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Editorial

Helicobacter pylori: the primary cause of duodenal ulceration or a secondary infection?

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INTRODUCTION

It is generally accepted that *Helicobacter pylori (H. pylori)* infection has a role in duodenal ulceration. Eradication of *H. pylori* accelerates healing compared with placebo in the absence of control of gastric secretion and reduces ulcer recurrence. There is increasing evidence, however, that it may not be the primary cause of duodenal ulceration, but that it may be a secondary factor in a number of cases. This possibility is supported by four sets of observations:

1 *Geographical distribution*

In India and China there is a difference in prevalence of duodenal ulceration between the rice eating areas of the south and the drier wheat and millet eating areas of the north despite a similar high prevalence of *H. pylori* infection[1-3]. There is a similar situation along the West Coast of Africa. In the coastal area in the south where there is a diet of yams, sweet potato, manioc, plantains, rice and some white flour, the prevalence of duodenal ulceration is higher than in the northern savannah regions where much of the diet is millet. Both areas have a similar prevalence of *H. pylori* infection[4,5]. Again in Fiji the Indian population adhering to their traditional diet has twice the incidence of duodenal ulceration compared to the Fijian population despite similar *H. pylori* infection rates[6,7].

2 *H. pylori-negative duodenal ulceration*

There are many reports of *H. pylori*-negative duodenal ulceration unrelated to non-steroidal anti-inflammatory drugs (NSAIDs) varying in prevalence between 14% and 72% (Table 1)[8-26]. The figures from more developed countries suggest that *H. pylori*-negative duodenal ulceration occurs more frequently in areas where the overall prevalence of *H. pylori* infection in the community is low[20,27]. A paper from Greater Rochester, New York[11], reports a 48% prevalence of *H. pylori*-negative in white patients and 15% in non-white, with an overall prevalence of 39%. Parsonnet[28] has conducted a world-wide survey of reports and gives a figure of 40% *H. pylori* negative duodenal ulcers. Kurata *et al*[27] calculated that only between 48% and 64% of peptic ulcers are *H. pylori*-positive.

Table 1 Endoscopy reports of *Helicobacter pylori*-negative duodenal ulcer (DU) unrelated to NSAIDs

Authors	Places	Year	% *H.pylori*-negative DU
Oshowo[8]	UK, London	1999	30
Jones[9]	UK, Manchester	1986	41
Maher[10]	USA, Rochester	1987	43
Jyotheeswaran *et al*[11]	USA,Rochester	1998	39
Greenberg *et al*[12]	USA, Harvard	1997	40
Gislason *et al*[13]	USA, Baltimore	1997	30
Fenger *et al*[14]	Greenland (Inuit)	1997	50
Mirghani *et al*[15]	Sudan, Khartoum	1994	38
Kontou and Katelaris[16]	Australia, Sydney	1997	32.5
Uyub *et al*[17]	Malaysia, N. Peninsular	1994	
	Malayans		72
	Non Malayans		14
Petersen *et al*[18]	USA, N. Carolina	1996	26
Lanza *et al*[19]	USA, Houston	1996	30
Bruno *et al*[20]	USA, Military Hospital	1997	75
Sprung and Apter[21]	USA, Florida		
	Retrospective	1998	68
	Prospective	1998	69
Dres Pest *et al*[29]	Argentina	1996	33
	Early DU		59
	Chronic DU		22
Parsonnet[28]	All countries (meta-analysis)	1998	40
Sprung and Gano[22]	USA, Florida (retrospective)		52
Ciociola *et al*[23]	USA	1999	27
Henry and Batey[24]	Australia	1998	33
Pilotto *et al*[25]	Italy	2000	18.6
Lahaie *et al*[26]	Canada	2000	38

3 *Early cases of duodenal ulceration may be H. pylori-negative*

Dres Pest[29] from Argentina found a 78% incidence of *H. pylori* infection in patients with a history of chronic ulceration and only 41% in patients with a short history. He suggests that many patients with a short history may be free from *H. pylori* infection.

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4 Recurrence after eradication

Laine *et al*[30] from N. America have done a meta-analysis of seven trials subjected to strict criteria and report a recurrent duodenal ulcer rate of 20% within 6 months of *H. pylori* eradication in patients not on NSAIDs. Two other reports[31,32] excluding NSAIDs give figures of a 6% endoscopic recurrence within 3 years and of 18.9% clinical relapse within 7 years after eradication in patients remaining *H. pylori*negative. There are many other reports of recurrent ulceration in patients remaining *H. pylori* negative after eradication in which NSAID users have not been excluded.

DISCUSSION

The above findings strongly suggest that *H. pylori* infection is not a prerequisite for duodenal ulceration and that *H. pylori* infection when it occurs may be only a secondary factor.

It has been suggested that the differences mentioned in the geographical distribution of duodenal ulcer may be due to the higher prevalence of Cag A and Vac A virulent strains of *H. pylori* in these areas, but there is no evidence to support this[33-39].

The long held concept that duodenal ulceration is the result of a combination of increased acid output together with factors such as reduced bicarbonate in the duodenum reducing the ability of the duodenum to cope with the presenting acid level still remains valid. There may be other factors-smoking, genetic or dietary. Smoking has a chronic effect of increasing the ability to secrete acid[40]. There is convincing evidence that the differences in geographical or ethnic distribution of duodenal ulceration may be diet related[41,42]. Duodenal ulceration is less common in areas where unrefined wheat, certain pulses and millets form the staple diet and more common in areas where rice, refined maize or wheat flour, yams, manioc, plantains or sweet potatoes are the staple foods. Experiments in our laboratory on animal peptic ulcer models have confirmed the protective action against ulceration of the lipids present in certain food from areas of low duodenal ulcer prevalence and have shown that stored milled white rice and its oil are ulcerogenic[43-46]. There are several reports[47-62] showing the protective effect of certain dietary essential fatty acids, phospholipids and phytosterols against peptic ulceration in several experimental animal models.

In conclusion, the findings suggest that duodenal ulceration does occur independently of *H. pylori* infection and that *H. pylori* infection which may be coincidental or be acquired subsequently contributes to the chronicity of the ulceration. Subsequent infection is more likely to occur in areas where the prevalence of *H. pylori* infection is high. Treatment reducing acid secretion and raising the pH may contribute to *H. pylori* infection in ulcer patients.

This is presented as a paper for discussion and it is hoped that readers will respond with their points of view in the correspondence section of the journal.

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