RESEARCH ARTICLE

Incidence of non-steroidal anti-inflammatory drugs induced gastric discomfort in patients with knee osteoarthritis

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Abstract

Background: Osteoarthritis is an age related degenerative disease seen predominantly in the elderly. Non-steroidal anti-inflammatory drug (NSAID) is a major therapeutic component in the management of osteoarthritis. Selective NSAID was developed to reduce the incidence of gastric irritation and erosion caused by the regular NSAIDS.

Methods: All elderly patients with clinical and radiographic features of osteoarthritis were included in the study. Some patients were placed on regular NSAIDS while others were placed on selective NSAIDS, being randomly selected. The trial was carried out in a private clinic over three years. Proton pump inhibitor was added as soon as patients complain of abdominal discomfort.

Results: Osteoarthritis was made up of 30.9 % of the total rheumatology cases seen over the three years period. Both patients on non-selective and selective NSAIDS presented with gastric discomfort. Symptoms were more noticeable in patients on non-selective NSAIDS. Females were more affected. Only two patients (2.1%) presented with symptomless gastro-intestinal bleeding. Proton pump inhibitor was helpful in majority of patients.

Conclusion: Gastric discomfort is very common in elderly patients on NSAIDS. Selective NSAIDS is not an exception though better than non-selective NSAIDS. Contributory factors may be co-intake of low dose aspirin and few others on corticosteroid and anticoagulant.

Key words: NSAIDS, Gastric discomfort, Osteorthritis, Elderly.

Introduction

Peptic ulcer disease is a heterogeneous group of disorder involving the gastrointestinal tract and results from an imbalance between the aggressive forces of acid and pepsin and the defensive mechanism of the gastric mucosa[1-3]. There has been a decline in the prevalence of uncomplicated peptic ulcer disease since the discovery of *Helicobacter pylori*, however, among the elderly people has been found a rise in admission for ulcer haemorrhage and perforation. The rise has been attributed to the increased use of NSAIDS and low dose aspirin[4]. Symptoms usually do not correlate with the severity of mucosa damage. Elderly patients however need to understand the prudent use of NSAIDS to prevent serious complications[5,6]. NSAIDS are commonly prescribed for a variety of musculoskeletal conditions such as rheumatoid arthritis, systemic lupus erythematosus and osteoarthritis[7].

NSAIDS cause damage to the gastric mucosa through inhibition of gastric prostaglandin synthesis. The inhibition leads to the reduction in the level of protection of the gastric mucosa by the prostaglandin (PGE2, PGI2) and also leads to alteration in mucus and bicarbonate production as well as blood flow into the gastric mucosa, all of which are prostaglandin dependent functions[8]. When NSAID is taken orally, it dissociates in the gastric lumen and concentrates in the gastric mucosa. Once within the gastric mucosa cell, acidic NSAID inhibit prostaglandin production and prostaglandin dependent cell protection function[9]. NSAID gain access to the gastric mucosa via three routes. Direct contact of the ingested drug with the gastric mucosa, indirect route via secretion in the bile and backward reflux into the stomach, and systemic route via circulation in the blood[10].

Materials and Methods

Elderly patients aged 50 years and above that presented with clinical and radiological features of knee osteoarthritis were included in the study. Exclusion criteria include- known ulcer patients, past history of ulcer disease or gastrointestinal

bleeding, and patients on concomitant anticoagulant or steroid. All rheumatology cases seen over 3 years were noted and all cases of primary osteoarthritis of the knee were extracted and the percentage of knee osteoarthritis in the total rheumatology cases determined. Patients were randomly selected, some were placed on regular NSAIDS (diclofenac, ibuprofen), and others on selective NSAID (e.g. Celebrex). Patients that developed symptoms of gastric irritation were given proton pump inhibitor (omeprazole).

Results

Osteoarthritis represented 30.9% of the total cases seen over 3 years. Gastrointestinal disturbances were noted in both groups (regular and selective NSAIDS). The disturbances were more noticeable in patients on regular NSAIDS. Total of 84 patients presented with gastrointestinal disturbances (80.8%), 24 males (28.6%) and 60 females (71.4%). Proton pump inhibitor was helpful in majority of symptomatic patients. Two patients (1.9%) however presented with symptomless gastrointestinal bleeding while eight patients (7.7%) were lost to follow-up.

Discussion

There are so many people on NSAIDS both prescribed and over-the-counter consumption[11]. There is an increased prevalence of NSAIDS induced gastrointestinal injury because of widespread use of the drug[12]. The readily availability of NSAIDS as over-the- counter medications adds to the incidence of gastrointestinal injury because people tend to consume more than the recommended doses[13]. Some of the studied patients combined two or more NSAIDS.

The pathogenesis of NSAID- induced gastrointestinal mucosa injury is complex[14,15]. The direct-injury hypothesis suggests that both NSAID-mediated direct acidity damage and the suppression of prostaglandin synthesis are necessary to induce gastric damage[14]. The first insult to the gastro-duodenum mucosa is as a result of the acidic property of the NSAIDS, and the later mucosa damage is as a result of active hepatic metabolites of NSAIDS and the NSAID-related decrease in the gastric mucosa prostaglandins[14,15]. When the hepatic metabolites in the bile are secreted into the duodenum, they cause mucosa damage to the stomach by duodenogastric reflux and to the small intestine by antegrade passage through the gastrointestinal tract[15].

Prostaglandins maintain an intact gastric mucosa barrier by increasing secretion of mucus and bicarbonate maintaining mucosal blood flow, and decreasing acid-secretion[16]. Suppression of prostaglandin synthesis can occur systemically with both oral and parenteral NSAID therapy[16]. The antiplatelet activity of some NSAIDS in low doses may cause bleeding from pre-existing ulcers[17]. There are two isoforms of the enzymes cyclo-oxygenase (cox) and NSAIDS inhibit both isoforms[18]. The isoform cox1 produces protective prostaglandins in the stomach and the isoform cox2 is inducible at sites of inflammation[19,20]. Researchers have developed a new type of NSAIDS that specifically inhibits cox2 while sparing cox1[19]. Selective inhibitors should theoretically provide analgesics and anti-inflammatory effects of older NSAIDS with a reduced risk of gastro-intestinal injury. It was however found out that the selective cox2 are not completely devoid of gastric mucosa injury[20].

When NSAIDS irritate the gastric mucosa, they weakens the resistance to acid, causing gastritis, ulcers, bleeding, or perforation[21]. The damage ranges from superficial injury to single or multiple ulcers, some of which may bleed. The clinical manifestations seen in our patients include dyspepsia, nausea and vomiting. Only very few presented with diarrhea. Two patients however presented with symptomless gastro-intestinal bleeding. The clinical features however do not correlate with the severity of the mucosa damage[22]. The NSAIDS differ with regard to their risk of inducing upper gastro-intestinal bleeding and or perforation[23,24].

Elderly patients are especially at risk for NSAID-induced gastro-duodenal mucosa injury because of their multiple medical conditions and polypharmacy. Risk factors include concomitant corticosteroid or anticoagulant therapy[25]. Patients with a history of peptic ulcer disease and gastritis are also at risk[26].

The prevalence of endoscopically confirmed gastro-intestinal ulcers in NSAIDS users is quoted to be between 15 and 30%. Between 12 to 30% of NSAID induced ulcers are gastric ulcer, whereas 2 to 19% are duodenal ulcers. NSAID-induced ulcers are symptomatic only in 1% of patients after 3 to 6 months and in 2 to 4% of patients after one year[27]. This study has shown that 8 out of 10 elderly patients on prolonged NSAIDS eventually develop some degree of gastro-intestinal discomfort, and that the symptoms are more noticeable in elderly women. It is therefore advisable that drugs causing gastro-intestinal toxicity as a consequence of a systemic effect should be co-prescribed with suitable prophylactic agents such as proton pump inhibitors and misoprostol in elderly patients[28,29]. The importance of gastro-protection is vital in preventing patient morbidity and mortality especially in patients with a number of risk factors which include patients over the age of sixty years, smokers, patients with a history of peptic ulcer disease, or concomitant use of anti-coagulants, bisphosphonates, or corticosteroids.

Table 1: Spectrum of rheumatology cases seen over 3 years (July 2009- June 2012)

Serial No.	Condition	Number	Male	(%)	Female	(%)
1	Osteoarthritis	104	32	30.8	72	69.2
2	Rheumatoid arthritis	12	4	33.3	8	66.7
3	Cervical spondylosis	36	23	63.9	13	36.1
4	Lumbar spondylosis	25	21	56	14	44
5	Low back pain	48	37	77.1	11	22.9
6	Gout	28	22	78.6	6	21.4
7	SLE	6	1	16.7	5	83.3
8	Shoulder pain syndrome	12	4	33.3	8	66.7
9	Hypermobility syndrome	8	0	0	8	100
10	Fibromyagia	6	0	0	6	100
11	Polymyalgia rheumatica	2	0	0	2	100
12	Bursitis	4	3	75	1	25
13	Trigger finger	16	6	37.5	10	62.5
14	Sjorgren's syndrome	1	0	0	1	100
15	Reiter's syndrome	1	1	100	0	0
16	Septic arthritis	2	0	0	2	100
17	Lateral epicondylitis	2	2	100	0	0
18	Medial epicondylitis	2	2	100	0	0
19	Scleroderma	2	0	0	2	100
20	Psoriatic arthropathy	1	1	100	0	0
21	Plantar fasciitis	7	2	28.6	5	71.4
22	Carpal tunnel syndrome	3	1	33.3	2	66.7
23	Archilis tendinitis	8	1	12.5	7	87.5
	Total	336	160		176	

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