Is the immune hyporesponsiveness of uraemic patients a protective factor for severe COVID-19 pneumonia?*

¿Es la hiporrespuesta inmune de la uremia un factor de protección contra la neumonía grave por COVID-19?

Dear Editor,

COVID-19/SARS-CoV-2 infection is a serious health problem with an unprecedented social and political response. The clinical expression of this new disease has been defined in the general population.[1] However, few articles have been published on this infection in patients with chronic kidney disease with or without renal replacement therapy (RRT).

A group from China published an interesting report of their experience at a haemodialysis centre. None of their 37 positive cases with a mean age of 66 years (55-81) had serious pneumonia. The six deaths from COVID-19 were attributed to other causes (cardiovascular and hyperkalaemia), with a death/infection rate of 16%. The authors considered this outcome less aggressive than expected in these frail patients, and it was attributed to their abnormal cellular immunity and inability to develop a "cytokine storm".[2]

The Sociedad Española de Nefrología (S.E.N.) [Spanish Society of Nephrology] has created a registry of COVID-19 cases. In the report of April 11, included 868 patients, mean age 67 years ±15, on RRT. A 72% developed pneumonia and approximately 5% required mechanical ventilation (10% were admitted ti intensive care unit (ICU).[3] This represented a death/infection rate of 22.7% (69.5% haemodialysis, 3.5% peritoneal dialysis and 26.8% kidney transplanted patients) — i.e. 7% higher than reported by the group from China, possibly differences in epidemiology and comorbidity – were not reported, plus they presented a larger number of cases. Comparison of this death/infection rate with the Spanish Ministry of Health data, which includes all cases in Spain, reveals that this rate is approximately 12% higher in patients on RRT. These data are dynamic and of debatable reliability since it is process subject to constant change, however the definitive numbers might be close to the data presented.

Patients with kidney diseases have an abnormal immune response. The main factors involved are the toxicity of uraemia, abnormal kidney metabolism of immune system molecules and the effects of RRT (materials used in dialysis, fluids, immunosuppressant drugs, etc.). Various forms of dysfunction have been reported in uraemic patients: monocyte senescence, B and T cell lymphopenia, deficient activation of lymphocytes secondary to increased apoptosis, reduced co-stimulation signal on the part of antigen-presenting cells, epigenetic changes in white blood cells and haematopoietic stem cells, and an accumulation of inflammatory cytokines (IL-1β, IL-18, IL-6, IL-8 and TNFα). These, along with an increase in oxidative stress, are the cause of a situation of chronic inflammation.[4,5]

An article by Ma et al. found that the count of T cell, T helper (Th) cells, cytotoxic killer T cells, natural killer (NK) cells and B lymphocytes were lower in haemodialysis patients with COVID-19 than in patients with COVID-19 without chronic kidney disease, and healthy controls. In addition, IL-4, IL-6 and TNFα levels were lower in patients with COVID-19 on haemodialysis than in all other comparator groups.[2]

Moreover, prior studies with related viruses (SARS and MERS) in the general population have found that the serious cases presented very high cytokine levels,[6] a pathophysiological condition known as a "cytokine storm". This excessive response results in suppression of immunological activity, cardiovascular instability, metabolic acidosis and massive cell damage, which is characteristic of many septic states and it is independent of the aetiology.[7]

Some drugs (IL-7, steroids, anakinra and others) have been used to mitigate this exaggerated immune response; and, in kidney patients we have extracorporeal blood (EBPTs) to combat sepsis, especially with the use high-adsorption membranes such as CytoSorb®, AN69 or oXiris®.[7,8]

While the quantity and quality of scientific evidence for making recommendations on the use of EBPTs in sepsis is insuffcient and non uniform, it is important to stress that most studies have been conducted in patients with bacterial sepsis. In cases of serious viral infection, such as influenza A infection, it has been found to be beneficial. It has been found to have the potential to remove Ebola virus with a system of lectin affinity plasmapheresis.[9,10]

As COVID-19 research continues, from a clinical perspective efforts must continue to be made to join forces to acquire knowledge and gain experience at a faster-than-usual pace. One contribution that nephrologists might make would be to promote and assist with early use of l continuous extracorporeal purification techniques in seriously ill patients in the general population, as well as in nephrology patients. Nephrologists might also share their knowledge and experience in managing the hypercoagulability of COVID-19 patients that

DOI of original article:
https://doi.org/10.1016/j.nefro.2020.05.002.

* Please cite this article as: Florit EA, Diekmann F. ¿Es la hiporrespuesta inmune de la uremia un factor de protección contra la neumonía grave por COVID-19?. Nefrologia. 2021;41:223–224.

could interfere with blood purification techniques. Finally, the information obtained at the different centres that have tested these techniques and other treatments should be orchestrated and shared swiftly by international scientific associations.

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https://doi.org/10.1016/j.nefroe.2020.05.006

Kidneys also speak Spanish☆

Los riñones también hablan español

Dear Editor,

Recently, the conclusions of a Kidney Disease: Improving Global Outcomes (KDIGO) consensus conference were published.[3] The main objective of the conference was to standardise nephrology nomenclature for scientific articles written in English, guided by the essential principle of improving understanding on the part of (English-speaking) patients.[3,4] From a Spanish-speaking point of view, it is striking that one of the main recommendations made was to use the term "kidney" instead of the term "renal" for general descriptions of kidney function and kidney disease, as it was stated that (in an English-language context) the noun "kidney" is more familiar than the adjective "renal".[3]

Curiously, this decision did not appear to extend to a change in nomenclature for anatomical structures (e.g. "renal artery") or historically established names (e.g. the United Kingdom's "Renal Association") (which seems to be reasonable). In another logical decision, the Greek prefix "nephro- "(Spanish "nefro-") was retained for syndromes, kidney diseases and kidney functions (nephritic, nephrotic, nephropathy, nephrology and so on)[3], since revising these terms would seem excessive and might even lead to a change in the name of the International Society of Nephrology (ISN) itself. Hence, a group of 10 nephrologists from nine different countries, not all Spanish-speaking, recently brought to the attention of the ISN[5] the need for different nephrology associations (ideally, both national and supranational) to make efforts similar to the

DOI of original article:
https://doi.org/10.1016/j.nefro.2020.11.002.
☆ Please cite this article as: Bover J, Bosch R, Ureña P, Trinidad P, Jara A, Górriz JL, et al. Los riñones también hablan español. Nefrologia. 2021;41:224–226.