Effect of Prednisolone and Rejection Episodes on Granzyme B Transcript Levels after Kidney Transplantation

Christoffer Borst[1,2], Claus Bistrup[1], Ying Liu[2], Jan Thoning[1,2] and Martin Tepel[1,2]
1) Odense University Hospital, Department of Nephrology; and 2) University of Southern Denmark, Department of Cardiovascular and Renal Research

Background

For patients with end-stages kidney disease, renal allograft transplantations are the best treatment of choice. Kidney donors are matched to recipients. In cases of high risk transplantations, immunosuppression of patients are intensified. To reduce incidence of acute rejection, standard treatment is supplemented with Prednisolone.

In patients where the immunosuppression are intensified by adding of Prednisolone, changes in immune cell activity may be reflected.

We have made a prospective trial and monitored mononuclear cell activity in blood.

Methods

Kidney transplanted patients from 2011-2012 were included. Peripheral blood samples were repeatedly collected every week after transplantation for 4 consecutive weeks. RNA was extracted from mononuclear cells using established technology. Transcripts of Granzyme B were analyzed using quantitative real-time PCR.

Results

The immunosuppressive treatment consisted of Basiliximab/Thymoglobulin/ Immunoabsorption, Tacrolimus and Mycophenolate Mofetil. Prednisolone was administered to 32 patients (Fig.1). Granzyme B was significantly correlated to Prednisolone treatment (Fig 2-4). Confounders by donor or recipient data (Table 1-2) were tested by Multivariate Analysis and found non-significant.

Conclusion

Administration of Prednisolone reduces Granzyme B transcripts after kidney transplantation. Repeated measurements showed that the two groups reached the same level of Granzyme B transcripts after 1 month.
It also shows that acute administration of intravenous Prednisolone, to patients with rejection, give an acute decrease in Granzyme B transcripts, that again returns to start values after 1 month.

Figure1.

ABO-incompatible recipient were treated differently than other recipients.
5 patients were classified high risk and given Prednisolone.
14 patients had kidney failure within the first month and given acute Prednisolone.

a) Immunosuppression (standard to all: Tacrolimus and Mycophenolate Mofetil)
b) Tx-operation (Department of Vascular Surgury, Odense University Hospital)
c) One month after Tx-operation

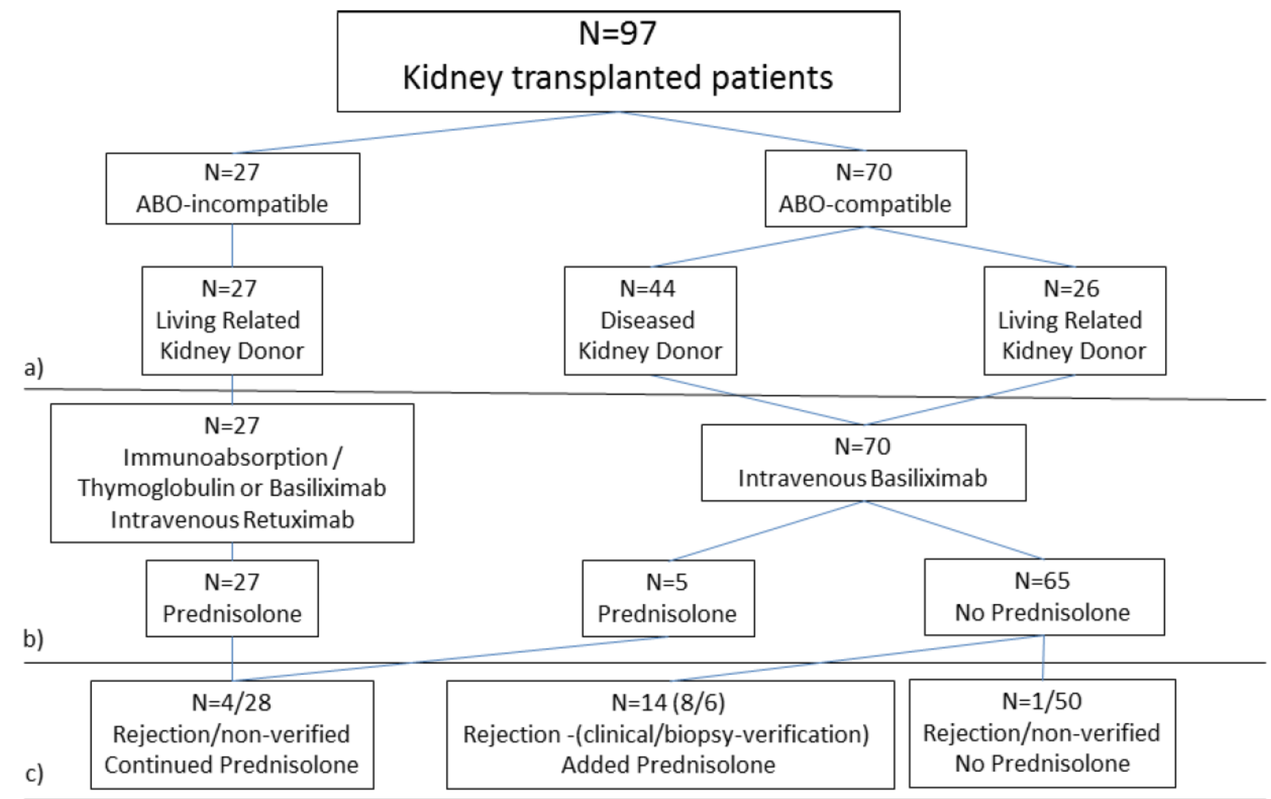

Table 1.

Recipient and donor were similarly matched in the ABO-compatible and incomptible group. Male/female (m/f)

	Recipient sex	Recipient age	Donor sex	Donor age	HLA I	HLA II
ABO-comp.	44/26 m/f	49 1 year	34/33 m/f	51 1 year	2.0 0.1 counts	0.8 0.1 counts
ABO-incomp	17/10 m/f	47 3 year	10/17 m/f	53 2 year	2.3 0.2 counts	0.9 0.1 counts

Figure 2.

mRNA GranzymeB/GAPDH-ratio were normally distributed after log-transformation. log(GranzymeB) were significantly (P<0.0001) lower at day one in the ABO incompatible group. Both groups had a significant (P<0.0001) positive slope. ABO incompatible had a significantly (P<0.0001) steeper slope. After one month log(GranzymeB) tends towards the same level. (Longitudinel Analysis, T-test between Regression Models)

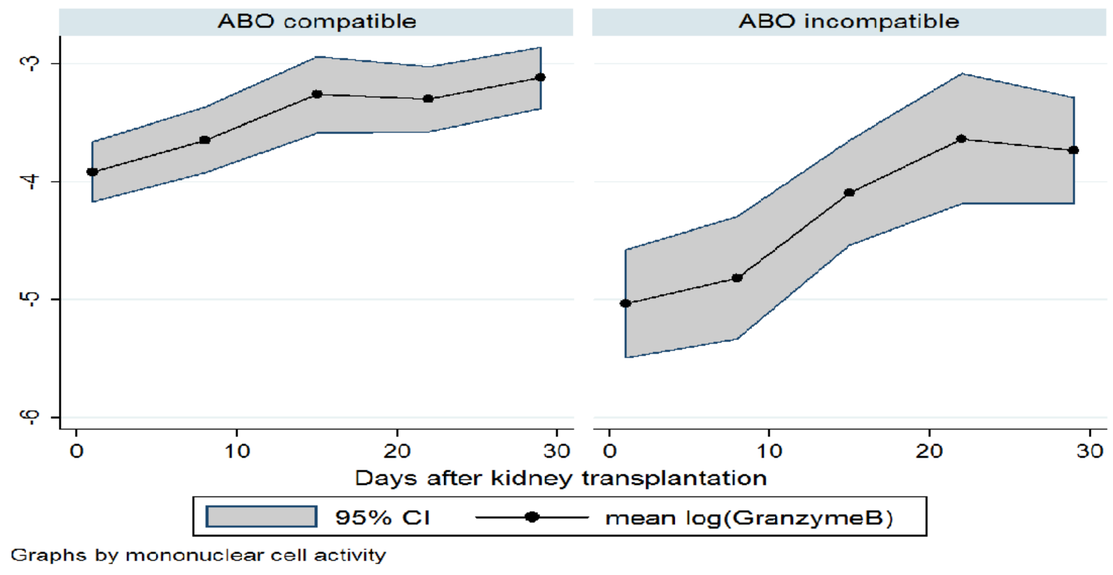

Figure 3.

Acute intravenous Prednisolone given to patients with rejection made a significant (P<0.0001) fall in log(GranzymeB).

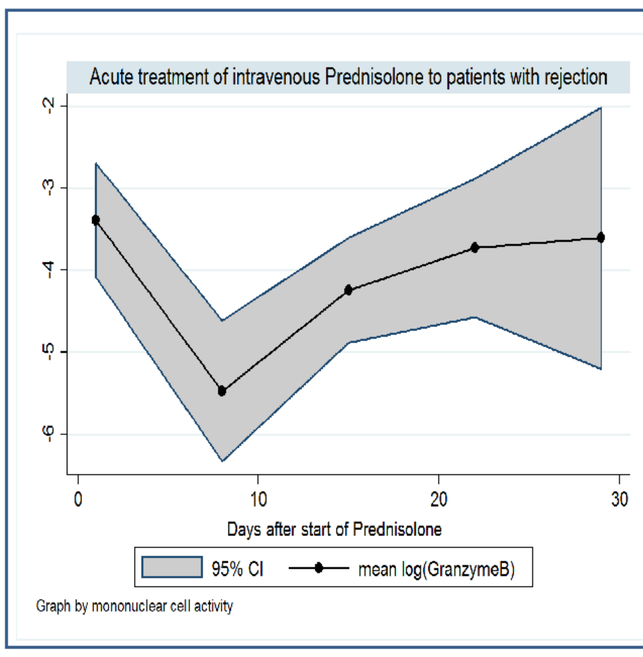

Figure 4.

Acute intravenous Prednisolone made a significant (P<0.005) decrease in delta log-(GranzymeB) compared to ABO-comp/incomp. (Kruskal-Wallis Test)

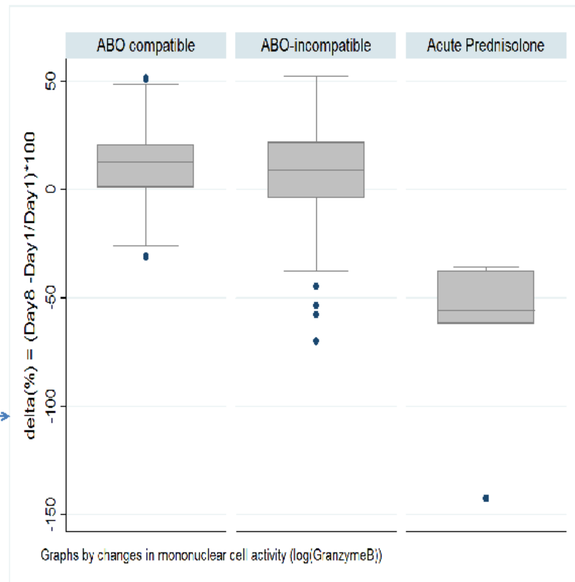

Table 2.

Standard bloodsample monitoring of recipients were similar between the two groups. Creatinine-ratio = (day_0-day_x)/ day_0 (Crea)

	Lympho-cytes Day 1	Mono-cytes Day 1	Tacro-limus Day 1	Tacro-limus Day 29	Crea-ratio Day 1	Crea-ratio Day 29
ABO-comp	0.9 0.1 10E9/l	0.7 0.0 10E9/l	19.7 1.0 ng/mL	13.6 0.5 ng/mL	0.44 0.03	0.76 0.02
ABO-incomp	0.9 0.1 10E9/l	0.6 0.0 10E9/l	16.1±1.1 ng/mL	15.4 0.8 ng/mL	0.50 0.03	0.79 0-02

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Contact: cborst@health.sdu.dk

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