

Assessment of Responsiveness to No Treatment (ther. 0), Treatment with Steroids and Cyclophosphamide (ther. 2), Treatment with Steroids Alone (ther. 3) in 177 Patients with Glomerulonephritis and Nephrotic Syndrome (NS)

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Abstract

Background: The patients with glomerulonephritis and nephrotic syndrome (NS) are heterogeneous for renal function, type and severity of renal lesions and urinary excretion of proteins with different molecular weight. The patients after biopsy have different functional outcomes: remission (24-hour proteinuria <2.0 g/24 hour); persistent nephrotic syndrome with normal or decreasing renal function; progression to end stage renal disease (ESRD); reduction of eGFR $<50\%$ of baseline.

Methods: Aim of the present study is the evaluation of functional outcome according to treatments. Three types of treatment were considered: no treatment (ther. 0), treatment with immuno-suppressive drugs steroids and cyclophosphamide in combination, (ther. 2); treatment with steroids alone (ther. 3). It is interesting to assess the functional outcome according to these 3 types of therapy and the clinical, functional, histological and proteinuric parameters associated with the different outcomes.

Results: 22 patients reached Remission after (ther. 0), 55 patients reached remission after (ther. 2); 20 patients reached remission after (ther. 3). The comparison of 22 remission patients with (ther. 0) with 55 remission patients with (ther. 2) show no significant differences for baseline and last eGFR, GGS%, TID score and AH score; otherwise, the 22 patients with (ther. 0) show highly significant lower values of TUP/C (0.0001), IgG/C (0.001), α_2 m/C (0.04), Alb/C (<0.0001), α_1 m/C (<0.0001) (**Table 1**).

39 patients progressed to ESRD, 14 with (ther. 0), 23 with (ther. 2) and 2 with (ther. 3). The patients progressing to ESRD with (ther. 2) compared with patients reaching Remission with (ther. 2) showed that the ESRD patients treated with (ther.2) have significant lower value of baseline eGFR (<0.0001) and significant higher values of histologic and proteinuric parameters: TUP/C (0.006), IgG/C (0.06), α_2 m/C (0.05), Alb/C (<0.007), α_1 m/C (<0.0001) and last 24h P(<0.0001) (**Table 1**).

Conclusion: The decision to treat the NS patients with immunosuppressive treatment with steroids and cyclophosphamide may be dependent on the evaluation of functional, histologic and proteinuric parameters.

Introduction

The patients with glomerulonephritis and nephrotic syndrome (NS) are heterogeneous for renal function, type and severity of renal lesions and urinary excretion of proteins with different molecular weight. The patients followed for rather long time after biopsy may have different functional outcomes: remission (24-hour proteinuria <2.0 g/24 hour); persistent nephrotic syndrome with normal or decreasing renal function; progression to end stage renal disease (ESRD); reduction of eGFR $<50\%$ of baseline value. Several articles showed that high urinary excretion of some proteins is associated with progression.

Aim of the present study is the evaluation of functional outcome according to treatment [1-5]. Three types of treatment were considered: no treatment (ther. 0), treatment with immu-

no-suppressive drugs such as steroids and cyclophosphamide in combination (ther. 2); treatment with steroids alone, (ther. 3). It will be interesting to assess the functional outcome according to these 3 types of therapy and the clinical, functional, histological and proteinuric parameters associated with the different type of outcome.

The first aim of the study was to compare all parameters in patients reaching Remission without treatment with those reaching Remission after treatment with steroids and cyclophosphamide.

A second aim was to compare the patients reaching Remission with treatment with steroids and cyclophosphamide in comparison to patients reaching ESRD notwithstanding a treatment with Steroids and Cyclophosphamide [6-9].

Table 1: Comparison of functional, histologic and proteinuric parameters in patients reaching remission without therapy (ther. 0) and patients reaching remission after treatment with steroids and Cyclophosphamide (ther. 2). The patients reaching Remission without treatment show high significantly lower values of all proteinuric parameter.

Remission n. 97 patients	Age	eGFR	e G F R last	Fol. up	High BP	GGs%	T I D score	TUP/C	IgG/C	α2m/C	Alb/C	α1m/C	Last 24hP
Rem. ther. 0 n. 22	38,9	90.7	81.8	12	9 (41%)	5.9	1.29	2437	92	3.11	1955	16.6	0.64
p value comparing Rem ther. 0 vs ther. 2		0.86	0.55	---	---	0.91	0.37	0.0001	0.001	0.04	<0.0001	<0.0001	0.56
Rem. ther. 2 n. 55	40.8	81,3	85.0	33	30 (55%)	6.2	1.58	4454	210	8.41	3836	34.2	0.56
Rem ther. 3 n. 20	39.8	73.2	73.2	61	12 (60%)	9.9	1.11	5087	236	4.92	4256	44.8	0.32

Table 2. Comparison of functional, histologic and proteinuric parameters in 55 patients reaching Remission after treatment with steroid and cyclophosphamide (ther. 2) and 23 patients progressing to ESRD notwithstanding treatment with Steroids and Cyclophosphamide (ther. 2). The ESRD patients show lower value of baseline eGFR and significantly higher values of histologic and proteinuric parameters.

ESRD n. 39 patients	Age	Bas. eGFR	Last eGFR	Fu up	High BP	GGs%	T I D score	TUP/C	IgG/C	α2m/C	Alb/C	α1m/C	Last 24hP
ESRD ther. 0 n. 14	43	44.6	8.6	126	3 (93%)	18.7	2.18	6759	492	21.92	5028	97.7	5.56
ESRD ther. 2 n 23	44.2	45.7	7.7	181	9 (83%)	21.7	3.09	7134	309	15.76	5862	80.9	8.58
P value comparing Rem ther 2 vs ESRD ther 2		<0.0001	<0.0001		0.001	<0.0001	0.002	0.006	0.06	0.05	0.007	<0.0001	<0.0001
Rem. ther. 2 n. 55	40.8	81,3	85	241	30(55%)	6.2	1.58	4454	210	8.41	3836	34.2	0.56

Patients and Methods

Between January 1992 and april 2006 469 patients performed renal biopsy; 177 have nephrotic syndrome (NS: proteinuria: ≥3.5 g/24 hour) (follow up 87.2±75.5 months) and 203 have persistent non-nephrotic proteinuria (PP). In evry type of outcome according to type of therapy several clinical, functional, histological and proteinuric parameters were evaluated: age, baseline eGFR, last eGFR, percentage of Global Glomerular sclerosis (GGs%), degree of Tubulo-Interstitial-Damage evaluated by a score from 0 to 6 (TID score 0-6) and degree of Arteriolar Hyalinosis evaluated by a score from 0 to 3 (AH score 0-3) and the urinary excretion of several proteins of different molecular weight expressed as mg of protein per g of urinary creatinine: Total Urinary proteins (TUP/C), IgG/C, α2m/C, Alb/C, α1m/C, last 24-hour proteinuria [10-15]. The functional outcome was: Remission reached in 97 patients: 22 patients untreated with immuno-suppression (ther. 0); 55 treated with Steroids and Cyclophosphamide (ther. 2) and 20 treated with Steroids alone (ther. 3).

Progression to ESRD was observed in 39 patients, 14 untreated with immuno-suppression (ther. 0), 23 treated with Steroids and Cyclophosphamide (ther. 2) and 2 with steroids alone (ther. 3). The first aim of the study was to compare all parameters in patients reaching Remission without treatment (ther. 0) with those reaching Remission with treatment with steroids and cyclophosphamide (ther. 2). The second aim was to compare the patients reaching Remission with treatment with (ther. 2) with patients reaching ESRD notwithstanding a treatment with im-

muno-suppression with Steroids and Ciclophosphamide(ther. 2) [16-19].

Results

22 patients reached Remission without (ther. 0), 55 patients reached remission after (ther. 2); 20 patients reached remission after (ther. 3). The comparison of 22 patients with (ther. 0) with 55 patients with therapy (ther. 2) show no significant differences for baseline and last eGFR, GGs%, TID score and AH score; otherwise, the 22 patients with (ther.0) show significantly lower values of TUP/C (0.0001), IgG/C (0.001), α2m/C (0.04), Alb/C (<0.0001), α1m/C (<0.0001) (**Table 1**).

39 patients progressed to ESRD, 14 with (ther. 0), 23 with (ther. 2) and 2 with (ther.3). The comparison of patients progressing to ESRD with therapy (2) with patients reaching Remission with therapy (2) showed that the ESRD patients treated with therapy (2) are characterized by significant lower value of baseline eGFR (<0.0001) and significant higher values of GGs% (<0.0001), TID score (0.002), AH score (<0.0001) and significant higher values of all proteinuric parameters :TUP/C (0.006), IgG/C (0.06), α2m/C (0.05), Alb/C(<0.007), α1m/C (<0.0001) and last value of UPT/C (<0.0001) (**Table 2**) Taken together these result show that spontaneous Remission in untreated patients is associated with significantly lower values of all proteinuric markers in comparison to patients reaching Remission after (ther. 2) that show higher values of all proteinuric markers; thus Remission is possible without treatment in patients with low values of all proteinuric markers. Progression

to ESRD in patients treated with (ther. 2) show that the patients may reach ESRD notwithstanding (ther. 2); these patients have significantly lower value of baseline eGFR and significantly higher values of all histologic and proteinuric parameters [20-22].

Conclusion

The decision to treat the NS patients with immunosuppressive treatment with steroids and cyclophosphamide may be dependent on the evaluation of functional, histologic and proteinuric parameters.

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