Papers and Originals

Lesions Associated with Gastroduodenal Haemorrhage, in Relation to Aspirin Intake

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Summary: The incidence of aspirin ingestion during the week preceding overt gastroduodenal bleeding was recorded in 582 patients. A positive aspirin history was found in 80% of patients with acute gastric lesions, in 63% of those in whom no lesion was found, in 52% of those with a chronic duodenal ulcer, and in 49% of patients with a chronic gastric ulcer. In a control series of 542 consecutive patients without overt bleeding admitted to the same wards during part of the time of this investigation the aspirin incidence was 32%.

The difference in aspirin habits between these two series confirms that aspirin is a factor in precipitating overt haemorrhage in acute and chronic peptic ulcers, and that it is an important cause of bleeding from the stomach or duodenum, or both, in the absence of a chronic peptic ulcer.

Introduction

Bleeding or hyperaemia around particles of aspirin in the stomach was seen through a gastroscope in 80% of 16 patients who had had aspirin placed in the stomach through a tube (Douthwaite and Lintott, 1938). Paul (1943), in a similar study of 209 patients, saw superficial ulceration or hyperaemia in 40% of patients after ingestion of aspirin. However, he considered these changes were due to previous chronic gastritis. Weiss *et al.* (1961) found haemorrhagic areas in the stomach on diagnostic gastroscopy in 43% of 30 patients with gastrointestinal symptoms; each gastroscopy was repeated after aspirin, and seven patients showed hyperaemia and six frank haemorrhages in the region of aspirin particles in addition to the changes noted previously. They ascribed the initial changes to trauma from aspiration with a tube before gastroscopy and suggested that this was the explanation for the high incidence of haemorrhage found by Douthwaite and Lintott (1938). Multiple acute erosions mainly on or near the lesser curvature of the stomach have been found in post-gastrectomy specimens after preoperative aspirin ingestion (Muir and Cossar, 1955; Croft and Wood, 1967).

Though the mechanism of bleeding after aspirin ingestion is still obscure some facts are known. Occult blood loss occurs in a large proportion of those who ingest aspirin (Stubbe, 1958; Pierson *et al.*, 1961; Wood *et al.*, 1962), and the amount is reproducible for each individual (Croft and Wood, 1967). However, Parry and Wood (1967), using a radiochromium method, showed that overt haemorrhage associated with recent aspirin ingestion was not related to susceptibility to occult bleeding on further aspirin challenge.

Previous investigations of patients with overt bleeding (Alvarez and Summerskill, 1958; Allibone and Flint, 1958; Parry and Wood, 1963) have produced conflicting information regarding the incidence of a recent history of aspirin in the presence of acute or chronic peptic ulceration. We report a prospective study, which is a continuation of the work of Parry and Wood (1963), undertaken to determine the incidence of aspirin ingestion during the week preceding haematemesis or melaena in patients with various gastroduodenal lesions.

Patients Studied and Methods

We studied 615 patients with haematemesis and/or melaena, all but 48 of whom were admitted consecutively to the two wards of one medical unit. Twenty-nine who were unable to give a reliable history and four who had taken phenylbutazone or indomethacin were excluded from the study. Diagnosis of the gastroduodenal lesion possibly responsible for the haemorrhage was based on the night secretion test (Chandler and Watkinson, 1953), gastroscopy, and barium meal examination, which were all carried out within five days of admission. The stomach was not emptied with a tube before gastroscopy, and this examination was omitted in many patients (Table I) for various reasons, including immobility of the neck or advanced age, especially in women. If the gastroscope was passed but no satisfactory view obtained the examination was recorded as omitted. As the heat of the bulb may cause petechiae, such lesions were ignored unless superficial ulceration accompanied them, in which case the patients were classed as having acute gastric lesions. This group included a few patients with acute shallow ulcers. A barium meal examination was carried out on all patients except a few in whom the diagnosis was made at operation or necropsy. Liver function tests (serum bilirubin, alkaline phosphatase, zinc and thymol turbidities, and serum alanine aminotransferase) were performed in 59% of the group of patients in whom no lesion was found; four patients had abnormal results which all reverted to normal later, and follow-up of these patients failed to reveal evidence of liver disorder.

Of the 582 patients studied, 171 had a duodenal ulcer, 109 had a gastric ulcer, 25 had an acute gastric ulcer or erosion, and in 162 no lesion was found (total 467, Tables I and II). In 115 patients various less common diagnoses were made (Table III). The patients were divided into those who had or had not taken aspirin during the seven days preceding the haemorrhage (Table II).

Results

Of 542 patients who had not bled, 174 (32%) had taken aspirin (Table II), and of 582 patients who had bled, 325 (56%) had taken aspirin. In comparing these two large groups of patients a highly significant relationship was found between the taking of aspirin and gastroduodenal haemorrhage ($\chi^2 = 63.1$,

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$P < 0.001$).§ Excluding the 115 patients with less common diagnoses (Table III) we were left with the 467 patients with the first four diagnoses in Table II, of whom 264 (56.5%) had taken aspirin. The difference between the incidence of a history of aspirin in this group and that in the control group was also highly significant ($\chi^2 = 60.0$, $P < 0.001$).

Eighty per cent. of patients with acute lesions and 63% of those in whom no lesion was found had taken aspirin during the week before the bleeding (Table II). This difference was not significant ($\chi^2 = 2.1$, $P > 0.10$).

Fifty-two per cent. of patients with a duodenal ulcer and 49% with a gastric ulcer had a positive aspirin history. This difference was also not significant ($\chi^2 = 0.16$, $P > 0.50$).

§ The value of χ^2 given in each case was that obtained in a χ^2 test for homogeneity of proportions. The corresponding P value is that critical level at which the stated value of χ^2 was tested for significance.

TABLE I.—Extent of Investigation by Gastroscopy and Night Secretion Test in Each Group

Diagnosis	Aspirin History	Total No. of Patients	% investigated by	
			Gastroscopy	Night Secretion Test
No lesion found	Positive	102	55	87
	Negative	60	45	76
Acute lesion	Positive	20	90	80
	Negative	5	40	80
D.U.	Positive	89	28	75
	Negative	82	30	82
G.U.	Positive	53	47	64
	Negative	56	52	75
All patients		467	44	78

TABLE II.—Aspirin History and Gastrointestinal Lesion Found

Diagnosis	Aspirin		No Aspirin	
	No.	%	No.	%
No lesion found ..	102	63.0	60	37.0
Acute lesion ..	20	80.0	5	20.0
D.U. ..	89	52.1	82	47.9
G.U. ..	53	48.7	56	51.3
Total ..	264	56.5	203	43.5
Less common diagnoses (Table III) ..	61	53.0	54	47.0
No bleeding (patients admitted for other conditions) (Parry and Wood, 1963) ..	174	32.1	368	67.9

TABLE III.—Aspirin History in Less Common Diagnoses

Diagnosis	No. of Patients	
	Aspirin	No Aspirin
Hiatus hernia ..	12	12
Carcinoma of stomach ..	9	11
Previous partial gastrectomy ..	7	6
Anastomotic ulcer ..	6	5
Oesophageal varices ..	4	6
Chronic duodenal and gastric ulcers ..	7	4
2 Chronic lesions—e.g., D.U. and hiatus hernia ..	9	6
Chronic and acute lesions ..	9	4
Total ..	61	54

TABLE IV.—Percentage Distribution of Patients According to Diagnosis, Age, and Aspirin History. Percentage in Each Diagnostic Group by Age

Age Group	All Patients					Patients who took Aspirin				
	No Lesion Found and Acute Lesion (187 patients)	D.U. (171)	G.U. (109)	Less Common Diagnoses (115)	Total Patients (582)	No Lesion Found and Acute Lesion (122)	D.U. (89)	G.U. (53)	Less Common Diagnoses (61)	Total Patients (325)
21-40	12.3	12.3	4.6	8.7	10.1	12.3	16.8	3.8	6.6	11.1
41-50	12.9	18.7	10.1	11.3	13.7	14.8	15.7	9.4	14.7	14.2
51-60	23.5	24.0	18.3	24.4	22.9	25.4	24.7	15.1	26.2	23.7
61-70	23.0	24.6	29.4	31.2	26.3	21.3	22.5	39.6	32.8	26.7
71-80	20.3	14.6	29.4	13.9	19.1	17.2	12.4	24.6	13.1	16.3
80+	8.0	5.8	8.2	10.4	7.9	9.0	7.9	7.5	6.6	8.0

The difference between the aspirin history in the combined group with an acute lesion and with no lesion, and in the combined group with duodenal and gastric ulcer, was highly significant ($\chi^2 = 9.0$, $P < 0.005$).

A history of aspirin-taking was found in a little over half of those with less common diagnoses, except in the group with both chronic and acute lesions, and in the group with chronic duodenal and gastric ulcers, where it was present in about two-thirds (Table III). Thirty-seven patients (6.4% of the total series of 582) had two lesions which might have caused the bleeding.

Whether or not the patients took aspirin, about 65% were between 51 and 80 years of age and about a quarter were over 70 (Table IV). If all the cases are taken together the proportion in each age group with an aspirin history fell with advancing age (but not in those over 80). However, the calculated slopes of these downward trends were not significant at the 10% level (Table V).

TABLE V.—Analysis of the Proportions of Patients Taking Aspirin for Dependence on Age

Clinical group	Estimated drop in percentage taking aspirin between age 21-40 and age 80+	χ^2	
No lesions and acute lesions	10.4	0.77	> 0.35
D.U. ..	8.9	0.43	> 0.50
G.U. ..	1.1	0.004	> 0.95
Less common diagnoses ..	15.3	0.82	> 0.35
All patients ..	9.9	1.84	> 0.15

Chandler and Watkinson (1953) defined high night acidity as a pH of 1 to 2 in each hourly gastric aspiration specimen, nocturnal neutralization as a rise of gastric juice pH from low levels to 5.5 or above during the night, and achlorhydria as a pH above 3.5 in the gastric juice throughout the night. The rise and fall of gastric juice pH was irregular in some patients whom we termed as showing a non-specific secretion pattern. A large proportion of our patients with a duodenal ulcer had a high night acidity and the majority of those with acute lesions had achlorhydria in the night secretion test (Table VI). This test was of less diagnostic value in patients with chronic gastric ulcers, 21% of whom had a high night acidity and 38% achlorhydria. In patients in whom no lesion was found to account for the haemorrhage, this test in our hands was also not much help in diagnosis.

TABLE VI.—Relation of Final Diagnosis to Night Secretion Pattern

Diagnosis	Aspirin History	Total No.	Night Secretion Test Pattern: Percentage With			
			High Night Acidity	Nocturnal Neutralization	Achlorhydria	Non-Specific Pattern
No lesion found	Positive	102	18	21	44	17
	Negative	60	28	16	28	28
Acute lesion	Positive	20	6	0	82	12
	Negative	5	0	0	100	0
D.U.	Positive	89	56	10	18	16
	Negative	82	69	9	10	12
G.U.	Positive	53	21	29	38	12
	Negative	56	21	36	38	5

TABLE VII.—Prospective Series of Overt Haemorrhage and Aspirin History

Authors	Days before Bleeding for which Aspirin history obtained	No Overt Bleeding		Overt Bleeding					Gastroscopy %
		No. of Patients	Positive Aspirin History %	No. of Patients	Positive Recent Aspirin History (%)				
					D.U.	G.U.	Acute Lesion	N.A.D.	
Alvarez and Summerskill (1958)	3	103	17	103	44	33	42	74	40
Allibone and Flint (1958)	14	100	38	100	50	73	73	Not stated	Not stated
Parry and Wood (1963)	7	542	32	96	57	40	100	93	Not stated
Present Series	7	—	—	582	52	49	80	63	44

Discussion

Parry and Wood (1963) showed that 32% of 542 consecutive patients admitted to two wards of a general hospital with no evidence of recent overt gastrointestinal bleeding had taken aspirin during the previous week (Table II). In the present series of patients admitted to the same two wards with recent haemorrhage 49% or more, depending on the diagnosis, had taken aspirin during this time. The incidence of aspirin was highest in patients with acute lesions and in those in whom no lesion could be found.

In some reported series of patients with overt gastrointestinal haemorrhage gastroscopies were not performed and it was assumed that bleeding was due to an acute lesion on the basis of the history and the absence of a chronic lesion on the barium meal examination (Muir and Cossar, 1955; Jennings, 1965). In planning the present series precision of diagnosis was considered cardinal to a further understanding of the problem, and all available methods of investigation were used in a large proportion of the patients.

The incidence of a positive recent aspirin history in the presence of a chronic peptic ulcer was about 50% in three of the series of cases summarized in Table VII, but less in that of Alvarez and Summerskill (1958). This may have been due to variation in the periods selected for the aspirin history (3 to 14 days in the different reports).

Alvarez and Summerskill (1958) found acute lesions on gastroscopy in 17% of those admitted with overt haemorrhage, and the aspirin incidence was 42% in this group. In the present series 7% had acute lesions and 80% of these had recently taken aspirin. It is difficult to explain these discrepant findings; perhaps differences in diagnostic criteria played a part.

In patients in whom no gastroduodenal lesion was apparent Parry and Wood (1963) found an aspirin incidence of 93%, but in the present study it was 63% in a similar group of patients. The reduced figure may be related to the smaller number in the earlier study or to the fact that the aspirin histories were recorded by one observer in that series. Allibone and Flint's (1958) controls were acute surgical patients, and Parry and Wood (1963) studied consecutive patients on admission to a general medical ward. Alvarez and Summerskill's (1958) controls were outpatients with gastrointestinal problems, and these had a lower aspirin incidence (17%).

Seven per cent. of the present series admitted with overt haemorrhage had two lesions, and this emphasizes the need for accurate diagnosis by adequate investigation of all patients. However, it is usually impossible to say which of the two lesions has bled, or whether both have bled.

Chandler and Watkinson (1953) found a high night acidity in 77% of patients with a duodenal ulcer and a nocturnal neutralization pattern in 82% of patients with a chronic gastric ulcer. In the present study 63% of patients with a duodenal ulcer had a high night acidity, but only 33% with a chronic gastric ulcer showed a nocturnal neutralization pattern. The proportion of duodenal ulcers which are not diagnosed by a barium meal examination on one occasion has been estimated as varying from 5–10% (Eusterman, 1936; Hussar, 1948) to

one-third (Littman and Bernstein, 1962). If patients with high nocturnal gastric acidity who have bled without apparent cause were to have another barium meal performed about a year later more duodenal ulcers might come to light.

Though the group in which no lesion was found had a higher aspirin incidence than the duodenal ulcer or chronic gastric ulcer groups, the incidence was lower than in the small group in which acute gastric lesions were found. The differential aspirin incidence between these last two groups (Table II) (which was not statistically significant) might be partially explained by the presence of some patients with undiagnosed duodenal ulcers in the group in which no lesion was found. In support of this suggestion about a fifth of the patients in whom no lesion was found had a high night acidity (Table VI); in contrast this was very infrequently found in the small group in which an acute gastric lesion was actually identified.

Though the peak number of patients in the whole series who took aspirin were in the later age ranges, it was the younger age groups which tended to have the highest proportion of patients taking aspirin. Although these trends did not reach statistical significance (Table V) they suggest either that older people take aspirin less commonly, which seems unlikely, or that their gastric mucosae are protected against aspirin in some way, and that when they suffer gastroduodenal haemorrhage it is due in part to some other factor(s).

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