Evaluation of Selected Markers of the Immune System in Children of Renal Transplant Recipients

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ABSTRACT

Objective. The aim of this study was to evaluate whether chronic use of immunosuppressive drugs during pregnancy in women after renal transplantation affects the concentration of immunoglobulin G (IgG) and IgM in the serum of their children.

Material. Seventy-eight children aged 1 day to 15 years were enrolled. The study group consisted of 39 children born to renal transplant recipient mothers. The control group comprised 39 children whose mothers had not received immunosuppressive medications during pregnancy and were born at similar gestational age.

Methods. Serum concentrations of IgG and IgM were evaluated with the use of agglutination immunoassays on Siemens or Cobas device. Age-adjusted reference values for immunoglobulins formulated by Wolska-Kusnierz et al were used. Statistical analysis was performed with the use of Statistica 10.0 software with P value $<.05$ considered significant.

Results. Normal IgG concentrations were found in 82.05% (32) of children from the study group and 79.49% (31) of the control group. IgG concentrations below normal range were observed in 12.82% (5) of children from the study group and in 15.38% (6) of the control group. Normal concentrations of IgM were found in 53.85% (21) of children from the study group and in 61.54% (24) of the control group. Decreased levels of IgM were observed in 38.46% (15) of children from the study group and 35.9% (14) of the control group. There were no significant differences regarding the analyzed values between the groups.

Conclusion. The exposure to chronic intrauterine immunosuppression had no significant effect on the concentration of IgG or IgM in children born to kidney transplant recipients.

THE ROLE of the immune system is to defend the organism against infections. Despite the fact that there are certain differences concerning the immune system between the adult, child, and neonate, the newborn is sufficiently protected against infections if the mother is healthy, the pregnancy ends at term, and the newborn is breastfed from the beginning. If any of these conditions are not fulfilled, the risk of infection increases [1].

The measurement of the immunoglobulin G (IgG), IgM, and IgA serum concentrations is one of the basic methods used to assess human immune functions. Decreased levels of these immunoglobulins occur in primary and secondary immunodeficiencies [2].

The development of transplantation medicine is inevitably associated with an increasing number of pregnant transplant recipients who chronically receive immunosuppressants and automatically with an increasing number of neonates exposed to those drugs [3]. The impact of immunosuppressive medications on the immune system of the newborns is particularly interesting.

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The objective of the study was to evaluate whether immunosuppressive drugs administered to pregnant renal transplant recipients (RTRs) had any effect on serum concentrations of IgG and IgM of their children. The impact of birth weight, gestational age, and particular immunosuppressive treatment in the group with decreased IgG and IgM levels were also assessed.

MATERIAL AND METHODS

Seventy-eight children were enrolled in the prospective study. They were examined in the First Department of Obstetrics and Gynecology, Medical University of Warsaw. The study group consisted of 39 children, aged 1 day to 15 years, born to RTRs. The control group comprised 39 children aged 1 day to 14 years whose mothers had not received immunosuppressive medications during pregnancy. The patients from both groups were born during similar a period and at similar gestational age. The most common drugs administered to mothers from the study group were tacrolimus, glucocorticosteroids, cyclosporine, and azathioprine.

Serum concentrations of IgG and IgM were evaluated with the use of agglutination immunoassays on Siemens or Cobas device. Age-adjusted reference values for IgG and IgM for immunoglobulins formulated by Wolska-Kusnierz et al were used.

Gestational age, birth weight, age at the time the research was conducted, and immunosuppressive treatment in patients with diminished immunoglobulin were analyzed.

Statistical analysis was performed with the use of Statistica 10.0 software. Fisher's exact test and the χ^2 test were applied and P values $<.05$ were considered significant.

RESULTS

Normal IgG concentrations were found in 82.05% (32) of children from the study group and 79.49% (31) of the control group ($P = .775$). IgG concentrations below normal range were observed in 12.82% (5) of children from the study group and in 15.38% (6) of the control group ($P = .746$).

Adequate concentrations of IgM were found in 53.85% (21) of children from the study group and in 61.54% (24) of the control group ($P = .494$). Decreased levels of IgM were observed in 38.46% (15) of children from the study group and 35.9% (14) of the control group ($P = .815$; Table 1).

Within the study group, decreased concentrations of IgG were observed in patients with birth weight ranging from 1660 to 2520 g and born at 31 to 37 weeks of gestation. In the control group, decreased levels of IgG occurred in patients with birth weight from 1190 to 3100 g and who were born at 28 to 36 weeks of gestation.

In the study group, diminished concentrations of IgM were found in patients with birth weight ranging from 580 to 3160 g and born at 27 to 38 weeks of gestation. In the control group, decreased levels of IgM were observed in patients with birth weight 1190 to 3700 g and born at 27 to 40 weeks of gestation (Table 2).

In the analyzed material, decreased IgG levels were found in 3 of 27 (11.1%) patients from the study group and in 6 of 26 (26.1%) controls born before 37 weeks of gestation ($P = .175$). Diminished IgM concentrations were observed in 11 of 27 (40.7%) children from the study group that were delivered preterm and 9 of 23 (39.1%) prematurely delivered controls ($P = .90$).

Regarding the age of patients at the time the research was performed, IgG concentrations below the reference range were found in 5 children from the study group: two of them were younger than 2 months of age, whereas the remaining three were aged 5 to 10 years.

Decreased concentrations of IgM were found mainly in the youngest children: 14 of 15 lowest values (93.3%) occurred in children younger than 15 months of age. In the control group, all diminished IgM concentrations were found in children aged younger than 15 months (Table 2).

All 5 patients with IgG levels below the reference range were prenatally exposed to azathioprine and glucocorticosteroids: one mother received solely azathioprine and glucocorticosteroid; two received azathioprine, glucocorticosteroids, and tacrolimus; and the remaining two received azathioprine, glucocorticosteroids, and cyclosporine.

Decreased concentrations of IgM were found in 15 children from the study group. Their mothers received the following immunosuppressive therapy during pregnancy: one

Table 1. Patients in Particular Age Intervals With Normal and Decreased Levels of IgG and IgM

	IgG				IgM			
	RTR		Control Group		RTR		Control Group	
Age	Normal	Decreased	Normal	Decreased	Normal	Decreased	Normal	Decreased
1–7 d	7/10 (70%)	1/10 (10%)	5/11 (45.45%)	4/11 (36.36%)	0	10/10 (100%)	0	11/11 (100%)
8 d–2 mo	1/2 (50%)	1/2 (50%)	2/2 (100%)	0	0	2/2 (100%)	0	2/2 (100%)
3–5 mo	0	0	1/1 (100%)	0	0	0	1/1 (100%)	0
6–9 mo	1/1 (100%)	0	0	0	0	1/1 (100%)	0	0
10–15 mo	3/3 (100%)	0	2/2 (100%)	0	2/3 (66.67%)	1/3 (33.33%)	1/2 (50%)	1/2 (50%)
16–24 mo	3/3 (100%)	0	4/4 (100%)	0	3/3 (100%)	0	4/4 (100%)	0
2 1/12–5 y	10/10 (100%)	0	9/10 (90%)	1/10 (10%)	9/10 (90%)	0	9/10 (90%)	0
5 1/12–10 y	6/9 (66.67%)	3/9 (33.33%)	6/7 (85.71%)	1/7 (14.29%)	6/9 (66.67%)	1/9 (11.11%)	7/7 (100%)	0
10 1/12–14 y	0	0	2/2 (100%)	0	0	0	2/2 (100%)	0
14 1/12–18 y	1/1 (100%)	0	0	0	1/1 (100%)	0	0	0
All	32/39 (80.05%)	5/39 (12.82%)	31/39 (79.49%)	6/39 (15.38%)	21/39 (53.85%)	15/39 (38.46%)	24/39 (61.54%)	14/39 (35.90%)

Abbreviations: RTR, children of renal transplant recipients (study group); IgG, immunoglobulin G; IgM, immunoglobulin M.