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Antiplatelet Activity of Aspirin in the Prevention of Cardiovascular Disease in a Tertiary Care Hospital, Bangalore, India

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Abstract

Objective: The present study is aimed to evaluate to Antiplatelet Activity of Aspirin in the Prevention of Cardiovascular Disease. Methodology: Cardiovascular disease (CVD) is a group of general category diseases that affects the heart and the circulatory system. CVD is caused by disorders of the heart, blood vessels that includes coronary heart diseases (CHD), congestive heart failure (CHF), stroke, Hypertension (HTN), peripheral artery disease (PAD) and rheumatic heart disease (RHD). The leading cause of death in India is CVD, India will notice a large number of people between 35 and 64 years die of CVD over the next 30 years as well as an increasing level of morbidity due to CVD. Drug therapy is a pillar of CVD prevention in such individuals and its cost/effectiveness ratio seems particularly favorable. Low-dose aspirin is a well-known, effective, cheap, and easy to use preventive drug. Drugs in a tertiary care hospital is a retrospective observational cross-sectional study, Patients who were satisfying the inclusion criteria was enrolled into the study conducted for the period of 6 months. Data collection form and other relevant source from Medical Record department are used as source of data and materials. Result: In our study 150 cases were examined in tertiary care hospital who were prescribed with Aspirin in cardiology department among that 108(72 %) were male and 42 (28%) were female. Accompanying major age group having CAD is 60-70 years i.e. 41(27.33 %) and 50-60 yrs. i.e. 39(26%). Regarding co-morbidity where aspirin was used, 34.67% of patients had CAD with HTN and 26.67% patients had CAD alone. Aspirin was mostly indicated for ischemia 50(33.33%) and Myocardial infarction 48(32%).In tertiary care hospital 150 mg of aspirin was highly used 50.67% followed by 75 mg 44%. Conclusion: Since 58.67% of prescription consist of aspirin in combination with other Antiplatelet drugs when compared with aspirin alone (41.33%), combination drug seems to be more effective in CAD patients.

Keywords: Cardiovascular disease, aspirin, Prescription, Prevention.

Introduction

Aspirin is a non-steroidal anti-inflammatory drug that has potent antiplatelet actions. Aspirin was initially used as an analgesic and antipyretic drug before its anti-inflammatory properties were discovered. Aspirin also has antithrombotic effects due to the inhibition of cyclo-oxygenase activity in platelets, which reduces the extent of thromboxane A2 formation and consequently the aggregability of platelets. Prophylactic low-dose aspirin therapy reduces the risk of future cardiovascular events in a variety of clinical settings. The maximum effect of aspirin in reducing risk of myocardial infarction is achieved soon after the initiation of therapy (Pawar, Shahani and Maroli, 1998).

Coronary artery disease (CAD) is mainly due to atherosclerosis (plaque in artery walls) of the inner lining of the blood vessels that supply blood to the heart. CAD begins when hard cholesterol substances (plaques) are deposited within a coronary artery. The plaques narrow the internal diameter of the arteries which may cause a tiny clot to form, which can obstruct the flow of blood to the heart muscle. This reduces the supply of oxygen and nutrients to the heart muscles, which is essential for proper functioning of heart. This may eventually result in a portion of heart being suddenly deprived of its blood leading to death of that area of heart tissue resulting in a chest pain or heart attack (Brizzio, 2012).

Aspirin's mechanism of action involves inhibition of platelet activation and aggregation, which was first described in 1971 by British pharmacologist John Vane. He demonstrated that the main mechanism of action was the irreversible inhibition of the platelet-dependent enzyme cyclooxygenase (COX), thereby preventing the synthesis of prostaglandins. Subsequent researcher's identified two COX iso

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enzymes, COX-1 and COX-2. In platelets, the COX-1 enzyme produces thromboxane A2, a powerful promoter of platelet aggregation. Thus, aspirin, by irreversibly inactivating COX- 1, thereby blocking the generation of thromboxane A2, derives a potential antiplatelet effect. Platelet activation and aggregation with subsequent activation of the clotting cascade play critical roles in the onset of acute occlusive vascular events, such as MI and occlusive cerebrovascular accident (CVA) (Pawar, Shahani and Maroli, 1998).
For primary prevention, the balance between benefits and risks of aspirin use is less clear because the absolute benefits of aspirin are generally lower than those in secondary prevention. Current guidelines largely ignore any differences in bleeding risk and recommend that aspirin be used widely for primary prevention in those at moderately raised risk of coronary heart disease. It has also been suggested that, since age is a major determinant of the risk of coronary heart disease, daily aspirin should be started in all people above a specific age, either alone or in combination with other drugs. To date, six completed randomized trials have evaluated the benefits and risks of low-dose aspirin for the primary prevention of cardiovascular disease. The PHS and BDT used aspirin regimens of 325mg every other day and 500mg/day, respectively, whereas the TPT and HOT used 75mg/day of aspirin and the PPP and WHS used 100mg/day of enteric-coated aspirin. The results demonstrate that aspirin therapy is associated with a significant reduction in the risk of cardiovascular events in both sexes (Dai and Ge, 2011).

Aspirin The regulation of several homeostatic mechanisms, including hemostasis, renal function, gastric acid secretion and blood pressure control, is modulated locally through eicosanoid synthesis. Inhibition of the constitutive prostaglandin G/H synthase pathway responsible for the production of these mediators is essentially responsible for the side effects associated with the long term administration of aspirin. Gastrointestinal complications, such as bleeding and perforation, are observed with greater frequency in individuals on nonsteroidal anti-inflammatory therapy. The incidence and severity of these complications are effected by the dosage regimen, the duration of treatment and the type of formulation used (plain vs enteric-coated) (Campbell et al., 2007; Pawar, Shahani and Maroli, 1998).

Deaths from myocardial infarction (MI) and stroke are mostly in older individuals. The incidence of venous thromboembolism is also higher in these patients (Heit et al., 2001). Apart from patients with venous thromboembolism and atrial fibrillation, who re quire anticoagulant therapy, antiplatelet drugs are the drugs of choice in preventing cardiovascular disease (Hirsh et al., 2001). Aspirin (acetylsalicylic acid) is the most widely used antiplatelet drug, while clopidogrel is slightly more effective, but much more expensive than aspirin (Calverley, 2001).

Materials and Methods

Study was conducted at tertiary care hospital. It is 300-bedded tertiary hospital having different specialties' like medicine, surgery, orthopedics, pediatrics, obstetrics and gynecology. All the inpatient in hospital who are treated for Aspirin in cardiology department in Tertiary care hospital. Eligible patients were enrolled based on inclusion and exclusion criteria. Structured data collection was used for collecting the details. This form mainly contains demographic details, social habits, current medication, past medical and medication history, laboratory investigations, and other relevant data needed for present study were collected from patient's progress records, treatment chart, and laboratory reports.

The data collected are subjected for various drug-drug interaction and ADR by using, primary (Micromedex), secondary and tertiary resources which are available in clinical pharmacy department. The collected information was documented and subjected for assessment using suitable statistical method. Descriptive statistical analysis has been carried out in the present study. Simple percentage calculations were used and expressed using charts and graphs by MS. Excel.

Result and Discusion

Retrospective study was conducted on antiplatelet activity of aspirin in the prevention of cardiovascular disease in a tertiary care hospital Bangalore. In our study 150 cases were examined in tertiary care hospital who were prescribed with Aspirin in cardiology department among that 108(72 %) were male and 42 (28%) were female.

Of the population studied, 20.66% of smokers and 11.34% of alcoholic were found to be under Aspirin therapy and 68% were nonsmokers and non-alcoholics. Regarding co-morbidity where aspirin was used, 34.67% of patients had CAD with HTN and 26.67% patients had CAD alone. Table 1

Table 1: Indication of Aspirin

INDICATION	NUMBER	PERCENTAGE %
MI	48	32%
THROMBOLIC STROKE	8	5.33%

ANGINA	32	21.34%
ISCHEMIA	50	33.33%
ATRIAL FIBRILLATION	12	8%

Aspirin was mostly indicated for ischemia 50(33.33%) and Myocardial infarction 48(32%). In tertiary care hospital 150 mg of aspirin was highly used 50.67% followed by 75 mg 44%.

Major prescriptions of Aspirin were with Statin 73.33%, and PPI 70% followed by antihypertensive drugs 53.33%. Among 150 prescriptions, 41.33% of prescriptions were with aspirin alone whereas 58.67% of prescriptions consists aspirin with other antiplatelet drugs. Table2 ,3 Among the total patients, most patients are admitted for 1-3 days 55.33%, whereas 33.33% were admitted for 4-5 days.

Table 2: Concurrent Drugs Prescribed

DRUG	No. of prescription	Percentage of prescription
ANTIBIOTICS	28	18.67%
NSAIDS	56	37.33%
ANTIEMETIC	27	18%
ANTIDIABETIC	32	21.33%
DIURETICS	59	39.33%
ANTIHYPERTENSIVE	80	53.33%
VITAMINS	4	2.66%
STATINS	110	73.33%
CORTICOSTERIODS	4	2.66%
ANTICONVULSANTS	8	5.33%
ANTIPSYCHOTIC	3	2%
ANTI ALLERGIC	8	5.33%
LEVOTHYROXINE	6	4%
ANTIASTHMATIC	14	9.33%
PPI	105	70%
ANTICOAGULANTS	35	23.33%
ANTACIDS	15	10%
IRON PRODUCTS	3	2%
ANTIANGINAL	34	22.67%
INSULIN	11	7.33%

Table 3: Use of Aspirin

USE OF DRUG	NO.OF PRESCRIPTION	PERCENTAGE %
ASPIRIN ALONE	62	41.33%
ASPIRIN WITH OTHER ANTIPLATELETS DRUGS	88	58.67%

The tolerability of aspirin is of importance, both in primary and secondary prevention. It is probably underestimated in everyday practice because all the primary and secondary trials that have been conducted did not include patients at increased risk of gastrointestinal hemorrhage or patients with aspirin intolerance. In studies involving elderly subjects, a clear excess of adverse events has occurred even at lower dosages (Nascitz et al., 1990). The risk of gastrointestinal bleeding is the most common serious adverse event associated with long-term aspirin use, while cerebral hemorrhage can also occur.

As with other NSAIDs, inhibition of gastrointestinal prostaglandin synthesis by aspirin commonly causes upper gastrointestinal symptoms. The bleeding and antithrombotic effects of aspirin are inseparable because both result from platelet inhibition of prostaglandin metabolism and thromboxane 2 synthesis (Calverley et al., 2001). The adverse-effect profile of aspirin is determined by dose, duration of administration and associated structural and hemostatic abnormalities. The risk seems to be higher at the beginning of treatment; patients in the first 2 months of therapy are at the greatest risk of a major upper gastrointestinal complication. Thereafter the risk goes down and reaches a plateau at around 6 months (de Abajo et al., 2001). The majority of conditions for which aspirin is required necessitate prolonged periods of exposure.

Whether the gastrointestinal bleeding risk is dose related remains controversial. In fact, the bleeding rate appears constant within the range of 75–325mg/day, but increases above 325mg. Even at low doses there is a bleeding risk. Weisman observed that patients who received low-dose aspirin (<325mg/day) were 2.5 times more likely to have gastro- intestinal tract bleeding than those in the placebo group (Weisman and Graham, 2002). Elderly subjects are particularly at risk of gastro intestinal hemorrhage with aspirin because of the high likelihood of having an underlying gastric ulcer or a drug-drug interaction. Aging alters the absorption, distribution, metabolism and excretion of many drugs; elderly patients are often prescribed multiple drugs for different conditions, making them susceptible to major drug-drug interactions (Calverley et al., 2001). Concomitant use of low-dose aspirin and NSAIDs at high doses puts patients at high risk of upper gastrointestinal bleeding (de Abajo et al., 2001). A 12-month, double-blind, ran domised placebo-controlled trial evaluated the ad verse effects of enteric-coated aspirin (100mg daily) in 400 healthy subjects aged >70 years without preexisting vascular disease at the time of entry. Gastrointestinal symptoms were reported by 18% of aspirin-treated subjects and 13% of those receiving placebo (RR = 1.4, $p = 0.08$). Corresponding values for the occurrence of clinically overt gastrointestinal bleeding were 3% and 0%, respectively, and the mean hemoglobin level decrease was higher in patients receiving aspirin than in those receiving placebo (0.33 g/dL vs 0 g/dL, $p < 0.05$). Faulkner et al. (1988) indicated in a case-control study of 230 patients aged ≥60 years with bleeding ulcers that sub jects on aspirin were 2–3 times more likely to be admitted to hospital with bleeding ulcers than those aged <60 years.

In order to quantify the effect of aspirin on the risk of hospitalization for GI bleeding among an elderly nursing home population, Quilliam et al. undertook a case-control study involving 3433 patients with a first hospitalization for a bleed and13 506 control individuals. After adjustment, the odds of aspirin use were not significantly different between cases and controls. Although present, the risk associated with use of aspirin is small. The number needed to treat to harm one resident with aspirin was 467 (Quilliam et al., 2001). In a case-control study in patients aged 40–79 years, de Abajo and Garc´ ia Rodr´ iguez et al. observed that the use of low-dose aspirin for prophylaxis of cardiovascular disorders increased the risk of upper gastrointestinal bleeding in the general population by 2-fold for all age categories (de Abajo et al., 2001). Concerning the risk of hemorrhagic stroke with aspirin therapy, the analysis of He.J. et al. (1998) estimated it to be 12 events per1000 persons receiving aspirin, irrespective of participants characteristics. In summary, the risk of bleeding with aspirin>325 mg/day seems to be dose-related in young and old patients; it may be greater in older subjects because they require more prolonged treatment with aspirin. It is difficult to determine whether the higher incidence of adverse events of aspirin detected in elderly is due to the age of the patient or to comorbid conditions or associated treatments.

Conclusion

Cardiovascular disease (CVD) is a group of general category diseases that affects the heart and the circulatory system. CVD is caused by disorders of the heart, blood vessels that includes coronary heart diseases (CHD), congestive heart failure (CHF), stroke, Hypertension (HTN), peripheral artery disease (PAD) and rheumatic heart disease (RHD). Throughout the world high morbidity and mortality is associated with CVD. Coronary artery disease (CAD) is mainly due to atherosclerosis (plaque in artery walls) of the inner lining of the blood vessels that supply blood to the heart. Prevalence shows more male suffered from CAD and age group of 60-70years with the significant risk factor of alcoholic (20.66%) and smoker (11.34%).

Regarding co-morbidity where aspirin was used, 34.67% of patients had CAD with HTN and 26.67% patients had CAD alone. Aspirin was mostly indicated for ischemia (33.33%) and Myocardial infarction (32%), among them 150 mg of aspirin was highly used 50.67% followed by 75 mg 44%. Summarily, 150 cases were evaluated for antiplatelet activity of aspirin in the prevention of cardiovascular disease in a tertiary care hospital. In this study, it was observed that the risk for coronary artery disease increased with increasing age. Hypertension and diabetes were the most common co-morbid conditions associated with coronary artery disease. The most commonly prescribed drug classes for main indications in coronary artery disease were anti-platelet drugs 169 (99.41%) followed by anti-hyperlipidemias 110 (73.33%), PPI drug 105(70. %) . Since 58.67% of prescription consist of aspirin in combination with other Antiplatelet drugs when compared with aspirin alone (41.33%), combination drug seems to be more effective in CAD patients.

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