REDUCTION OF ALBUMINURIA AFTER THERAPY WITH AMINAPHTONE. A REPORT OF 40 CASES

F. Godino, A. Di Maggio , Unit of Nephrology, SS. Annunziata Hospital, Taranto, Italy

Objectives:

Albuminuria is a renal epiphenomenon of a generalized endothelial damage, and defines the prognosis of renal diseases and the cardiovascular risk.

Control of blood pressure or metabolic syndrome, and medications acting on glomerular hemodynamics, such as drugs effective on the RAAS, have an anti-proteinuric effect.

A further approach could target endothelial dysfunction. Aminaphtone is a synthetic molecule effective in treating the loss of integrity of capillaries sustained by the production of endothelin-1 and the expression of adhesion molecules.

We performed a retrospective review of our cases of albuminuric outpatients who had been treated with aminaphtone.

Methods:

Out of a population of about 1500 patients referred to our nephrology clinic, 50 albuminuric subjects were selected because:

1) they had been treated with aminaphtone, 75 mg orally twice a day, for 91-251 days (median 171);
2) albuminuria had been tested no more than 30 days before the start of therapy with aminaphtone, and retested when the drug was still taken, or no later than 30 days after its suspension;
3) during the observation period, they had not undergone variations of other concomitant medications with possible effects on albuminuria, such as ACE inhibitors (ACEi) or AT receptor blockers (ARB).

To avoid errors due to the collection of 24-hours urine, we defined as albuminuric the patients with albumin concentration higher than 30 mg/L on a sample of early morning urine.

Results:

The table contains the patients' data.

The duration of therapy with aminaphtone ranged between 91 and 251 days (median 171).

Forty out of the 50 patients showed an albuminuria reduction.

The albuminuria variations are represented in Figure 1.

They showed no correlation with gender, age, diabetes, treatment with ACEi and/or ARB, with the days of aminaphtone therapy or with the changes in serum creatinine and eGFR (MDRD) at the end of the observation period.

Almost all patients (48 out of 50) had hypertension. Also the 2 patients with normal blood pressure showed a decrease of albuminuria.

There was a significant difference between patients in which albuminuria decreased and those where it increased with respect to basal plasma creatinine and eGFR. Figure 2 shows the scatterplot of percent changes of albuminuria versus baseline creatinine and eGFR.

Using the cut-offs of 1.5 mg/dl for creatinine and 45 ml/minute for eGFR to separate the patients into 2 groups, it can be observed (Figure 3) that the average percent changes in albuminuria differ significantly between the group with creatinine <1.5 mg/dl (N = 32) vs that with creatinine >1.5 mg/dl (N = 18) (P <0.003), and between the two groups with eGFR greater (N = 32) and lower (N = 18) than 45 ml/min (P <0.02).

Patient	Age [yrs]	Gender	Lenght of therapy [days]	Diabetes	Hypertension	Creatinine [mg/dl]	eGFR [ml/min]	ACEi	ARB	albuminuria basal [mg/dl]	albuminuria final [mg/dl]
AA	54	F	186	YES	YES	0,90	69,3	YES	YES	326	142
AD	77	M	175	NO	YES	1,33	55,4	NO	YES	884	908
AF	67	M	147	YES	YES	1,10	71	YES	NO	1640	1112
AF	80	M	176	YES	YES	1,98	34,7	YES	NO	138	152
AG	41	M	159	NO	NO	1,14	75,2	NO	YES	180	137
BF	51	F	161	YES	YES	0,67	98,6	NO	YES	100	15
CB	78	M	119	YES	YES	2,01	34,3	YES	YES	460	410
CC	60	M	228	NO	YES	0,98	82,9	YES	NO	1980	1318
CF	86	M	175	NO	YES	1,94	35	NO	YES	61	112
CG	67	M	205	YES	YES	1,22	63	NO	YES	2011	1640
CI	77	F	168	YES	YES	0,83	70,9	NO	YES	70	56
CN	58	M	147	NO	YES	1,20	66,1	NO	YES	80	61
CV	73	M	187	YES	YES	1,12	68,3	YES	NO	1090	541
DC	72	M	196	NO	YES	1,85	38,4	NO	YES	420	444
DO	74	M	212	YES	YES	1,80	39,4	NO	YES	196	77
DP	55	M	169	NO	YES	1,15	70,2	YES	NO	50	36
DR	79	F	195	YES	YES	0,51	123,6	NO	YES	50	41
DS	69	F	129	YES	YES	0,61	103,4	YES	YES	60	31
FA	68	M	157	NO	YES	1,11	70	NO	YES	346	304
FC	61	F	161	NO	YES	1,87	29,1	NO	YES	143	125
FR	68	F	184	YES	YES	2,92	17	NO	YES	78	60
GA	82	F	168	YES	YES	1,43	37,3	YES	NO	100	50
GN	71	M	174	YES	YES	2,50	27,2	YES	NO	300	322
GV	69	M	166	YES	YES	1,13	68,4	YES	YES	585	597
LU	78	M	107	NO	YES	1,37	53,4	YES	NO	152	28
LV	64	M	106	YES	YES	1,56	47,9	YES	YES	227	189
LV	69	M	196	YES	YES	1,20	63,8	YES	NO	84	52
MM	81	F	194	NO	YES	1,14	48,6	NO	YES	109	36
MM	67	F	174	YES	YES	1,16	49,5	NO	YES	62	49
MN	67	M	187	YES	YES	0,90	89,5	YES	YES	315	246
NL	58	F	245	YES	YES	0,88	70,1	NO	YES	70	46
NM	89	M	91	NO	YES	1,50	46,8	YES	NO	206	126
NR	71	F	188	YES	YES	1,20	47,1	NO	YES	74	39
PA	78	F	119	YES	YES	1,30	42,1	NO	YES	34	12
PA	75	F	251	YES	YES	2,10	24,4	NO	YES	143	198
PG	69	M	152	YES	YES	0,80	101,9	YES	NO	137	93
PM	72	F	133	NO	YES	3,90	12	YES	NO	380	410
PM	62	F	154	YES	YES	2,70	19	YES	NO	1220	1280
PP	71	F	187	YES	YES	1,94	27	NO	YES	102	114
PS	59	F	154	YES	YES	1,18	49,8	NO	YES	80	69
RE	73	F	201	YES	YES	1,59	33,8	NO	YES	328	212
RG	65	M	96	NO	YES	4,18	15,3	NO	YES	404	81
SG	69	M	173	NO	YES	1,00	78,7	NO	YES	200	182
SM	58	M	181	YES	YES	1,80	41,4	YES	NO	938	638
TC	72	M	135	NO	NO	0,91	87	NO	NO	411	189
TF	77	M	103	YES	YES	0,99	77,9	NO	YES	211	191
TG	72	M	179	YES	YES	0,90	88,2	YES	YES	174	123
VA	80	M	124	YES	YES	3,41	18,6	YES	NO	997	945
VE	72	M	210	YES	YES	1,19	63,9	NO	YES	220	161
ZI	79	M	140	YES	YES	1,45	49,9	NO	YES	88	27

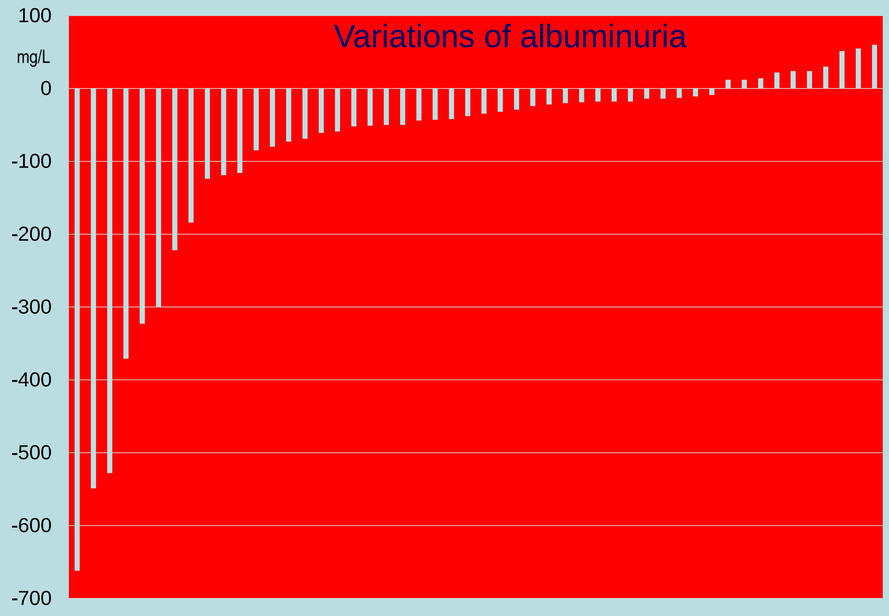

Figure 1. Changes in albuminuria after treatment with 75 mg b.i.d. aminaphtone in 50 patients [baseline value = zero]

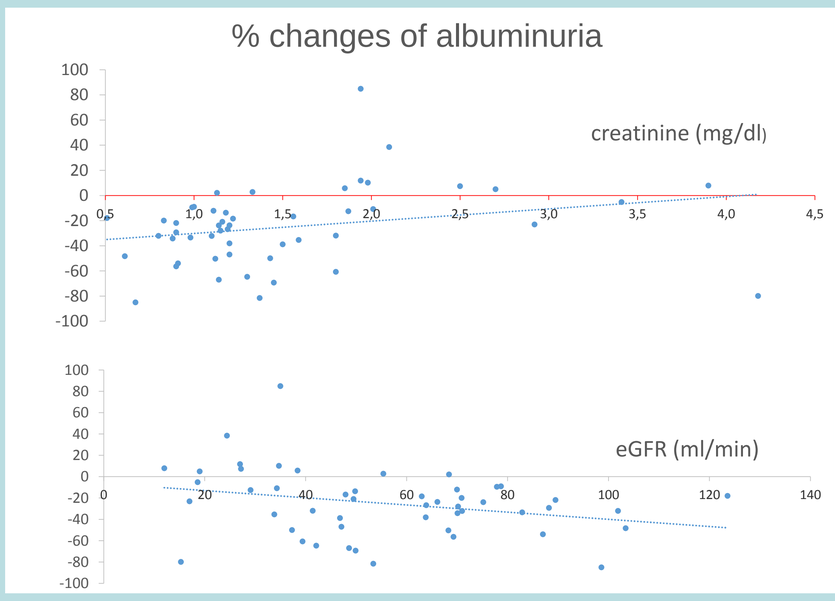

Figure 2. Scatterplots of the percent changes of albuminuria vs baseline creatinine [top box] and vs eGFR [lower box] [N = 50].

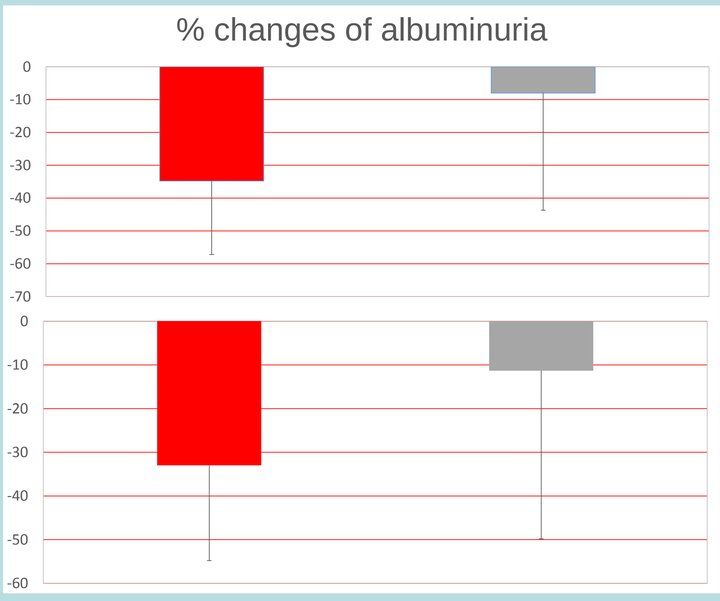

Figure 3. Top box: percent changes of albuminuria in patients with creatinine lower (N = 32, red) and higher (N = 18, gray) than 1.5 mg/dl (mean and SD, P <0.003). Lower box: percent changes of albuminuria in patients with eGFR higher (N = 32, red) and lower (N = 18, gray) than 45 ml/minute (mean and SD, P <0.02).

Conclusions:

Our observations seem to indicate a direct action of aminaphtone on albuminuria reduction, at least in the initial stages of kidney disease, perhaps through a different mechanism from that of drugs traditionally used for their activity on the RAAS.

References

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2) Bertini M. "Endothelial Protector Drugs" and Diabetes: Is there a Role for these drugs? J Diabetes Obes. 2015; 1:1-3.
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