ALLOPURINOL THERAPY FOR HYPERURICEMIA REDUCES INFLAMMATION AND PROGRESSION OF RENAL DISEASE IN MODERATE CHRONIC KIDNEY DISEASE

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INTRODUCTION Hyperuricemia is a common finding in patients with metabolic syndrome and in those with cardiovascular and renal disease. Moreover, the elevation in uric acid levels observed after fructose ingestion, with a consequent reduction in nitric oxide, may lead to a reduced glucose uptake in the skeletal muscle, hyperinsulinemia, and insulin resistance. Clinical studies showed the beneficial effects of lowering uric acid therapies on several markers of cardiovascular and renal disease. To date, however, there is no evidence indicating that such therapies, that are not free of risk, may reduce cardiovascular events. In the mean time, few data are available regarding the effect of allopurinol in patients with chronic kidney disease.

AIM OF STUDY was to monitor if Allopurinol therapy reduces inflammation and slows down the progression of renal disease in patients with moderate to severe chronic kidney disease

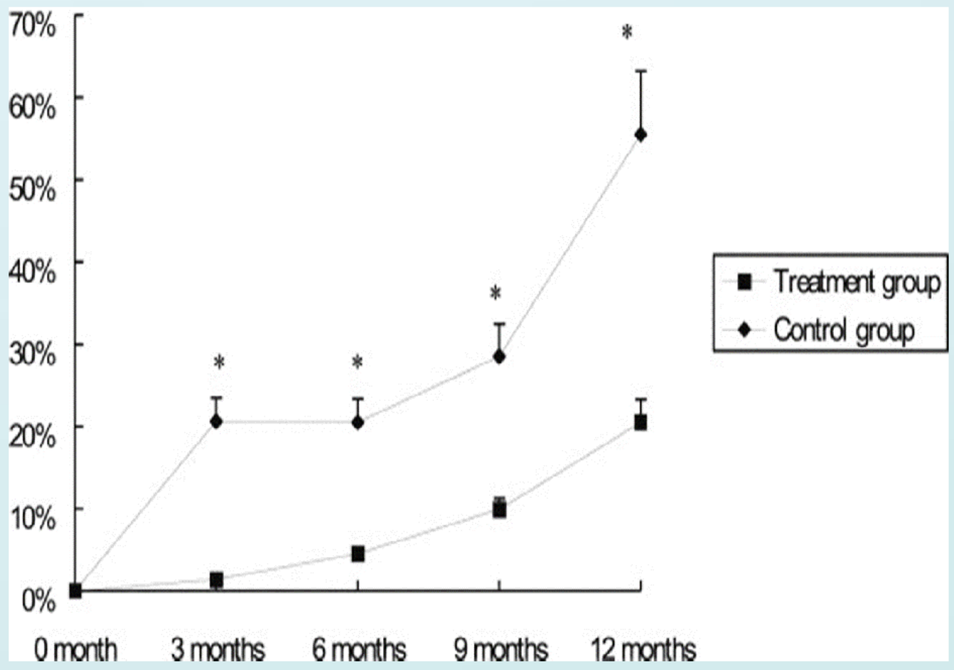
MATERIAL AND METHODS: We conducted a prospective, randomized trial of 125 patients with estimated GFR (eGFR) 30-59 ml/min. Patients were randomly selected either to treatment with allopurinol 100 mg/d (n= 52) or to continue the usual therapy (n =63). Clinical and biochemical, including inflammatory parameters were followed at baseline and after 3, 6, and 12 months of therapy. The objectives of study were the monitoring of renal disease progression (modifications of eGFR) and cardiovascular events that needed hospitalization.

RESULTS: Serum uric acid, C-reactive protein levels and IL-6 were significantly decreased in subjects treated with allopurinol. In the control group, eGFR decreased 2.2 1.2 ml/min/1.73 m², and in the allopurinol group, eGFR decreased less, with 1.7 0.8 ml/min/1.73 m² after 12 months. Allopurinol treatment slowed down renal disease progression independently of age, gender, association with diabetes, levels of C-reactive protein, IL-6, albuminuria, and renin-angiotensin system blockers use. After a mean follow-up time of 12 months, 32 patients (24%) suffered a severe cardiovascular event that needed hospitalization. Diabetes mellitus, previous coronary heart disease, and C-reactive protein levels increased cardiovascular risk. Allopurinol treatment reduced risk of cardiovascular events in 63% of cases, compared with standard therapy. Only in 6 cases (4.8%) the allopurinol therapy was stopped because the occurrence of side effects.

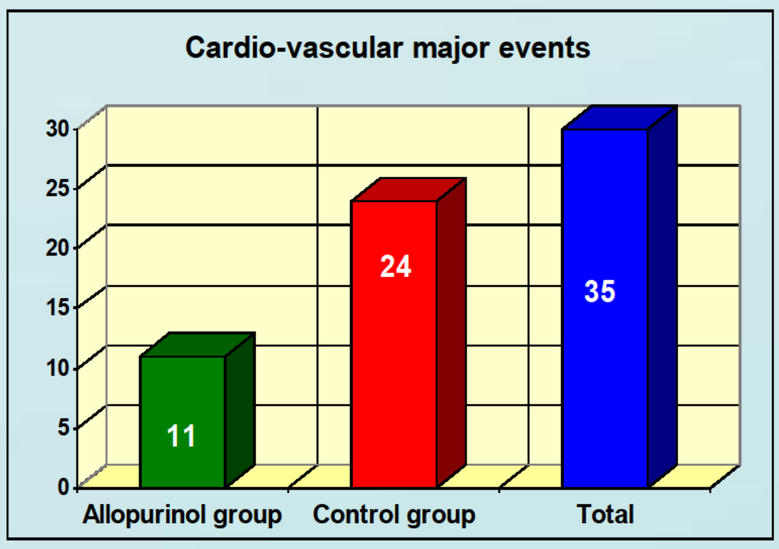
Demographic Characteristics study groups

	Allopurinol Group (62 pts)	Control Group (63 pts)	*P* value
Age	56.5±11.7	57.3±14.6	*NS*
Gender (F/M)	32/30	33/30	*NS*
Body weight (kg)	77.6±11.3	78.4±13.7	*NS*
ArterialHT – Systolic -Diastolic	146±25 89±21	139±29 85±26	*NS* *NS*
Diabetes mellitus	18/62	19/63	*NS*
Creatinine Clearance (ml/min/1.73)	47.2±10.9	46±11.2	*NS*
Proteinuria (g/24 hrs)	1.09± 0.67	1.13±0.73	*NS*
RAAS blockers	41/62	44/63	*NS*
Calcium-channel blockers	27/62	26/63	*NS*
Statins treatment	38/62	40/63	*NS*

MEAN PERCENTAGE OF CHANGE (Decrease)IN CREATININE LEVELS



Allopurinol group	Hs-CRP mg/L	IL-6 pg/mL
Basal	4,5±1.8	3.9± 1.5
6 months	3±1.6	3.5± 1.3
12 months	2.6±1.3	3± 1.1
Control group		
Basal	4.2±1.9	4± 1.6
6 months	3.9±1.7	3.8± 1.5
12 months	3.5±1.5	3.9± 1.7



•**CONCLUSION**: Allopurinol decreases C-reactive protein and IL-6 levels and seems to slow down the progression of renal disease in patients with moderate to severe chronic kidney disease. In addition, allopurinol reduces serious cardiovascular events, need for hospitalization and, consecutively, the medical costs in these subjects.

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H) Clinical Nephrology, CKD. H1) Lab methods, progression & risk factors for CKD 1-5, nutrition in CKD, renal diseases (except GNs and cystic diseases).
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DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM THE NETHERLANDS MAY 31 - JUNE 3 2014