



Rh Immune Globulin in Pregnancy: Relationship to Autism Development

J.H. Miles, T.N. Takahashi, Division of Medical Genetics
University of Missouri-Columbia

Abstract

Autism is believed to be predominately a genetic disorder. However, recent increases in the prevalence of autism have raised the possibility that certain environmental exposures may cause or potentiate the development of autism. The most debated factor has been the increased exposure of children to mercury in the form of thimerosal, a preservative used to stabilize vaccines. Previous studies have concentrated on postnatal vaccines, however, we reasoned that exposure in pregnancy might have a greater effect on the developing nervous system. Since only Rh- women receive Rh immune globulin during pregnancy, any effect of Rh immune globulin exposure should be mirrored by an increased percentage of Rh-mothers of autistic children. We conducted a structured telephone survey to determine the blood type and Rh immune globulin exposure of mothers of autistic children and controls. We found no difference in the Rh- status of autism mothers compared to controls and found no evidence to suggest an etiologic role for thimerosal in the development of autism.

Introduction

Autism is a neuropsychiatric disorder of childhood which has a complex and undoubtedly very heterogeneous etiology. Based on the high heritability factor (0.85 to 0.92), geneticists believe autism is predominately a genetic disorder. However, during the last 15 years there has been a dramatic increase in the apparent incidence of autism with increases in prevalence rates soaring from 1 in 2-5,000 to 1 in 2-500 children. It is unclear whether this is due to a true increase in the incidence of the disorder or to a combination of increased recognition of the symptoms and broadening of diagnostic criteria. Since there are no genetic epidemics, a major question is whether any environmental factors are responsible for the increased prevalence of autism. Because mercury is known to be neurotoxic in sufficiently high doses, it has been theorized that thimerosal, an organic mercury-based preservative used in vaccines, may be a cause for the increased prevalence of autism. Previous immunization studies investigating possible links with autism have focused on postnatal vaccines such as the Measles-Mumps-Rubella vaccine (MMR). This study focuses on prenatal thimerosal exposure in the form of Rh immune globulin or RhoGam, an immunization given to Rh- women after delivery of an Rh+ baby to prevent blood incompatibility in future pregnancies. Until 2001, RhoGam was manufactured with thimerosal as a preservative. The purpose of our study was to determine whether there is any evidence of a relationship between the development of autism and the exposure to Rh immune globulin/thimerosal during the mid trimester of pregnancy.

Methods

Subjects

Study subjects included mothers of 201 children with autism who were evaluated at the Missouri Autism Center between 1995 and 2003. Each child with autism met DSM-IV, CARS and our center based version of the ADI scoring protocol. Independent diagnostic evaluations were conducted by a child psychiatrist and a neuropsychologist. Subjects with a known syndrome or metabolic disorder were excluded from this study.

Control pregnancies consisted of 224 non-autistic siblings, 24 Down syndrome families and 13 families with other genetic disorders.

Evaluation

A structured telephone survey was carried out to determine the blood type of autism mothers and control mothers. Results were verified by review of pregnancy, delivery and immunization histories. Each family was sent Release of Information forms to send to their obstetrician, birthing hospital and pediatrician or health clinic where immunizations were received.

Structured Telephone Questionnaire

Questions	Answer	Level of certainty			
		Absolutely certain	Pretty sure	Think so	Don't know
Mother's ABO blood type	A B O				
Mother's Rh type	Rh- Rh+				
Father's ABO blood type	A B O				
Father's Rh type	Rh- Rh+				
History of Rh sensitization	Yes No				
Rhogam in pregnancy	Yes No				
Rhogam dose	Date Gest age Reason				
Did mother get any other vaccines in pregnancy?	Yes No Hep B Influenza Rubella				
Full siblings	Rhogam Yes No				
Maternal half sibs	Rhogam Yes No				
Immunizations	UTD Delay Unk				

Results

- no significant difference in the Rh- status of autism mothers (19.5%, 30/154), Down syndrome mothers, (25%; 6/24) or genetic clinic mothers (23.1%; 3/13)
- exposure to Rh immune globulin during pregnancy was comparable for autism mothers (12.9%; 26/201) and Down syndrome mothers, (15%; 4/27)
- Rh immune globulin exposure during pregnancies of non-autistic sibs of children with autism was similar to the exposure in the autism pregnancies (12.9% vs 12.6%)

Demographics of Autism Group (N=201)

Male:Female ratio	4:1 (161:40)
Mean age (SD)	8.0 (5.9)
Ethnicity	
Caucasian	92%
African American	3%
Asian	1.5%
Biracial/other	3.5%

	Autism	Non-autistic sibs	Down Syndrome control
Rh-	19.5%	23.3%	25%
Rh immune globulin exposure	12.9%	12.6%	15%

Conclusions

- no indication that pregnancies of children with autism were any more likely to be complicated by Rh immune globulin/thimerosal exposure than those of controls
- no evidence of an etiologic role for thimerosal in the development of autism.

Future studies:

- analysis of total thimerosal and organic mercury exposure for each autistic child and control.
- determine whether exposure to Rh immune globulin correlates with any specific subset of autism patients