ABO and Rh blood groups in patients with cholelithiasis and carcinoma of the gall bladder

M Pandey, A Gautam, V K Shukla

Department of Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221 005, India
M Pandey, *senior resident*
A Gautam, *lecturer*
V K Shukla, *reader*

Correspondence to:
Dr Shukla.

BMJ 1995;310:1639

Carcinoma of the gall bladder is a common malignancy in Eastern Uttar Pradesh and Western Bihar regions of India, constituting 4·4% of all malignancies and 0·3% of admissions to University Hospital, Varanasi.[1] Since the first report by Aird *et al* in 1953,[2] showing an association between blood group A and gastric cancer, numerous other reports have documented a high incidence of blood group A in various cancers including salivary gland, colon, uterus, ovary, pancreas, kidney, bladder, and cervix.[3] There has been no previous report of association between gall bladder carcinoma and any specific blood group. Juvonen and Niemela[4] studied 171 patients with symptomatic gall stones and found no association with any blood group, although patients with blood group A had multiple stones. Blood groups are differentially distributed in various socioeconomic, geographical, and ethnic groups. We studied the distribution of ABO and Rh blood groups in patients with carcinoma of the gall bladder and cholelithiasis, comparing it with the blood group distribution in our population.

Patients, methods, and results

Distribution of ABO and Rh blood groups was recorded in 69 patients with carcinoma of the gall bladder and 152 patients with cholelithiasis presenting to the department of surgery, University Hospital, Banaras Hindu University, Varanasi. Patients coming for routine surgical operations such as hernia, hydrocele, appendicitis, lipoma, and sebaceous cyst (n=673) and blood donors (n=367) served as controls. Statistical analysis was carried out by χ^2 test using MS-Basic epistat and MSTAT statistical packages.

The ABO blood group distribution is shown in the table. Of the 1040 controls 40 (3·8%) were Rh negative. Among the cholelithiasis group, eight (5·3%) were Rh negative, while only one (1·4%) patient with carcinoma of the gall bladder was Rh negative ($P > 0·05$).

Blood group distribution in patients with cholelithiasis, carcinoma of the gall bladder, and controls. Results are numbers (and percentages) of patients

Blood group	Cholelithiasis	Carcinoma of gall bladder	Blood donors	Routine surgery	Total
A	34 (22·4)	23 (33·3)	81 (22·1)	159 (23·6)	297
Expected value	35·8	16·3	86·4	158·5	
χ^2	0·1	2·8	0·3	0·0	
B	54 (35·5)	16 (24·8)	113 (30·8)	215 (31·9)	398
Expected value	48·0	21·8	115·8	212·4	
χ^2	0·8	1·5	0·1	0·0	
O	54 (35·5)	12 (17·5)	162 (44·1)	254 (37·7)	482
Expected value	58·1	26·4	140·3	257·2	
χ^2	0·3	7·9	3·4	0·0	
AB	10 (6·5)	18 (26·1)	11 (3·0)	45 (6·7)	84
Expected value	10·1	4·6	24·5	44·8	
χ^2	0·0	39·0	7·4	0·0	
Rh negative	8 (5·3)	1 (1·4)	12 (3·3)	28 (4·2)	

$\chi^2 = 63·64$, df=9, $P < 0·0005$.
*Figures in parenthesis show range.
χ=Contribution of each cell to χ^2.

Comment

Like previous workers,[4] we found the distribution of blood groups in patients with cholelithiasis to be the same as that of the general population. The present study, however, shows an increased frequency of carcinoma of the gall bladder in blood groups A and AB compared with the control population, which is similar to the previously reported increased incidence of blood group A in carcinoma of the stomach, colon, uterus, and cervix.[2,3]

The increased risk of development of gastric and colonic cancers in patients with blood group A has been explained by the expression of Forssmann antigen in these cancers. Forssmann antigen is structurally similar to the blood group antigen A. Because of this similarity, antibodies to A probably also attack precancerous and cancerous cells expressing this antigen. People with blood groups A and AB lack antibodies to A and so are more prone to develop these carcinomas.[3] A similar mechanism may be responsible for the high incidence of carcinoma of the gall bladder observed in patients with blood groups A and AB in this study.

It is also possible that there may be genes associated with a factor or factors that confer a favourable prognosis, closely related to the genes responsible for the expression of the blood group antigens; these may be inherited together.[5] Further studies on the blood group antigenic determinant in tumour tissues with clinicopathological correlation might further elucidate this relationship.

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(Accepted 4 April 1995)

GR106642X: a new, non-ozone depleting propellant for inhalers

Simon C O Taggart, Adnan Custovic, David H Richards, Ashley Woodcock

Correspondence to:
Dr Woodcock.

BMJ 1995;310:1639-40

Metered dose inhalers are the most popular choice of drug delivery system for treating asthma and chronic airflow limitation. Unfortunately, they contain chlorofluorocarbon propellants, which contribute to the depletion of stratospheric ozone.[1] The Montreal Protocol of 1987 has therefore called for a gradual phasing out of manufacture of chlorofluorocarbons in all developed countries by 1996. Inhalers containing chlorofluorocarbons have been given a temporary exemption, but there remains considerable environmental pressure for their early withdrawal.

GR106642X (1, 1, 1, 2-tetrafluoroethane) is a new propellant which does not deplete ozone. It has been used alone, with no other excipients, to reformulate salbutamol. We investigated the safety and efficacy of the new non-ozone depleting formulation for salbutamol in a randomised, double blind, placebo controlled, crossover comparison with the traditional salbutamol inhaler containing chlorofluorocarbons 11 and 12 (Ventolin, Allen and Hanburys) in protecting adults with asthma from bronchoconstriction induced by histamine.

Subjects, methods, and results

The study was approved by the local research and ethics committee of the university hospitals of south

North West Lung Centre, Wythenshawe Hospital, Manchester M23 9LT
Simon C O Taggart, *honorary research registrar*
Adnan Custovic, *honorary research registrar*
Ashley Woodcock, *consultant respiratory physician*

Glaxo Research and Development, Stockley Park West, Uxbridge, Middlesex UB11 1BT
David H Richards, *clinical research manager*

Manchester. During three weeks, 24 non-smoking, asthmatic subjects with bronchial hyperresponsiveness to histamine at screening (with a dose arbitrarily defined as $<3{\cdot}9$ μmol, which represents the cumulative dose required to cause a 20% drop in post-saline forced expiratory volume in one second with a dosimeter and Yan's protocol[2]) attended for testing on three occasions not less than 24 hours but not more than 7 days apart. At each visit, provided that forced expiratory volume in one second was within an arbitrarily defined 15% of the result at the screening visit, the subjects took two puffs with a Volumatic spacer from one of three different inhalers—delivering placebo GR106642X; salbutamol 100 μg plus GR106642X (new inhaler); or salbutamol 100 μg plus propellants 11 and 12 (traditional inhaler). The subjects then rested for 30 minutes before their bronchial responsiveness to histamine was measured. Throughout the study each subject was monitored for any adverse events.

Log normalised values of bronchial responsiveness to histamine were compared between treatments with analysis of covariance appropriate to a three period crossover,[3] in which the terms for treatment sequence, period, and forced expiratory volume in one second before challenge with histamine were included. Equivalence of effect between the treatments with salbutamol was defined as a ratio of less than 4 (equivalent to a difference of two doubling doses of histamine) as in inexperienced subjects successive results after challenge with histamine are likely to be within 1·87 doubling doses of one another.[4]

All 24 subjects (10 men, 14 women; mean age 37 years) completed the study without systemic side effects attributable to the new propellant. Twenty two subjects were maintained on regular inhaled steroid prophylaxis (median dose 400 μg/day) and two on sodium cromoglycate.

Equivalence of effect was shown between new and traditional inhalers (ratio (90% confidence interval) 1·06 (0·63 to 1·79, P=0·842)), but both these treatments were found to be significantly more protective of bronchoconstriction induced by histamine than the placebo (new inhaler *v* placebo 3·35 (1·92 to 5·83, $P<0{\cdot}001$), traditional inhaler *v* placebo 3·14 (1·86 to 5·31, $P<0{\cdot}001$)). The table shows the effects of the treatments.

Summary of effects of treatment in 24 asthmatic subjects

	Treatment		
	Placebo GR106642X	Salbutamol 200 μg plus GR106642X	Salbutamol 200 μg plus propellants 11 and 12
Before challenge with histamine:			
Mean (SD) forced expiratory volume in 1 second (l)	2·74 (0·76)	2·84 (0·77)	2·79 (0·79)
Mean (SD) forced vital capacity (l)	3·69 (0·98)	3·78 (0·96)	3·80 (0·97)
After challenge with histamine*:			
Geometric mean (cv) forced expiratory volume in 1 second (l)	0·78 (3·54)	3·06 (1·85)	2·66 (3·81)
Adjusted mean (cv) forced expiratory volume in 1 second (l)	0·84 (1·43)	2·83 (1·43)	2·66 (1·43)

cv=Coefficient of variance.
*Cumulative dose of histamine ($<3{\cdot}9$ μmol) causing a 20% drop in forced expiratory volume in one second.

Comment

We have shown in asthmatic adults with bronchial hyperresponsiveness an equivalence of effect between 200 μg salbutamol delivered with GR106642X (an almost universal dose for the relief of symptoms) and the same dose delivered with propellants 11 and 12 in the protection from bronchoconstriction induced by histamine. This finding does not necessarily imply equivalence of effect at all doses of salbutamol as 200 μg rests on the plateau of the dose-response curve.[5] Nor does it imply equivalence of effect in all other methods of inducing bronchoconstriction, although a degree of association probably exists between them.

The results of our study suggest that the new, non-ozone depleting formulation for salbutamol is a promising alternative to current metered dose inhalers containing chlorofluorocarbons. The introduction of the new formulation would ensure continuity of choice of treatment in subjects with asthma and chronic airflow limitation.

This study was supported by Glaxo Group Research. DHR is employed by Glaxo.

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(Accepted 31 March 1995)

BMJ audit: time to decisions and publication

We aim to make a decision on publication within eight weeks (56 days); to reject papers that are unsuitable for external peer review within two weeks (14 days); and to publish a paper within eight weeks of acceptance.

Between July 1994 and December 1994 we made a decision within 56 days for 83% of all papers submitted and for 64% of those we accepted. We accepted 73% within 66 days (10 days over target), and the mean time to accept a paper was 51 days. We met our target of rejecting papers without peer review within 14 days 46% of the time; 73% were rejected within 24 days (10 days over target), and the average time to reject such papers was 21 days. We published 40% of papers within 56 days of acceptance, 67% within 10 weeks, and 87% within 12 weeks. A comparison with previous audits is shown in the table.

Results of "BMJ" audits. Values are percentages unless stated otherwise

	Decision within 56 days		Accepted papers		Rejected papers			Publication times after acceptance		
Audit	All papers	Accepted papers	Decision within 66 days	Mean time to acceptance (days)	Decision within 14 days	Decision within 24 days	Mean time to reject without peer review (days)	Within 8 weeks	Within 10 weeks	Within 12 weeks
1993:										
Jan-June	88	73	85	41	37	76	19	38	72	95
July-Dec	86	62	75	50	40	84	18	27	66	85
1994:										
Jan-June	88	64	76	48	40	84	18	13	24	57
July-Dec	83	64	73	51	46	73	21	40	67	87