Original Article

Non-Steroidal Anti-Inflammatory Drugs: Identifying the Risk Factors in the Patients

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ABSTRACT

OBJECTIVE: The objective of this study was to identify the risk factors in NSAID users.

STUDY DESIGN AND SETTING: Comparative prospective study, performed at the Department of Pharmacology and Therapeutics BMSI, JPMC with the collaboration of Departments of Medicine and Rheumatology JPMC Karachi from February 2008 to August 2008.

MATERIALS AND METHODS: This study was performed on endoscopically diagnosed patients of NSAID induced peptic ulcers, in whom a clinical trial was performed between Ranitidine (H2 Receptor blocker) and new proton pump inhibitor Esomeprazole. Eighty Patients were selected and evaluated for presence of risk factors and dyspepsia after consumption of NSAIDs or low dose aspirin for last 6 months to 1 year. They were asked to fill in a specially designed proforma regarding the use of NSAIDs, which also included the questions for their social setup, habits and diseases for which they were taking them. All the patients were tested for presence of H. pylori infection and anti-H. pylori IgG antibody titers were determined by enzyme-linked immunosorbent assay. Patients taking anticoagulants and steroids were excluded from the study.

RESULTS: Important factors that have been shown to increase the risk of NSAID-associated GI complications in our study included female gender (76%) presence of H.pylori infection (71%), combination of two NSAIDs (23.75%) and high-dose NSAID use (20%). Other factors that may increase risk include social habits like heavy consumption of tea (30%), pan or Gutka consumption (8.75%). Current evidence supports that H. pylorus potentates the risk of NSAID-induced gastrointestinal ulcers or clinical events, and a strategy of H. pylori testing and treatment in NSAID users may be adopted.

CONCLUSIONS: The incidence of NSAID related gastrointestinal problems was present in 10-15% of patients who belonged to high risk group. Identifying them is strongly recommended to avoid serious complications. H. pylori infection may also be eradicated before initiating NSAID therapy.

KEY WORDS: Non-steroidal anti-inflammatory drugs (NSAIDs), Helicobacter pylori (H. pylori), Gastrointestinal (GI).

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the pharmaceutical agents which are widely used in general medical practice, highly effective in relieving the pain and inflammation associated with osteoarthritis and rheumatoid arthritis,[1-3] but it is well recognized that these agents are associated with substantial gastrointestinal effects which are harmful to the patients.[4,5] NSAIDs affect locally due to diffusion and ion trapping; and systematically by inhibition of prostaglandins, which plays a protective role in the stomach.[6-8] Treatment guidelines suggest that patients with one or more risk factors for NSAID associated ulcers should be prescribed preventive treatment[2]. Despite these recommendations, gastroprotective strategies (e.g. acid suppressive drugs or gastroprotective agents) appear to be under-utilized in patients who receive NSAIDs. A study conducted in the Netherlands, using data from early 1996 to mid-2002, found that only 7.9% of NSAID users during this time period received a preventive therapy. Of these, 6.6% received gastroprotective agents, and an additional 1.3% received COX-2 inhibitors. A greater percentage of patients with one or two risk factors for upper gastrointestinal injury received gastroprotective drugs but over 80% of these patients were provided with no preventive strategy. A large treatment gap persists, despite an increase in the overall prevalence of use of gastroprotective strategies from 5.1% in 1996 to 15.9% in 2002.[3] Despite their inherent problems, traditional NSAIDs are consumed on a daily basis by more than 30 million people worldwide, and they account

for a vast number of prescriptions, around 20 million annually in the UK and 70 million annually in the US.[4] Multiple strategies are available to reduce the risk for NSAID associated gastrointestinal complications. First, risk may be reduced by using non-NSAID analgesics. Second, use of the minimum effective dose of the NSAID may reduce risk. Third, co-therapy with a proton pump inhibitor or misoprostol may be desirable in at-risk patients. Fourth, use of cyclo-oxygenase-2 inhibitors (after evaluating its safety in particular case) may also reduce the risk for gastrointestinal events, although this benefit is eliminated in patients who receive aspirin and cyclo-oxygenase-2 inhibitors as it negates the gastrointestinal benefits of these drugs[2,4-6].

MATERIALS AND METHODS

This study was conducted from February 2008 to August 2008 at the Department of Pharmacology and Therapeutics BMSI, JPMC with the collaboration of Department of Medicine and Rheumatology Jinnah Post Graduate Medical Centre, Karachi. The study was performed on endoscopically diagnosed patients of NSAID induced peptic ulcers, in whom a clinical trial was performed between Tablet Ranitidine 300-mg twice a day (H_2 Receptor blocker) and new proton pump inhibitor Esomeprazole 40-mg OD. Patients were evaluated on day 1, day 15, day 30, day 45 and day 60 for relief of dyspepsia by monitoring their gastrointestinal symptom rating scale (GSRS) and for healing of peptic ulcers by upper gastrointestinal endoscopy at day 1 and day 60. Patients were asked to fill a specially designed proforma regarding the use of NSAIDs, which also included the questions for their social setup, habits and diseases for which they were taking them. All the patients were tested for presence of H. pylori infection and anti-H. Pylori IgG antibody titers were determined by enzyme-linked immunosorbent assay.

Patients of either sex, age between 40-75 years, with history of using NSAIDS or low dose aspirin for at last 6 months to 1 year, or those giving history of dyspepsia and severe heart-burn following the use of non-selective NSAIDS were also included.

Patients suffering from other gastrointestinal problems e.g. esophagitis, gastric carcinomas, patients with impaired renal function and liver diseases and those taking anticoagulants or steroids were excluded from the study.

RESULTS

Among 80 study subjects 19 (23.75%) were males and 61 (76.25%) were females. Important factors that have been shown to increase the risk of NSAID-associated GI complications in our study included, increasing age, female gender (76%) presence of H.pylori infection (71%), combination of two NSAIDs (23.75%) and high-dose NSAID used (20%). Other factors that may increase risk include social habits like heavy consumption of tea (30%), pan or Gutka consumption (8.75%) **Table I**. Patients using non-selective NSAIDs for 6 months to 1 year were more prone to develop the complication. The most common disease in terms of prescription of NSAIDs was Osteoarthritis (37.5%). Other reasons for NSAID prescription are detailed in **Table II**. The non-selective NSAIDS which were commonly prescribed for a vast range of indications were Diclofanec (30%) followed by Ibuprofen (20%) and Aspirin (20%) as detailed in **Table III**. Fifty percent patients were found to be using them over the counter. Presence of H.pylori infection was commonest risk factor and this association was found to be positive in 54 (71%) and negative in 24 (30%) patients.

TABLE I:
RISK FACTORS ASSOCIATED WITH PATIENTS

Risk Factor	No of Patients
Tea or coffee consumption	24 (30.0%)
Two NSAIDs combined	19 (23.75%)
High doses of NSAIDs	16 (20.0%)
Duration of NSAIDs use >6 months	14 (17.50%)
Pan or gutka consumption	07 (8.75%)

TABLE II:
DISEASES FOR WHICH NSAIDS WERE PRESCRIBED

Diseases	No. of Patients
Osteoarthritis	30 (37.5%)
Rheumatoid Arthritis	22 (27.5%)
Orthopedic reasons	13 (16.2%)
Gynecological disorders	08 (10%)
Headaches/Body aches	05 (6.25%)
Fever	02 (3.2%)

TABLE III:
COMMONLY USED NSAIDs

Name of Nsaid	No. of Patients
Diclofanec	24 (30%)
Ibuprofen	16 (20%)
Aspirin	16 (20%)
Naproxen	10 (12%)
Indomethacin	08 (10%)
Mefenamic acid	06 (8%)

DISCUSSION

Although a small proportion of patients who use NSAIDs can develop the complications related to GI tract, but as these drugs are used extensively so this small proportion turns out to be a large absolute number [6]. Drugs like NSAIDs can hardly be avoided in patients of arthritis as these drugs not only relieve the agony of pain which cripples the quality of life and causes emotional and psychological stress to these patients but also decrease the inflammation and swelling. Aspirin is also widely used for its antiplatelets action in patients of myocardial infarction and stroke.

The GI related complications are seen in 10-15% of patients and are common in association with H.pylori infection.[8] Females suffer more than males probably because they develop Rheumatoid arthritis more frequently as compared to males and after menopause the incidence of osteoporosis is also increased.

Helicobacter pylori infection in NSAID users is associated with an increased ulcer incidence. The result that H.pylori infection is a risk factor for peptic ulcers in patients receiving NSAIDs is consistent with the studies conducted by Chan et al, Davidovic et al and Yajima H et al.[9-11] According to AGA (American Gastroenterologists Association) recommendations to gastroenterologists, a consensus panel called for consideration of routine screening for Helicobacter pylori infection for all patients at high risk of gastrointestinal complications about to initiate NSAID therapy.

Patients who used these drugs at high doses or in combination for longer durations are more prone to develop this disease[6].

SUGGESTIONS

While prescribing these drugs indications and risk factors for both GI and cardiovascular complications should be carefully reviewed. The drugs with low profile for side effects may be prescribed along with antisecretory and gastro-protective agents. Duration and dosage of these drugs should be monitored in high risk patients. Combination of two non-selective NSAID therapy should be avoided.

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