

The Prevalence of NSAID related ulcer and Helicobacter pylori related ulcer in Hasan Sadikin General Hospital Bandung Indonesia.

Ali Djumhana *), Sujono Hadi*) and Makmuri Jusuf**)

*)SubDivision Gastroenterohepatology Departement of Internal Medicine

**)Departement of Pathology Anatomy

Hasan Sadikin General Hospital-Medical Faculty University Of Padjadjaran
Bandung – Indonesia

Abstract

Background: NSAID and Helicobacter pylori (Hp) are major causes of gastroduodenal ulcers. Previous study reported that prevalence of Hp in patient who took NSAID were lower than who did not take NSAID. The aim of this study are to compare the prevalence of Hp infection in patients with ulcer and non ulcer in those who took NSAID and did not take NSAID for their medication and to compare the proportion of NSAID related ulcer and Hp related ulcer in patients with gastric ulcer (GU) and duodenal ulcer (DU).

Material and Methods: Between January 1995 and December 1996, a retrospective study was done to 162 patients who were proven to have ulcer and non ulcer by endoscopic examination. Patients were divided into NSAID user group and non NSAID user group based on their drug history. Infection of Hp were tested by CLO and histopathology.

Result and Conclusion: Between January 1995 and December 1996, 162 patients were studied, they consisted of 64 patients with gastroduodenal ulcer (33 GU and 31 DU) and 98 patients without ulcer (NU). Age ranged from 16 to 78 years old, 84 patients were male and 78 patients were female. The median age of GU was 60 years, DU was 48 years and NU was 44 years. Among patients with ulcer, the prevalence of Hp infection was 6/40 (15%) in NSAID users compare to 21/24 (87.5%) in non NSAID user ($p < 0.001$). Among patients NU the prevalence of Hp infection was 13/39 (33.3%) in NSAID users compare to 35/59 (59.3%) in non NSAID user ($p < 0.05$). There was no significant difference of Hp infection between ulcer group and NU group in patients who took NSAID (15% vs 33.3%; $p > 0.05$). Significant difference of Hp infection was found in ulcer group and NU group in non NSAID user (87.5% vs 59.3%; $p < 0.05$). Among patients with ulcer, 34/64 (53.1%) were NSAID user without Hp infection and 21/64 (38.1%) were non NSAID user with Hp infection ($p < 0.05$). Among patients with GU, 28/33 (84.8%) were NSAID user without Hp infection and 2/33 (6%) were non NSAID user with Hp infection ($p < 0.001$). Conversely among patients with DU, 6/31 (19.4%) were NSAID user without infection and 19/31 (61.3%) were non NSAID user with Hp infection ($p < 0.01$). We therefore conclude that prevalence of Hp infection in patients with ulcer and without ulcer who took NSAID were lower than those who did not. The NSAID related ulcer was more frequent than Hp related ulcer. Gastric ulcers were found more frequent in patients with positive NSAID usage, but duodenal ulcers were found more frequent in patients with Hp infection.

Introduction

Most of gastroduodenal ulceration were caused by Hp infection and NSAID, only a small part of them were caused by other etiology such as Zollinger Ellisson Syndrome and Crohn's disease. The use of NSAID in most people is common by the older people, it is related to high prevalence of musculoskeletal disorders. NSAID toxicity in gastrointestinal tract has many forms such as erosion and bleeding, ulcer, perforation and dyspepsia. Gastroduodenal ulcer occurred in more than 25% of patients who took NSAID for long time (1,2). Effect of NSAID to gastrointestinal tract is mainly at gastric mucosa. A case control study showed that gastric ulceration in NSAID user was 3 fold greater than control, but the prevalence of duodenal ulcer in NSAID user was lower than control. This study also reported that the mean age of gastric ulcer and duodenal ulcer were 61 and 47 years, respectively (3). Symptom of NSAID related ulcer is not classical. One study reported that 55% of the patients with ulcers were asymptomatic (4), another study reported that one-third of the patient who developed adverse gastrointestinal event were not classically (5). After Warren and Marshall discovered the Hp, concept of pathogenesis and treatment of peptic ulcer disease changed dramatically. Duodenal ulcer has an association with chronic active gastritis at the antral and body of the stomach. Chronic active gastritis developed after infection of Hp for several years. Contribution of bacterial factors such as virulence, density and host factors such as genetic susceptibility, gastroduodenal microcirculation, alcohol consumption, smoking etc may lead to ulcer formation. Gastric ulcer has an association with atrophic gastritis. Atrophic gastritis developed after long time infection of Hp (6,7). There is no question that NSAID or Hp alone cause clinically relevant ulcers. However a subset of subjects with NSAID induced ulcers with positive for Hp is low. Some studies demonstrated the benefit of Hp eradication before NSAID medication, but other studies reported that no difference in prevalence of ulcers between eradication and non eradication groups (8,9,10,11).

Material and Methods

From January 1995 to December 1996 a retrospective study was done on 162 dyspeptic patients who were proven to have ulcers and non ulcers by endoscopic examination. The study was done at SubDiv. of Gastroenterology Department of Internal Medicine, Dr Hasan Sadikin General Hospital-Faculty of Medicine, University of Padjadjaran Bandung Indonesia.

The inclusion criteria were no antibiotics treatment within the last 2 weeks, no history of bismuth therapy and no H₂ blockers or Proton Pump Inhibitor treatment within the last 2 weeks. NSAID user was patient who took NSAID in at least 8 weeks. Two biopsy specimens were taken from antrum, corpus and fundus. Hp infections were examined by CLO and histopathology. Hp infection was considered when Hp found histopathologically regardless of CLO result. Chi square test was used to compare the prevalence of Hp infection and the proportion of NSAID related ulcers and Hp related ulcers.

Result

Between January 1995 and December 1996, 162 patients were studied, consisted of 64 ulcers and 98 non ulcers patients.(Table 1)

Table.1. Characteristics of patients.

		Ulcer	Non ulcer	
No of patients		64	98	
Age(y)	: range	16 – 78	21 - 72	
	: mean	53.4±14.4	43.7±14.7	p<0.05
Sex	: M	43	43	
	: F	21	55	p<0.01
Smoking	:	20	34	ns
Alkohol	:	0	0	ns
NSAID user:	Hp(+ve)	6(15%)	13(33.3%)	ns
	Hp(-ve)	34(85%)	26(66.7%)	
Non NSAID user :	Hp(+ve)	21(87.5%)	35(59.3%)	p<0.05
	Hp(-ve)	3(12.5%)	24(41.7%)	

The mean age of ulcer group was older than non ulcer group(p<0.05%) and male was more frequent in ulcer group(p<0.01). There was no significant difference of prevalence of Hp infection between ulcer and non ulcer in NSAID user patients (p>0.05).In non NSAID user Hp infection was more prevalent in patient with ulcers(p<0.05).Among patients with ulcer, the difference of Hp infection between NSAID and non NSAID user was highly significant (p<0.001).Of patient with non ulcer, the difference of Hp infection in NSAID and non NSAID user was also significant(p<0.05).

The median age of gastric ulcer,duodenal ulcer and non ulcer 60,48 and 44 years old.(Table. 2.)

Table.2. Characteristic of Gastric ulcer,Duodenal ulcer and Non Ulcer patients

		GU	DU	NU
Median age(y)		60	48	44
Sex	M	23	20	43
	F	10	11	55
NSAID user	Hp(+ve)	2	4	13
	Hp(-ve)	28	6	26
Non NSAID user	Hp(+ve)	2	19	35
	Hp(-ve)	1	2	24

In gastric and duodenal ulcer patients the proportion of male twice fold than female (p<0.01), whereas in non ulcer patients female was more common than male but this not significant statistically (p>0.05).The majority(90%) of patients with gastric ulcer were NSAID user,conversely among patients with duodenal ulcers 70% were non NSAID user.The prevalence of Hp infection among non NSAID users with DU and GU were 91%.and 66.7% respectively

In contrast the prevalence of Hp infection among NSAID users with DU and GU were 40% and 6% ,respectively.

Discussion

Our study found that the mean age of patients with ulcer were older than non ulcer, median age of GU , DU and NU patients were 60,48 and 44 years, respectively. Male to female ratio was 2:1. Russel found that the mean age of GU and DU were similar to our result, but mean age in NU was 54 years. The population of Russell's study were patients with Rheumatoid arthritis(3). The prevalence of Hp infection in ulcer and non ulcer patients who took NSAID were lower than those who did not take, and this result was not difference with other investigators(12,13). Low prevalence of Hp infection in NSAID user is not clear yet. It may be that NSAID had an effect as anti bacteria. Another possibility is that the patient with Hp infection may had dyspeptic symptom more often and therefore avoid taking NSAD. Contribution of Hp infection in ulcer development with patient who was taking NSAID is controversial.

We found that the total NSAID related ulcer more frequent than Hp related ulcer. The proportion of NSAID related ulcer in GU and DU patients were 90% and 30% respectively. Previous study reported tha the proportion of NSAID related GU was 25-30%(1,2). Another study reported that the proportion of DU in NSAID user not difference with non NSAID user (5). One study in USA indicated that most of GI complication cases occurred in patients using non prescription NSAID.(14). Our study found that the proportion of NSAID related ulcer was greater than Hp related ulcer. It means that the people who had been consuming NSAID in our country was greater than western country. Although the prevalence of Hp infection in population is high but the prevalence of Hp related ulcer is lower than NSAID related ulcer. Our assumption is that the strain of Hp in our country is less virulent than Hp in western country.

References

1. Borody TJ, Brand LS, Adam P et al. Helicobacter pylori negative gastric ulcer. *Am.J.Gastroenterol.* 1992;98:569-574
2. Marshall BJ: The Campylobacter pylori story. *Scand.J.Gastroenterol.* 1988;23 (sup);50-56
3. Russel RI: Peptic ulceration in rheumatoid arthritis in NSAID induced ulcers a distinct disease :Graham DY(ed). *Excerpta Medica.Inc.Princeton.* 1991;18
4. Soll A. Pathogenesis of NSAID drug-related Upper gastrointestinal toxicity. *Am.J. Med.* 1998;105:10S-16S
5. McCarthy D. Nonsteroidal anti-inflammatory Drug-related gastrointestinal toxicity : Definition and Epidemiology. *Am.J.Med.* 1998;105;3S-9S
6. Sippone P, Sappala K, Arisyne M et al. Gastritis and gastroduodenal ulcer; a case control study of risk toxic duodenal or gastric ulcer in patients with gastritis. *Gut.* 1989;30;922-929.
7. Alam K, Schubert T, Bologna S D, Ma CK: Increase of Hp on antral biopsy associated with severity of acute and chronic inflammation and likelihood of duodenal ulceration. *Am.J.Gastroenterol.* 1992;97;424-428

8. Sung JY: H.pylori contribute to NSAID gastroduodenal damage; Yes. International work shop on Helicobacter pylori. Hong Kong. 1996
9. Laine L: H.pylori contribute to NSAID gastroduodenal damage; No. International work shop on Helicobacter pylori. Hong Kong. 1996
10. Blanci Porro G, Parente F, Imbesi V et al. Role of Hp in ulcer healing and recurrence of gastric and duodenal ulcers in long term NSAID user: response to omeprazole dual therapy. Gut. 1996;39:22-26
11. Allison MC, Howatson AG, Torrance CJ et al. Gastrointestinal damage associated with the use of non steroidal anti inflammatory drugs. N. Engl. J. Med. 1992;327:749-754.
12. Laine L, Marin Sorensen M, Weinstein WM. NSAID associated gastric ulcers do not require Hp for their development. Am. J. Gastroenterol. 1992;87:1398-1402
13. Caslli M, Pazzi P, LaCorte et al. Campilobacter like organism, NSAID and gastric lesions in patients with rheumatoid arthritis. Digestion. 1989;44:101-104
14. Peura DA, Lanza FL, Gostout CJ, Foutch PG. The American Colledge of Gastroenterology Bleeding Registry: preliminary findings. Am. J. Gastroenterol. 1997;93:924-928.

Dimuat dalam Journal of Gastroenterology & Hepatology, 14(3):A2, March 1999