IS BASILIXIMAB INDUCTION, A NOVEL RISK FACTOR FOR NEW ONSET DIABETES AFTER TRANSPLANTATION FOR LIVING DONOR RENAL ALLOGRAFT RECIPIENTS?

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Introduction

- New Onset Diabetes after Transplant (NODAT) is an important complication in kidney transplant recipients
- NODAT has been associated with increased risk of cardiovascular disease, susceptibility to infection, patient death and graft loss.
- The use of Interleukin-2 (IL-2) receptor antibodies to prevent acute rejection has been increased in recent past.
- Anti-CD25 monoclonal antibodies (MAbs) are directed against the IL-2 receptor affect the proliferation of T lymphocyte that leads to loss of regulatory T lymphocyte, which is also associated with the pathogenesis of diabetes mellitus (DM).
- This regulatory lymphocyte controls the occurring of various autoimmune illnesses.
- It was studied that Basiliximab, a chimeric CD25 [interleukin (IL)-2] MAbs, by affecting populations of T lymphocytes, indirectly may affect β-cell function leading to impaired glucose homeostasis in these patients.
- However, there is paucity of clinical data in this regard.
- Therefore, we undertook this study to compare the incidence of NODAT in renal transplant recipients who received induction with IL-2 receptor blockers compared to those who did not and also identified the risk factors associated with NODAT in these patients.

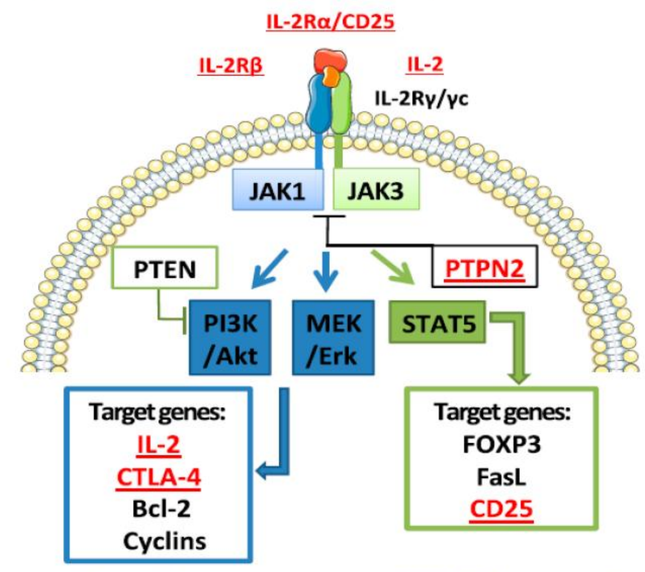
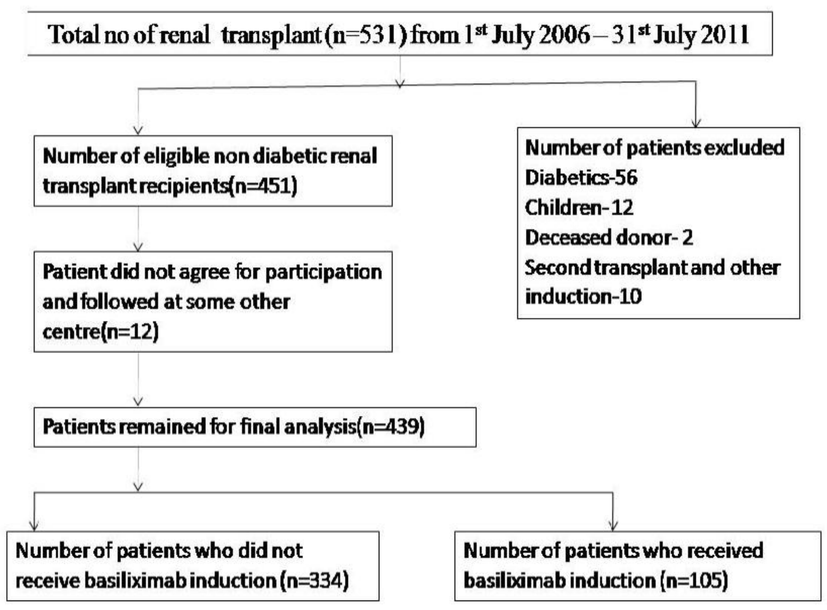


Figure : IL-2 receptor and action on FOXP3 (T regulaory cells)

Aims

- To compare the incidence of NODAT in renal transplant recipients with and without basiliximab induction along with calcineurin inhibitors and steroids
- To prove the hypothesis that basiliximab is an independent risk factor for development of NODAT in these patients.

Material and Methods



Material and Methods

Diagnosis of NODAT

Daily blood sugar level before breakfast, lunch and dinner during the kidney transplant unit stay by nursing staff as per our institute protocol.

NODAT: FPG ≥126mg/dl or 2-hour plasma glucose ≥200mg/dl

Impaired glucose tolerance (IGT): 2-hour plasma glucose ≥140mg/dl

Impaired fasting glucose (IFG): Fasting plasma glucose ≥110mg/dl and ≤126mg/dl).

The patients with IFG, IGT, and those with occasional rise in blood sugar level on monitoring with glucometer and requiring insulin therapy were **leveled as transient hyperglycemia**.

Statistical Analysis: The differences in mean values between two groups were compared using the Students' t' test. The percentage of categorical variables between two groups were compared using nonparametric Mann-Whitney U test, Chi-square or Fisher exact probability test as when appropriate. Multivariate logistic regression analysis was used to determine the factors predicting NODAT with NODAT as dependent variable. A P-value < 0.05 was considered statistically significant.

Results

	Without basiliximab (n=334)	With basiliximab (n=105)	P value
Age – Mean(SD)	36.38 (10.9)	37.08 (11.28)	0.57
Body mass index (SD)	21.05 (2.71)	21.36 (2.9)	0.31
Donor category Parents Siblings Spouse Offspring	146 (40.3%) 104 (28.4%) 102 (27.9%) 10 (2.7%)	41(39%) 29(27.6%) 32(30.4%) 3 (3 %)	NS
Immunosuppression			
Tacrolimus based	221/334 (66.1%)	72/105 (68.5%)	0.72
Tac level(trough level in ng/ml at 3 months)	9.09±1.62	8.68±1.51	0.08
Cyclosporine based	113/334 (33.9%)	33/105 (31.5%)	0.73
Cyclosporine trough level (mcg/L at 3 months)	177.63±28.08	173.69±26.77	0.44
acute rejection	63/334 (18.8%)	5/105 (4.7%)	0.001
HCV infection	12/334 (3.5%)	5/105 (4.7%)	0.51
CMV infection	22/334 (6.5%)	9/105 (8.5%)	0.001
Overall hyperglycemia (Transient hyperglycemia +NODAT)	102/334 (30.5%)	44/105 (41.9%)	0.03
NODAT	56/334(16.7%)	34/105 (32.3%)	0.005
Transient hyperglycemia	46/102	10/44	0.016
Duration of dialysis (months)	6.8(4.3)	10.3(7.7)	0.001
Duration of follow up (months)	28(22.7)	30.7(23.6)	0.27

Table 1: Demographic profiles, clinical characteristics, transient hyperglycemia and NODAT between patients without and with basiliximab induction

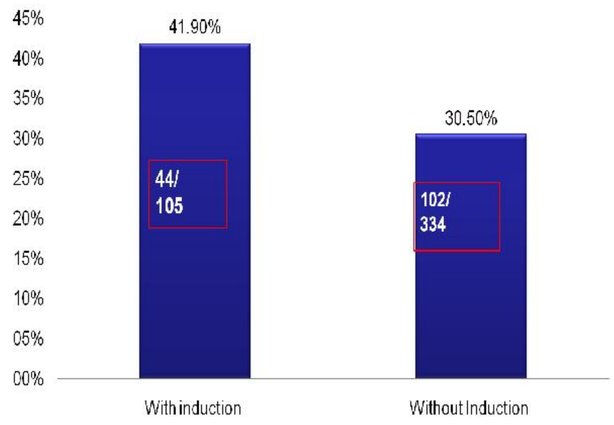


Figure 1 Overall Hyperglycemia (Transient hyperglycemia, IGT, IFT and NODAT)

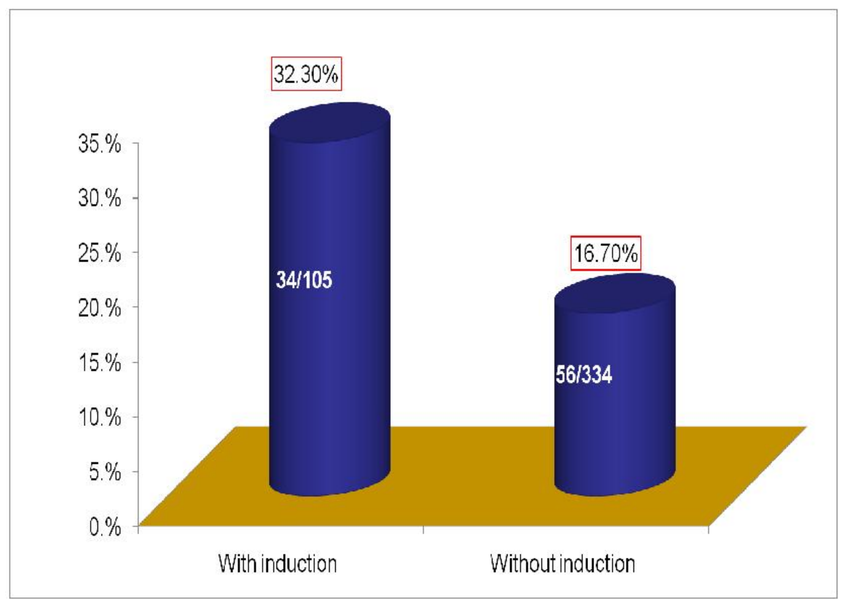


Figure 2. NODAT at 3 Month

Variables	Odds ratio	95% Confidence Interval	P value
Age (per year)	0.98	0.96-1.01	0.27
BMI(Kg/m^2)	1.02	0.93-1.17	0.61
Cyclosporine based regimen	2.43	0.74-8.02	0.14
Tacrolimus based regimen	2.65	0.83-8.43	0.09
Hepatitis C virus infection	6.37	2.28-17.7	0.001
Cytomegalovirus disease	0.66	0.24-1.81	0.42
Acute rejection	0.76	0.36-1.60	0.48
Induction(IL-2 R blocker)	2.31	1.37-3.88	0.002

Table 2: Multivariate logistic regression analysis showing the predictor of NODAT in renal transplant recipients.

Conclusions

- ✓ Basiliximab induction in renal allograft recipient is an independent risk factor associated with development of NODAT in renal transplant recipients.
- ✓ Acute rejection episodes were significantly less with the use of basiliximab induction, which is the main purpose of the use of this drug and therefore the study does not negate the use of basiliximab induction.
- ✓ These observation needs to be confirmed in randomized controlled trial.

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