

Modifications in relaxin's serum levels during acetate-free biofiltration (AFB): only a new biomarker?

Valeria Cernaro¹, Antonio Lacquaniti¹, Grazia Giorgianni², Davide Bolignano³, Michele Buemi^{1,*}

¹ Chair of Nephrology, Department of Internal Medicine, University of Messina, Messina, Italy.

² Clinical Experimental Department of Medicine and Pharmacology, Section of Endocrinology, University of Messina, Messina, Italy.

³ CNR-IBIM, Clinical Epidemiology and Physiopathology of Renal Diseases and Hypertension of Reggio Calabria, Reggio Calabria, Italy.

Summary

Aims. We evaluated relaxin's behaviour during a haemodialytic session and the effects of its intradialytic variability on blood pressure.

Methods. We enrolled 25 patients and evaluated relaxin's levels during a haemodialytic session. We also dosed interdialytic relaxin and enrolled 10 healthy subjects and 16 patients with III stage chronic renal failure as controls.

Results. Haemodialyzed patients have relaxin's baseline concentrations higher than healthy controls, but lower than chronic patients. During the treatment, relaxin is removed; it increases again throughout the interdialytic phase. Furthermore, relaxin's pre- haemodialytic concentration positively and significantly correlates with systolic, diastolic, and mean BP; such correlations disappear at the end of the treatment.

Conclusion. Relaxin's removal during the treatment may intervene in the pathogenesis of intradialytic hypertension. Hence, relaxin could be not only a new biomarker but also an active player in the intradialytic variations of blood pressure.

Key words

Acetate-free haemodialysis; Blood pressure; Pleiotropic hormone; Relaxin; Intradialytic hypertension.

Relaxin is a 6 kDa-peptidic-hormone which plays a role in the renal and systemic haemodynamic changes of pregnancy³. It also exerts pleiotropic actions, particularly at the cardiovascular level¹. We evaluated, for the first time, relaxin's behaviour during a haemodialytic (HD) session and the potential effects of its intradialytic variability on arterial blood pressure (BP).

We recruited 25 patients (male/female, 10/15; mean age, 62.7±14 years; dialysis vintage in months, 36 [10-284]; residual GFR 2.3±0.6 ml/min) receiving dialytic treatment, three times a week, with AFB (Acetate Free Biofiltration) technique. Blood samples were obtained from upstream of the haemodialyzer at the beginning and at the end of the session, and from downstream at the beginning. Relaxin's serum levels were assessed by the Human Relaxin-2 RIA Kit, Phoenix Pharmaceuticals, Inc[®]. All values were normalized to volume, considering haematocrit and serum albumin. We also dosed relaxin during the interdialytic period and enrolled 10 healthy subjects and 16 patients with III stage chronic renal failure (CRF) as controls.

* Corresponding Author: Via Salita Villa Contino 30, 98100 Messina, Italy; Phone: +39.090.2212396; Fax: +39.090.2935162; Email: buemim@unime.it.

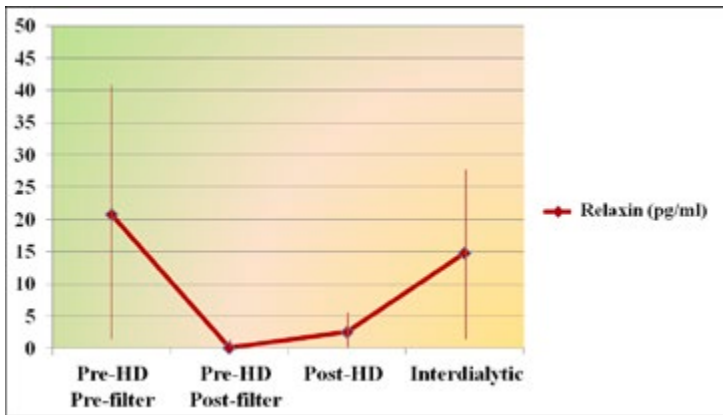


Figure 1. Relaxin's behaviour during HD treatment.

We observed that HD patients had relaxin's baseline concentrations (pre-HD, 20.81 ± 17.86 pg/ml) significantly higher than healthy controls (2.28 ± 2.19 pg/ml, $P < 0.001$), but lower than CRF patients (35.47 ± 30.94 pg/ml, $P = 0.018$). Throughout the HD session, relaxin was removed (**Fig.1**) by the filter (from 20.81 ± 17.86 to 2.54 ± 3.07 pg/ml, $P < 0.001$); it increased again during the interdialytic phase (14.80 ± 11.63 pg/ml, $P < 0.001$). Additionally, relaxin's pre-HD concentration positively and significantly correlated with systolic ($r = 0.72, P < 0.0001$), diastolic ($r = 0.61, P = 0.0011$), and mean ($r = 0.75, P < 0.0001$) BP; such correlations disappeared at the end of HD treatment.

Relaxin induces vasodilatation, as already established²; hence, it is usually negatively related to BP. Conversely, our data show a direct correlation between pre-HD relaxin and BP. The high baseline relaxin's levels in HD patients could express a compensatory mechanism to the increase in BP due to the fluid accumulation occurring between two consecutive HD sessions. The correlation between relaxin and BP is lost at the end of the treatment most likely because, during the HD session, the volume removal exerts a major role in influencing BP compared to that of vasoactive factors (endothelin-1, angiotensin II, relaxin, etc) in most patients. Contrariwise, in those subjects who show a volume-independent intradialytic hypertension (about 8-15% of HD patients), relaxin's removal by HD could play a significant role in determining BP's increase. Thus, relaxin could be not only a new biomarker but also an active player in the intradialytic variations of BP.

References

- 1) Bani D. (2008) Relaxin as a natural agent for vascular health. *Vasc Health Risk Manag.* 4(3):515-24.
- 2) Conrad KP, Shroff SG. (2011) Effects of relaxin on arterial dilation, remodeling, and mechanical properties. *Curr Hypertens Rep.* 13(6):409-20.
- 3) McGuane JT, et al. (2009) Role of relaxin in maternal systemic and renal vascular adaptations during gestation. *Ann N Y Acad Sci.* 1160:304-312.