (in kg) ÷ height (in meters) squared. A detailed examination of these patients was then followed to exclude any systemic manifestation of above mentioned diseases or stigmata/complications of diabetes in these patients. Patients selected through this procedure were then told about the blood samples to be taken and analyzed in the laboratory. After entering all relevant data in the proforma of this study, lab request forms were carefully filled and signed.

Lab reports were collected and reports were then entered in the proforma. Patients not fulfilling the criteria or fulfilling the exclusion criteria were removed from the proforma.

Table-1: Comparison of age and BMI between both the groups.

Demographic Variables	Group A (n=60)	Group B (n=60)	*p*-value
Age	50.30±7.99	49.78±7.78	0.720
BMI	25.80±1.86	25.91±1.84	0.168

Values are expressed as mean ± SD

Table-2: Comparison of uric acid levels between both the groups.

Uric Acid level	Group A (n=60)	Group B (n=60)
≤ 445µmol	54(80%)	60(100%)
> 445µmol	6(10%)	0(0%)

$p = 0.012$

Data collected through a carefully designed structured questionnaire. Data had been analyzed using SPSS version 10. Mean and standard deviation (SD) was calculated for all quantitative variables like age and BMI. Frequencies and percentages were described for gender, marital status, socioeconomic status and uric acid levels. Independent sample t-test was used to compare age and BMI. "Chi square" test was then used to compare the gender and uric acid between both groups. $p<0.05$ was taken as significant.

RESULTS

There were 60 patients in each group. All patients who were taking low dose Aspirin were placed in group "A" and all those patients who were not taking low dose Aspirin were placed in group "B".

Age and BMI for both the groups are described in table 1. In group A there were 56.7 % males and 43.3 % females. In group B there were 53.3 % males and 46.7 % female. Both the groups were comparable with respect to age (p=0.720), BMI (p=0.168) and gender (0.714). Patients in both the groups (100%) were married and all (100 %) belonged to middle class socioeconomic group.

In group A, 90% of the patients had uric acid ≤ 445 umol/l and 10% of the patients had uric acid > 445umol/l. whereas in group B 100% of the patients had uric acid ≤ 445 umol /l (p=0.012), which is statistically significant difference between the two groups (table 2).

DISCUSSION

It is a matter of great concern that a significant number of diabetic patients land up with complication in the emergency department, these include myocardial infarctions, cerebrovascular accidents and renal failures. Cardiovascular disease is the major cause of morbidity and mortality in patients with diabetes mellitus[2]. The pathophysiology of cardiovascular disease in diabetes involves cardiac risk factors, including hypertension, dyslipidemias, smoking, genetic factors, hyperglycemia, insulin resistance, metabolic abnormalities, oxidative/glycoxidative stress, inflammation, endothelial dysfunction, a procoagulant state and myocardial fibrosis[3]. Specific vascular, myopathic and neuropathic alterations have been suggested to be responsible for the excessive cardiovascular morbidity and mortality in diabetes. These alterations manifest themselves clinically as coronary heart disease, congestive heart failure and / or sudden cardiac death. In order to contain this emerging epidemic of CVD in DM[4-6], diabetic patients should ideally have excellent glycemic control, a low normal blood pressure and low levels of low-density lipoprotein cholesterol, and be taking an angiotensin-converting enzyme inhibitor and aspirin, which may go some way to contain the emerging epidemic of cardiovascular disease in diabetes mellitus. The most important of which was a meticulous blood glucose control. However despite meticulous blood glucose control, a significant number of patients had myocardial infarctions. American Diabetic Association (ADA) had clear indications for instituting aspirin therapy in these patients. But despite the fact that it is very clearly mentioned and the benefit of the therapy cannot be denied, very small numbers of patients were actually taking aspirin. Despite the overwhelming

benefits of aspirin therapy, one important side effect in these patients is the incidence of hyperuricemia.

There is paucity of research work both nationally and internationally on this subject. However mini-dose aspirin, even at a dosage of 75 mg/day, caused significant changes in renal function and UA handling within one week[15].

Hyperuricemia is important because of its direct relationship with the incidence of myocardial infarctions[13]. As the difference was significant between the two groups and patients follow up regularly in medical OPDs, so these patients, in addition to routine monitoring of blood glucose should also be monitored for raised uric acid levels. Aspirin therapy as per recommendations should be started in these patients and uric acid is monitored regularly and once it is found that uric acid levels are increased then aspirin therapy can be stopped and other anti platelet drugs like clopidogrel can be started.

CONCLUSION

Aspirin in low doses cause hyperuricemia and regular monitoring of uric acid is mandatory to prevent its adverse effects.

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