WCN24-AB-1937

RENOPROTECTIVE EFFECT OF 3RD GENERATION CALCIUM CHANNEL BLOCKERS

MARTÍNEZ SERVENTI, JOAQUÍN; MORALES, DIEGO; CANTELI, MARCELA; BERNASCONI, AMELIA; HEGUILÉN RICARDO

NEPHROLOGY UNIT, HOSPITAL GENERAL DE AGUDOS "JUAN A. FERNÁNDEZ", BUENOS AIRES, ARGENTINA

INTRODUCTION

Drugs that inhibit the renin-angiotensin axis (RAS) have largely recognized renoprotective properties. Third generation dihydropyridine calcium channel blockers like lercanidipine (LER), blocking "L" as well as "T-type" calcium activated channels, reduce intraglomerular pressure and urine protein excretion (UprotV) and also might stabilize renal function in several nephropathies.

The main aim of this study was to compare the renoprotective efficacy of the addition of losartan (LOS) or LER to patients (Ps) with chronic kidney disease (CKD) receiving monotherapy with enalapril (ENL).

METHODS

Stage 2-3 CKD Ps with controlled hypertension (HT), receiving ENL (10-20 mg/d) for >12 months and displaying UprotV <2 g/d, were included.

Serum creatinine (Scr), as well as UprotV and clinical parameters were assessed at baseline and at 4 ± 1 month interval after being randomly assigned to fixed dose of Losartan (LOS) or lercanidipine (LER).

The primary outcome of interest was the survival time until the composite event (doubling Scr and/or > 50% increase in UProtV). All data are expressed as mean (SD), median (IQR) or proportions otherwise indicated.

The Kaplan-Meier product limit estimator and the Log-rank test were used to compare event-free survival among the two treatment groups.

After adjustment for potentially correlated variables the proportional hazard (Cox) regression analysis was used to evaluate whether such outcome was dependent on the following covariates: treatment arm, gender, diabetes, tobacco use, or the presence of dyslipemia, Odds ratios with the appropriate 95% confidence intervals are reported.

All tests were 2 sided, and p values < 0.05 were considered statistically significant.

The statistical analysis was carried-out with "RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA URL http://www.rstudio.com/".

RESULTS

- The main characteristics of the studied cohorts are shown in Table 1.
- Seventy-eight (43 men) 48 – 61-year-old, CKD (55.1% type 2 diabetic) Ps were recruited.
- LOS (50 mg/d) was added in 38 while LER (10 mg/d) in 40.
- Dyslipemia (DLP) was present in 34 (43.6%), tobacco use in 28 (35.9) and 37 (47.4%) individuals were on diuretics, with no differences between treatment arms.
- The addition of LOS or LER produced no relevant changes in BP.
- The median (95%CI) time until the outcome event was 7.9 (7.0-8.8) and 8.2 (7.3- 9.1) years for LOS and LER groups respectively (p: NS. Log-rank test). (Fig 1.)
- Poor controlled DBT (OR 2.99, 95%CI 1.24 – 7.24 p:0.015) and tobacco use (3.95, 1.85 – 8.44; p:0.0001) associated with worsening renal outcomes in this cohort of CKD individuals. (Fig 2.)

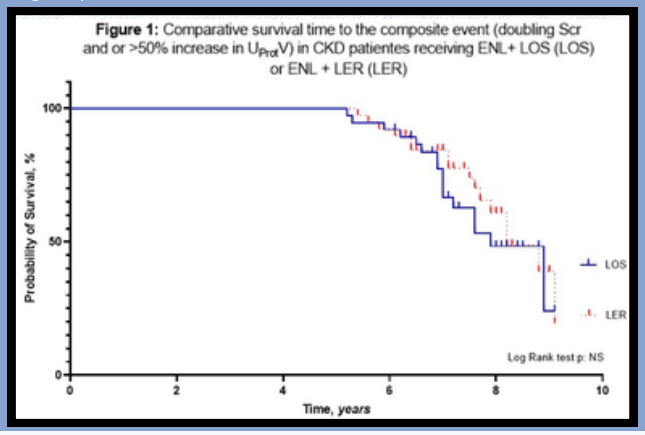
Table 1. Main characteristics at baseline

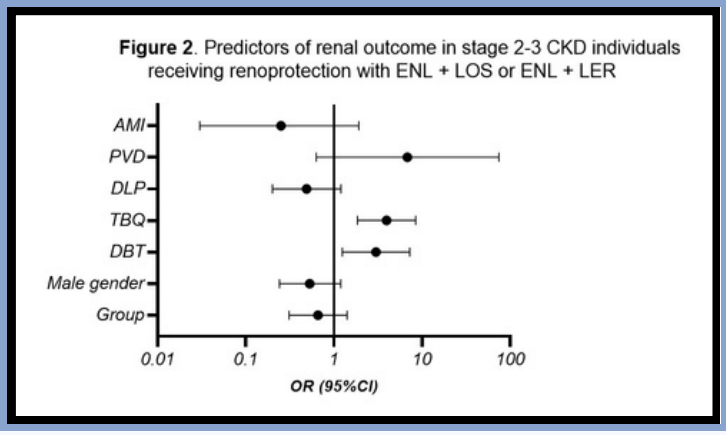
	LOS (n: 38)	LER (n: 40)	p
Gender; *M/F*[&]	22/16	21/19	NS
Age, *years* *	54.8(3.5)	54.8(3.8)	NS
Weight, *kg* *	86.4(13.4)	81.1(13.2)	NS
DBT, *n (%)* [&]	19 (50,0)	24 (60,0)	NS
Insulin, *n (%)* [&]	9 (23.7)	8 (20.0)	NS
Oral Anti-DBT, *n (%)* [&]	12 (31.6)	14 (35.0)	NS
AMI previous, *n (%)* [&]	7 (18.4)	6 (15.0)	NS
PVD, *n (%)* [&]	4 (10.5)	3 (7.5)	NS
Tobacco, *n (%)* [&]	16 (42.1)	12 (30.0)	NS
Dyslipidemia; *n (%)* [&]	16 (42.1)	18 (45.0)	NS
Diuretics, *n (%)* [&]	19 (50.0)	18 (45.0)	NS
AAS, *n (%)* [&]	19 (50.0)	23 (57.5)	NS
Statins, *n (%)* [&]	24 (63.2)	19 (47.5)	NS
SBP, *mmHg* * [#]	146.1 (8.8)	147.3 (6.2)	NS
DBP, *mmHg* * [#]	86.4(5.5)	87.1 (5.7)	NS
ENL dose, *mg/d* ** [$]	17.5 (5.0)	20.0 (5.0)	NS
S-Creat, *mg/dL* * [#]	1.5 (0.1)	1.5 (0.1)	NS
eGFR (CKD-EPI), *mL/min* * [#]	48.7 (9.3)	49.6 (9.9)	NS
Proteinuria, *g/d* ** [$]	1.3 (0.3)	1.4 (0.4)	NS
Baseline Serum K, *mmol/L* * [#]	4.8 (0.3)	4.8 (0.3)	NS

AMI: Acute myocardial infarction; PVD: Peripheral vascular disease; AAS: Acetylsalicylic acid; SBP and DBP: Systolic and diastolic blood pressure respectively; ENL: enalapril.

* Mean (SD), ** Median (interquartile range). [&] Yates corrected chi square.

[#] Unpaired Student´s "t" test. [$] Wilcoxon-Mann Whitney test





CONCLUSIONS

1. The addition of LER to standard therapy with ENL has similar renoprotective properties than ENL plus LOS.

2. Adequate control of some modifiable (tobacco exposure) and/or non-modifiable conditions (DBT) may help reduce the risk of worsening renal function.

3. LER could be preferred for those Ps not responding to the dual blockade of the RAS or for whom such measures produced adverse consequences like hyperkalemia.

4. Additional studies in a larger number of individuals are mandatory to corroborate the benefits of this group of agents.