Comparison of the Influence of ACE Inhibitor Lisinopril (LN) and ATII Receptor Antagonist Losartan (LS) in Patients with Idiopathic Membranous Nephropathy (IMN) and Nephrotic Syndrome (NS)

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Introduction

Idiopathic membranous nephropathy (IMN) is a clinicopathological entity defined by the presence of proteinuria, commonly in nephrotic range, and by diffuse and uniform thickening of the glomerular basement membranes (GBMs) due to the deposition of subepithelial immune deposits (1). Membranous nephropathy remains the most common cause of the nephrotic syndrome in adults. The disease may slowly progress to renal failure, but a number of patients maintain normal renal function and may even have spontaneous remission of proteinuria (2). The clinical feature most commonly used to predict the course of the disease is the sustained high levels of proteinuria in a six months period post diagnosis as well as the initial creatinine clearance and the rate of change in renal function over this six-month interval (3). Before considering the so-called specific therapy of IMN, the importance of a well-planned symptomatic therapy must be noted. The use of non-specific, non-toxic agents, ie, angiotensin-converting enzyme (ACE) inhibitors and/or antagonists of angiotensin receptors, for both hypertension control and their renoprotective effect, is supported by evidence from high-quality studies (4-5). In several experimental models of renal disease progression, ACE inhibitors and angiotensin II receptors antagonists were equally renoprotective, which suggested that reduction of renal angiotensin II activity is crucial for the preservation of glomerular structure and function (6)

In the present study we compare the effects of an ACE inhibitor, lisinopril (LN) and an angiotensin II receptor antagonist, losartan (LS) in patients with nephrotic syndrome due to idiopathic membranous nephropathy.

Materials and methods

Twenty seven patients, 13 male, 14 female, of mean age 51.3±15.4 years, with biopsy proven IMN and NS were studied. The study patients were devided in two groups defined by the administration of lisinopril (n=13) or losartan (n=14). Both groups were under medication for a period of nine months. At the beginning and at the end of the medication period serum creatinine (CR), albumin (AL), total cholesterol (CHO) as well as 24-hour proteinuria (PR) and mean arterial pressure (MAP) were determined. We compared the parameters' changes between the two groups throughout the medication period. Values are given as mean±SEM. Statistical analysis was performed using the SPSS program. ANOVA for repeated measures was performed to test the timing effect of the studied parameters during the study. A paired t-test was used to compare the differences between the studied parameters at the different time intervals along the study. P values less than 0.05 were considered to be significant.

Results

In group A patients showed no change in renal function during the medication period. Their serum albumin increased since the 1st month of therapy and continued to increase until the end of the 9th month during the medication period. Total cholesterol levels were significantly lower since 5th month of medication. Proteinuria was also significantly reduced since 1st month and throughout medication period, (Table 1). It should be noted that despite the reduction of proteinuria and increase of albumin, 10 patients had higher than 1.5g/24hour and 6 of them albumin lower than 3g/dl at the end of the study.

MAP was also significantly lower during therapy with lisinopril (Table 1).

In group B patients had stable renal function at baseline and throughout therapy. Serum albumin levels significantly increased since the first month of therapy and were maintained stable throughout the nine-month treatment with losartan. Serum cholesterol levels were kept unchanged throughout medication period. Proteinuria was also significantly reduced since the 1st month of therapy and remained decreased until the end of therapy. We should comment that at the end of the study , 8 of the patients presented proteinuria higher than 2g/24hour and 3 of them had nephrotic range proteinuria. Mean blood pressure was also significantly lower since the 1st month of treatment and throughout therapy (Table 1).

We found no statistically significant difference between the two groups in evolution of CR (p=0.32), AL (p=0.29), CHO (p=0.24), PR (p=0.41) and MAP (p=0.61) levels.

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Table 1. Mean serum (±SEM) levels of creatinine, albumin and total cholesterol, 24-hour urinary protein excretion, and mean blood pressure before and after treatment with lisinopril (LIS) or losartan (LOS) in patients with idiopathic membranous nephropathy (IMN) and nephrotic syndrome (NS).

		During therapy (months)						
		Baseline	1	3	5	7	9	P*
Creatinine(mg/dl)	LIS	1.27±0.48	1.25±0.43	1.26±0.40	1.27±0.41	1.27±0.39	1.30±0.39	NS●
	LOS	1.11±0.36	1.17±0.25	1.11±0.27	1.12±0.23	1.17±0.22	1.18±0.21	NS
Albumin (g/dl)	LIS	2.27±0.41	2.50±0.48	2.63±0.50	2.70±0.55	2.93±0.52	3.09±0.59	<0.001
	LOS	2.93±0.40	3.25±0.48	3.48±0.47	3.54±0.47	3.58±0.40	3.53±0.41	<0.001
Cholesterol (mg/dl)	LIS	347.38±81.44	342.76±108.6	326.23±89.04	313.76±90.17	284.23±92.08	276.53±68.92	<0.001
	LOS	305.8±57.8	284.6±79.2	266.5±57.5	276.9±86.3	278.1±87.3	269.4±84.5	NS
Proteinuria (g/24hour)	LIS	4.82±2.26	2.97±1.08	2.39±1.05	2.15±0.81	2.03±0.93	1.83±0.72	<0.001
	LOS	4.55±1.09	3.26±1.33	2.92±2.10	2.66±1.84	2.73±2.21	2.66±2.03	<0.001
MAP (mmHg)	LIS	107.15±11.93	95.76±7.18	95.15±7.43	94.92±6.40	94.61±6.91	95.61±6.42	<0.001
	LOS	104±9.9	99.6±5.7	96.7±5.9	97.4±5.9	96.2±6.0	97.1±5.9	<0.001

* Time-dependent differences vs baseline values.; ● Not (statistically) significant.

Conclusions

In patients with IMN and NS the administration of ACE inhibitors or AT II receptor antagonists results in similar effects on renal function, hypoalbumimemia, hypercholesterolaemia, proteinuria and arterial pressure.

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