PREGNANCY AFTER KIDNEY TRANSPLANTATION: OUTCOMES, TACROLIMUS DOSES AND TROUGH LEVELS

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INTRODUCTION AND AIM:

Although pregnancy after kidney transplantation has been considered as high risk for maternal and fetal complications, it can be successful in properly selected patients. It is well known that pregnancy can induce changes in the plasma concentrations of some drugs, however, there has been very limited information about tacrolimus pharmacokinetics during pregnancy. In this study, we evaluated the tacrolimus doses, blood level and the outcomes of pregnancies in kidney allograft recipients.

METHOD:

Between 2004 - 2014, we found 16 pregnancies in 12 kidney allograft recipients in our center. We reviewed the files and data reports including fetal outcomes, graft function, complications, tacrolimus trough levels and the doses. We analysed the tacrolimus trough levels and doses before pregnancy, during pregnancy (monthly) and postpartum period.

RESULTS:

Throughout the pregnancy, we aimed to achieve tacrolimus trough levels between 4-7 ng/ml. All patients were on triple immunosuppression including tacrolimus, azathioprine and prednisolone. The demographic features of the patients were given in Table 1.

A total 11 out of 16 (68.7 %) pregnancies were successful, the mean weight gain was 12.5 ±1.66 kg. One patient developed gestational diabetes mellitus and two had preeclampsia. While 5 out of 11 babies were found to have low birth weight, 4 of them were premature. Two patients had lost their grafts, one due to acute rejection and second was due to progression of chronic allograft dysfunction.

We have shown that tacrolimus doses need to be significantly increased to keep appropriate trough levels during pregnancy (the doses; before: 3.20 ± 0.9, first trimester: 5.03 ± 1.5, second trimester: 6.50 ± 1.8, third trimester: 7.30 ± 2.3, post-partum: 3.5 ± 0.9 mg/day). Biochemistry and tacrolimus trough levels and doses were given in table 2.

Table 1: Demographic Features of the Patients

Patient Number (n)	12
Pregnancy Number (n)	16
Pregnancy Age (mean ± sd)	28 ± 5
Body Mass Index (mean ± sd)	22.5 ± 4.3
Hypertension (n, +/-)	1/11
Diabetes Mellitus (n, +/-)	0/12
Mismatch Number (median) (minimum, maximum)	4 (0 – 6)
Pretransplantation Dialysis Modality HD/PD (n)	5/7
Living / Deceased Donor (n)	9/3
Duration To Pregnancy (month,mean ± sd)	28.4 ± 4.3

Table 2: Biochemistry And Tacrolimus Trough Levels And Doses

	Before Pregnancy	1. Trimestr	2. Trimestr	3. Trimestr	Postpartum
Tacrolimus Dose (mean ± sd)	3.20 ± 0.9[(a,b,c)]	5.03 ± 1.5[(a)]	6.50 ± 1.8[(b)]	7.30 ± 2.3(c)	3.5 ± 0.9
Tacrolimus Trough Level (mean ± sd)	5.7 ± 1.1[(d)]	5.0 ± 1.1	5.6 ± 1.0	6.2 ± 0.5	7.9 ± 1.7[(d)]
Hemoglobin (gr/dl, mean ± sd)	12.20 ± 1.7[(e)]	11.60 ± 1.5	10.80 ± 1.37[(e)]	11.12 ± 1.35	11.93 ± 1.32
Albumin (gr/dl, mean ± sd)	4.2 ± 0.3[(f)]	3.88 ± 0.4	3.60 ± 0.5[(f)]	3.58 ± 0.58	3.96 ± 0.48
Creatinine (gr/dl, mean ± sd)	0.77 ± 0.21	0.76 ± 0,20	0.86 ± 0.30	0.90 ± 0.23	0.88 ± 0.24
eGFR (MDRD) (ml/min, mean ± sd)	92 ± 26	93 ± 25	87 ± 30	80 ± 24	84 ± 28

a , b, c, d p<0.0001, p<0.0001, p<0.0001, p=0.004,
e: p=0.002, f: p=0,001

CONCLUSION:

In conclusion, the dose of tacrolimus needs to be increased to provide safe and stable tacrolimus trough levels during the pregnancy. Although pregnancy can be succesful in most cases, it should be kept in mind that there are increased risk of maternal and fetal complications including allograft loss, low birth weight, spontanous abortus, and preeclampsia.

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