The incidence of Non Steroidal Anti-Inflammatory drugs as a causative agent of peptic ulcer diseases.

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Abstract

Non steroidal anti-inflammatory drugs(NSAIDs) it is anti-inflammatory drugs .Many people take an anti-inflammatory drug for arthritis, muscular pains & to protect against blood clots form. These drugs sometimes affect the mucus barrier of the stomach and allow acid to cause an ulcer. About 2 in 10 stomach ulcers are caused by anti-inflammatory drugs. The discovery that the primary mechanism behind NSAID-associated upper GI side-effects was through systemic inhibition of COX-1-mediated prostaglandin synthesis in the gastric mucos. COX-2 selective NSAIDs, continues to carry significant risk of injury to the gastro-duodenal mucosa possibly because COX-2 selective NSAIDs are not totally COX-2 specific, but also inhibit COX-1 to a certain degree. Acidic NSAIDs, including aspirin, may also have a topical irritant effect on the gastric mucosa. Indeed, there is evidence of significant localized foci and damaged cells only 16 minutes after administration of aspirin. Patients & methods.A three hundred-forty four patient including by this study all of them complaining of signs symptoms of peptic ulcer & the diagnosis confirm by endoscopy examination .Results:- A 170(49.4%) patients with gastric ulcer & 174(50.6%) patients with duodenal ulcer. A gastric ulcer patients. A forty seven (27.65%) patients were consider as NSAIDs users .the duration of using NSAIDs was divided into acute(less than 3 months) & chronic states so 28(59.6)% was acute user while 19(40.4)% was chronic user .A duodenal ulcer patients . A twenty-two (12.7%) patients were consider as NSAIDs users .the duration of using NSAIDs was divided into acute & chronic states so 12(54.5)% was acute user while 10(45.5)%was chronic user . A significant difference was detected between gastric ulcer & duodenal ulcer which indicate that NSAIDs mostly cause gastric ulcer than duodenal ulcer & this is due to the fact that these agents affecting the defense mechanism of gastric mucosa in both topical & systemic administration. Conclusion:-A high causing rate of NSAIDs in inducing peptic ulcer .Reducing the administration of analgesia as possible as & to be limiting to really indication .It is better to used anti-ulcer agent in combine with the NSAIDs agents especially in long term therapy .

Key words:-peptic ulcer, non-steroidal anti-inflammatory drugs.

Introduction

Non steroidal anti-inflammatory drugs (NSAIDs) are anti-inflammatory agents. There are various types and brands. For example: aspirin, ibuprofen etc. Many people take an anti-inflammatory drug for arthritis, muscular pains, etc. Aspirin is also used by many people to protect against blood clots forming. These drugs sometimes affect the mucus barrier of the stomach and allow acid to cause an ulcer. About 2 in 10 stomach ulcers are caused by anti-inflammat -ory drugs. NSAIDs are among the most widely used drug in the world (**1**)., particularly common among elderly patients; approximately 10–20% of those aged 65 years or over have a current or recent prescription(**2**) . A study conducted in primary care practices in the UK found that the number of NSAID prescriptions per month increased steadily with age, with the highest NSAID use among those over 75 years (**3,4**) .The major problem with NSAIDs is the occurrence of side-effects, which primarily affect the GI system, but also the renal and cardiovascular systems.**(5)** Indeed, non-selective NSAIDs account for approximately 25% of all reported drug adverse events in the UK(**6**) . As these drugs are commonly used in the elderly, their side-effects can pose a significant risk these (**7**)..

NSAIDs inhibit the COX enzyme, which exists in two forms , thus suppressing the transformation of arachidonic acid to

prostaglandins.(8) This action is central to their anti-inflammatory and analgesic properties. COX exists in two isoforms: COX-1, which is constitutively expressed in most tissues ,producing prostaglandins that regulate normal cell activity; and COX-2, which is virtually undetectable in most tissues under normal physiological conditions, but can be induced in the presence of inflammation, tissue damage or malignant transformation (8–10).The anti-inflammatory effects of NSAIDs appear to be largely attributable to inhibition of COX-2, and their upper GI side-effects to inhibition of prostaglandin synthesis in the gastric mucosa, mediated via COX-1.(8–11)

The discovery that the primary mechanism behind NSAID-associated upper GI side-effects was through systemic inhibition of COX-1-mediated prostaglandin synthesis in the gastric mucosa provided the rationale for the development of COX-2 selective NSAIDs, which might be expected to reduce the risk of upper GI toxicity, while retaining the beneficial anti-inflammatory effect. The use of NSAIDs, including COX-2 selective NSAIDs, continues to carry significant risk of injury to the gastro-duodenal mucosa. (12) This is possibly because COX-2 selective NSAIDs are not totally COX-2 specific, but also inhibit COX-1 to a certain degree. Furthermore, studies in rats have shown that gastric mucosal damage requires inhibition of both COX-1 & COX-2(13,14) . **Systemic and topical effects of NSAIDs decrease gastric mucosal defenses'** .Several components of gastric mucosal defense are influenced through the systemic effects of NSAIDs, including the secretion of mucus and bicarbonate ions. Mucus has an important role in protecting the mucosa from bacterial colonization and mechanical injury, and forms a microenvironment over sites of superficial injury, allowing rapid restitution to occur. By reducing the secretion of mucus and bicarbonate ions, NSAIDs diminish the mucosal defenses to injury . Moreover, NSAIDs adversely affect mucosal blood flow and immunecyte function, which impairs the usually rapid rate of epithelial cell turnover and repair (15,16). Acidic NSAIDs, including aspirin , may also have a topical irritant effect on the gastric mucosa. Indeed, there is evidence of significant localized foci and damaged cells only 16 minutes after administration of aspirin (17) . Topical irritant effects on the epithelium are not, however, as strongly implicated in the development of gastro-duodenal pathology as the systemic effects of NSAIDs (18).. **Gastric acid plays a central role in NSAID-associated gastro-duodenal injury** .The net effect of the systemic and topical effects of NSAID s on the upper GI system is to impair the mucosal barrier to gastric acid, which, together with the corrosive action of pepsin, exacerbates the initial damage, potentially resulting in deeper erosions and peptic ulceration. Intra-duodenal administration of a non-selective NSAID caused marked macroscopic gastric mucosal damage in pylorus-ligated rats when the luminal pH was 2.0 or 4.0, but damage decreased when the luminal pH was raised to 5.5 or 7.0 (19,20). A more recent study has shown that acid plays a key role in the development of acute gastric mucosal lesions in NSAID-treated rats, and that NSAID-induced reduction in gastric mucosal blood flow only occurs in the presence of acid (20). Elevation of the intra-gastric pH is, therefore, key in the management and prevention of NSAID-associated upper GI side-effects. Patients with a Helicobacter pylori infection have an increased risk of bleeding from NSAID-associated peptic ulcers, higher doses and concomitant use of oral anticoagulants and corticosteroids are frequently noted as drug-related risk factors (21-23). The US Food and Drug Administration (FDA) estimated that 2–4% of chronic NSAID users will develop upper gastrointestinal bleeding, a symptomatic ulcer, or an intestinal perforation each year (24). The mortality rate among patients who are hospitalized for NSAID-induced upper gastrointestinal bleeding is about 5–10% (25). Deaths from gastrointestinal toxic effects of NSAIDs are assumed to be the 15th most common cause of death in the United States (26).

The aim of study:-

1- to estimate the incidence of NSAIDs as causative agent in inducing peptic ulcer diseases in Kirkuk city .

2-compare Kirkuk city incidence with the other countries.

Patients & methods

This study carried out in kirkuk city from June 20008 to September 2010 .A three hundred-forty four patient including by this study all of them complaining of signs symptoms of peptic ulcer & the diagnosis confirm by endoscopy examination .A questioner was performed include the following information age , sex, history of arthritis , other joints problems, cardio-vascular diseases , stress , history & duration of taking NSAIDs(acute those take medication for less than 3 months while chronic more than 3 months) & the period between using of NSAIDs & GIT complaining .The patients divided according the endoscopy repot into those with gastric ulcer & those with duodenal ulcer as showed in table -1- .urease test performed on biopsy taken to exclude H-pylori as causative agents of ulceration .

Statistical analysis:-

Its done by using chi-square .

Results

This study was performed on 344 peptic ulcer patients aged 30-72 years (mean = 54.6 years), 123(35.75%) were female & 221(64.25%) were male .A 170(49.4%) patients with gastric ulcer & 174(50.6%) patients with duodenal ulcer .A47(27.65%) out of 170patients with gastric ulcer were NSAIDs users & a twenty two(12.7%) out of 174 pstients with duodenal ulcer were NSAIDs users see table-2-

A gastric ulcer patients , 54(31.8%) were female while 116(68.2%) were male. A forty seven (27.65%) patients were consider as NSAIDs users, A 27(57.4)% were male&20(42.6)% were female .A28(59.6)% was smoker while19(40.4)% was non smokers .A35(74.2%) were under stress & 12(25.5)% consider as stressless .The duration of using NSAIDs was divided into acute & chronic states so 28(59.6)% was acute user while 19(40.4)% was chronic user . According to the reason to use NSAIDs as known it used either due to joints reason (rheumatoid, arthritis …etc) 33(70.2)% while 14(29.8)% their cause to used it cardiovascular or cerebrovascular (anti-thrombic agents) .As showed in table -3-

A duodenal ulcer patients , 69(39.7%) were female while 105(60.3%)were male. A twenty-two (12.7%) patients were consider as NSAIDs users, A 13(59)% were male& 9 (41)%were female .A15 (68.2)% was smoker while 7 (31.8)% was non smokers .A18(81.8)% were under stress & 4 (18.2) % consider as stressless .the duration of using NSAIDs was divided into acute & chronic states so 12(54.5)% was acute user while 10(45.5)%was chronic user . According to the reason to use NSAIDs as known it used either due to joints reason (rheumatoid, arthritis …etc) 17(77.3)%while 5 (22.7)% their cause to used it cardiovascular or cerebrovascular (anti-thrombic agents) .As showed in table -3-.

Discussion

Using of NSAIDs representing the second common cause of peptic ulcer after H-pylori infection . A significant difference was detected between gastric ulcer & duodenal ulcer which indicate that NSAIDs mostly cause gastric ulcer than duodenal ulcer & this is due to the fact that these agents affecting the defense mechanism of gastric mucosa in both topical & systemic administration , this in agreement with others studies (15-16) . the estimating incidence of NSAIDs inducing peptic ulcer is in agreement with (Jurg Metzger ..et al 2001) they estimate that incidence of NSAIDs inducing peptic ulcer up to 32% & in agreement with (Ali E Al-Sanafi, Hassan KH Rijab 2005) they reach to nearly closed results&10–20% of those aged 65 years or over have a current or recent NSAID prescription (2) .

A major causative factor (60% of gastric and up to 90% of duodenal ulcers) is chronic inflammation due to Helicobacter pylori that colonizes the antral mucosa . In patients using NSAIDs with concurrent H pylori infection, the risk for side effects is increased and questionable whether the effects are additive or synergistic. In terms of providing optimal patient care, adequate management of peptic ulcer disease will allow optimization of pain management with NSAIDs, as continuation of these useful medications can provide these patients with increased quality of life and pain control.(29,30, 31).

Almost all deaths from NSAID-related gastrointestinal adverse effects occur in elderly

persons and elderly women seem particularly susceptible (31). Patients with a Helicobacter pylori infection have an increased risk of bleeding from NSAID-associated peptic ulcers (32). Higher doses (22) and concomitant use of oral anticoagulants and corticosteroids (23) are frequently noted as drug-related risk factors

Although there is no significance differences between NSAIDs users & non-users in regarding of sex, stress state , duration of using it , smoking & the reason of using it , but still there is a high percentage to be observe .This may indicate that combination of more than one risk factor increasing the possibility of developing peptic ulcer .

Conclusion

1-A high causing rate of NSAIDs in inducing peptic ulcer .

2-Two causative agent may found together in one patient complaining of peptic ulcer .

Recommendation

1-reducing the administration of analgesia as possible as & to be limiting to really indication .

2-it is better to used anti-ulcer agent in combine with the NSAIDs agents .

3- Haphazard using of NSAIDs may be a real problem facing our community . Education programs for doctors & population are needed .

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Table-1- distribution of patients according to ulcer site :-

Total number	Gastric ulcer	Duodenal ulcer
344	170	174

Table -2-distribution of NSAIDs users & non-users according to ulcer site:-

Patients	Gastric ulcer	Duodenal ulcer	$\chi 2$
NSAIDs user	47 (27.65%)	22 (12.7%)	*
Non-NSAIDs user	123(72.35%)	152(87.3%)	

*** statistical significance(p<0.01)**

Table -3-NSAIDs users according to ulcer site profile :-

NSAIDs user		Gastric ulcer	Duodenal ulcer	χ^2
Sex	Male	27(57.4%)	13(59%)	**
	Female	20(42.6%)	9(41%)	
Smoking	Smoker	28(59.6%)	15(68.2%)	**
	Non-smoker	19(40.4%)	7(31.8%)	
Stress	Under stress	35(74.5%)	18(81.8%)	**
	Not under it	12(25.5%)	4(18.2%)	
Duration of takingNSAIDs	Acute	19(40.4%)	10(45.5%)	**
	Chronic	28(59.6%)	12(54.5%)	
Reason of using NSAIDs	Joints cause	33(70.2%)	17(77.3%)	N*
	Cardiovascular causes	14(29.8%)	5(22.7%)	

** Statistical non significance