54TH ERA-EDTA CONGRESS
Madrid, Spain June 3rd-6th 2017 www.era-edta2017.org

Circulating Galectin-3 levels are associated with respiratory and renal dysfunction in patients with chronic obstructive pulmonary disease

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Introduction and Aims

Chronic obstructive pulmonary disease (COPD) may induce profound effects on cardiac function and systemic consequences, including CKD that occurs frequently in COPD patients. Plasma galectin-3 has been linked to the CKD and heart dysfunctions in cohort studies. The aim of this study was to evaluate the cross-sectional correlations of galectin-3 with respiratory and renal functions in COPD patients.

Methods

This is a cross-sectional study with 42 COPD patients recruited between January and December 2015 in Fortaleza, Ceará, Brazil. Also, healthy volunteers were included as a control group. Patients with previous diagnosis of renal diseases were excluded. Respiratory function was evaluated through forced expiratory volume (FEV) score and gasometry parameters. Renal parameters as creatinine, urea, eGFR (MDRD formula) and urinary albumin-creatinine ratio (ACR) were evaluated. Renal biomarkers were measured in specific serum and urine samples aliquots by sandwich ELISA: NGAL (R&D systems), urinary MCP-1 (R&D systems). Galectin-3 was measured using ELISA too (R&D systems). Spearman correlation was applied in cross-sectional correlations analyses.

Results

Patients' mean age was 67.9 ± 9.6 years in COPD patients and 57% were female. COPD patients had a significant increased in PaCO2 (52±10 vs. 46.7±3.9 mmHg, p=0.017) and systolic blood pressure (p=0.038) compared with healthy group. Moreover, patients had increased in ACR [6.25 (median), interquartile range (IQR 2.4–13.3) vs. 1.1 (IQR 0.3–2.8) mg/g creatinine; p=0.012] and significant decrease in eGFR (78.7±28.4 vs. 104.9±14.3 mL/min, p<0.001) in comparison with healthy group. Urinary MCP-1 was higher in COPD patients [74 (IQR 37.7-175.4) vs. 38.5 (IQR 14.5-85.9) pg/mg creatinine] and no difference regarding serum and urinary NGAL. Increased levels of galectin-3 were observed in COPD patients [1.5 (IQR 0.8-2.4) vs 0.5 (IQR 0.3-1.3) ng/mL; p<0.01] mostly in severe COPD. In cross-sectional correlations analyses only galectin-3 had significant correlation with decrease in FEV score (r=-382, p=0.04), decrease of eGFR (r=-0.557, p=0.001) and decrease of PaO2 (r= -0.463, p=0.007) in COPD patients. Also, when COPD group were divided by galectin-3 quartiles, patients with higher galectin-3 levels (quartile 4) had significant decrease in FEV score, eGFR and PaO2 (p<0.01 for all).

Table 1. General characteristics of COPD patients and control group.

	COPD (n=36)	Control (n=13)	P
Age (years)	67.9 ± 9.6	60 ± 7.0	0.01 [b]
Gender, male, n (%)	20 (43)	6 (46)	0.868 [a]
BMI (kg/m^2)	25±6	25.5±2.0	0.657 [b]
SBP (mmHg)	130 (115. 140)	120 (110. 120)	0.038 [c]
DBP (mmHg)	80 (75. 80)	80 (70. 80)	0.949 [c]
Hypertension, n (%)	22 (47)	3 (23)	0.023 [a]
Hypertension + Dyslipidemia	1 (3)	-	-
Hypertension + CHF	1 (3)	-	-
GOLD stage	46±19	-	-
Moderate, n (%)	16 (44.4%)	-	-
Severe, n (%)	13 (39.3%)	-	-
Very severe, n (%)	7 (21.2)	-	-
Time of disease (years)	6.8±5.05	-	-
Time of smoking (years)	34.62±17.34	-	-
Laboratory data			
Hemoglobin (g/dL)	14.2±1.6	13±4.4	0.138 [b]
Hematocrit (%)	43.3±4.7	39.1±13.4	0.128 [b]
Platelets (/mm^3)	263±70	184±124	0.070 [b]
PO_2 (mmHg)	31.6±12.7	35±12.4	0.428 [b]
PCO_2 (mmHg)	52±10	46.7±3.9	0.017 [b]
Triglycerides (mg/dL)	121±40	117±71	0.873 [b]
Total Cholesterol (mg/dL)	202±37	202±78	0.978 [b]
Albumin (g/dL)	4.2±0.3	4.1±0.2	0.899 [b]
Fast Glucose (mg/dL)	95.5±24	92±11	0.633 [b]

BMI – Body mass index; SBP – Systolic bloodpressure; DBP – Diastolic blood pressure; CHF- Congestive heart failure; VEF_1 – Forced expiratory volume in 1s; PO_2 – Partial oxygen pressure; PCO_2 – Partial pressure of carbon dioxide. Data expressed as mean ± standard deviation for normally distributed variables, median and interquartile interval for continuous variables with non-normal distribution, or percentage for absolute data. Significant p<0.05. [a]Chi-square test; [b]Student t test; [c]Mann-Whitney test.

Table 2. Traditional and novel biomarkers among COPD patients and control group.

	COPD (n=36)	Control (n=13)	P
Serum Creatinine (mg/dL)	0.76 ± 0.24	0.72 ± 0.14	0.617 [a]
Serum Urea (mg/dL)	31.7 ± 10.9	25.8 ± 6.7	0.086 [a]
eGFR (mL/min/1.73m^2)	78.7 ± 28.4	104.9 ± 14.3	<0.001[a]
Microalbuminuria (mg/g-Cr)	6.25 (2.4.13.3)	1.1 (0.3. 2.8)	0.012[b]
Na^+ (mEq/L)	140.5 ± 3.7	141.3 ± 5.4	0.587[a]
K^+ (mEq/L)	4.6±0.9	4.9±0.46	0.432[a]
Serum NGAL (ng/mL)	98.4±32.1	82.3±24.2	0.078[a]
Urinary NGAL (ng/mg-Cr)	6.3±4.9	8.1±7.2	0.149[a]
Urinary MCP-1 (pg/mg-Cr)	74 (37.7. 175.4)	38.5 (14.5. 85.9)	<0.05[b]
Serum Galectina-3 (ng/mL)	1.5 (0.8. 2.4)	0.5 (0.3. 1.3)	<0.01[b]

eGFR – Estimated glomerular filtration rate using MDRD equation; Na^+ - sodium; K^+ - potassium; NGAL - neutrophil gelatinase-associated lipocalin ; MCP-1 – monocyte chemoattractant protein-1. Data expressed as mean ± standard deviation for normally distributed variables, median and interquartile interval for continuous variables with non-normal distribution. Significant p<0.05. [a]Student t test; [b]Mann-Whitney test.

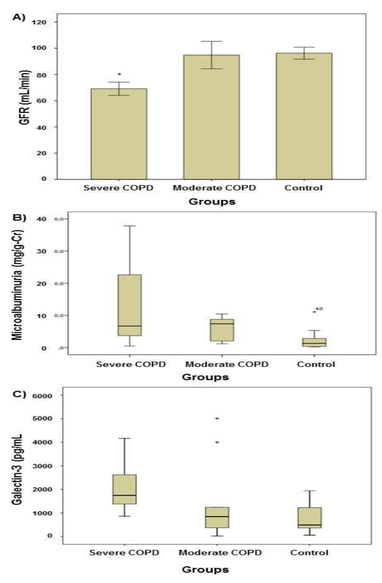

Figure 1. Biomarkers levels among COPD patients according to severity and comparison with control group. A) Mean GFR levels according to VEF1 groups (severe and moderate), p<0.05 severe vs. moderate COPD and COPD vs. control; B) Median and interquartile ranges of microalbuminuria according to VEF1 groups (severe and moderate), p<0.05 severe vs. moderate COPD and COPD vs. control; C) Median and interquartile ranges of blood galectin-3 according to VEF1 groups (severe and moderate), p=0.003 severe vs. moderate COPD and COPD vs. control.

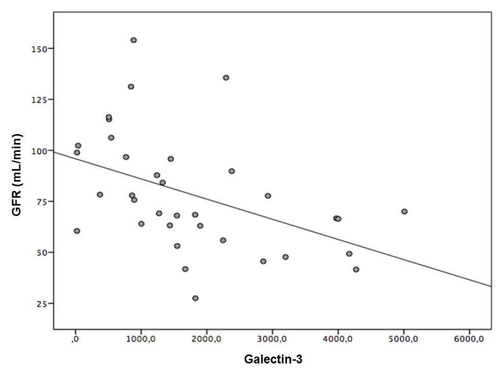

Figure 2. Inverse correlation between galectin-3 levels and GFR.

Conclusions

Higher circulating galectin-3 levels were found in COPD patients and were associated with decrease in eGFR and factors related with severe COPD as decrease in FEV score and in PaO2. Further prospective studies are needed to evaluated the prognostic value of galectin-3 in detect CKD in COPD patients.

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DOI: 10.3252/pso.eu.54ERA.2017
ePosters supported by F. Hoffmann- La Roche Ltd.
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