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Response to "Experience with dulaglutide in an obese diabetic patient on incremental peritoneal dialysis". Response to related letter

Contestación a «Experiencia con dulaglutida en un paciente diabético y obeso en diálisis peritoneal incremental». Respuesta a carta relacionada

Dear Editor,

We appreciate the interest in our work shown by the authors of this letter.[1] We fully agree with the comment on the cardiovascular benefits of GLP-1 receptor agonists (GLP-1 RAs) as an excellent treatment option in patients with type 2 diabetes mellitus (T2D) and obesity on peritoneal dialysis (PD). However, to date, there is no published evidence on the experience of using these drugs in PD patients.

By the technical data sheet the administration of GLP-1 RAs analogues are not indicated in patients with estimated glomerular filtration rate (eGFR) < 15 ml/min/1.73 m^2. However, it should be remembered that this compound is divided by chemical structure into incretin-mimetics and human GLP-1 analogues; and the latter, which include liraglutide, dulaglutide and semaglutide, are not eliminated by the renal route, but are metabolized by proteolytic enzymes. No specific organ has been identified as the main route of elimination.[2,3] Furthermore, the pathway by which GLP-1 RAs may provide renal benefit is currently not well understood, but probably involves a combination of direct and indirect effects, such as stimulation of natriuresis at the proximal tubule level, inhibition of the renin angiotensin system, decreased renal hypoxia, decreased glomerular atherosclerosis, and improved glycemic control, blood pressure and weight reduction, among others.[4,5]

Therefore, although patients with Stage 5 chronic kidney disease (CKD) (defined by an eGFR < 15 ml/min/1.73 m^2) with or without renal replacement therapy (hemodialysis, PD or renal transplantation) have not been included in the large pivotal studies of GLP-1 RAs,[6] the results coming from different randomized clinical trials with small sample size and case series, mainly in the advanced CKD,[7] hemodialysis[8] and renal transplantation[9] populations, show that patients undergoing PD could also benefit from the efficacy of GLP-1 RAs in improving glycemic control, lowering blood pressure and weight

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loss.[10,11] Recently, the working group of the "*Effect of semaglutide versus placebo on the progression of renal impairment in subjects with type 2 diabetes and chronic kidney disease*" (FLOW) study, a Phase 3 clinical trial involving more than 3000 patients with DM2 and moderate-severe CKD (eGFR 25–75 ml/min/1.73 m^2 and albumin-creatinine ratio 300–5000 mg/g) (NCT03819153), the first to include kidney disease outcomes as a primary endpoint, which will define the clinical efficacy and renal safety of semaglutide (GLP-1 RAs), expected to be completed in 2024, decided to halt the trial based on the recommendation of the independent data monitoring committee that concluded that the results of an interim analysis met certain predetermined criteria for stopping the trial early due to the efficacy of the drug against the stated endpoints.

Additionally, our group recently published a case series with similar characteristics to the case discussed by the authors of this letter, and we found that the use of GLP-1 RAs in three obese diabetic patients on incremental hemodialysis (iHD) was safe and effective for glycemic and weight control, as well as blood pressure and other control targets that delay diabetic complications. This allowed our patients to maintain one weekly hemodialysis session and facilitate their inclusion in renal transplant waiting lists.[8] The latter, in relation to the improvement in obesity parameters, which is a limiting factor for inclusion on the transplant waiting list, as was also noted in another series of two cases published by Touzot et al.[12] All these previously mentioned benefits could indirectly contribute to the preservation of residual renal function (RRF), which is fundamental for both patient survival and PD technique survival, without neglecting its effect on the improvement of morbidity and mortality.[13]

Therefore, we thank and congratulate the authors for their recent case description of their experience using another GLP-1 RA in incremental peritoneal dialysis.

Ethical responsibilities

The study complied with the principles set forth in the Declaration of Helsinki. The authors declare that they have the informed consent of the subject studied and respect the patient's right to privacy. For this research, no experiments were performed on human beings or animals.

Conflict of interest

The authors declare that they have no conflicts of interest or financial support.

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Mesangial and endocapilar proliferative glomerulonephritis and scabies infection: A causal or circumstantial relationship?

Glomerulonefritis proliferativa mesangial y endocapilar e infección por escabiosis. ¿Una relación causal o circunstancial?

Dear Editor,

IgA-dominant postinfectious glomerulonephritis (PIGN) is a morphological variant of PIGN that is increasingly common in our environment. Unlike classic post-streptococcal PIGN, in which there is deposition of C3 and IgG or C3 only, it is characterised by the dominant deposition of IgA at the glomerular level. It usually coexists with less intense positivity for IgG, IgM or C3, and histological patterns of mesangial or extracapillary proliferation have also been described.[1,2]

IgA PIGN mainly affects elderly men with different comorbidities, mainly diabetes mellitus, but also tumors, alcoholism or HIV[2] infection. It is more aggressive than the classic variant, with a poor prognosis and in most cases (70–80% begins with acute renal failure, proteinuria, hematuria and hypocomplementemia). The differential diagnosis should be made with post-streptococcal PIGN and IgA nephropathy. It is usually associated with active infections caused by *Staphylococcus aureus*, frequently methicillin-resistant, but there are also cases due to other staphylococci, and some are occasionally due to gram-negative bacteria of urinary origin and parvovirus B19.[3,4] The most common focus is cutaneous, but there are descriptions of respiratory, bone, urinary and cardiac infections.[5–7]

Here we are presenting the clinical case of a patient with a pathological diagnosis of IgA PIGN after cutaneous superinfection in the context of scabies.

She is a 59-year-old woman with no personal history of interest, except for follow-up by dermatology in the context of a pruritic skin reaction, classified after a skin biopsy as chronic eczematous dermatitis. She inniciated treatment with cyclosporine, with inadequate response; also she received treatment with ivermectin due to skin superinfection of *Sarcoptes scabiei* (Norwegian scabies associated with immunosuppressive treatment).

After 3–4 weeks of starting antiparasitic treatment, she went to the emergency room due to oedema, dyspnoea on minimal exercise and decreased diuresis, with little response to depletion treatment. The analytical control revealed acute renal failure (urea 176 mg/dl, creatinine 2.28 mg/dl, that were previously normal, and a serum K of 6 mEq/dl) with nephritic syndrome (albumin 2.8 g/dl, triglycerides 324 mg/dl, protein/creatinine ratio (PCR) 16,116 mg/g, haematuria ++ and HTN that is difficult to manage). Regarding the rest of the complementary tests, the proteinogram and complement were within range (C3 155.7 mg/dl, C4 32 mg/dl), with increased IgA (629 mg/dl), and autoimmunity and viral serologies were negative. A renal ultrasound was performed, which reported normal-sized kidneys with preserved cortical thickness without duct dilation. Subsequently, a progressive deterioration of renal function was observed (peak creatinine 3.4 mg/dl), thus an ultrasound-guided renal biopsy was performed with an anatomopathological result of mesangial and endocapillary proliferative glomerulonephritis with an epithelial crescent and deposits of C3 and IgA at the glomerular level

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