Reported ABO Rhesus blood groups and administration of anti-Rh D immune globulin in pervasive developmental disorders.

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Abstract

Objectives

To examine the frequency of ABO and Rhesus (Rh) blood groups of people diagnosed with pervasive developmental disorders (PDD) and their mothers as recorded by the primary caregiver.

Design

Cross sectional study of a database of records held at the University of Sunderland, UK

Participants

Maternal and participants records of 313 people diagnosed with pervasive developmental disorders and 66 controls not diagnosed were examined for the frequency of maternal and participant ABO and Rh blood groups and frequency of Rh-negative mothers who received Rh D immune globulin.

Results

Univariate analysis showed a significant difference in the frequency of blood type O for maternal control participants (OR 1.82, 95% CI 1.06-3.13, p=0.027) compared to mothers of PDD participants. There was also a significant difference in blood type A (OR 5.60, 95% CI 1.66-18.90, p=0.003) and blood type O (OR 0.16, 95% CI 0.04-0.60, p=0.003) for patients diagnosed with autism. No difference was found between groups for rhesus blood groups or administration of Rh D immune globulin to Rh-negative mothers.

Conclusions

Further research is needed to ascertain the relevance of ABO and Rh blood groups to pervasive developmental disorders.

Introduction

The ABO(H) and Rhesus (Rh) antigen systems are the formal blood group nomenclature used in modern haematology. The differentiation of blood groups using the ABO system is reflective of genetic differences in surface antigens expressed on blood erythrocytes, A, B and neither respectively, and consequently different plasma antibodies. The Rh blood grouping, so-called because it was first studied in rhesus monkeys, is used to describe the presence or absence of the D antigen on the surface of erythrocytes and is usually designated alongside the ABO grouping. The majority of people in the UK tend to be Rh-positive (84%) rather than negative (National Blood Service). Rh incompatibility, as defined as exposure of a Rh-negative person to Rh-positive blood, causes hemolytic disease of the

newborn (HDN) and is preventable by the administration of anti-Rh D immune globulin (anti-D or RhoGAM) to previously exposed Rh-negative mothers.

Variance in the frequency of ABO blood groupings are well known to occur in different ethnic populations as a result of genetic differences (Daniels, 1996). Migration and subsequent inter-population marriage has lead to many of the ancestral homogeneous blood groupings prevalent in specific populations being lost. Britain, for example, shows the greatest frequency of the O phenotype, present in approximately 45% of the population, followed by A (43%), B (9%) and AB (3%) (National Blood Service). The dispersion of blood groups is probably due to the historical migration of other ethnic groups to Britain such as the Celts, Saxons, Romans, and Vikings.

Associations between ABO and Rh blood groupings and increased susceptibility to certain diseases, such as ischaemic heart disease in men (Whincup *et al*, 1990), cancer (Neugut *et al*, 1996) and childhood asthma (Ronchetti *et al*, 2001) have been documented. Possible associations with psychiatric diagnoses such as depression have also been suggested but not substantiated (Singg & Lewis, 2001). Research examining the link between ABO rhesus blood groups and schizophrenia has suggested that rhesus incompatibility may be a risk factor (Hollister *et al*, 1996) implying a possible role for genetic susceptibility. Examination of blood/plasma in pervasive developmental disorders as a biological media has been reported for a variety of biochemical measures (*e.g*. Fatemi *et al*, 2002) although comparatively little work has been conducted on blood group classification as possible factors.

This study investigated the distribution of ABO and Rh blood groups amongst people diagnosed with autism, Asperger syndrome and autism spectrum disorder (Wing, 1996) and their mothers compared to controls, along with rates of administration of Rh D immune globulin among Rh negative mothers.

Method

Subjects

Maternal and/or patient ABO and rhesus blood groups were obtained from parental reports stored on an electronic database of people formally diagnosed with autism (n=95, mean age=6.9 years, SD=6.1), Asperger syndrome (n=66, mean age=8.3 years, SD=4.8), and autism spectrum disorder (Wing, 1996) (n=152, mean age 4.9 years, SD=4.6). Responses were compared with parental reports from a group of controls not diagnosed with pervasive developmental disorder (n=66, mean age=7.6 years, SD=8.7). All participants were residents of the UK and Ireland. Ninety five percent and 93% of mothers and fathers respectively were Caucasian.

Statistical analysis was conducted to identify significant (P=0.05) differences between autism groups and controls using SPSS for Windows™ (v10.1 SPSS Inc. Chicago, IL, 2000). Significant results are expressed as odds ratio (OR), 95% confidence intervals (CI) and P-values. All data are held at the Autism Research Unit at the University of Sunderland under the 1998 Data Protection Act. The study was conducted following guidelines supplied by the University of Sunderland Ethics Committee.

Results

Analysis of the distribution of ABO and rhesus blood groups amongst mother and their offspring are shown in table 1 and 2 respectively.

Table 1 Number of cases by ABO blood groupings (percentage of recorded cases per diagnosis). Smaller numbers of cases for individual diagnostic groups reflects missing responses.

	Autism (16)	Asperger (12) Syndrome	ASD (25)	Controls (11)
Child blood groups				
A	10 (63)*	2 (17)	7 (28)	2 (18)
B	1 (6)	2 (17)	1 (4)	1 (9)
AB	1 (6)	0 (0)	1 (4)	0 (0)
O	4 (25)*	8 (67)	16 (64)	8 (73)
	Autism (95)	Asperger (65) Syndrome	ASD (151)	Controls (66)
Maternal blood groups				
A	37 (39)	18 (28)	61 (40)	20 (30)
B	14 (15)	11 (17)	16 (11)	5 (8)
AB	2 (2)	1 (2)	5 (3)	1 (2)
O	42 (44)	34 (52)	69 (46)	40 (61)*

* Significant at p<0.05.

Knowledge of maternal blood group were high: ABO blood group = 99.4%, rhesus blood group = 83.3%, compared to knowledge of child's blood group: ABO blood group = 16.8%, rhesus blood group = 13.5%. Univariate analysis showed a significantly increased frequency of blood type O for mothers of control participants (blood type O: OR 1.82, 95% CI 1.06-3.13, p=0.027) compared to PDD groups. There was also a significant difference in

blood group for participants diagnosed with autism (blood type A: OR 5.60, 95% CI 1.66-18.90, p=0.003; blood type O: OR 0.16, 95% CI 0.04-0.60, p=0.003). There were no significant differences in patient or maternal rhesus groupings between any of the groups.

Table 2 Number of cases by rhesus blood group (percentage of recorded cases per diagnosis).

	Autism (14)	Asperger (10) Syndrome	ASD (19)	Controls (8)
Child rhesus group				
Negative (-)	3 (21)	2 (20)	7 (37)	3 (38)
Positive (+)	11 (79)	8 (80)	12 (63)	5 (62)
	Autism (80)	Asperger (57) Syndrome	ASD (127)	Controls (52)
Maternal rhesus group				
Negative (-)	20 (25)	9 (16)	26 (20)	10 (19)
Positive (+)	60 (75)	48 (84)	101 (80)	42 (81)

Additional analysis of data from rhesus negative mothers for numbers in receipt of Rh D immune globulin showed no significant difference in frequency between groups (autism: 10 of 20, 50%; Asperger syndrome: 6 of 9, 67%; ASD: 20 of 26, 77%; Controls: 6 of 10, 60%).

Discussion

The results of this pilot study show that mothers of control participants were significantly more likely to be type O blood group than mothers of participants diagnosed with PDD. Participants diagnosed with autism were significantly more likely to be reported as type A blood group and less likely to be type O when compared to other PDD groups and controls.

The reliance on parental reports rather than direct blood phenotyping of participants reflects the preliminary, exploratory basis of this study. The high reporting rates amongst mothers of participants is indicative of the routine nature of screening pregnant women in the UK for ABO and Rh blood group to counter the possible risk of HDN. Conversely, the low response for their offspring is perhaps more representative of a newborn screening policy in the UK that, aside from Phenylketouria and congenital hypothyroidism, does not routinely take or examine blood samples. Given the low number of responses for participant groups,

the significant findings associated with blood groups from the autism diagnostic group must be considered as preliminary and require further investigation.

Bearing in mind the limitations of this study, the implications of a significant difference in blood grouping for families where a PDD diagnosis has been given are far-reaching. Genetic factors as one possibility for conferring susceptibility to acquiring developmental disorders through specific blood groups, could offer a new direction for studies of molecular genetics. Preliminary anthropological data has suggested several factors such as disease infection and diet show strong relationships to blood groups (Martin, 2000), although formal epidemiological studies are lacking to substantiate many of the hypotheses.

Formal studies of Rh ABO blood phenotyping are needed to ascertain any significant relationship with developmental disorders. Future studies should also examine other blood classification systems (*e.g.* Lewis, MNSs) utilising advances in molecular technology.

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