IS ANTIPROTEINURIC EFFECT OF ACE-INHIBITORS CONSTANT THROUGHOUT THE DAY?

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INTRODUCTION

It has been demonstrated that a low dose of ACE-inhibitor (ACE-I) has the same effectiveness as a higher dose in lowering blood pressure, but with a shorter duration of action, so that the patient is unprotected for a relevant part of the day. However, if the same occurs also for the antiproteinuric effectiveness is not known. In our prospective study, we aimed to recognize if proteinuria varies throughout the day with different doses of ACE-I administered once a day.

SUBJECTS AND METHODS

Between the 1st of January 2012 and the 1st of September 2012 we enrolled normotensive patients with a 24-hours urinary protein excretion between 1 and 3 grams/day and estimated glomerular filtration rate (eGFR) > 30 ml/min. Patients should have discontinued any therapy with anti-angiotensin agents, anti-aldosteronic or immunosuppressive agents from at least 3 months. At the time of enrollment, participants performed three consecutive timed urine collections (from 8 a.m. to 2 p.m., morning collection; from 2 p.m. to 8 p.m. evening collection; and from 8 p.m. to 8 a.m. of the following day, night collection), on which urinary protein/creatinine ratio (UPC ratio) was calculated.

Soon after, a single daily dose of ramipril 2.5 mg was administered at 8 a.m. for 10 days. At day 10 the three consecutive time-matched collections were repeated and at day 11 the dosage of ramipril was increased to 10 mg for other 10 days. At the day 20, a new timed collection was obtained. Our study was approved by the Local Ethical Committee, and all participants gave written informed consent. Statistical analysis was performed using PASW Statistics 18, the level of significance was set at p-values <0.05.

Table 1: urinary protein/creatinine ratio (g/g) according to timed collection and therapeutic regimen.

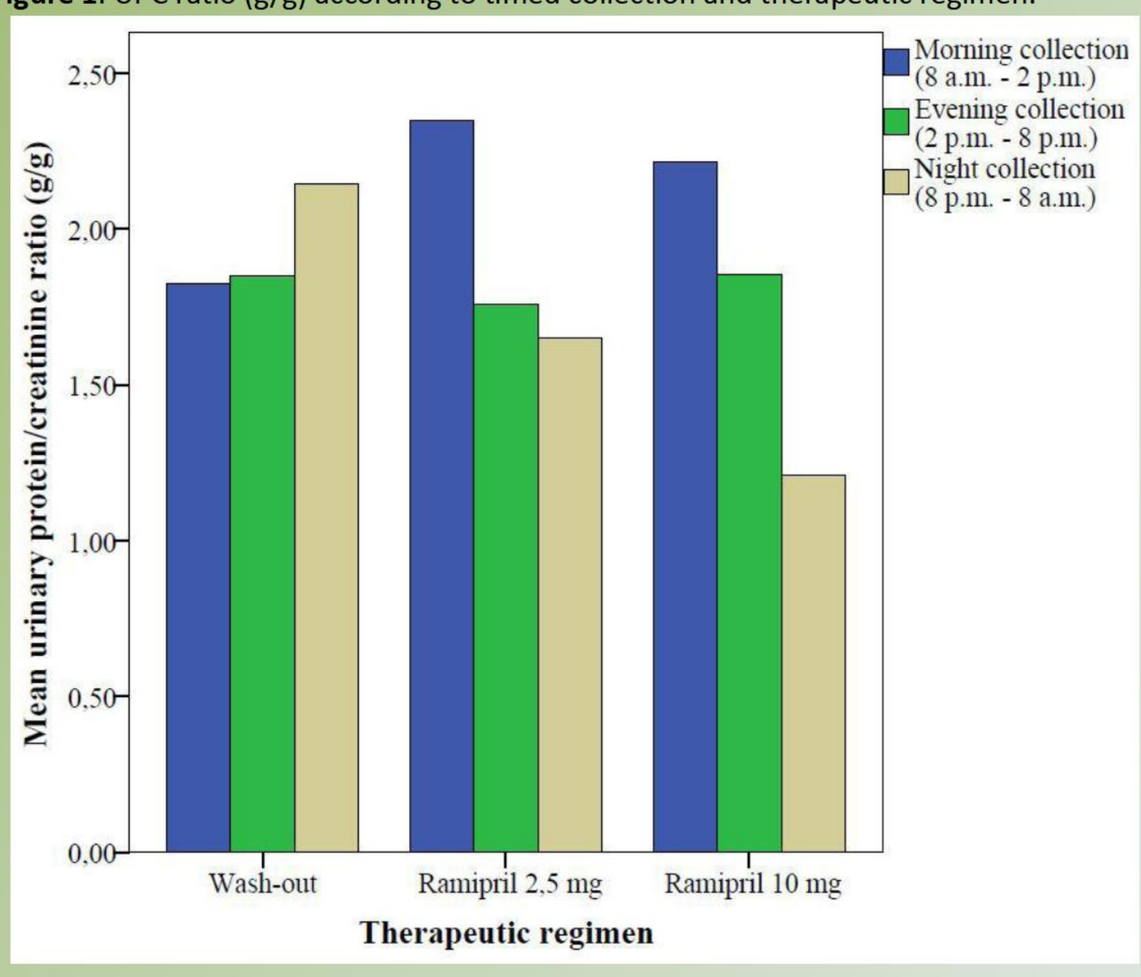
	No Ramipril	Ramipril 2.5 mg/day	Ramipril 10 mg/day	p
Morning collection (8 a.m. – 2 p.m.)	1.83 ± 0.95	2.35 ± 1.83	2.21 ± 1.74	0.516
Evening collection (2 p.m. – 8 p.m.)	1.85 ± 0.74	1.76 ± 0.80	1.38 ± 0.61	0.246
Night collection (8 p.m. – 8 a.m.)	2.14 ± 2.19	1.61 ± 0.99	1.29 ± 0.90	0.212
p	0.659	0.231	**0.016**	

Data are expressed as mean standard deviation. p = ANOVA level of significance.

RESULTS

Eleven patients (3 women) met the inclusion criteria and completed the study. ACE-I therapy was well tolerated, without significant variations of blood pressure, eGFR or plasma potassium. Mean eGFR at enrollment was 46.3 16.6 ml/min, mean age 55 19 years. In the first part of the study (without ramipril therapy), UPC ratio was maintained quite stable throughout the 24 hours, without any significant difference between the three consecutive time-matched collections (Table 1, Figure 1). After the administration of ramipril 2.5 mg/day, a non-significant reduction of the UPC ratio during the 24 hours was observed, without significant differences between the three timed collections (Table 1, Figure 1). By contrast, after the administration of ramipril 10 mg/day we found a significant reduction of the UPC ratio during the 24 hours (p=0.016, Table 1), with lower levels during the evening and the night collection as compared with the morning collection, (p=0.048 and 0.032, respectively, data not shown).

Figure 1: UPC ratio (g/g) according to timed collection and therapeutic regimen.



CONCLUSIONS

Our findings show that administration of ACE-I induces dose dependent antiproteinuric effects only after several hours, and no residual effect lasts over the 24 hours. Also, this finding suggests that an antiproteinuric effect lasting 24-hour could be obtained administering the drug in two daily doses (i.e. in the morning and in the evening) and that higher dosage induces higher effect.

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