PREGNANCY AND DELIVERY MANAGEMENT IN WOMEN WITH TRANSPLANTED KIDNEY

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Introduction

Successful long-term postoperative rate of kidney transplantation is now increasing. Nowadays more than 25 000 kidney transplantation have been performed. One-year survival of allografts and recipients reaches 80% and 93%, accordingly. The most important evidence of patient's successful rehabilitation after kidney transplantation is woman's ability to give birth to a healthy child.

Approximately one of 50 reproductive aged women with functioning renal transplant becomes pregnant. According to the data of American National Register of Pregnancy Cases after Transplantation the most pregnancy cases after renal transplantation results in delivery of healthy newborns. So that, the study of this problem is now actual not only for transplantologists but also for obstetricians and gynecologists.

When renal function declines in pregnancy of graft loss occurs, it may be difficult to determine whether this is due to pregnancy (which is considered to be 18%) or represents the "natural history" of renal transplant function decreasing (about 15%).

Absence of experience of obstetricians/gynecologists in management of pregnancy after renal transplantation usually contributes to advise the pregnancy termination. But it has been established pregnancy termination in women with renal transplant is accompanied with the increased risk of grafts losses. Sometimes women decided to prolong pregnancy are managed by transplantologists only that could increase risk of obstetrical complications.

The aim of our study was to present the tactics of pregnancy and delivery management of women after renal transplantation.

We conducted clinical and laboratory examination of 35 pregnant women who had previously undergone kidney transplantation. Before the transplantation all the patients had been suffering from different renal pathology (glomerulonephritis,

pyelonephritis, congenital anomalies of urinary tract) resulted in chronic renal failure which demanded haemodialysis and peritoneal dialysis during the period of 18 and 14 months, accordingly.

Menstrual disorders and pelvic inflammatory diseases were the most frequent gynecological pathology.

Cadaveric kidney transplantation was performed if there were donor tissue compatibility. Under general anesthesia renal transplant was placed in the right or left iliac area (fossa iliaca) extraperitoneally; intercommunication between renal and iliac vessels was established by "end-to-end" or end-to side" anastomosis using uninterrupted vascular suture. Creation of neoureterovesical anactomosis using uninterrupted absorbable suture allowed to restore urine passing. All women were given immunosuppressive therapy in postoperative period. Two-compound therapy included azathioprine (5-100 mg) and glucocorticoids (prednisolone or methylprednisolone); three-compound therapy combined azathioprine, glucocorticoids and cyclosporin A (3-35mg/kg).

All renal allograft recipients were recommended contraception for at least a 18-month period after operation until stable normalization of transplant function. The duration of a period between transplantation and pregnancy varied from 1.5 to 9 years (in the majority cases - 2 years).

Among 35 patients 23 were primigravida (nullipara) and 8 and 4 were gravida 1 and 2, accordingly. It is important to note that in 3 patients became pregnant after the repeat kidney transplantation because of the previous graft loss.

All the previous pregnancies were terminated; in the most cases pregnancy termination was perfomed on medical recommendation probably due to limited knowledge and apprehension of obstetricians about future patient’s state.

During the gestational period patients continued to receive immunosuppressive therapy - glucocorticoids (all patients) and cyclosporin A (32 women). Azathioprine was excluded due to its teratogenic effects. Besides this all women received vitamins, metabolic medications.

All renal allograft recipients underwent clinical and laboratory examination during gestation. Blood tests and urinalises, renal function tests, hormonal and immunological investigations, fetal and transplanted kidney ultrasound, uteroplacental, fetoplacental and renal graft’s doppler waveforms recording, fetal cardiomonitoring and daily blood pressure monitoring were dynamically evaluated.

Special attention was paid to creatinine and urea as well as cyclosporin A blood level as these parameters are considered to be the most important in the assessment of transplanted kidney function.

Renal transplant function was normal in the beginning of pregnancy in all excluding 2 patients: blood and urinary tests, blood creatinine level corresponded to normal parameters, systolic and diastolic blood pressure did not exceed 150 and 90 mm Hg, respectively. It is important to note there was no deterioration of kidney transplant function in all allograft recipients before pregnancy.

As far as pregnancy progresses the main parameters of renal transplant function are dynamically changed: we noted moderate decreasing of creatinine and urea blood levels as well as moderate increasing of glomerular filtration rate until the end of the III trimester. Since this period gradual increasing of creatinine and urea blood concentration and declining of glomerular filtration have been observed.

According Doppler sonography data, changes of renal transplant haemodynamics have occurred in pregnancy and resulted in progressive decrease of resistant index (RI) due to high intensity of blood flow velocity and mostly diastolic component. This process is especially expressed in the period from 13 to 16 weeks of gestation. According to the raised renal transplant blood flow intensity glomerular filtration rate is increased with accompany of moderate decreasing of urea and creatinine blood levels. Starting with 37 weeks and during 3-4 weeks postpartum renal blood flow velocity decreases moderately resulted in resistant index increasing. The same changes of renal haemodynamics are characteristic of normal pregnancy and explained by hormonal influence.

Thus, worsening of renal transplant function in the III trimester and postpartum is of physiological character and transitory.

Proteinuria is a significant parameters of renal allograft suffering. Nowadays proteinuria is considered to be a marker of chronic transplant rejection. In our study 2 patients had moderate proteinuria before pregnancy (0,6 and 0,75 g/L/day). In other women constant proteinuria with level that did not exceed 0,5 g/L/day was found at the beginning of pregnancy. Moderate increasing of protein excretion during gestation we did not consider as a sign of renal transplant pathology in case it is not combined with arterial hypertension. In our research only 4 patients demonstrated proteinuria with hypertension higher than 160 and 100 mm Hg after 26 weeks of pregnancy. In 18

women hypertension with blood pressure level up to 140/90 - 150/90 mm Hg was recorded before the pregnancy and demanded minimal antihypertensive therapy.

Metabolism and pharmacokinetics of cyclosporin A during gestation are of a great importance. The maintenance of a certain cyclosporin A level is necessary for prevention of renal transplant rejection. Cyclosporin A concentration varied from 98 to 130 ng/ml and tended to decrease despite the increase of the dose of this medication.

The most common gestational complications in women with renal allografts were early toxicosis, anemia, pyelonephritis, intrauterine growth retardation. Anemia with hemoglobin level less than 100g/L took place in 6 patients before pregnancy. It was often caused by deficient erythropoietin production due to a reduction of functional renal mass. Other causes included deficiencies of iron, folate, and cyanocobalamin. Besides iron administration refractory iron-deficiency anemia usually demanded vitamin supplementation (folic acid, cyanicobalamin) as well as recombinant human erythropoietin. Because the absorption of oral iron is limited, many patients required iron *I.V.* during pregnancy.

Anemia due to deficient erythropoietin production in usually takes place in patients with chronic renal transplant dysfunction. In our study anemia caused by deficient erythropoietin production due to chronic renal allograft nephropathy had 1 patient. In other case of erythropoietin production deficiency renal transplant function was stable during the II and III trimesters, and anemia was efficiently treated by recombinant human erythropoietin.

Urinary tract infection observed in 10 patients. Moreover, chronic pyelonephritis of renal allograft in 2 patients was diagnosed before pregnancy. If diagnostic criteria of renal transplant pyelonephritis were revealed antibacterial therapy was included in the treating management. We did not observed obstructive pyelonephritis that can be explained by topographoanatomical location of pregnant uterus and transplanted kidney that excludes constriction of ureter.

Pregnancy ended in labor in 33 cases. Term labor took place in 24 cases, preterm labor - in 9 patients. Pregnancy was terminated preliminary by miscarriage in 2 women. 28 patients were delivered by cesarean section. The mean term of delivery was 34±2,4 weeks. During the operation all renal transplant recipients were given methylprednisolone (500-750 mg) to prevent acute crisis of allograft rejection. According into consideration expressed immunosupression and high risk of purulent

complication the duration of postoperative antibacterial therapy was 10 days. Azathioprine administration was resumed after delivery.

Among 33 alive neonates average weight of born at term was 3005±154.9 g and born prematurely - 2053+173.2 g. The frequency of intrauterine infection in neonates was 9% (toxoplasmosis, hepatitis B).

Puerperium was normal in all women. Detailed clinical and laboratory examination did not reveal any deterioration of renal transplant function due to pregnancy.

Breast-feeding was prohibited for all our patients because immunosuppressive drugs pass into the mother's milk that could result in deep depression of immune system of newborns.

Summarizing our results we can conclude we conclude that pregnancy can proceed successfully in women with transplanted kidney if it is starts not earlier than 2 years after transplantation, in absence of severe proteinuria and significant hypertension that can point at satisfactory allograft function. During pregnancy immunosuppressive therapy including glucocorticoids and/or cyclosporin A should be given in minimal doses. Azathioprine must be excluded because of its teratogenic effect. Pregnant women with transplanted kidney should be followed up by obstetrician and transplantologist once in two weeks in the I-st and II-nd trimesters and weekly in the III trimester. Management of these patients demands special attention in renal transplant function control (blood pressure, proteinuria level, creatinine and urea blood concentration).

Satisfactory function of transplanted kidney before pregnancy provides more opportunities for uncomplicated gestation.