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## Experience with dulaglutide in a diabetic and obese patient on incremental peritoneal dialysis

## Experiencia con dulaglutida en un paciente diabético y obeso en diálisis peritoneal incremental



Dear Editor,

We read with interest the case recently published by De la Flor et al. "Efficacy and safety of semaglutide in a diabetic and obese patient on incremental hemodialysis. Does it also contribute to preserving residual renal function?",<sup>1</sup> to which we would like to contribute our experience in incremental peritoneal dialysis (PD).

Diabetic kidney disease is associated with an excessive increase in morbidity and mortality, especially of cardiovascular origin, and also increases progression of CKD.<sup>2</sup>

Glucagon-like peptide type 1 receptor agonists (GLP-1 ARs) are a family of antihyperglycemic drugs that have demonstrated strong reduction of HbA1c levels, low risk of hypoglycemia, weight reduction and cardiovascular and renal benefits.<sup>3</sup> In addition, the authors also describe favorable effects on preservation of residual renal function (RRF) in a patient on incremental hemodialysis.<sup>1</sup> However, experience in dialysis patients is limited.<sup>4</sup>

We present a 71-year-old male with type 2 diabetes mellitus, kidney disease secondary to diabetic nephropathy and repeated episodes of renal stones, arterial hypertension, dyslipidemia and a history of past tobacco use. His body mass index (BMI) was 32.9 kg/m<sup>2</sup> and his abdominal perimeter, 110 cm.

He started PD in 2020 incrementally with two exchanges per day, one of 2000 cc of physioneal® 40 1.36% and one of nocturnal icodextrin; he was in temporary contraindication for kidney transplantation due to grade 1 obesity. Serum creatinine was 6.39 mg/dl, glomerular filtration rate (GFR) measured by CKD-EPI was 8 ml/min/1.73 m<sup>2</sup>, creatinine clearance (ClCr) and urea clearance (KrU) were 12.2 and 6.1 ml/min/1.73 m<sup>2</sup>,

respectively, both in 24-h urine; the GFR by mean level of ClCr and KrU was 9.2 ml/min/1.73 m<sup>2</sup> and proteinuria was 1.680 mg/24 h.

Despite good glycemic control with 18 UI/day of insulin glargine, dulaglutide was added to the treatment due to its effect on weight reduction and to improve metabolic control in PD, with the expectation of making possible renal transplantation. The starting dose was 0.75 mg subcutaneously weekly, increasing to 1.5 mg/weekly at 1 month, with good tolerance and no hypoglycemia.

At the beginning of the treatment there were no data for hyperhydration. At 4 weeks there was a significant reduction in the percentage of fat mass (26.8%) and an increase in lean mass (20.2%). At 44 weeks the weight loss was 10.4 kg, insulin requirements were reduced by more than 50%, glycated hemoglobin (HbA1c) was reduced by 16.4% and BMI by 11.6%; as for the lipid profile, triglycerides were reduced by 44.7%, total cholesterol by 47.3% and LDL by up to 65.5%. During follow-up, the dose of antihypertensive drugs was reduced, an effect that can probably be attributed to the decrease in weight, as well as the decrease in insulin therapy.

From the renal point of view, diuresis remained around 2 L/day. ClCr and KrU initially fell, as did total weekly Kt/V (at the expense mainly of renal Kt/V) to gradually increase throughout the evolution until stabilizing. Urinary creatinine and urea excretion, normalized to kilo of weight, increased from week 12 of treatment. The normalized protein catabolism rate (nPCR) was stable (Table 1). The patient received a kidney transplant 14 months after starting treatment with dulaglutide.

To date, case series have been published with GLP-1 ARs in PD that have proven their efficacy and safety, but to our knowledge there is no previous experience with these drugs

**Table 1 – Analytical evolution monitoring and parameters of peritoneal dialysis.**

	Basal	Week 4	Week 8	Week 12	Week 20	Week 28	Week 36	Week 44
<i>Analytical, glycemic and body composition parameters</i>								
Hb (g/dl)	11.3	11.3	10.8	10.3	11.4	14	14.2	12.3
Na+ (mmol/l)	138	136	138	140	137	138	139	145
K+ (mmol/l)	5.2	4.5	4.7	5.1	4.5	4.8	4.6	4.6
Serum albumin (mg/dl)	3.8	4	3.7	5.1	4.5	4.8	4.6	4.6
Triglycerides (mg/dl)	188	278	138	147	135	144	144	104
Total cholesterol (mg/dl)	188	145	97	123	118	125	121	99
HDL cholesterol (mg/dl)	34	33	29	36	31	34	35	38
LDL cholesterol (mg/dl)	116	65	40	58	60	62	57	40
Serum glucose (mg/dl)	206	128	109	96	82	84	85	87
HbA1c (%)	6.1	5.4	5.46	5.2	NA	5.1	NA	NA
Weight (kg)	89.5	87.6	86.8	85.8	85.3	83.5	80.4	79.1
IMC (kg/m) <sup>2</sup>	32.9	32.2	31.9	31.5	31.3	30.7	29.5	29.1
Abdominal circumference (cm)	110	109	106	106	104	104	104	102
Lean tissue index (kg/m) <sup>2</sup>	16.8	20.2	13.3	15.3	NA	13.5	14.8	NA
Fat tissue index (kg/m) <sup>2</sup>	14.9	10.9	17.4	15.2	NA	15.8	13.9	NA
Absolute overhydration (liters)	0.3	0.9	1.1	1	NA	-0.2	0	NA
Insulin glargine (IU/day)	18	14	12	10	10	10	10	8
Dulaglutide (mg/week)	0.75	1.5	1.5	1.5	1.5	1.5	1.5	1.5
<i>Evolution of residual renal function and dialytic parameters</i>								
Serum creatinine (mg/dl)	7.1	7.3	8.1	8.5	8.2	9	9.2	9.7
CKD-EPI (ml/min/1.73 m) <sup>2</sup>	7	7	6	6	6	5	5	5
Serum urea (mg/dl)	151	134	129	150	126	149	141	144
Creatinine urine (mg/dl)	76	52	37	59	NA	73	NA	73
Urea urine (mg/dl)	968	618	470	827	NA	843	NA	753
Residual diuresis (ml/24 h)	1.800	2.000	2.000	2.000	NA	1.700	NA	1.900
KrU (ml/min)	8	6.4	5.1	7.7	NA	6.7	NA	6.9
ClCr <sub>o</sub> (ml/min/1.73 m) <sup>2</sup>	13.4	9.9	6.3	9.6	NA	9.5	NA	9.9
GFR (ml/min/1.73 m) <sup>2</sup>	10.7	8.15	11.4	8.65	NA	8.1	NA	8.4
CIU (l/wk)	109.5	89.4	77.8	104.4	NA	90.5	NA	94.2
Kt/V weekly total	2.52	2.08	1.83	2.47	NA	2.22	NA	2.33
Kt/V weekly peritoneal	0.57	0.58	0.63	0.65	NA	0.57	NA	0.61
Kt/V weekly renal	1.95	1.50	1.20	1.82	NA	1.65	NA	1.72
ClCr (l/wk)	150.3	105.3	82	111	NA	104.6	NA	108.3
ClCr (l/wk/1.73 m) <sup>2</sup>	132.8	93.9	73.4	99.7	NA	96.3	NA	100.1
Cr U/kg (mg/kg)	15.4	11.8	8.4	13.7	NA	14.8	NA	17.5
U U/kg (mg/kg)	194.4	141.6	108.3	192.3	NA	171.3	NA	180.8
nPCR (g/kg/day)	1.1	0.9	0.8	1.2	NA	1.1	NA	1.1
CAC (mg/g)	340	NA	NA	NA	NA	NA	NA	481
PAS (mmHg)	129	132	112	128	145	130	127	130
PAD (mmHg)	68	63	74	65	70	66	66	62

CAC: albumin/creatinine ratio; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration estimate of glomerular filtration rate; ClCr: creatinine clearance; ClCr<sub>o</sub>: creatinine clearance in 24 h urine; CIU: urea clearance; Cr U/kg: urinary creatinine excretion per kilogram of body weight; Hb: hemoglobin; Hb1Ac: glycated hemoglobin; HDL: high-density lipoprotein cholesterol; GFR: glomerular filtration rate; BMI: body mass index; K+: plasma potassium; KrU: renal clearance of residual urea; Kt/V: dialysis treatment efficacy; LDL: low-density lipoprotein cholesterol; NA: not assigned; Na+: plasma sodium; nPCR: normalized protein catabolism rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; U U/kg: urinary urea excretion per kilogram of body weight.

in patients on incremental PD or their effect on RRF, which is important.<sup>5,6</sup>

As described by De la Flor et al.,<sup>1</sup> we observed a significant decrease in weight, abdominal perimeter and HbA1c and an improvement in blood pressure control, lipid profile and preservation of RRF. In our group, we consider that RRF brings great benefits to dialysis patients, so we adjusted the dosage of GLP-1 ARs accordingly.<sup>7</sup>

The 2022 KDIGO (Kidney Disease: Improving Global Outcomes) guidelines on the management of diabetes emphasize the cardiovascular and renal benefits of GLP-1 ARs.<sup>2</sup> Weight reduction is a fundamental objective in the nephroprotection of patients with diabetic RD and obesity is an important limitation for inclusion in the renal transplant waiting list.<sup>8</sup> On

the other hand, preservation of RRF is essential for the survival of the technique in PD.<sup>9</sup> In addition to the cardiovascular benefits, GLP-1 ARs can be an excellent treatment option in diabetic and obese patients on PD.

In our experience, dulaglutide has proven to be an effective and safe option in obese diabetic patients on incremental PD with metabolic and RRF benefits.

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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.<sup>1</sup> 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<sup>2</sup>. 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.<sup>2,3</sup> 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.<sup>4,5</sup>

Therefore, although patients with Stage 5 chronic kidney disease (CKD) (defined by an eGFR < 15 ml/min/1.73 m<sup>2</sup>) with or without renal replacement therapy (hemodialysis, PD or renal transplantation) have not been included in the large pivotal studies of GLP-1 RAs,<sup>6</sup> the results coming from different randomized clinical trials with small sample size and case series, mainly in the advanced CKD,<sup>7</sup> hemodialysis<sup>8</sup> and renal transplantation<sup>9</sup> 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