Author's response to reviews

Title: Cardiovascular risk and mortality in end-stage renal disease patients undergoing dialysis: sleep study, pulmonary function, respiratory mechanics, upper airway collapsibility, autonomic nervous activity, depression, anxiety, stress and quality of life: A prospective, double blind, randomized controlled clinical trial.

Authors:

Israel R Santos (ireissantos@uol.com.br)
Aline R Danaga (ardanaga@yahoo.com.br)
Isabella C Aguiar (isabellacarvalhocauguiar@gmail.com)
Ezequiel F Oliveira (ezequielo_fisio@hotmail.com)
Ismael S Dias (ismaelsouza.fisio@gmail.com)
Jéssica J Urbano (jjulioti@yahoo.com.br)
Nina T Fonsêca (ninat23@hotmail.com)
Aline A Martins (a_line_am@hotmail.com)
Leonardo M Ferraz (leo.macario@uol.com.br)
Vigilio Fernandes (fernandesvirc@hotmail.com)
Vinicius AT Fernandes (vifernandes@hotmail.com)
Viviane CD Lopes (vivianelopes.enf@hotmail.com)
Fernando SS Leitão Filho (fernandostudart@uol.com.br)
Sergio R Nacif (pro_ar@uol.com.br)
Paulo TC Carvalho (ptpaulo@uninove.br)
Luciana Maria M Sampaio (lucianamalosa@uninove.br)
Lílian C Giannasi (odontogiannasi@uol.com.br)
Salvatore Romano (salvatore.romano@ibim.cnr.it)
Giuseppe Insalaco (insalaco@ibim.cnr.it)
Ana Karina F Araujo (karinafachini@uninove.br)
Humberto Dellè (hdelle@uninove.br)
Nadia Karina G Souza (nadia.uimaraes@uninove.br)
Daniel Giannella Neto (dgiannella@terra.com.br)
Luis Vicente F Oliveira (oliveira.lv@uninove.br)

Version: 2 Date: 10 September 2013

Author's response to reviews: see over
Dear Executive Editor

Hayley Henderson, BioMed Central- Editorial Office - BMC Nephrology

Dear Editor,

Please find enclosed a manuscript entitled: “Cardiovascular risk and mortality in end-stage renal disease patients undergoing dialysis: sleep study, pulmonary function, respiratory mechanics, upper airway collapsibility, autonomic nervous activity, depression, anxiety, stress and quality of life: A prospective, double blind, randomized controlled clinical trial.” which we are submitting for exclusive consideration of publication as an Study Protocol in BMC Nephrology.

STUDY PROTOCOL CHECKLIST

- The study protocol was reviewed and all suggested changes were made. The article was formatted according to the rules for authors according to BMC Nephrology.

- Checklist was performed according to the CONSORT Statement and made the adjustments for randomized controlled clinical study to meet the CONSORT criteria.

- We are sending to you attached copies of the documents approved by the institutional ethics committee, proof of registration of the Protocol in Brazilian Registry of Clinical Trials – REBEC (http://www.ensaiosclinicos.gov.br/rg/step_1/462/) and also proof of approval of funding of the study.

- The study is part of a Master’s thesis and Ph.D. from the Graduate Program in Rehabilitation Sciences of the Research Board of the Nove de Julho University - UNINOVE and was approved by a committee of experts external peer review, in accordance with the attached statement.

- Our protocol is in the recruitment phase and collecting clinical data from patients’ records and has not been published on the study results.

- We made the insertion of a new version of the article, with all the suggested changes and also changes to meet the criteria of the CONSORT Statement.

This study protocol followed the CONSORT guidelines and was registered with the World Health Organization Universal Trial Number (UTN) U1111-1127-9390, and Brazilian Registry of Clinical Trials - ReBEC (RBR-7yhr4w), and has been approved by the Human Research Ethics Committees of the Nove de Julho University, São Paulo, Brazil (process number 220506/2009). All the authors have read and approved the enclosed version of the manuscript, and declare that there are no conflicts of interest related to the subject treated in this paper.
Chronic kidney disease is one of the most serious public health problems, and the increasing prevalence in developed and developing countries has led to a global epidemic. Cardiovascular complications are the leading cause of death in patients receiving conventional hemodialysis for end-stage renal disease. The high risk for cardiovascular disease results from the additive effect of multiple factors, including hemodynamic overload and several metabolic and endocrine abnormalities more or less specific to uremia.

Sleep disorders are common in patients with renal insufficiency. A higher prevalence of sleep apnoea has been observed in the chronic kidney disease compared with estimates in the general population. Increased rates of sleep apnoea have been described in patients with various renal-related diagnoses including dialysis, renal transplant, early-stage chronic kidney disease, proteinuria and mainly in end-stage renal disease patients.

It is unknown whether is a causative association in either direction between chronic kidney disease and sleep apnoea, or whether the two diseases represent clinical sequelae from a more common disease process, such as diabetes mellitus, hypertension or neuropathy. Given the complexity and variety of renal disease associated with sleep apnoea, there may be different grounds for each particular association.

The extracellular fluid volume and metabolic derangements that characterize the uremic state likely contributes to sleep apnoea in the dialysis population. Sleep apnoea causing direct renal insults from haemodynamic changes, ischaemic stress, or an intermediary conditions such as hypertension, can lead to early chronic kidney disease and proteinuria. In this sense, the high prevalence of sleep apnoea in end-stage renal disease patients and the associated clinical implications warrant vigilance in diagnosis and treatment of sleep apnoea in kidney disease.

A prospective, double blind, randomized controlled clinical trial is proposed to address the effects of nocturnal hemodialysis compared to daytime hemodialysis on sleep variables, pulmonary function, respiratory mechanics, upper airway collapsibility, autonomic nervous activity, depression, anxiety, stress and quality of life in end-stage renal disease patients. The measurement protocol will include body weight; height; BMI; neck, waist, and hip circumferences; heart and respiratory rates; blood pressures; Mallampati index; tonsil index; heart rate variability; maximum ventilatory pressures; negative expiratory pressure test, and polysomnography (sleep study), as well as the administration of specific questionnaires addressing sleep apnoea, excessive daytime sleepiness, and quality of life.

Our hypothesis is that the whether weight gain due to volume overload observed during interdialytic period will influence the degree of collapsibility of the upper airway due to narrowing and predispose to upper airway occlusion during sleep, and to investigate the influences of haemodialysis in the physiological variables of sleep, and autonomic nervous system, and respiratory mechanics and thereby compromise the quality of life of end-stage renal disease patients.

Thank you for your consideration of our work!

Sincerely,

Daniel Giannella-Neto, Ph.D.

Editor-in-chief - Diabetology & Metabolic Syndrome – BMC Biomed Central

Luis Vicente Franco Oliveira, Ph.D.

Sleep Laboratory

Master and Doctoral Degree Program in Rehabilitation Sciences.

Nove de Julho University – UNINOVE. São Paulo, SP, Brazil.