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Original Research Paper

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AN OBSERVATIONAL STUDY TO ASSESS THE GASTROINTESTINAL SIDE EFFECTS OF LOW DOSE ASPIRIN THERAPY FOR PRIMARY AND SECONDARY PREVENTION OF CARDIOVASCULAR EVENTS

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ABSTRACT

Cardiovascular disease is a leading cause of mortality in many parts of the world. Low-dose aspirin is widely used for the prevention of cardiovascular disease and is a standard measure of therapy for primary and secondary prevention of CVD. Aspirin is associated with upper gastrointestinal side effects including ulcers and bleeding.This study has been undertaken with an aim of assessing the occurrence of upper GI side effects with low dose aspirin in a tertiary care setting .

Materials and methods : An observational study on 106 patients who were on low dose aspirin therapy was done to assess the occurrence of various gastrointestinal side effects . Patients who were on low dose aspirin therapy for both primary and secondary prevention of CVD were included in the study.

Results : Out of the total 150 patients assessed who were on low dose aspirin therapy, 106 patients had gastrointestinal side effects. 18.86% had dyspepsia, 21.69% had nausea alone , 16.98% had both nausea and vomiting , 0.94% had an episode of haematemesis , 30.18% had heartburn ,11.32% patients had heartburn and ulceration. No incidence of major GI bleeding was noted . 60.37% patients were on concomitant proton pump inhibitor therapy. 32.18% had recovered after therapy while 56.25% were found to be recovering.

Conclusion : It was found that dyspepsia ,nausea , vomiting , heartburn and ulceration were the commonly occurring side effects among patients treated with low dose aspirin therapy. Proton pump inhibitors were used to overcome the aspirin induced GI side effects . The side effects were found to have reduced after PPI therapy .

KEYWORDS : CVD, Low dose aspirin , GI side effects, proton pump inhibitors

Low-dose aspirin reduces the cardiovascular risk and is recommended for the primary and secondary prevention of myocardial infarction and stroke. The use of low-dose daily aspirin, typically in the range of 75–325 mg/d, continues to rise as a result of increasing evidence of its benefits in primary and secondary prevention of cardiovascular events.[1] Aspirin causes irreversible acetylation of platelet COX and inhibition of platelet function. It is the permanent suppression of platelet TxA_2 formation that is thought to underlie the cardioprotective effect of aspirin.[2]Aspirin reduces the risk of serious vascular events in high-risk patients especially in patients with previous myocardial infarction by 20%–25%. For primary prevention, this absolute risk must be carefully weighed against the benefits of aspirin ; such assessments are currently limited by a lack of data from general populations.[3]Aspirin in regular doses may result in epigastric distress, heart- burn, dyspepsia, nausea, vomiting , can cause erosive gastritis and GI ulceration along with serious haemorrhage .[4,5,6] Even low-dose aspirin (≤100 mg/d) can result in such adverse events [7] and studies have also pointed out that low-dose aspirin is associated with a lower risk for GI adverse events than higher doses.[8]Also low doses of aspirin have been shown to increase the incidence of serious GI bleeds and intracranial bleeds in placebo-controlled trials.[9] But since the overall benefits from the use of low dose therapy is more in comparison to the risk of side effects, most often the therapy is continued despite occurrence of side effects . Drugs to reduce the GI side effects like PPI can prevent discontinuation of therapy . This study has been undertaken to assess the various GI side effects of low dose aspirin therapy and usefulness of the intervention with PPI therapy in reducing the side effects .

Materials and Methods:

An observational study was conducted on 150 patients to assess the GI side effects of low dose aspirin therapy in a tertiary care setting in Chennai. The trial protocol was submitted to the institutional ethics committee and the study was initiated on approval from the institutional ethics board. A total of 106 patients who were found to have various gastrointestinal side effects were included for assessment . Patients who were on low dose aspirin therapy for both primary and secondary prevention of CVD were included in the study.

The various demographic particulars of the patients including age, sex, clinical diagnosis, the treatment given, drugs administered, details of route of administration of the drugs and dosing were recorded. All the ADRs that were reported were included along with the period of report of the effect and the treatment measures along with further prevention strategies undertaken were noted and analysed. The details on co administration of other drugs and possible drug interactions was also assessed along with history of comorbid conditions. The severity assessment, causality assessment and outcome assessment of the ADRs were done.

Results :

Descriptive statistics was used for analysis and the data was analysed using percentage calculations. Out of the total 150 patients assessed who were on low dose aspirin therapy, 106 patients had gastrointestinal side effects. 79 were male patients and 27 were female patients . The male patients were in the age group of 42 to 72 and female patients were in the age group of 53-68. 20 patients had dyspepsia, 23 patients had nausea alone , 18 patients had both nausea and vomiting , 1 patient had an episode of haematemesis , 32 patients had heartburn ,12 patients had heartburn and ulceration. No incidence of major GI bleeding was noted . 36 patients were on propton pump inhibitor (PPI) therapy. 28 patients had stopped PPI after initial therapy . The therapy was withdrawn for a brief period of time in the patient with haematemesis and was reintroduced with PPI therapy.

The adverse drug reactions(ADR) were assessed using the Hartwigs criterion and the causality assessment was done using the Naranjos probability scale of assessment. The outcome of the ADR was recorded as not recovered, recovered, recovering, and unknown.

DISCUSSION

Aspirin has been shown to be effective as a preventive therapy among patients at risk of developing CVD (primary prevention) as well as among patients who suffer from one or more CVD events (secondary prevention). [10,11,12]

This study was undertaken to assess the various GI side effects of low dose aspirin therapy and to assess the usefulness of the intervention with PPI therapy in reducing the side effects so that it is

possible to outweigh benefit vs risk . Patients who were on low dose aspirin therapy for both primary and secondary prevention of CVD were included in the study. The data obtained was analyzed with reference to the various demographic details, severity of the adverse drug reactions , the causality assessment using the Naranjo scale and assessment of the outcome of the various adverse drug reactions after treatment with proton pump inhibitors . A total of 150 patients on low dose aspirin therapy were assessed. 106 patients were found to have gastrointestinal side effects. The prevalence of GI adverse effects was estimated to be 71%. There was a male preponderance to the occurrence of side effects . It was found that 74.52 % were male patients and 25.47 % were female patients . The male patients were in the age group of 42 to 72 and female patients were in the age group of 53- 68.

It was found that dyspepsia ,nausea , vomiting , heartburn and ulceration were the commonly occurring side effects among patients treated with low dose aspirin therapy. The patients were also found to be treated with other standard medications for the primary conditions .

Table :1 Gastrointestinal side effects associated with low dose aspirin therapy (n=106)

ADR	Frequency	Percentage (%)	No.treated with PPI	(%)
Dyspepsia	20	18.86	3	15
Nausea	23	21.69	-	-
Nausea & vomiting	18	16.98	18	100
Mild Haematemesis	1	0.94	1	100
Heart burn	32	30.18	30	93.7
Heart burn & ulceration	12	11.32	12	100
Major GI bleeding	Nil		-	

Factors associated with an increased risk of upper GI complications during low-dose aspirin therapy include aspirin dose, history of ulcer or upper GI bleeding, age > 70 years, concomitant use of NSAIDs (including COX-2-selective NSAIDs), and Helicobacter pylori infection. Proton pump inhibitors were used to overcome the aspirin induced GI side effects . Studies have pointed out that co-administration of a gastroprotective agent such as proton pump inhibitors (PPIs) may be useful for alleviating the upper GI side effects associated with use of low-dose aspirin.[13]

18.86%patients had dyspepsia, 21.69% patients had nausea alone , 16.98% patients had both nausea and vomiting , 0.94% patients had an episode of haematemesis , 30.18% patients had heartburn ,11.32% patients had heartburn and ulceration. No incidence of major GI bleeding was noted .(Table 1) The most common ADRs associated with the use of low dose aspirin was heart burn.The adverse drug reactions were classified as mild, moderate and severe using the ADR severity assessment scale of Hartwigs.[14] 69.81% were of mild nature, 23.58% were of moderate type and 6.60 of severe nature.(Table 2) Majority of the reactions were of mild severity.

Table 2: Hartwigs severity scale (n=106)

Severity	Frequency	Percentage (%)
Mild	74	69.81
Moderate	25	23.58
Severe	7	6.60

The causality assessment was done using Naranjo causality assessment scale . The Naranjo Algorithm is a questionnaire designed by Naranjo et al for determining the likelihood of whether an ADR is actually due to the drug rather than the result of other factors. It is also called the Naranjo Scale or Naranjo Score.[15] 17.92% were found to be definite , 30.18% were probable and 51.88% were possible natured. (Table3)

Table 3: Causality assessment (n=106)

Causality	Frequency	Percentage
Definite	19	17.92
Probable	32	30.18
Possible	55	51.88
Doubtful	-	-

A total of 64 patients received treatment with proton pump inhibitors for the adverse effects. 32.81% recovered, 56.25 % were found to be recovering and in 10.93% the outcome was unknown.(Table 4) The low dose therapy was withdrawn for a brief period of time in the patient with haematemesis and was reintroduced with PPI therapy. The side effects were found to have reduced after PPI therapy .

Table 4: Outcome assessment (n= 64)

Outcome	Frequency	Percentage
Not recovered	-	-
Recovered	21	32.81
Recovering	36	56.25
Unknown	7	10.93

Conclusion:

It was found that dyspepsia ,nausea , vomiting , heartburn and ulceration were the commonly occurring side effects among patients treated with low dose aspirin therapy. Proton pump inhibitors were used to overcome the aspirin induced GI side effects . The side effects were found to have reduced after PPI therapy.

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