Cognitive impairment in chronic kidney disease

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The literature widely reports the direct association between declining renal function and cognitive impairment,[1-4] showing that, for each decrease of 15 ml/min/1.73 m^2 in glomerular filtration rate, there is a cognitive decline similar to that of 3 years of aging.[5] Recently, a meta-analysis reported that chronic kidney disease (CKD) is an independent risk factor for cognitive decline,[6] and this can be a determining factor in quality of life.[7]

Studies have shown that cognitive impairment is associated with the severity of renal disease and the prevalence of this condition is particularly high in patients undergoing hemodialysis - comprising up to 60% of the population.[8,9]

The mechanisms involved in the cognitive impairment etiology are not completely understood. The effects of uremic toxins directly contribute to cognitive decline. However, the persistence of cognitive deficits despite adequate dialysis doses, indicates that other factors contribute to the cerebral disorder.[7]

Changes in cerebral hemodynamics may play a role in the pathogenesis of cognitive impairment among patients in hemodyalisis.[10,11] Cerebral vasomotor reactivity is the vasodilator response to increases in blood concentration of carbon dioxide. This response may be impaired in the presence of cognitive impairment. Old age, depression and white matter injury are associated with cognitive impairment and with changes in cerebral vasomotor reactivity.[12] However, few studies provide information on the best way to intervene in cerebral hemodynamics.

Neurological manifestations of HD patients impose unique diagnostic and therapeutic challenges due to the heterogeneity of conditions that are commonly associated with them.

In this issue of the Brazilian Journal of Nephrology (JBN), the authors, Matta *et al.,* present a review article about the topic. The authors, with integrity, address the question of cognitive impairment and the mechanisms involved in this dysfunction. In this same JBN edition, the paper by Silva *et al.* assesses the relationship between the cognitive ability of 75 patients undergoing hemodialysis and their sociodemographic and clinical characteristics. Importantly, the authors have proposed different cutoff points used in the literature for the instrument employed in cognitive screening. Cognitive ability was directly related to education and *per capita* income; and inversely related to age. The study found no clear correlations between cognitive impairment and hemodialysis process. Eventually, a larger number of patients may need to demonstrate this relationship widely reported in the literature. However, the study highlights the importance of cognitive alterations on patient prognosis, a condition very little appreciated in the clinical evaluation of CKD. Based on these findings, it is interesting that all patients with CKD were subjected to assessments of changes in cognitive ability.

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There is recent preliminary evidence supporting the role physical activity plays in the prevention or delay of cognitive decline. Thus, there is now a new adjuvant therapeutic strategy against cognitive decline based on a non-pharmacological method. Early research was based on the identification of mechanisms involved in neuronal protection through physical exercises, showing an association between high levels of physical activity and higher cognitive capacity.[13]

Our research group has been engaged to investigate possible associations between physical activity and cognitive function in hemodialysis patients. In an observational study of 102 patients, we found a strong association between physical activity and improved cognitive function, independently of confounding variables. It was found that the most active patients had a lower risk of severe cognitive impairment as compared to those irregularly active and inactive. Patients classified as active obtained better scores on cognitive function (Mini Mental State Examination) tests, when compared to sedentary and irregularly active individuals.[14]

Given these findings, and based on the hypothesis that changes in cerebral hemodynamics may possibly influence the pathogenesis of cognitive impairment, we started a randomized clinical trial, which aims to evaluate the effects of intradyalitic physical training on cerebral blood flow, cognitive function and quality of life in hemodialysis patients. The study is ongoing, with exciting preliminary results.

Although the neuroprotective role of physical activity on cognitive decline is not fully understood, its implementation in hemodialysis centers is recommended by the possibility of cardiovascular protection - clearly described in the literature.

In future studies, it is vital to consider new strategies for encouraging hemodialysis patients towards this change in behavior for their proper compliance with physical activity protocols.

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