ROLE OF ASPIRIN IN DIABETES MELLITUS PATIENTS: A REVIEW

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ABSTRACT

Diabetes is one of the most common non-communicable diseases worldwide. India suffers from rising prevalence in both urban and rural areas due to lack of public awareness of the disease, limited health facilities, high cost of treatment, suboptimal glycemic control and increased diabetic complications. It is observed that Diabetics are twice as likely to suffer cardiovascular events such as heart attack and stroke as per the American Diabetes Association. Type 1 Diabetes is more commonly seen to develop in childhood or adolescence whereas Type 2 Diabetes is seen to develop at any age. Type 2 diabetes is most common in people over the age of 40. However, the role of aspirin in primary prevention in patients without cardiovascular disease is controversial. As a secondary prevention medication, aspirin is effective in preventing cardiovascular events in patients with pre-existing cardiovascular disease. Indeed, in low risk patients, the modest benefit of reducing major vascular events may be offset by increased bleeding risks such as intracranial and gastrointestinal bleeding. Hence, Diabetes mellitus is seen to be associated with a significant increased risk of both primary and recurrent atherothrombotic events and thereby complicating aspirin therapy.

KEYWORDS: Aspirin, diabetes mellitus, prevention, cardiovascular disease.

INTRODUCTION

Diabetes mellitus (DM) is a condition of high blood sugar levels due to absolute insulin deficiency or relative insulin deficiency. Sugar levels in the frame typically fluctuate at certain times of the day. Diabetes mellitus (DM) is commonly referred to as a "sugar" and it is the most common endocrine disorder.[1] The American Diabetes Association (ADA) suggests that human beings with diabetes are two times more probable to have cardiovascular disorders like a coronary heart assault or stroke. ADA best recommends day by day aspirin at a dose of 75 to 162 milligrams. Low-dose of aspirin can assist in lessening person's danger of experiencing a cardiovascular event. Aspirin is suggested for human beings with diabetes who have a record of cardiovascular disease. Diabetes affects more than 23.6 million people in the United States. Although believed to be underreported, this metabolic disorder is the seventh leading cause of death, with mortality occurring at a rate nearly twice that of individuals without the disease. Mortality is attributed to macro-vascular complications such as peripheral vascular disease, cardiovascular disease (CVD), and stroke.[2]

Classification of Diabetes

Type I diabetes mellitus (T1DM) is a metabolic disease that affects almost 1 million Americans. Prolonged hyperglycaemia results in extended occurrence of secondary complications such as retinopathy, neuropathy, coronary heart disease and osteoporosis.[3] Type 2 diabetes mellitus (T2DM) accounts for about 90% of all diabetes cases. Type 2 diabetes has a reduced response to insulin, defined as insulin resistance. In this state, insulin is ineffective and initially encountered by increasing insulin production to maintain glucose homeostasis, but over time insulin production decreases, leading to T2DM. T2DM is most commonly seen in people over the age of 5 years.[4] Gestational diabetes mellitus (GDM) is defined as any degree of impaired glucose tolerance that occurs or is first detected during pregnancy. It occurs during the second and third trimester of pregnancy and is characterized by marked insulin resistance as a result of the release of placental hormones. GDM can be classified into A1GDM and A2GDM. GDM that is managed without medication and responds to nutritional therapy such as diet- controlled is called as A1GDM. Conversely, GDM managed with pharmacotherapy to achieve adequate glycaemia control is defined as A2GDM.[5]

Signs and symptoms
Typical symptoms of diabetes, such as polyuria, polydipsia, and binge eating, are common in T1DM and T2DM with very high blood sugar. Excessive weight loss is common only in type 1 diabetes and goes long-undetected in T2DM. Unexplained weight loss, fatigue and restlessness, and body aches are also common signs of undiagnosed diabetes.[6]

Pathophysiology of diabetes mellitus
Diabetics have a shorter platelet lifespan, leading to increased production of platelets in the bone marrow. Platelets upregulate glycoprotein IIb/IIIa and P2Y12 signalling, which increases platelet aggregation and adhesion leading to probability of forming blood clots. This makes aspirin therapy potentially valuable in these patients to reduce platelet activation and aggregation. However, diabetics have several prothrombotic mechanisms that may also trigger the response to aspirin ingestion causing the inhibition of aspirin's action on the anticoagulant pathway (e.g. Nitric oxide) when glucose levels are high.[7]

Role of aspirin in diabetes mellitus patients
Aspirin therapy (75-162mg/day) as a primary prevention strategy in patients with type 1 or 2 diabetes at increased risk of cardio vascular disease is considered in the (10-year risk >10%). This includes most men aged >50y and women aged >60y with more than or equal to 1 additional major risk factors (family history of CVD, hypertension, smoking, dyslipidaemia, albuminuria). Evidence is insufficient to recommend aspirin for primary prevention in lower- risk patients, such as men aged <50y and women aged <60y without other major risk factors. Therefore, aspirin (75- 162mg/day) is recommended as secondary prevention strategy in patients with diabetes and history of cardio vascular disease (CVD).[8]

Mechanism of action in cardiovascular disease
The optimal dose of aspirin has efficacy and safety of 75 to 100 mg standard dose 300 to 325 mg of aspirin per day in 17,000 patients undergoing coronary artery angioplasty. A study result showed that low-dose aspirin (75-100 mg) had similar efficacy to high-dose aspirin in preventing death and cardiovascular events. However, in terms of safety, low-dose aspirin had a superior safety profile due to a lower incidence of bleeding events. In the USA the most common low-dose pill is 81mg.[7]

Dose of aspirin in cardiovascular disease with diabetes mellitus
According to a 2019 report, the American Diabetes Association only recommends daily aspirin at a dose of 75 to 162 milligrams per day for people with diabetes and a history of cardiovascular disease.[9]

Adverse Effects for Aspirin
Shakiness or nervousness, sweating, feeling clammy, light headedness, dizziness, a sense of weakness, confusion, ulcers, bleeding and blurred vision.[2]

Implications of aspirin uses
Aspirin did not have a significant risk on the primary endpoint of cardiovascular events and bleeding in diabetic patients compared with controls. The major adverse cardiovascular events (MACE) were significantly lower with aspirin.[10]

Prevention
The role of aspirin as number one prevention in patients who have a low-chance profile for cardiovascular activities is questionable, especially because of excessive chance of intracranial and gastrointestinal bleeding related to aspirin use. However in diabetes excessive blood glucose ends in osmotic impact and oxidative stress, which in the long run boosts up the atherosclerosis process for which aspirin maybe a suitable medication therapy.[7]

Current guidelines for aspirin use in reducing blood sugar levels

Sr.no	Organization	Primary prevention	Secondary prevention
1.	American Heart Association/American Stroke Association	Recommended for individuals whose cardiovascular risk outweighs the risks associated with treatment (10-year risk of cardiovascular events >6- 10%).	Heart attack and stroke survivors are advised to take regular low-dose aspirin for secondary prevention
2.	Heart attack and stroke survivors are advised to take regular low-dose aspirin for secondary prevention	Recommended for all patients over the age of 50	Low-dose aspirin or clopidogrel is recommended for all patients with established cardiovascular disease
3.	U.S. preventive Services Task Force	It is recommended for men aged 45-79 years when the potential benefit from reduced myocardial infraction outweighs the potential harm from increased bleeding. It is recommended for women aged 55-79 where the potential benefits from reducing ischemic stroke outweigh the potential harm from increased bleeding.	Like primary prevention
4	Canadian Cardiovascular Society	Not recommended for use in men or women without signs of vascular disease	Indefinite treatment with low-dose aspirin is recommended for all patients following a

			major cardiovascular event.
5.	European Society of Cardiology	Recommended when the risk of cardiovascular death at 10 years of age is markedly increased and blood pressure is controlled.	Lifelong low-dose aspirin therapy recommended for all patients with cardiovascular diseases, including diabetics, unless contraindicated [11].

Apart from medication management treating Diabetes also involves **non-pharmacological therapy** approach as follows:

Diet: It has been demonstrated that diabetes patients have better glycemic control and blood lipids when they eat a diet high in whole grains, fruits, vegetables, legumes, nuts, moderate alcohol consumption, and fewer refined grains, red/processed meats, and sugar-sweetened beverages.[12] The following items are permitted for free consumption: Water, green leafy vegetables, tomatoes, onions, cucumbers, aubergines, peppers, and a vegetable salad with no cream are all that are included. any tea, coffee, or beverage brand with few or no calories. The majority of carbohydrates should come in the form of starches (polysaccharides), which include things like bread, potatoes, maize, rice, and beans.[13]

Exercise
Aerobic exercise: Large muscular groups are repeatedly and continuously moved during an aerobic workout. Aerobic energy-producing systems are primarily used during exercises including walking, cycling, jogging, and swimming. Exercises utilising free weights, weight machines, your own body weight, or elastic resistance bands are all considered to be resistance (strength) training. Exercise that increases flexibility increase joint range of motion. Exercises that improve balance improve gait and reduce falls. Yoga and tai chi are examples of exercises that incorporate resistance, flexibility, and balance.[14]

Patients care
If you have diabetes and are concerned about your cardiovascular risk, ask your doctor about daily aspirin. They may not recommend it for you, especially if you have no history of cardiovascular disease, heart attack, or stroke. You should also talk to your doctor before taking aspirin every day if you are over 70 years old, drink alcohol, are at frequent, risk of bleeding such as gastrointestinal bleeding or haemorrhagic stroke and if having any medical or dental treatment.[2]

Self-management of diabetes: There are seven key self-care behaviours in people with diabetes that predict good outcomes. These are healthy eating, physical activity, blood sugar monitoring, medication adherence, good problem-solving skills, healthy coping skills, and risk reduction behaviours. Diabetes self-care activities are behaviours that people with diabetes undertake to successfully manage the disease themselves. These seven behaviours were found to be positively correlated with good glycaemic control, fewer complications, and improved quality of life.[15]

CONCLUSION
The use of aspirin for patients with cardio vascular disease absolutely exceeds the threat of bleeding, which makes the function of aspirin for secondary prevention undisputed. A modest gain has additionally been established in number one prevention; however, the trade-off of aspirin initiation as opposed to the multiplied threat of intracranial and gastrointestinal bleeding is extra unsure in sufferers without an overt cardio vascular disease. When selected for number one cardio vascular disease prevention, aspirin should be prescribed at the dose of (i.e., 75–100mg), the uncoated formulations with better bioavailability.

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