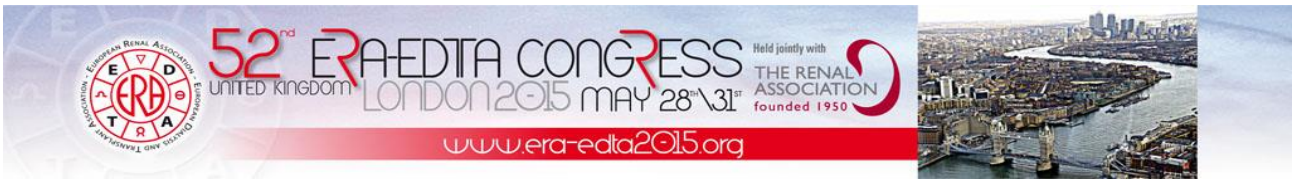

PODOCYTURIA IN FABRY DISEASE IS ELEVATED IN UNTREATED VS TREATED ADULT PATIENTS AND DOES NOT CORRELATE WITH PROTEINURIA OR RENAL FUNCTION

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Abstract

Purpose: We assessed the degree of podocyturia in controls and in Fabry disease patients with vs without agalasidase beta therapy, and correlated podocyturia with proteinuria and renal function.

Methods: Prospective controlled study in 11 healthy subjects (Group 1) and in 17 Fabry individuals (Group 2). Controls were defined as patients without clinical morbidities. Fabry disease was diagnosed in all cases by low enzymatic α-galactosidase activity and by characterization of the molecular enzyme mutation. Group 2 was thereafter divided in Group 2A, which received agalasidase beta (n=12), and Group 2B, which included untreated cases (n=5). Variables included: Age, gender, hypertension, diabetes, proteinuria, MDRD4, podocyte count per 10 20x microscopy power fields, and number of podocytes per gram of urinary creatinine. Podocytes were identified by epifluorescent microscopy employing antibodies against synaptopodin. All Fabry patients were on enalapril and/or valsartan treatment. Wilcoxon signed ranks test was used; results are expressed as mean±SD unless expressed otherwise. Spearman coefficient was employed for correlations.

Results: Group 1 vs Group 2 were not different as to age (48±17.11 vs 41.4±12.5) years or gender (M 45% vs M 47%); proteinuria, 0 vs 1.46±1.06 g/day, p<0.0001; MDRD4, 92.73±21.62 vs 54.35±41.62 ml/min, p=0.01; podocyte count, 0.37±0.30 vs 1±0.82 cells, p<0.0089; podocytes/gram of urinary creatinine, 50.00±28.88 vs 87.53±17.79 cells/gram urinary creatinine, p<0.001. Groups 2A vs 2B: Age, 43.42±12.01 vs 36.4±13.67 years, p<0.0001; gender, M 47% vs M 42%, p=ns; proteinuria, 1.70±1.19 vs 0.90±0.40 g/day, p<0.0001; MDRD4, 54.25±37.36 vs 54.60±35.58 ml/min, p=ns; podocyte count, 0.55±0.25 vs 2.09±0.63 cells, p<0.0001; podocytes/gram of urinary creatinine, 61.80±44.90 vs 149.26±32.68 cells/gram urinary creatinine, p<0.0001. Hypertensives, Group 2A, 3 (25%); Group 2B, 0. Correlations Group 2A: Podocyturia-proteinuria, ρ= -0.47 p=ns; podocytes/gram of urinary creatinine-MDRD4, ρ=0.56 p=0.05. Group 2B: podocytes/gram of urinary creatinine-MDRD4, ρ= -0.41 p=ns; podocytes/gram of urinary creatinine-proteinuria, ρ=0.67 p=ns, MDRD4-proteinuria, ρ= -0.95 p<0.01.

Conclusions: Fabry subjects display higher levels of podocyturia compared with controls. Fabry treated patients display a negative correlation between podocyturia and proteinuria

and a positive correlation with renal function. Fabry untreated subjects display a significant higher degree of podocyturia despite being younger and with lower proteinuria levels which is independent of proteinuria or renal function. Therapy with agalasidase beta may protect against irreversible podocyte loss, may contribute to improved renal function despite some degree of hypertension, and should be recommended to all patients with Fabry disease to decrease irreversible podocyte loss.