The Failure of Neonates to Form Red Blood Cell Alloantibodies in Response to Multiple Transfusions

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Red blood cell alloantibody production was studied in 90 neonates who received a mean of 14.1 transfusions (range 2–35) from an average of 8.9 donors during the first three months after birth. Standard antibody detection procedures were done with the use of a selected red blood cell panel. No unexpected alloantibodies were detected. These findings suggest, at a 99% confidence level, that neonates do not make red blood cell alloantibodies in response to transfusion, indicating that repeated compatibility testing is probably unnecessary. Thus, following initial antibody screening and compatibility tests, further compatibility testing can be eliminated. (Key words: Neonatal transfusion; Red blood cell alloantibody; Red blood cell compatibility testing) Am J Clin Pathol 1987; 87: 250–251

THE American Association of Blood Banks Standards no longer require repeated red blood cell (RBC) compatibility testing for neonatal patients (younger than four months) who have no RBC alloantibodies detected in the first testing procedures. Before following these guidelines and to evaluate RBC alloantibody formation by neonates, we studied the incidence of alloantibody production in 90 neonates who received multiple (1,269) transfusions.

Materials and Methods

Blood samples were obtained from 90 neonates admitted to the University of Minnesota Hospitals newborn intensive care unit. Only patients who had been transfused at least three weeks earlier were included to provide an arbitrary minimum time interval during which patients could have produced antibodies.

RBC alloantibody detection tests were done by conventional test tube methods with the use of six-cell panel (three pools of two cells each) of saline-suspended pa-painized or untreated RBCs. Tests were incubated at 4 °C, room temperature (RT), or 37 °C, in saline or albumin media and included an antiglobulin phase when appropriate. Patients’ sera were also screened by the rou-

tine procedures used in the University Hospitals’ Blood Bank with pooled Spectrogen Duo® screening cells I and II (Biological Corporations of America, Westchester, PA 19830) with incubations at RT and 37 °C and carried through the antiglobulin phase (Table 1). All tests were read microscopically. Test procedures were selected to provide optimum conditions for detection of antibodies in the Rh, Kell, Duffy, Kidd, MNS, Lewis, and P systems.

Statistical analysis of the data was done using a Klopper-Pearson confidence interval limit for proportions (binomial) table at 99%.

Results

The 90 neonates studied received a total of 1,269 transfusions, an average of 14.1 transfusions per neonate (range 2–35). The average number of different donor exposures was 8.9 for a total of 802 donor exposures to these 90 patients. No unexpected RBC alloantibodies were detected in their sera.

Statistical evaluation using Klopper-Pearson confidence interval tables (binomial) for N = 1,269 indicates that the likelihood of a neonate making an antibody is 0–0.6%, using a confidence interval limit of 99% (P = 0.01). Giblett calculated that at least 23% of blood transfusions exposed the recipient to foreign antigens, exclusive of AB and Rh, but that there was only a 1.1% overall observed antibody stimulation from a random unit of blood despite the 23% chance of exposure. Given this 1.1% expected antibody production, we should have observed 13.9 examples of antibody resulting from the 1,269 transfusions. Because we found none, the data are significant at the P = 0.01 level. If statistical evaluation is based on the 802 different donors used, the range of expected antibody formation is 0–0.75%, and our findings are significantly less (P < 0.01) than the 1.1% predicted rate as calculated by Giblett.

Discussion

The reason(s) for reduced or absent RBC alloantibody formation in neonates is not established. The neonatal
period is a state of relative immunodeficiency during which newborns are particularly vulnerable to bacterial, viral, and protozoal infection. Newborns localize infection poorly, mount a sluggish antibody response to injected antigens, and are relatively anergic. Both in vivo and in vitro studies suggest that there are a number of immature or dysfunctional components of the neonatal afferent and efferent arms of the immunologic mechanism leading to a state of physiologic hyporesponsiveness. The impairment in antibody production by neonates can be corrected by transplanting macrophages from adults, which implies that the host (neonatal) macrophages may be defective or viral, and protozoal infection. Newborns localize infection due to a period of relative immunodeficiency during which they are particularly vulnerable to infection. This period is also characterized by a state of physiologic hyporesponsiveness in newborns, which is thought to be due to a lack of functional T and B cells.

Other studies suggest a state of relative immunodeficiency in the neonate with respect to T-cell function. Newborn infants, particularly those born prematurely, have a significantly lower rate and degree of skin sensitization to dinitrochlorobenzene, a decreased response to intradermal phytohemagglutinin, although the response of newborn lymphocytes to this agent is intact. This diminished skin test response may reflect not only monocyte and macrophage dysfunction, but also a lack of the components of the inflammatory response as well as lymphocyte dysfunction. Thus, newborn infants may not be fully immunocompetent until four to six months of age.

Our study was carried out on a specific population (neonates) whose members were critically ill and/or premature, and this subset of patients may be unusually immunologically suppressed. Therefore, even though these data cannot be generalized to other populations, they can be applied to neonates who are multiply transfused. Because this study indicates that neonates have a very low, if not nonexistent, incidence of RBC alloantibody formation compared with adults, repeated RBC compatibility testing for non-ABO antibodies may be eliminated for these patients. Therefore, if unexpected antibodies are not detected in initial compatibility testing and group ABO Rh0 compatible RBCs are used for neonatal transfusions, repeated RBC compatibility testing can be eliminated during the neonatal period, consistent with the present standards of the American Association of Blood Banks.

References


Table 1. RBC Alloantibody Detection Procedures

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<th>Antiglobulin Serum Used</th>
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