

ABO blood group and secretor status in relation to clinical characteristics of peptic ulcers

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EDITORIAL SYNOPSIS A large series of peptic ulcer patients divided into groups according to those who bled, those who required operation, and those who had neither bleeding nor operation showed a dissociation between ABO blood group and secretor status. Patients who had undergone operation showed a higher proportion of non-secretors for both gastric and duodenal ulcers than others. Ulcer patients who bled showed an increased frequency of blood group O compared with the others, but there was no difference as between the operation and non-operation groups. A careful statistical analysis of results and review of previous work on this subject makes the findings in this paper important, particularly as a possible guide to prognosis.

Possible relationships between genetic factors and ulcer prognosis have received attention since the discovery by Aird, Bentall, Mehigan, and Roberts (1954) that there is an association between blood group O and liability to peptic ulcer.

Clarke, Cowan, Edwards, Howel-Evans, McConnell, Woodrow, and Sheppard (1955) analysed their data on blood group and duodenal ulcers according to macroscopic, *i.e.*, mainly operative and radiological, evidence of ulceration, and found that the trend was towards an increased proportion of patients of blood group O in their radiological material. Further investigation showed that one hospital had contributed most of these patients and that here there was a particularly high admission rate for bleeding ulcers; but the subject was not pursued. Later Peebles Brown, Melrose, and Wallace (1956) demonstrated a slight trend towards an increase in group O patients in their operative material, and a more marked one if all patients with a haematemesis or perforation were compared with the rest; even so the result was not statistically significant.

Clarke, Edwards, Haddock, Howel-Evans, McConnell, and Sheppard (1956) showed duodenal ulcers to be commoner in those who were incapable of secreting ABH blood group substances in their mucous secretions, this property being inherited independently of ABO blood group. These findings have been confirmed by others and extended to cover gastric ulcers (Wallace, Peebles Brown, Cook, and Melrose, 1958; Doll, Drane, and Newell, 1961).

Wallace *et al.* (1958) found that duodenal ulcer patients of blood groups A/AB/B who were non-secretors were more likely to come to operation than secretors, the difference being statistically significant. The same tendency was probably also present in persons of blood group O. Clarke *et al.* (1956) found a small, but statistically insignificant, excess of ABH non-secretors in their operative duodenal ulcer material compared with cases diagnosed by radiography only, but Newman, Naifeh, Auer, and Buckwalter (1961) in the U.S.A. were unable to show any difference at all.

One reason for the disagreement may be that some years can elapse before an ulcer bleeds or its symptoms become sufficiently severe or persistent to warrant an operation; consequently no differences might be found between the different genetic groups in each clinical category if analyses were made early in the course of the disease, whereas they might be found later. It seemed worthwhile, therefore, to re-examine the clinical characteristics of peptic ulcers in relation to blood group and secretor status and to ensure that a substantial number of patients were included whose ulcers had not given rise to any complications for at least five or 10 years after their initial diagnoses.

METHOD

To simplify the contrasts, patients were excluded if they had a history of perforated ulcer, or of combined gastric and duodenal ulcers, or if another lesion, such as a

hiatus hernia, could have influenced symptoms or prognosis. There remained patients whose ulcers had caused pain, obstruction, or haemorrhage; by combining the first two categories bleeding ulcers could be compared with non-bleeding and, within both groups, a comparison could be made between those patients who had required operation and those who had not.

For the blood group studies the groups were:

Group 1 consisted of patients who had not bled and had not been operated on. Many of these patients formed part of a consecutive series whose ABO blood groups had been studied previously (Doll, Swynnerton, and Newell, 1960). Others were obtained by re-examining patients who had participated in a controlled trial of treatments for duodenal ulcer (Friedlander, 1954) or who had been included in a series examined to determine the risk of gastric cancer after a routine diagnosis of gastric ulcer (Doll, Avery Jones, Pygott, and Stubbe, 1957). These last two groups had attended hospital in 1950 or 1951 so that 84% of the gastric ulcer patients (117 out of 130) and 79% of the duodenal ulcer patients (111 out of 143) were known to have survived for 10 years or more after the initial diagnosis of the ulcer without any complication having arisen.

Patients forming groups 2 (bleeding, but no operation), 3 (no bleeding, operation performed), and 4 (bleeding, operation performed) were obtained from the records of the Gastroenterological Department of the Central Middlesex Hospital. All gastric ulcer patients were included who were admitted for haemorrhage or for operation between 1950 and 1962, and all duodenal ulcer patients who were admitted between 1953 and 1962. In all cases the hospital records were examined and patients were retained in each category only when their subsequent course was consistent with their initial classification.

For the secretor status studies the same broad categories were used but the material differed as secretor status had not been determined in consecutive ulcer cases. The data used were obtained in part by a re-examination of the cases reported by Doll *et al.* (1961) in their survey of the occurrence of peptic ulceration and other diseases in relation to secretor status at the Central Middlesex Hospital, a study in which ulcer symptoms and prognosis

were not investigated. Since that report secretor status had been determined by the same method for more ulcer patients, mainly for those falling into groups 2, 3, and 4. It was therefore necessary only to augment group 1 and this was done by using the patients who were specially interviewed in the blood group study. Another difference between the series is that admissions for haemorrhage in groups 2 and 4 and for operation in groups 3 and 4 were occasionally at hospitals other than the Central Middlesex Hospital, although all the patients had attended there at some time.

RESULTS

Tables I and II give the basic figures and Tables III and IV comparisons of ABO blood group and secretor status frequencies in the different clinical categories.

Patients with bleeding at some time in their ulcer's history had an increased frequency of blood group O when compared with those whose ulcers had caused pain or obstruction. The difference is small, but it is present for both gastric and duodenal

TABLE I
PATIENTS WITH GASTRIC OR DUODENAL
ULCERS DIVIDED BY CLINICAL TYPE AND ABO
BLOOD GROUP

Type of Ulcer	Clinical Characteristics	No. Belonging to Blood Group				Total Patients
		O	A	B	AB	
Gastric	Pain only, no operation	65	53	9	3	130
	Bleeding, no operation	83	76	10	3	172
	Pain or obstruction, operation	123	132	35	9	299
	Bleeding, operation	100	51	11	9	171
	Total	371	312	65	24	772
Duodenal	Pain only, no operation	65	62	11	5	143
	Bleeding, no operation	202	116	19	6	343
	Pain or obstruction, operation	343	230	49	15	637
	Bleeding, operation	121	64	14	3	202
	Total	731	472	93	29	1,325

TABLE II

PATIENTS WITH GASTRIC OR DUODENAL ULCERS, DIVIDED BY CLINICAL TYPE, BLOOD GROUP, AND SECRETOR STATUS

Type of Ulcer	Clinical Characteristics	No. Belonging to Blood Group								No. Not Grouped	Total Patients	
		O		A		B		AB				
		Secretor	Non-secretor	Secretor	Non-secretor	Secretor	Non-secretor	Secretor	Non-secretor			
Gastric	Pain only, no operation	53	12	47	6	6	3	1	2	5	2	137
	Bleeding, no operation	9	5	15	5	4	0	0	0	0	0	38
	Pain or obstruction, operation	44	17	31	23	11	1	4	0	0	1	132
	Bleeding, operation	22	7	8	11	2	2	1	1	0	0	54
	Total	128	41	101	45	23	6	6	3	5	3	361
Duodenal	Pain only, no operation	43	22	43	19	7	4	3	2	3	0	146
	Bleeding, no operation	24	18	21	4	1	1	1	0	1	1	72
	Pain or obstruction, operation	72	43	39	35	7	10	3	3	0	1	213
	Bleeding, operation	17	12	11	4	2	1	0	1	0	0	48
	Total	156	95	114	62	17	16	7	6	4	2	479

TABLE III

RELATION BETWEEN CLINICAL CHARACTERISTICS AND BLOOD GROUP AND SECRETOR STATUS IN PATIENTS WITH GASTRIC ULCERS

<i>Clinical Characteristics</i>	<i>No. of Patients Examined</i>	<i>Percentage Group O</i>	<i>No. of Patients Examined</i>	<i>Percentage Non-secretor</i>
Pain only, no operation	130	50.0	137	18.2
Bleeding, no operation	172	48.3	38	26.3
Pain or obstruction, operation	299	41.1	132	33.3
Bleeding, operation	171	58.5	54	38.9
All types	772	48.1	361	27.1

Comparison between group O and other groups
 (i) bleeding v no bleeding, $\chi^2 = 6.558$, $n = 1$, $P = 0.013$.
 (ii) operation v no operation, $\chi^2 = 1.222$, $n = 1$, $P = 0.25$.

Comparison between secretors and non-secretors
 (i) bleeding v no bleeding, $\chi^2 = 2.251$, $n = 1$, $P = 0.14$.
 (ii) operation v no operation, $\chi^2 = 8.084$, $n = 1$, $P = 0.005$.

TABLE IV

RELATION BETWEEN CLINICAL CHARACTERISTICS AND BLOOD GROUP AND SECRETOR STATUS IN PATIENTS WITH DUODENAL ULCERS

<i>Clinical Characteristics</i>	<i>No. of Patients Examined</i>	<i>Percentage Group O</i>	<i>No. of Patients Examined</i>	<i>Percentage Non-secretor</i>
Pain only, no operation	143	45.5	146	32.2
Bleeding, no operation	343	58.9	72	33.3
Pain or obstruction, operation	637	53.8	213	43.2
Bleeding, operation	202	59.9	48	37.5
All types	1,325	55.2	479	37.8

Comparison between group O and other groups
 (i) bleeding v no bleeding, $\chi^2 = 6.002$, $n = 1$, $P = 0.014$.
 (ii) operation v no operation, $\chi^2 = 0.514$, $n = 1$, $P = 0.5$.

Comparison between secretors and non-secretors
 (i) bleeding v no bleeding, $\chi^2 = 0.287$, $n = 1$, $P = 0.6$.
 (ii) operation v operation, $\chi^2 = 4.236$, $n = 1$, $P = 0.04$.

ulcers and in neither case it is likely to be due to chance (in each group $P < 0.02$). No significant difference in blood group frequencies was, however, found between the operative and the non-operative groups ($P = 0.25$ for gastric ulcers and 0.5 for duodenal ulcers).

In contrast, when a comparison is made between the proportions of secretors and non-secretors no significant difference is found between patients with bleeding and non-bleeding ulcers ($P = 0.14$ for gastric ulcers and 0.6 for duodenal ulcers), but there is a highly significant difference between the operation and non-operation categories. Among the patients who have undergone operation the proportion of non-secretors is substantially higher, and the figures are again consistent for both types of ulcer ($P < 0.01$ and $= 0.04$ respectively).

DISCUSSION

The simplest explanation of these results is that the natural history of a peptic ulcer is affected by the patients' ABO blood group and secretor status, a suggestion that is implicit in most of the other studies referred to previously. Knowledge of the blood group or secretor status has not, in our experience, influenced the method of treatment; if it had, it would presumably have produced an excess of blood group O as well as of non-secretors among the operated on patients. Neither are the results

likely to have been produced by incomplete follow-up, which would be expected to diminish, rather than increase, the differences between the groups. They may, perhaps, have been influenced by the inclusion of a proportion of incorrectly diagnosed cases among the patients who were neither operated upon nor bled, but personal knowledge of the accuracy of the radiological diagnoses at the Central Middlesex Hospital has convinced us that this proportion is, at the most, very small. We do not believe it can have materially influenced the results which, in any case, lead to similar conclusions even if the patients in group 1 are omitted.

More important, perhaps, than the evidence for a genetic effect on ulcer prognosis, is the evidence of dissociation between the actions of ABO blood group and secretor status. This accords with the observation that the proportion of non-secretors in ulcer patients is the same irrespective of ABO blood group (Doll *et al.*, 1961), but it is not readily explained, and it is unclear whether the effects of ABO blood group and secretor status on peptic ulcers are associated with mucosal defence mechanisms or with variations in acid secretion.

Large amounts of blood group substances are found in the duodenal and gastric mucosa and in the gastric juice, probably being secreted in the non-parietal component. In all these situations the amount and type varies with the ABO blood group and secretor status (Glynn, Holborow, and Johnson,

1957; Szulman, 1960, 1962; Evans, McConnell, Donohoe, Sircus, and Crean, 1963), and their distribution may be taken to suggest that the substances play a part in the defence of the mucosa against peptic digestion.

Measurements of the relationship between the substances and acid and pepsin secretion provide conflicting results. Sievers (1959) and Hanley (1964) found that normal people of blood group O have significantly higher serum pepsinogen levels than do people of blood group A, whereas Niederman, Gilbert, and Spiro (1962) found a similar level in all groups. Hanley (1964) and Niederman *et al.* (1962) agree, however, that serum pepsinogen does not vary with secretor status.

Sievers (1959), using the tubeless test meal technique, found that achlorhydria was significantly more common amongst patients without gastrointestinal symptoms who belonged to blood group A than amongst those who belonged to group O. Similarly Purohit and Shukla (1960) showed that more acid was secreted in response to an alcohol test meal by young Indian medical students of blood group O than by those of groups A, AB, or B. Studies of duodenal ulcer patients, however, have not shown any differences in acid secretion according either to ABO blood group or secretor status (Peebles Brown *et al.*, 1956; Ventzke and Grossman, 1962).

The association between blood group O and liability to bleeding as an ulcer complication may, perhaps, be explained by the observation that normal people of blood group O have slightly lower plasma levels of factor VIII, antihæmophilic globulin, than do those of blood group A (Preston and Barr, 1964).

SUMMARY

The prognosis for peptic ulcer appears to be influenced by the patient's ABO blood group and ABH secretor status. Group O patients are more likely to suffer from bleeding than are those of groups A/AB/B but are not particularly likely to come to operation; by contrast non-secretors are not prone to suffer from bleeding although they do tend to come to operation more often than secretors. No explanation for this dissociated effect is known.

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