ORIGINAL ARTICLE

Losartan versus Valsartan in the treatment of hypertension of renal transplant recipients

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Arterial hypertension is a major risk factor for cardiovascular morbidity and mortality in renal transplant recipients. Steroids, cyclosporine A (CsA) and FK-506 contribute in the development of hypertension. Losartan and Valsartan, angiotensin II receptor type 1 antagonists (AT1), have been proved to be effective antihypertensive agents in the general population and in the renal transplant recipients. The purpose of the present retrospective study was to compare the safety and efficacy of losartan (L) and valsartan (V) in the treatment of hypertensive renal transplant (Rt) recipients.

Sixty four renal transplant recipients on antihypertensive therapy were included in the study because of inadequate blood pressure control, drug side effects or proteinuria. Three patients were withdrawn from the study because of inappropriate serum creatinine elevation. Forty patients (28 men), 41 years old, received L 3.86 years after renal transplantation at the dose of 25-100 mg/d and 21 patients (16 men), 41 years old, received V 4.21 years after renal transplantation (p:NS) at the dose of 80-160 mg/d. Systolic blood pressure (SBP), diastolic blood pressure (DBP), serum creatinine levels (CRs), K, uric acid, Ht and Hb were recorded before and every two months for a period of six months after L or V initiation. Proteinuria, number of antihypertensive agents, cyclosporine A (neoral) dose and blood levels were recorded before and at the end of the six month period. The percentage of abnormal blood pressure readings was calculated before and during the patients' follow up. Doubly multivariate repeated measures analysis of variance, repeated measures analysis of variance, Mc Nemar and independent t tests were used for statistical analysis.

Multivariate analysis showed that patients on V had statistically significantly (ss) lower DBP compared with patients on L (p:0.037). SBP/DBP was 145.17±15.78/91.60±9.72 mmHg, 138.03 ±10.74/87.14±7.98 mm Hg, 142.00±15.67/ 88.57±7.68 mmHg and 143.03±14.85/ 90.35±8.15 mmHg before 2, 4 and 6 months on L treatment respectively (pins/NS). SBP/DBP was 153.50± 12.25/90.5±9.71 mmHg, 142.00 ± 9.92 / 85.25±6.78 mmHg, 137.25 ± 10.93 / 85.75±6.74 mmHg and 133.25±8.92/84.00 ± 5.98 mmHg before, 2, 4 and 6 months on V treatment respectively (p:0.0005/NS). The number of abnormal blood pressure readings was reduced ss in the V group (p:0.001). The number of antihypertensive agents per patient was 2.00±0.87/2.09±0.83 before (L/V) and 1.67 ± 0.85 (p:0.001)/1.47±0.60 (p:0.001) after 6 months (L/V). CRs was 1.61±0.81/1.28± 0.32 mg/dl, 1.64±0.77/1.36±0.36 mg/dl, 1.66±0.86/1.40±0.37 mg/dl and 1.68±0.88/1.34±0.32 mg/dl before, 2, 4, and 6 months on L/V (p:NS/0.036) treatment respectively. Hb was 13.63 ± 2.72/13.15±2.05 g/dl, 13.39±2.28/12.65±1.93 g/dl, 13.00±2.18/12.51±2.01 g/dl and 12.85± 2.26/ 12.55±2.10 g/dl before, 2, 4 and 6 months on L/V(p:0.002/0.002) treatment respectively.

Valsartan is more potent than losartan as far as the reduction of DBP in the recommended doses and reduces ss the high abnormal blood pressure readings. L and V control efficiently SBP and DBP of hypertensive Rt recipients, lower significantly the need for other antihypertensive agents and cause significant fall of Hb.
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Hypertension occurs in about 70%-90%[1-4] of patients with renal transplantation. Rejection, immunosuppressive agents, recurrent renal disease, renal artery stenosis, native kidney disease, polycythemia, weight gain and renal failure are the best known causes of post-transplant arterial hypertension[3-6]. Post transplant arterial hypertension has been associated recently with reduced kidney graft survival[7-10] and the best management of it is not known.

Losartan and vaslartan competitively and selectively inhibit the actions of angiotensin II type 1 receptor (AT1). It has been shown that losartan and valsartan can be given and are effective in patients with essential hypertension or renal failure[11-14]. The blood pressure lowering effect of these agents has not been connected with hyperkalemia or serum creatinine changes but is accompanied by a significant reduction of proteinuria, in patients with renal function impairment[15,16]. Losartan and valsartan have already been given in hypertensive renal transplant recipients and have been proved to be effective[17,18].

The aim of this study was to compare the safety and efficacy of valsartan versus losartan in the treatment of hypertension of patients with renal transplantation and stable graft function.

Subjects and methods

Sixty four renal transplant recipients on antihypertensive therapy were selected to receive losartan or valsartan in an outpatient basis at Hippokratio General Hospital of Thessaloniki. They were given losartan or valsartan because of SBP > 140 mmHg and/or a DBP > 90 mmHg in two or more readings performed at different days, because of clinical conditions causing considerable discomfort (erythrocytosis, leg oedema, gum hypertrophy) or because of proteinuria. The conventional antihypertensive agents used were stopped 24 hours before losartan or valsartan initiation.

Three patients (one from the Losartan group and two from the Valsartan group) were withdrawn from the study because there was a raise of serum creatinine level > 0.5 mg/dl in the first 15 days of treatment (no renal artery stenosis was found). Finally forty patients (28 men), with a mean age 41.69±12.87 years (range 16.21-63.36), received losartan and twenty one patients (16 men), with a mean age 41.04±14.19 years (range 18.31-60.71) received valsartan. They had received triple or quadruple sequential drug immunosuppression. No patient had documented renal artery stenosis. No patient had salt depletion or any active disease at the time of drug initiation. Patients were excluded from the study if they had heart failure, major arrhythmias, myocardial infarction or stroke within the previous six months. Patients' demographic data are shown in table 1.

Table 1. Demographic data

	Losartan	Valsartan
- Male/female	28/12	16/5
- Mean age (years)	41.69±12.8	41.04±14.19
range	16.21-63.36	18.31-60.71
- Primary renal disease		
Glomerulonephritis	17	10
Interstitial nephritis	6	2
Hypertensive glomerulopathy	2	2
Polycystic kidney disease	8	2
Diabetic nephropathy	1	
Unknown aetiology	6	5
- Reasons for inclusion		
Inadequate control of BP	24	15
Leg oedema or gum hypertrophy	10	3
Erythrocytosis	1	0
Proteinuria	5	3

The initial dose of losartan and valsartan was given according to the needs of each patient. In cases with inadequate control there was a rapid augmentation of the dose at weekly intervals up to the highest recommended dose for each drug (100 mg/d for losartan and 160 mg/d valsartan) and after that a second drug was added if it was necessary.

Blood pressure measurement was done in the morning between 9.00 and 11.00 am, with the patient at sitting position, always by the same automated machine (auscilometric). Blood and urine samples were taken, after overnight fasting on outpatient basis, at baseline time and 2, 4 and 6 months after losartan or valsartan initiation. Serum creatinine, Ht, Hb, uric acid and potassium were measured at the same time intervals. Proteinuria (24 hour urine protein), drug dose, number of antihypertensive agents and cyclosporine levels were measured before the day of AT1 antagonist initiation and six months later.

Multivariate repeated measures analysis of variance was used to compare the effect of the drugs on measured parameters during the six month follow up. Repeated measures analysis was used to estimate the effect of each drug on measured parameters during time. Student's independent t test and paired t test were used appropriately to compare quantitative variables at baseline and 6 months after treatment initiation. Mc Nemar test was used to compare the abnormal blood pressure readings before and six months after initiation of losartan and valsartan treatment. A value of $p < 0.05$ was considered ss. Quantitative results were expressed as Mean ± SD. The Statistical Package for Social Sciences (SPSS) for Windows, version 10, was used.

Results

The time from renal transplantation that patients started AT1 antagonists was 3.86±2.85 years (range 0.6-10.96) for Losartan group and 4.21±3.12 years (0.08-10.67) for Valsartan group (p:NS). The blood pressure (systolic and diastolic) was not significantly different between groups the day before drug initiation. Doubly multivariate repeated measures analysis of SBP did not show ss difference between L and V group (table 2). Repeated measures analysis of SBP showed that here was no ss change in the L group while there was ss fall of SBP in the V group (p:0.0005).

Doubly multivariate repeated measures analysis of DBP between L and V group showed ss lower DBP in the V group (p:0.037). Repeated measures analysis of DBP showed that there was no ss change in either group during time (Table 3).

In the L group proteinuria was present in 11 pts at baseline and in nine at the end of six month period. In the V group proteinuria was present in 7 pts at starting day and in six at the end of follow up. Twenty four hour proteinuria decreased during the six month period but the change was not significant and there was no difference between groups (table 4).

Table 2. Levels of systolic blood pressure measured at baseline and bimonthly intervals after initiation of losartan and valsartan treatment (mmHg)

Months	BLM	+2	+4	+6
Losartan group°	145.17±15.78	138.03±10.74	142.00±15.67	143.03±14.85
Valsartan group°	153.50±12.25*	142.00±9.92*	137.25±10.93*	133.25±8.92*

°Doubly multivariate repeated measures analysis of variance p:NS *Repeated measures analysis of variance p:0.0005
BLM: baseline measurment

Table 3. Levels of diastolic blood pressure measured at baseline and bimonthly intervals after initiation of losartan and valsartan treatment (mmHg)

Months	BLM	+2	+4	+6
Losartan group°	91.60±9.72	87.89±7.98	88.57±7.68	90.35±8.15
Valsartan group°	90.5±9.71	85.25±6.78	85.75±6.74	84.00±5.98

°Doubly multivariate repeated measures analysis of variance p:0.037 BLM: baseline measurement

Table 4. Proteinuria and number of antihypertensive drugs the day before initiation of treatment and six months later

	Treatment initiation	Six months later
24 hour urine protein (g)		
Losartan group	0.20±0.46	0.16±0.22
range	(0.15-2.5)	(0.00-1.80)
Valsartan group	0.28±0.68	0.22±0.57
range	(0.10-3.00)	(0.00-2.50)
p:NS		
number of antihypertensives		
Losartan	2.00±0.87*	1.67±0.85*
Valsartan	2.09±0.83 **	1.47±0.60**

*p:0.001 **p:0.001

Table 5. Number of blood pressure readings above the normal range in losartan and valsartan group.

	Starting day cases	2nd month cases	4th month cases	6th month cases
Losartan group SBP	6	6	8	6
Losartan group DBP	4	2	2	2
Losartan group SBP+DBP	14	4	6	8
Total No of abnormal blood pressure readings	24[1]	12	16	16[1]
% of readings with uncontrolled hyp/sion	60	30	40	40
Valsartan group SBP	10	10	4	2
Valsartan group DBP	0	1	1	0
Valsartan group SBP+DBP	6	0	2	0
Total No of abnormal blood pressure readings	16[2]	11	7	2[2]
% of readings with uncontrolled hyp/sion	76.1	52.3	33.3	9.5

[1] Mc Nemar test p:NS

[2] Mc Nemar test p: 0.001

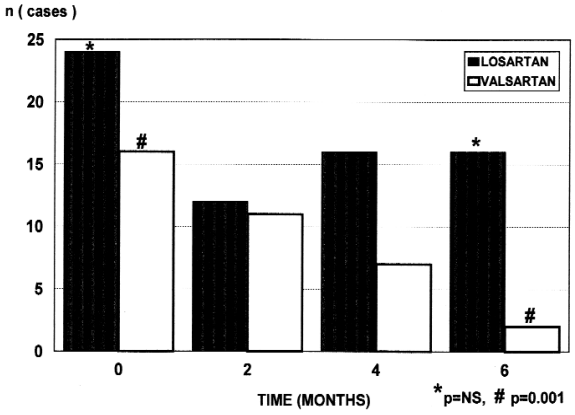

Figure 1. Total number of abnormal BP readings in the Losartan and Valsartan group.

Considering as a target SBP ≤ 140 and DBP ≤ 90 mmHg, the need for antihypertensive drugs decreased significantly in both groups but there was no ss difference between groups (table 4).

Losartan group at baseline presented high abnormal blood pressure (systolic blood pressure > 140 mmHg, or diastolic blood pressure >90 or both) in 24/40 readings and at the end of follow up in 16/40 readings (table 5). The Valsartan group, at starting day, presented high abnormal blood pressure in 16/21 readings while at the end of follow up in 2/21 readings. Mc Nemar binomial test showed that the difference of the number of uncontrolled readings in the losartan group was not ss, while in the valsartan group the difference of the uncontrolled readings between starting day and the end of follow up was ss (p:0.001). The incidence of high abnormal readings in the L group shows a fall at the second month of follow up after which there is a stabilization. On the contrary in the V group there is a steady decline in the incidence of abnormal readings during time (table 5, figure 1).

Serum creatinine levels in L group were ss higher compared with those of V group at starting day (p:0.038). Doubly multivariate repeated measures analysis of serum creatinine levels showed that there was no significant difference between groups during time. Repeated measures analysis of serum creatinine showed that there was a slight but ss raise in the V group (table 6).

Hematocrit and Hb were not different between groups at baseline and did not show any difference at the six month recordings. In spite of this there was a ss significant fall of Ht and Hb in both groups during time (table 7).

Analysis of uric acid and serum potassium levels did not show difference between L and V group during time (table 8). There was no case with hyperkalemia (K > 5.5 meq/l) during the six month period before and after losartan or valsartan initiation. Cyclosporine dose and levels measured at the initiation of losartan and valsartan treatment and six months later did not show ss difference (table 9). The antihypertensive drugs

Table 6. Mean serum creatinine levels measured at baseline and bimonthly intervals after initiation of losartan or valsartan treatment

Months	BLM	+2	+4	+6
Serum Creatinine (mg/dl)				
Losartan group°	1.61±0.81	1.64±0.77	1.66±0.86	1.68±0.88
Valsartan group°	1.28±0.32*	1.36±0.36*	1.40±0.37*	1.34±0.32*

°Doubly multivariate repeated measures analysis p:NS *Repeated measures analysis p:0.036

BLM: baeline measurement

Table 7. Mean Ht and Hb levels measured at baseline and bimonthly intervals after initiation of losartan or valsartan treatment

Months	BLM	+2	+4	+6
Ht(%)				
Losartan group[1]	42.25±7.66*	41.37±6.63*	40.44±6.46*	39.79±6.83*
Valsartan group[1]	41.09±6.11°	38.65±6.10°	38.10±5.77°	38.10±5.77°

*Repeated measures analysis p:0.018

°Repeated measures analysis p:0.001

[1]Multivariate repeated measures analysis p:NS

BLM: baseline measurement

Hb(g/dl)				
Losartan group[2]	13.63±2.72*	13.39±2.28*	13.00±2.18*	12.85±2.26*
Valsartan group[2]	13.15±2.05°	12.65±1.93°	12.51±2.01°	12.55±2.10°

*Repeated measures analysis p:0.002 °Repeated measures analysis p:0.002

[2]Multivariate repeated measures analysis p:NS

Table 8. Mean values of serum potassium and uric acid levels measured at bimonthly intervals before and after initiation of losartan treatment

Months	BLM	+2	+4	+6
Uric acid (mg/dl)				
Losartan group	7.02±1.48	7.25±1.45	7.30±1.34	7.17±2.03
Valsartan group	7.26±1.27	7.25±1.15	7.36±1.40	7.37±1.20

p:NS

BLM:baseline measurement

Potassium (mEq/L)				
Losartan group	4.34±0.54	4.51±0.50	4.40±0.52	4.37±0.52
Valsartan group	4.43±0.47	4.70±0.46	4.62±0.43	4.74±0.50

p:NS

Table 9. Cyclosporine dose and levels and AT1 antagonists' dose at baseline and six months after initiation of treatment

	At starting day	Six months later
Cyclosporine levels (ng/ml)		
Losartan group	110.28±47.81	93.13±40.06
Valsartan group	101.75±71.95	86.62±36.54
Cyclosporine dose (mg/dl)		
Losartan group	151.64±63.41	126.37±54.24
Valsartan group	158.33±75.96	145.23±65.00
AT1 antagonist dose (mg/d)		
Losartan	50.62±17.43*	61.87±24.01*
Valsartan	91.42±28.68	95.23±32.18

*p:0.002

that were substituted by L or V were: calcium channel antagonists, ß-adrenergic blockers, clonidine, minoxidil and furosemide. Losartan mean dose was ss higher at the end of the follow up while valsartan dose did not change significantly (table 9).

No case presented tahycardia or orthostatism. Side effects such as cough, angioneurotic oedema or dysgeusia were not recorded. Also there was remission of leg oedema (5/7 in the Losartan group and 2/2 in the Valsartan group) and gum hypertrophy.

Discussion

The best management of transplant hypertension has not yet been defined. Hypertension treatment requires individualization and this stands for hypertensive renal transplant recipients. Hypertension is a serious risk factor for cardiovascular morbidity and mortality and affects the progression of renal failure. Thus, long-term control of high blood pressure is mandatory. Calcium antagonists are able to reverse cyclosporine induced renal vasoconstriction[19] and currently are preferred for the hypertensive renal transplant recipients. However, recently it has been reported that these drugs could have deleterious side effects on patients with chronic allograft nephropathy[20].

We already have shown that angiotensin II AT1 receptor antagonists, a new class of antihypertensive agents, control blood pressure of hypertensive renal transplant recipients satisfactorily[17,18] and this is in agreement with the findings of others[21]. Losartan and Valsartan, despite their common mechanism of action, have pharmacologic differences that result in different efficacy and tolerability in patients with essential hypertension[22].

In this work we found that valsartan causes a ss fall of systolic blood pressure during time but no ss difference between L and V group was noticed (table 2). The comparison of diastolic blood pressure between groups showed that valsartan is more potent antihypertensive agent causing ss lower DBP (table 3). The need for other antihypertensive drugs was reduced ss in both groups (table 4) but there was no ss difference between groups neither at starting time nor six months later. The prevalence of uncontrolled hypertension was 60% and 76.1% at starting time and fell to 40% and 9.5% six months later in the L and V group respectively (table 5) and this suggests that valsartan becomes more efficacious during time. The blood pressure load defined by the percentage of high abnormal readings[23] during the six month period was reduced by both losartan and valsartan. This reduction was greater in the V than in the L group in all measured periods. Therefore the burden on the heart by the uncontrolled high BP probably was decreased more by V than by L. Having in mind that BP overload is considered better determinant of cardiac and vascular abnormalities than the casual readings of BP[24], these findings are important because it is already known that, in patients with hypertension, chronic BP overload induces myocardial and vascular damage. The effect of BP overload on the renal allograft during time is not known.

The effectiveness of Ag II AT1 antagonists may be influenced by receptor affinity, pharmacokinetic properties and access of the active drug to the sites of action. Valsartan has a 5-fold greater affinity than losartan and does not bind to other sites, like losartan, except the Ag II AT1 receptor[25]. It does not require biotransformation for its pharmacologic activity[26] and its clearance is 30% by the kidneys and 70% by the liver[27]. Much of the Ang II inhibiting effect of losartan can be attributed to its active metabolite EXP3174, a noncompetitive antagonist that binds to the AT1 receptors with 10-fold greater affinity than the parent compound and is about 15 to 20 times more potent in inhibiting Ang II induced pressor and contractile responses[28,29]. Losartan has no steady biotransformation metabolised by the cyp 450 isoform 3A4 and may be influenced by drugs such as cyclosporine A, antifungal agents, statins and antibiotics. Only 10% of losartan is excreted by the kidneys its clearance been made is almost exclusively by the liver (90%)[11]. The elimination half life of valsartan is longer than that of losartan. All these factors possibly contribute to the potency of action of each drug.

Both groups presented a small increase in serum creatinine that was ss in the valsartan group but no difference between groups was noticed (table 6). Possibly changes in the glomerular hemodynamics with a transient decrease in GFR were the cause. The elevation of serum creatinine > 0.5 mg/dl in three patients that were excluded from the study possibly is connected with

intrarenal atheromatous lesions favouring the development of intrarenal ischemia.

Stimulation of AT1 receptors of erythroid progenitor cells by Ag II is believed to increase red cell mass independently from circulating erythropoietin[30]. A statistically significant fall of Ht and Hb was noticed in both groups but no difference was noticed between groups (table 7). This fall has already been noticed[17,18,31] and is due to blockade of AT1 receptors which results in a decrease of red blood-cell mass independently of erythropoietin and initial haemoglobin levels.

No difference was noticed between groups as far as the 24 hour proteinuria which decreased at the end of the six month antihypertensive treatment though not ss. Interestingly two proteinuric pts from L and one from V group remained free from proteinuria. The presence of proteinuria points renal damage. This group of patients needs renal biopsy and a close and long term follow up before we draw any conclusions.

Side effects such as tachycardia (> 100 beats/min), orthostatism, cough, angioneurotic oedema and dysgeusia that have already been reported by others[32], were not noticed in our patients. The unwanted clinical conditions (erythraemia, leg oedema, gum hypertrophy) improved significantly in both groups.

Potassium and uric acid levels six months after initiation of losartan and valsartan treatment remained stable in spite the report that losartan has uricosuric effect in healthy people and causes a decrease in serum uric acid during chronic treatment[33,34].

The intrarenal renin-agiotensin system is significant for the growth, sclerosis and regulation of hemodynamics of the glomerulus[35]. TGF-β, connected with the angiotensin II production, is considered to be a significant fibrogenic factor implicated in a number of chronic diseases of the kidney[36]. The identification of molecular mechanisms of monocyte/macrophage infiltration in hypertensive nephrosclerosis might lead to the development of novel therapies. Oseopontin inhibition by AT1RAs has been connected with reduction of macrophage infiltration and tubulointerstitial injury[37]. Recent studies have shown that MCP-1 expression is increased in some forms of experimental hypertensive nephrosclerosis mediated by angiotensin II teceptors type 1[38]. The proof that AT1 receptor antagonists could decrease the synthesis and activation of TGF-β as well as blockade osteopontin and MCP-1 expression further supports the idea that these drugs are useful in the treatment of hypertension in renal transplant recipients[39].

Having in mind that losartan and valsartan do not cause changes in the cyclosporine blood levels and do not affect total serum cholesterol, triglycerides, ALAT, ASAT, or bilirubin[21] and furthermore based on the six month results of our study, we are justified to continue and examine the possible long term effect of losartan and valsartan on the chronic allograft nephropathy.

Valsartan proved to be a more potent antihypertensive agent than losartan and should be preferred in resistant cases of hypertension. Caution should be given in the first fifteen days of treatment with these agents in order to avoid possible inappropriate raise of serum creatinine even though there is no evidence of graft renal artery stenosis.

ΠΕΡΙΛΗΨΗ

Γ. Βέργουλας, Γρ. Μυσερλής, Β. Παπανικολάου, Δ. Γάκης, Ι. Κατσάρα, Ε. Ατματζίδης, Δ. Τακούδας, Α. Αντωνιάδης. **Σύγκριση της λαζαρτάνης και της βαλσαρτάνης στη θεραπεία της υπέρτασης ασθενών με λειτουργούν νεφρικό μόσχευμα.** Ιπποκράτεια 2001, 5 (4): 156-164

Η αρτηριακή υπέρταση είναι μείζων παράγοντας κινδύνου για την ανάπτυξη καρδιαγγειακής νοσηρότητας και θνητότητας στους ασθενείς με μεταμόσχευση νεφρού. Τα κορτικοστεροειδή, η κυκλοσπορίνη, και το τακρόλιμους είναι φάρμακα που συμβάλλουν στην ανάπτυξη υπέρτασης. Η λοζαρτάνη και η βαλσαρτάνη, ανταγωνιστές των υποδοχέων τύπου 1 της αγγειοτενσίνης ΙΙ (ΑΤ1), έχει αποδειχθεί ότι είναι αποτελεσματικοί αντιυπερτασικοί παράγοντες στο γενικό πληθυσμό και στους ασθενείς με νεφρική μεταμόσχευση. Ο σκοπός της παρούσας αναδρομικής μελέτης ήταν να συγκρίνουμε την ασφάλεια και την αποτελεσματικότητα της λοζαρτάνης (L) και της βαλσαρτάνης (V) στη θεραπεία υπερτασικών ασθενών με λειτουργούν νεφρικό μόσχευμα (Rt).

Εξήντα τέσσερις λήπτες νεφρικού μοσχεύματος που βρίσκονταν σε αντιυπερτασική θεραπεία περιλήφθηκαν στη μελέτη λόγω ανεπαρκούς ελέγχου της αρτηριακής πίεσης, ανεπιθύμητων δρά-

σεων των φαρμάκων ή λόγω λευκωματουρίας. Τρεις ασθενείς απεσύρθησαν από τη μελέτη λόγω μεγάλης ανόδου της κρεατινίνης του ορού. Σαράντα ασθενείς (28 άνδρες), ηλικίας 41 ετών, έλαβαν L 3.86 έτη μετά τη μεταμόσχευση σε δόση 25-100 mg/d και 21 ασθενείς (16 άνδρες), ηλικίας 41 ετών, έλαβαν V 4.21 έτη μετά τη νεφρική μεταμόσχευση (p:NS) στη δόση των 80-160 mg/d. Η συστολική (SBP) και η διαστολική αρτηριακή πίεση του αίματος (DBP), τα επίπεδα της κρεατινίνης του ορού (CRs), το K, το ουρικό οξύ, ο Ht and η Hb καταγράφηκαν πριν και ανά δίμηνο για διάστημα έξη μηνών μετά την έναρξη χορήγησης L ή V. Η λευκωματουρία, ο αριθμός των αντιυπερτασικών φαρμάκων, η δόση και τα επίπεδα της κυκλοσπορίνης καταγράφηκαν πριν και στο τέλος της εξάμηνης περιόδου. Το ποσοστό των μετρήσεων της αρτηριακής πίεσης εκτός του φυσιολογικού ορίου υπολογίσθηκε πριν και κατά τη διάρκεια της παρακολούθησης των ασθενών. Χρησιμοποιήθηκε διπλή πολυπαραγοντική ανάλυση επαναλαμβανομένων μετρήσεων, ανάλυση επαναλαμβανομένων μετρήσεων, Mc Nemar και t tests για μη ζεύγη τιμών.

Η πολυπαραγοντική ανάλυση έδειξε ότι οι ασθενείς that patients που πήραν V είχαν στατιστικά σημαντικά (ss) χαμηλότερη DBP συγκρινόμενοι με τους ασθενείς που έπαιρναν L (p:0.037). Η SBP/DBP ήταν 145.17±15.78 /91.60± 9.72 mmHg, 138.03±10.74/87.14±7.98 mm Hg, 142.00±15.67/88.57±7.68 mmHg και 143.03± 14.85/90.35±8.15 mmHg πριν 2, 4 and 6 μήνες σε θεραπεία με L αντίστοιχα (p:ns/NS). Η SBP/DBP ήταν 153.50± 12.25/90.5±9.71 mmHg, 142.00 ± 9.92 / 85.25±6.78 mmHg, 137.25 ± 10.93 / 85.75±6.74 mmHg και 133.25±8.92/84.00 ± 5.98 mmHg πριν, 2, 4 and 6 μήνες στους ασθενείς με θεραπεία V αντίστοιχα (p:0.0005/NS). Ο αριθμός των μετρήσεων της αρτηριακής πίεσης εκτός φυσιολογικών ορίων ελαττώθηκε ss στην ομάδα των ασθενών υπό V (p:0.001). Ο αριθμός των αντιυπερτασικών παραγόντων ανά ασθενή ήταν 2.00±0.87/2.09±0.83 πριν (L/V) και 1.67 ± 0.85 (p:0.001)/1.47±0.60 (p:0.001) μετά από 6 μήνες(L/V). Η CRs ήταν 1.61±0.81/1.28±0.32 mg/dl, 1.64±0.77/1.36±0.36 mg/dl, 1.66± 0.86 /1.40±0.37 mg/dl και 1.68±0.88/1.34±0.32 mg/dl πριν, 2, 4 και 6 μήνες σε θεραπεία με L/V (p:NS/0.036) αντίστοιχα. Η Hb ήταν 13.63 ± 2.72/13.15±2.05 g/dl, 13.39±2.28/12.65±1.93 g/dl, 13.00±2.18/12.51±2.01 g/dl και 12.85± 2.26/ 12.55±2.10 g/dl πριν, 2, 4 και 6 μήνες σε θεραπεία με L/V(p:0.002/0.002) αντίστοιχα.

Συμπερασματικά η V είναι πιο αποτελεσματική από την L όσον αφορά την ελάττωση της DBP στις προαναφερθήσες δόσεις και ελαττώνει ss τον αριθμό των μετρήσεων της αρτηριακής πίεσης εκτός των φυσιολογικών ορίων. Η L και η V ελέγχουν επαρκώς τη SBP και DBP των υπερτασικών λιπτών νεφρικών μοσχευμάτων, ελαττώνουν σημαντικά την ανάγκη για άλους αντιυπερτασικούς παράγοντες και προκαλούν ss πτώση της Hb.

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