Author’s response to reviews

Title: Long term hemodialysis aggravates lipolytic activity reduction and VLDL, LDL composition in chronic renal failure patients.

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Author’s response to reviews: see over
To editor of

“BMC Cardiovascular Disorders”

Dear Professor,

We are submitting for publication in “BMC Cardiovascular Disorders” after revision, the manuscript entitled: Long term hemodialysis aggravates lipolytic activity reduction and VLDL, LDL composition in chronic renal failure patients.

We have considered carefully the reviewers comments while revising our manuscript. You will find the responses to the comments. In the revised manuscript, we have marked the revised words or sentences by a red font.

Yours sincerely
Reply to comments from Reviewer 1:

1. This is not a real “prospective” design, but a cohort re-analyzed retrospectively. The details of hemodialysis (HD) therapy, dosage, efficiency are all missing. We need these data to address: if the HD really aggravates or induces these lipoprotein abnormalities?, or this results only from “correlations”? Please supply these data and address this in “Discussion”.

Reply to comments 1

- We have removed the term "prospective" from the text.
- We have provided in the manuscript the details of hemodialysis (HD) therapy (dosage and efficiency) and we have discussed it in the “discussion”.
- Patients were undergoing dialysis for 4 hours three times weekly, in order to achieving adequate dialysis (Kt/V = 1.2 ±0.18).

2. We learned from Table 1 and Figures (1 & 2) the VLDL, LDL were changed in different time episodes (T2, T3), which are not consistent with the variations of LPL (T3), HL (T1, T3). Is there any biological rationale to apply?, Can we infer from this observation that LPL is biologically more “dominant” than HL in manipulating lipoproteins of HD patients?

Reply to comments 2
VLDL amount and composition were changed at T2 and T3 whereas LPL activity remained stable.

- The decreased VLDL-cholesteryl esters contents might be related to the low transfer of CE from HDL to VLDL and of TG in the opposite direction, probably related to a decreased cholesterol ester transfer protein (CETP) activity.
- VLDL-PL is a substrate for HL activity and its decreased value was probably due to the low HL activity.

Several mechanisms may explain the high plasma VLDL-amounts and VLDL-TG concentrations.

Indeed, the LPL synthesis was probably insufficient to can hydrolyse the VLDL-TG, which would explain the high plasma VLDL-amounts and VLDL-TG concentrations in spite of unchanged LPL activity.

The decreased LPL synthesis could be attributed to a low animal proteins intake (<10% of total protein intake), in the diet in our HD patients, knowing that animal proteins are characterized by essential amino acids, needed for protein synthesis.

On the other hand, hemodialysis requires repeated use of heparin, which reduces the reserve of the both lipolytic enzymes, LPL and HL, facilitating their release from the endothelium of blood vessels. This phenomenon aggravates the LPL deficiency because the enzyme is not normally synthesized in uremic patients due to resistance to the insulin action.

3. Please make it concise of the “methodology” section, as these have largely been standardized

The “methodology” section is more concise as pointed out.
**Reply to comments from Reviewer 2:**

This abbreviation “hemodialysis duration (HD)” is not adequate. HD is usually used as the abbreviation of hemodialysis.

- We have took into account the abbreviation HD for the term hemodialysis in all the manuscript.