Recurrence of IgA Nephropathy after Transplantation: Altered IgA Glycosylation and Its CD89 Receptor as Biomarkers of the Disease and Effectiveness of Steroid Pulse Therapy for Recurrence

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Background and aim

IgA nephropathy is is the most common primary glomerular disease leading to end-stage renal disease. This disease is characterized by galactose deficient (Gd) IgA1 present in the circulation and deposited in the mesangium. IgG auto-antibodies against Gd-IgA1 and the soluble (s) CD89, (the Fc receptor of IgA), are also found complexed to IgA1 in the circulation. The origin of IgA nephropathy appears in the circulation compartment since some cases of subclinical IgA nephropathy donor kidneys showed clearance of IgA deposits after the graft in patients suffering with others kidney diseases The recurrence of the disease is frequent after transplantation. The use of corticosteroids seems to affect the recurrence rate of IgA nephropathy. In this study, we investigated the efficacy of IV pulse steroid treatment for IgA nephropathy recurrence. The predictive value of three markers : Gd-IgA1, IgG-IgA and IgA-sCD89 complexes was also assessed before the transplantation.

Methods

Kidney transplanted recipients treated with IV pulse steroids therapy for IgAN recurrence (R group, n=11) were compared to those without recurrence (NR group, n=13). R and NR were treated with low-salt diet, statins and ACE inhibitors or ARBs or both. If proteinuria was persistent (>1g/day) despite 3 months of supportive treatment, then steroid treatment was instituted as previously described by Pozzi and colleagues in the R group. Briefly, patients received 1g of methylprednisolone intravenously for three consecutive days at the beginning of the steroid course and again 2 and 4 months later. They were also given oral prednisone at a dose of 0·25 mg/kg every other day for 6 months. Following clinical and biological parameters were collected for each patient at different time points. Gd-IgA1 and IgA complexes containing IgG and sCD89 levels were determined in serum collected before and after transplantation. For Gd-IgA1, classical ELISA using the HAA lectin was performed and for complexes, ELISA plates were coated with anti-CD89 or IgG and revealed with anti-IgA antibodies.

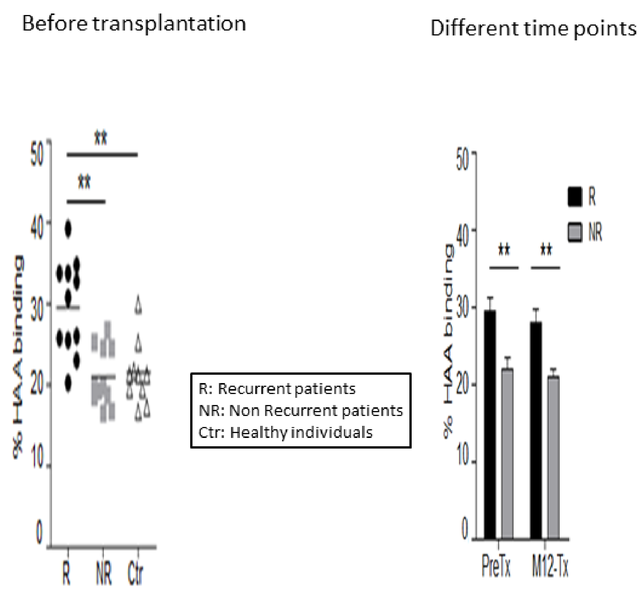
RESULTS

RESULT 1: Proteinuria was markedly reduced by steroids treatment in R group.
Table 1: Evaluation of the effectiveness and tolerance of the pulse corticosteroids treatment

	M6-pre-R-Tx	R-Tx	M6-post-Pozzi	M12-post-Pozzi	M6-pre-R-Tx vs R-Tx	R-Tx vs M6-post-Pozzi
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	P value	P value
ACEI/ARB introduction or increase (n)	6	10	10	9	0.04	NS
eGFR (ml/min per 1.73 m2)	54,0 (±12,9)	49,6 (±16,3)	50,4 (±11,9)	50,3 (±13,5)	0,14	0,92
Proteinuria (g/24 h)	0,6 (±0,3)	2,8 (±1,6)	0,4 (±0,3)	0,4 (±0,4)	0,002	0,001
Systolic BP (mmHg)	129,5 (±5,9)	128,9 (±7,6)	128,8 (±8,9)	125 (±14,4)	NS	NS
Diastolic BP (mmHg)	78,7 (±6,7)	76,9 (±5,4)	76,7 (±7,8)	76,88 (±5,9)	NS	NS
MAP (mmHg)	104,1 (±6,7)	102,9 (±4)	102,8 (±7,8)	100,9 (±9,6)	NS	NS
Blood glucose (mmol/l)	5,3 (0,6)	5,2 (±0,5)	5,5 (±0,9)	5,3 (±0,4)	NS	NS
Total cholesterol (mmol/l)	5,67 (±1,65)	6,22 (±2,99)	4,44 (±1,04)	5,45 (±1,05)	NS	NS

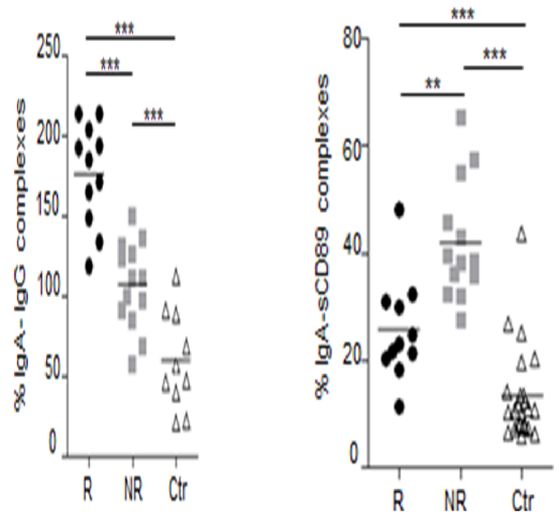
M6-pre-R-Tx = 6 months before recurrence, R-Tx= time of recurrence, M6-post-Pozzi=6 months after steroid pulse beginning, M12=12 months after steroid pulse beginning. eGFR : Estimated Glomerular Filtration Rate, BP : blood pressure, MAP : mean arterial pressure, ACEI : angiotensin-converting-enzyme inhibitor, ARB : angiotensin receptor blockers

Serum levels of Gd-IgA1



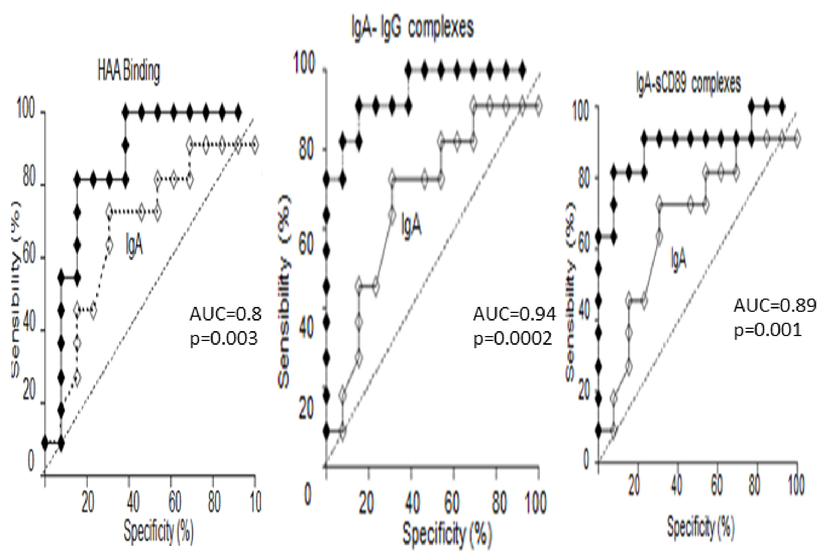
RESULT 2: Before and after transplantation, serum levels of Gd-IgA1 were significantly higher in R group compared to NR group or healthy controls .

Serum levels of IgA-IgG and IgA-sCD89 complexes before transplantation



RESULT 3: Before transplantation, serum levels of IgA-IgG were significantly higher in R group compared to NR group or healthy controls but values of IgA-sCD89 were lower in R group compared to NR group..

Receiver-operating-characteristic (ROC) curves



Result 4: The receiver-operating-characteristic (ROC) curve showed predictive power of each biomarker for IgA nephropathy recurrence.

CONCLUSIONS

Pulse IV steroid therapy seems to be an efficient and safe option for treatment of IgAN recurrence. Moreover, the levels of Gd-IgA1 and IgA complexes containing IgG or sCD89 were found as biomarkers of the disease recurrence before transplantation. Studies in larger cohorts are needed in order to confirm these findings, and refine the threshold at which these three immunological markers would identify a high risk of recurrence.

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L) Renal pathology. L2) Immune and inflammatory mechanisms.
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