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Influence of the ABO blood groups and secretor status on bleeding and on perforation of duodenal ulcer

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ABO BLOOD GROUPS IN RELATION TO DUODENAL ULCER

Since Aird, Bentall, Mehigan, and Roberts (1954) convincingly demonstrated a high incidence of blood group O in duodenal ulcer subjects there have been a number of confirmatory studies carried out in different ethnic groups and populations (McConnell, 1966).

Studies have also been undertaken to see if there is an especially strong association between blood group O and some particular category of duodenal ulcer patient. Brown, Melrose, and Wallace (1956) found that there was a marked association between blood group O and duodenal ulcer subjects requiring surgery, and also an association which fell short of statistical significance in subjects who had suffered perforation or bleeding compared with those in whom duodenal ulcer had been diagnosed by radiology alone. However, Langman and Doll (1965) did not find a high incidence of blood group O in subjects who came to operation in their series of 479 duodenal ulcers but found that the association of blood group O with bleeding was very significant. Horwich, Evans, McConnell, and Donohoe (1966) confirmed the association between blood group O and bleeding in duodenal ulcer subjects and demonstrated a high incidence of blood group O also in subjects who had sustained a serious gastro-duodenal bleed but did not have any radiologically demonstrable gastro-duodenal lesion.

In the study of Horwich *et al.* (1966) 125 subjects with perforated duodenal ulcer were blood grouped and 72 (58·1%) were found to be of blood group O compared with 50·6% in 549 subjects with duodenal ulcer which had not perforated or bled. Langman, Doll, and Saracci (1967) found 56·8% blood group O in a series of 192 patients with perforated duodenal ulcer as compared with 45·5% in duodenal ulcer subjects who had presented with pain or obstruction.

ABH SECRETION IN RELATION TO DUODENAL ULCER

The association between salivary ABH non-secretion and duodenal ulcer was first demonstrated by Clarke, Edwards, Haddock, Howel-Evans, McConnell, and Sheppard (1956) and later confirmed by Wallace, Peebles Brown, Cook, and Melrose (1958), Doll, Drane, and Newell (1961), Newman, Naifeh, Auer, and Buckwalter (1961), Ball (1962), Pringle, Wort, and Green (1964) and Fodor and Urcan (1966).

Studies designed to discover a relationship between ABH secretion and clinical categories of duodenal ulcer have shown a tendency for non-secretors to come to operation more frequently than secretors (Langman and Doll, 1965) but this was not confirmed by Horwich *et al.* (1966). Bleeding duodenal ulcer subjects have a similar incidence of ABH secretors as uncomplicated duodenal ulcer subjects (Langman and Doll, 1965; Horwich *et al.*, 1966). A small series of 125 perforated duodenal ulcers has been investigated for ABH secretion by Horwich *et al.* (1966) and 38 (30·4%) were non-secretors. This is a rather lower frequency than that found in bleeding ulcers or those which had caused only pain or obstruction.

THE PRESENT STUDY

The aims of the present communication are (1) to see if there is an association between blood group O and bleeding outside the gastrointestinal tract, *viz.*, menorrhagia; (2) to expand our series of blood grouped and secretor-typed perforated duodenal ulcer subjects to see if this clinical category is associated with either blood group O or non-secretion.

METHODS

MENORRHAGIA CASES These cases were ascertained by examining case records of women diagnosed as

having menorrhagia. Abstracts were made of case records which contained the patient's ABO blood group at the Liverpool Royal Infirmary (133 patients) and at the Women's Hospital, Liverpool (367 patients). Thirty-four patients were excluded from this series having been diagnosed as follows:

Diagnosis	*No. of Cases*
Endometriosis	24
Fibroadenoma	3
Thrombocytopenia purpura	2
Undifferentiated carcinoma	2
Thrombotic thrombocytopenia	1
Haemangiomatous malformation	1

Women with fibroids, adenomyosis, 'pelvic inflammation', and chronic cervicitis were included in the 466 patients remaining for analysis.

PERFORATED DUODENAL ULCER CASES These patients had all been surgically treated for perforated duodenal ulcer at two large Liverpool hospitals. A house visit was made, and at this visit a further history was taken and a sample of blood and saliva obtained. Patients were not included in this series if there was any history of overt gastroduodenal bleeding, or other lesion in addition to a duodenal ulcer visible on the barium meal.

CONTROLS The same general population controls as in the paper of Horwich *et al.* (1966) were employed. The clinical categories Ia and Ib of patients with duodenal ulcers who had not bled or perforated from Table II of Horwich *et al.* (1966) were used for comparisons with cases of perforated duodenal ulcers in this communication.

RED CELL GROUPING A tube technique was used (Lawler and Lawler, 1957) and was carried out within 24 hours of collecting the blood sample.

SECRETOR TESTING Saliva was tested in the usual manner for H, A, and B activity (Evans, McConnell, and Donohoe, 1964).

RESULTS

The blood groups of the menorrhagia patients are given in Table I. It will be seen that there is no association beteeen menorrhagia and blood group O in the total series; similarly no association was found either between blood group O and fibroids or between blood group O and hysterectomy.

The present series of 100 perforated duodenal ulcer patients was ascertained for 'perforation' whereas those analysed in the paper of Horwich *et al.* (1966) were abstracted from a large number of patients ascertained for 'duodenal ulcer'. No patient was included in both series. No patient who had sustained bleeding as well as perforation was included.

The blood groups and secretor status of patients with perforated duodenal ulcers are given in Table II. It is to be noted that only 60 of the 100 patients whose blood group were known in the present series could be traced for the purpose of secretor testing. There is no significant heterogeneity for either ABO blood group distribution or ABH secretor status between the series of perforated duodenal ulcer subjects from the paper of Horwich *et al.* (1966) and the present series.

TABLE I

THE ABO BLOOD GROUPS OF MENORRHAGIA PATIENTS

Series		*Blood Group*				*Total*	
		O	*A*	*B*	*AB*		
Control		3,146	2,648	546	170	6,510	
All	(L.R.I.)	61	45	12	4	122	466
Menorrhagia	(W.H.)	179	119	37	9	344	
Fibroids	(L.R.I.)	28	17	4	3	52	94
	(W.H.)	21	17	4	0	42	
Hysterectomy	(L.R.I.)	38	28	7	2	75	262
	(W.H.)	94	71	19	3	187	

L.R.I. Liverpool Royal Infirmary. W.H. Women's Hospital, Liverpool.

Heterogeneity between hospitals for blood groups O, A and B plus AB combined (2 degrees of freedom)

All menorrhagia patients	χ^2 0·212	$p > 0{\cdot}50$
Fibroids	χ^2 0·750	$p > 0{\cdot}50$
Hysterectomy	χ^2 0·007	$p > 0{\cdot}90$

Heterogeneity in O vs *non-O incidence* (1 degree of freedom)

Menorrhagia vs control	χ^2 1·757	$p > 0{\cdot}10$
Fibroid vs non-fibroid	χ^2 0·018	$p > 0{\cdot}50$
Hysterectomy vs non-hysterectomy	χ^2 0·172	$p > 0{\cdot}50$

TABLE II

THE ABO BLOOD GROUPS AND ABH SECRETOR STATUS OF PATIENTS WITH DUODENAL ULCERS

Phenotype		*Perforated Duodenal Ulcers*			*Duodenal Ulcers without Bleeding or Perforation from Paper of Horwich* et al. *(1966)*[3]
		Data from Paper of Horwich et al. *(1966)*[1]	*Present Series*[2]	*Total*	
O	S	53 } 73	17 } 55	128	174 } 278
O	ss	20 }	17 }		104 }
A	S	23 } 35	14 } 30	65	135 } 209
A	ss	12 }	5 }		74 }
B	S	7 } 12	2 } 13	25	33 } 48
B	ss	5 }	3 }		15 }
AB	S	4 } 5	0 } 2	7	8 } 14
AB	ss	1 }	2 }		6 }
Total		125	100	225	549

[1]Table II, category III. [2]Not all patients blood grouped in present series could be contacted for secretor testing.
[3]Table II, categories I a and I b.

Perforated Duodenal Ulcers
Heterogeneity between paper of Horwich *et al.* (1966) and present series for secretion $\chi^2 = 3{\cdot}79$; 1 degree of freedom; $p > 0{\cdot}05$.
Heterogeneity between paper of Horwich *et al.* (1966) and present series for blood groups O, A and B plus AB combined $\chi^2 = 1{\cdot}47$; 2 degrees of freedom; $p > 0{\cdot}10$.

The incidence of O expressed as a percentage of (O + A) is 66·32 for the 225 perforations and this is significantly greater than the corresponding percentage, 57·08, in the incidence of group O in duodenal ulcer patients who had not bled or perforated. (χ^2 for heterogeneity of incidence of blood groups O and A with one degree of freedom = 4·90; $P < 0{\cdot}05$.)

The non-secretor incidence amongst the 225 perforations was 65/185 = 35·13% which is very similar to the incidence of $\frac{199}{549} = 36{\cdot}25\%$ in the duodenal ulcer patients who had not suffered perforation or bleeding. (χ^2 for heterogeneity of incidence of secretion and non-secretion with one degree of freedom 0·07; $P > 0{\cdot}50$.)

DISCUSSION

Before entering into the complexities of gastric function in order to find a physiological link between gastroduodenal bleeding and blood group O it is necessary to consider whether blood group is not more closely correlated to faults in the coagulation and bleeding mechanisms. Preston and Barr (1964) have shown that there is a deficiency of factor VIII in subjects of blood group O as compared to other blood groups. The present work shows no influence of blood group on the likelihood of being admitted to hospital with menorrhagia with or without the presence of uterine fibroids. Furthermore, as hysterectomy is more likely to be performed for the more severe forms of uterine bleeding then it may be inferred from the present work that blood group O does not adversely affect the clinical course of menorrhagia by interfering with natural haemostasis. It could follow from these findings in menorrhagia patients that blood group O does not exert any significant influence on gastroduodenal bleeding by delaying haemostasis.

The series of bleeding duodenal ulcer patients reported by Horwich *et al.* (1966) showed blood group O as a percentage of (O + A) to be 67·7% which is very similar to the present figure for perforated duodenal ulcers (66·3%). It is to be noted that no patient was included in our perforation series if bleeding was known to have occurred at any time in the history. During the course of our investigations 52 patients possessing blood groups O and A have been encountered who have sustained both perforation and bleeding; 34 of these were of group O, an incidence as a percentage of O + A = 65·4 which is again a very similar figure. It would seem, therefore, that any hypothesis designed to explain the effect of blood group O must take into account the influence of this blood group on perforation of duodenal ulcer, as well as on gastroduodenal haemorrhage with or without duodenal ulcer.

In discussing the factors which would tend to keep the gastric and duodenal mucosa intact it is necessary to consider the mucosal cell turnover rate and the quantity and quality of the mucous secretion. Studies on the relation of these factors to blood group and secretor status in normal and duodenal ulcer subjects could clearly make a valuable contribution in this field. The opposing

factors which may be expected to cause mucosal injury and result in erosions and ulceration would certainly include the acid and pepsin secretions.

Several studies of acid secretion in relation to blood group in normal as well as duodenal ulcer subjects have been carried out and have shown results which have been conflicting. Renewed interest has been aroused by the recent experimental work of Emås and Grossman (1967) who infused porcine gastrin into cats to induce gastric secretion short of the maximum extent. The lesions described included gastroduodenal bleeding, mucosal erosions, and duodenal ulcer with perforation in some cases. It would seem, therefore, that further studies of acid secretion in man in relation to blood group would be well worth undertaking.

The incidence of ABH non-secretion is the same in patients who have perforated as in those who have neither bled nor perforated. It would seem, therefore, likely that the influence exerted on duodenal ulcer by the genes controlling ABH secretion on the one hand and the genes controlling the ABO blood groups on the the other are quite different. The evidence at present available strongly suggests that the ABO blood groups influence the clinical course of the disease, probably by determining the structure of the mucosa of the upper gastrointestinal tract. Less evidence is available concerning ABH secretor status, of various clinical categories, but the Liverpool data suggest that non-secretion may be more concerned with initiation of duodenal ulceration than with clinical course.

SUMMARY

It is known that there is a much stronger association between blood group O and duodenal ulcers which have bled than between blood group O and duodenal ulcers which have caused pain or obstruction without bleeding. Another common bleeding condition, namely menorrhagia, has been examined and the incidence of blood group O found does not differ from an appropriate large general control population. This finding suggests that blood group O does not specifically influence haemostatic mechanisms.

A previously published series of perforated duodenal ulcers which have not bled has been expanded. The incidence of blood group O in perforated duodenal ulcers is at a similar high level to that found in duodenal ulcers which have bled. The non-secretion incidence is, however, the same in perforated duodenal ulcers, duodenal ulcers which have bled, and in those which have caused pain and obstruction without either bleeding or perforating.

It would appear in the light of the evidence at present available that blood group O genes play a part in determining the severity of duodenal ulcer, probably by means of an effect on the mucosa of the upper gastrointestinal tract. The role of the genes controlling ABH secretion remains obscure, but they may be mainly involved in the predisposition to duodenal ulceration.

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