Hypertension and Donor Age in Living-Related Kidney Transplantation

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1. INTRODUCTION

Post-transplantational hypertension is one of the most important factors which has negative influence on survival of a graft and a patient. The objective of this study was to evaluate the influence of donor’s age on hypertension and the outcome in living-related transplantation of the kidney. Methods: The research included 52 recipients of the graft, 30 women and 22 men who received living-related kidney graft in 5 years period. In experimental group there were recipients of grafts who’s donors were 55 and older, and in control group recipients of graft who’s donors were younger than 55. Age and sex of the donor, glomerular filtration rate of the donated kidney, previous dialysis treatment, kidney disease and number of months after transplant were monitored. Blood pressure was measured once a day and average monthly value was assessed. Creatinine clearance was valued out in six months. Functional kidney graft after 60 months was considered the one with serum creatinine ≤150µmol/l. Statistical analysis included t-test, Fisher’s exact test, chi-square test, Kaplan–Meier curve and multivariant logistic regression. Results: Experimental group included 23 examinees who received grafts from donors 55 years old and above (18 men and 5 women, average age 31,69±10,5, who have been treated for 35,33±37,59 months), and control group of 29 examinees from donors younger than 55 (16 men and 13 women, average age 31,69±10,5, who have been treated for 21,03±25,59 months). Average age of the donors in experimental group was 62,43±10,0 and 45,31±5,24 in control group. Mean creatinine clearance of the donated kidneys was 47,87±10,5 ml/min in experimental group and 51,19±10,1 ml/min in the control group. Average systolic blood pressure was 146±20,0 mmHg, and in the control group 129±16,0 mmHg (p<0,001). Average diastolic blood pressure was 82,75% recipients of the control group. The average systolic blood pressure in experimental group was 146±20,0 mmHg, and in the control group 129±16,0 mmHg (p=0,005). Sixty months after transplantation graft was functional in 32,69% recipients of the experimental group and 82,75% recipients of the control group. In experimental group recipients of graft who’s donors were younger than 55 (16 men and 13 women, average age 31,69±10,5, who have been treated for 21,03±25,59 months) had significant influence on long-term survival of the kidney graft in the living-related transplantation. Survival of the graft in examinees without hypertension is significantly longer. Treatment of post-transplantational hypertension is one of the most important tasks in the treatment of patients with transplanted kidney.

Keywords: kidney transplantation, age of donor, graft survival, patient survival

2. OBJECTIVE

The objective of this study was to evaluate the influence of donor’s age on hypertension and the outcome in living-related transplantation of the kidney.

3. METHODS

The research included 52 recipients of the graft, 30 women and 22 men who received living-related kidney graft in five years period. Examinees were divided in experimental and control group. In experimental group there were recipients of grafts who’s donors were 55 and older, and in control group-recipients of graft who’s donors were younger than 55. All donors were psychophysical healthy adult persons. Upper age was not limited. Kidney with less glomerular filtration rate (measured with radioisotope renogram method–Tc99m DTPA) was taken from donors. After transplantation we used triple immunosuppressive therapy which included corticosteroids, azathioprine or mycophenolate mofetil and cyclosporine.

In all kidney graft recipients were monitored age and sex of the donor, glomerular filtration rate of the donated kidney, previous dialysis treatment, primary kidney disease and number of months after transplantation. Blood pressure were measured once a day and average monthly value were assessed. All graft recipients were assessed every one or two months (blood glucose level, lipids, blood cell count, blood urea nitrogen, creatinine, uric acid concentration, proteins, electrolytes, bilirubins, transaminases, urin, quantitative proteinuria, creatinine clearance by Cockcroft’s formula (3), kidney graft ultrasound, eye fundus and chest radiography).

Cyclosporine blood level were measured once monthly by fluorescence polarization immunoassay (AxSTYM). The outcome in living-related kidney transplantation after 60 months was defined as: functional kidney graft (serum creatinine ≤ 150 µmol/l), chronic graft nephropathy, other graft’s malfunction reasons (glomerulonephritis “de novo”, infective complications, postoperative complications), terminal graft insufficiency with return on hemodialysis and letal outcome with functional or non-functional kidney graft.

Numerical data are presented as measure of central values, arithmetic median and measure of dispersion, standard deviation. For hypothesis testing between two independent groups we used t-student test and Fisher’s exact test. For hypothesis testing of difference frequency (distribution) assessed parameters we used chi-square test. Survival of patients and grafts is presented by Kaplan-Meier curve (4). For all examinees in both groups were compared results of assessed parameters with the outcome of transplantation after 60 months. For risk assessment we used Odds ratio with 95% confidence interval.

For analysis of potential risk factors influence on function of kidney graft survival we made logistic regression analysis. Independent variable was serum creatinine level, and risk factor variable high blood pressure of recipient. Cross relation risk points on measure of correlation between function of kidney graft survival and influence of mentioned risc factors between experimental and control group. Potential risk factors used for multivariant logistic regression were monitoring age over 55 years and hypertension of corelation between function of kidney graft survival and influence of mentioned risk points on measured values.

4. RESULTS

Most frequent primary kidney disease were chronic glomerulonephritis...
in 15 (65%) recipients in experimental and 14 (48.72%) in control group. Diabetes mellitus was register in two recipients in control group (6.89%) and in experimental group there were no diabetes mellitus. Kidney graft recipients were treated by almost same average dose of cyclosporine, 2.22 ml in experimental and 2.26 ml in control group.

Average age of recipients was 33.27 years. In age from 30 to 39 there were 25 (48%) recipients, 15 in age from 20 to 29 years (28%), six in age from 40 to 49 and three in age from 10-19 and from 50 to 59 years. Mother was donor in 22 (42.4%), father in 15 (28.8%), brother in 7 (13.5%), sister in 6 (11.5%) and other family members in 2 cases (3.8%). Total average age of the donors was 51.4 (±9.7), in experimental group 62.43 (±4.10) years (55-72 years), and in control group 45.31 (±5.24) years.

We did not confirm statistical significant difference in age of recipients in experimental and control group. Average creatinine clearance value of donated kidney was 47.87 (±10.5) in experimental and 51.19 (±10.1) ml/min in control group, what is statistical significant difference (p=0.005).

From total 23 kidney graft recipients in experimental group there were 18 males (78.26%) and five females (21.74%), average age 34.86 (±6.54), which had previous hemodialysis for 35.33 (±37.59) months. Sixty months after transplantation graft was functional in 17 (32.69%) recipients, chronic graft nephropathy had five (21.73%), three recipients were returned on hemodialysis treatment (13.04%), and four patients has died (17.39%). In one case we confirmed „de novo“ glomerulonephritis (4.34%) over the biopsy. Average serum creatinine value of recipients in experimental group after 60 months was 279 (±224.00) µmol/l.

From 29 examinees in control group, 16 were males (55.17%), and 13 were females (44.83%), average age 31.69 (±10.9), which had previous hemodialysis for 21.03 (±25.59) months. Sixty months after transplantation kidney graft was functional in 24 recipients (81.75%), three (10.34%) recipients were returned on hemodialysis treatment and two patients has died (6.89%). Average serum creatinine value of recipients in control group 60 months after transplantation was 153.00 (±48.00) µmol/l.

We confirmed statistical significant difference between groups in sistolic and diastolic blood pressure values (table 1), but we did not register statistical significant difference in glucose blood level, cholesterol and triglycerides levels and hematocrit value.

According the prospects, there is statistical significant difference in creatinine blood level between the groups (p=0.005).

Difference of frequency high average sistolic pressure appareance between experimental and control groups is not random (p=0.011). It means that there is corelation between high average sistolic pressure and age of the donor.

Same conclusion we get over Fisher’s exact test (p=0.006). We have calculated OR=5.38 (95% CI: 1.41-21.75), which means that chances for appearance of high sistolic pressure, are at least 1,41 times higher in experimental, than in control group.

Difference of frequency high average diastolic pressure in experimental and control group is also not random (p=0.013), what confirms application of Fischer’s exacts test (p=0.009). Odds ratio (OR) for appearance high diastolic pressure in both groups is 5.85 (95%CI: 1.39-28.65). Chances for appearance of high diastolic pressure are at least 1,39 times higher than in control group.
of systolic and diastolic blood pressure, risk for rejection is 15,58 times higher, than in case when donor is younger person and recipient has not got high values of systolic and diastolic blood pressure. In case when donor is younger person, and recipient of kidney graft has high values of blood pressure, risk for high values of blood creatinine is 2,45 times higher.

If kidney graft recipient has not got high blood pressure, and donor is elder person, risk for high values of blood creatinine is 2,45 times higher.

Kidney graft function were monitored for five years. For interpretation of the results we used Kaplan-Meier’s curve. Possibility of graft survival in recipients with creatinine values over 150 μmol/l for five years period is 72,0%. As risk factors has been analysed high values of systolic and diastolic blood pressure and there were compared with groups without these risk factors. Possibility of survival in all cases until five years is good. (77,5%). Graft survival in recipients of both groups after 60 months is 77,5%. Five years graft survival of recipients in experimental group is about 70%, and of recipients in control group 82%. Difference is statistical significant (Figure 1).

Five years graft survival in recipients with average systolic blood pressure which is equal or less than 130 mm Hg is100 %. When average systolic blood pressure of recipient was higher than 130 mm Hg, graft survival is 50% (Figure 2).

In group of recipients with average diastolic blood pressure was equal or less than 80 mm Hg graft survival after 60 months is 96%. When diastolic blood pressure was higher than 80 mm Hg graft survival is about 70 % (Figure 3).

Kidney graft survival in recipients with creatinine blood values equal or less than 150 μmol/l is 100 %, and in group of recipients with creatinine blood values higher than 150 μmol/l, is about 72%. Difference is statistical significant (Figure 4).

5. DISCUSSION

Success of kidney transplantation is evaluate over the survival of graft and patient.

Today for calculation of graft’s and patient’s survival most frequent utilises Kaplan-Meier method (4), for half-life calculation of graft and patient. Survival of patients presents assessment of possibility that patient will be alive in period from the date of kidney transplantation until the date of death or last medical control (5). Graft survival presents assessment of possibility that kidney graft will function in period from the date of transplantation until the date of complete loss of function and recommended hemodialysis treatment, otherwise new transplantation or until the last medical control when graft was functional or until patient’s death (6). Graft stops to work when patient died, no matter that it had normal function before the death.

European and American studies declaim that patients surviving in living-related transplantation after first year is 83-92% (7), and after five years 70-79% (1, 6, 8). In our serial of patients five years survival of patients is 77,5% (9). In our study survival of patients in five years period is 77,5%. Age of donor significantly influence on graft survival, no matter is it living-related or cadaveric transplantation.

Influence of donor’s age on long-term graft survival is well-known for many years before. When donor is older, rate of long-term survival is lower (10). Kidney transplantation from older donors is in association with more often postpone graft function, acute rejection and early appearing of chronic graft rejection, and consequence is unsatisfactory function of kidney graft (11).

In our series of examinées five years graft survival in recipients which has got kidney from donor elder than 55 years, were 12 % less then in recipients which has got kidney from donors younger than 55 years, what is likewise as results from the other authors. High blood pressure is important risk factor with negative influence on function of graft survival and it appears in 80% patients after kidney transplantation, because the alterations in kidney graft, primary kidney disease or disease of the other organs. Correlation between blood pressure and long-term survival of the kidney graft is high significant (p<0,0001). It has been proofed that this correlation is available for measuring of blood pressure in different time intervals after the transplantation (1). In 60-70% recipients which has taken calcineurin inhibitors after the transplantation has developed high blood pressure, and a lot of studies showed that it is independent predictor of graft insufficiency (12). In patients with systolic blood pressure under 130 mm Hg half-time of graft survival is 14,5 years. When systolic blood pressure is 160 mm Hg half-time of graft survival is under 10 years (13). In our research we presented that in the group of recipients with average diastolic blood pressure was equal or less than 80 mm Hg, graft survival after 60 months is 96%. In the group of recipients with average diastolic blood pressure was higher than 80 mm Hg, percent of graft survival is 70%. We has also showed that in kidney graft recipients with average systolic blood pressure was equal or
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less than 130 mm Hg, percent of graft survival after 60 months is 100%, and when average systolic blood pressure of recipients was higher then 130 mm Hg, percent of graft survival is 50%. These results are similar as the results from the other authors (1).

Effective blood pressure control presents key of success for the improvement of long-time survival of the kidney grafts, because the therapy protects graft function and reduce risk of cardiovascular complications after transplantation. The most frequent value for monitoring of the kidney graft function is serum creatinine level, but there is no standard value in post-transplantational period.

The most frequent used serum creatinine levels is from 1,5 mg/dl or 135 μmol/L (14) and 2,0 mg/dL or 180 μmol/L (15). Our results demonstrate that creatinine level in control group has presented statistically significant difference comparing to creatinin level in experimental group (p=0,005), what approved inferior graft function associated with development of high blood pressure and poorly survival of recipients who have got kidney from older donors.

6. CONCLUSIONS

Age of the donor has significant influence on long-term survival of the kidney graft in the living-related transplantation. If kidney donated older person, and recipient of kidney graft has high sistolic and diastolic blood pressure, risk from rejection is 16 times higher, than in case when kidney donated younger donor and recipient is without hypertension. Survival of the graft in examinees without hypertension is significantly longer. Treatment of post-transplantational hypertension is one of the most important tasks in the treatment of patients with transplanted kidney.

REFERENCES


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