DIABETIS AND PERITONEAL DIALYSIS: literature review

by Jana Publication & Research

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I. INTRODUCTION :

Diabetic nephropathy (DNK) is a major health problem associated with an increased risk of morbidity and mortality. Treatment of MRD is challenging given changes in blood glucose homeostasis, unclear accuracy of blood glucose measurements, and altered kinetics of hypoglycemic drugs.

There is uncertainty regarding the optimal glycemic target in this population, although recent epidemiological data suggest that HbA1c ranges of 6–8%, as well as 7–9%, are associated with higher survival rates in diabetic patients on dialysis. Furthermore, treatment of diabetes in patients maintained on dialysis is challenging, and many hypoglycemic drugs are metabolized and excreted renally, necessitating dose adjustment or avoidance in dialysis patients. [1]

Diabetes, along with vascular disease, is the most common cause of end-stage renal disease (ESRD). Many authors have suggested that continuous ambulatory peritoneal dialysis should be the preferred treatment for diabetics with chronic kidney failure. However, controversy persists regarding the preferred treatment of dialysis in diabetic patients. Currently, the final choice of method will depend on the patient's clinical conditions, preferences, socio-professional environment, the availability of dialysis techniques, the personal beliefs of nephrologists, as well as local facilities and financial considerations. [2]

II. METHODOLOGY:

PubMed, Google Scholar, and Medline were searched for all literature on the management of diabetes in dialysis and peritoneal dialysis patients.

III. EPIDEMIOLOGY OF DIABETES

The incidence and prevalence of diabetes mellitus have increased significantly worldwide, particularly with improvements in living standards and lifestyle changes. Diabetic patients now live longer than when they were denied treatments such as dialysis. The number of adults with type 2 diabetes is expected to increase to approximately 642 million by 2040. This overall increase in the number of diabetics has a major impact on the development of diabetic kidney disease (DKD) and is expected to have a significant social and economic impact on care and management in the future [3,4].

DKD affects approximately 20 to 40% of diabetic patients progressing to ESRD, a major cause of significant morbidity and mortality. The WHO predicts that diabetes will be the seventh leading cause of death by 2030 [4,5].

The MAREMAR study conducted in 2016 in Morocco found a prevalence of diabetes reaching 16.8% in an adult population between 18 and 70 years old, with hypertension at 21.9%. It is therefore not surprising that MRD is the leading cause of ESRD among the Moroccan dialysis population, affecting more than 30% of all dialysis patients [6].

IV. EPIDEMIOLOGY OF DIABETES AND PD (HAS)

Studies based on national registries highlight differences in diabetic dialysis populations. Populations from the USRDS and MEDICARE registries differ from those from Canadian, Italian, Danish, and Dutch registries in that they have a higher prevalence of diabetes and a poorer prognosis.

The literature has demonstrated an increased risk of mortality in diabetic women over 55 years of age treated with PD compared to those treated with HD. This is a characteristic specific to US registries that has not been described in other continents.

The majority of the studies reviewed show that 2-year survival in diabetics under 55 years of age is better with PD than with HD.

However, in older diabetics, there is no evidence to suggest that 2-year survival is better or worse with PD than with HD, with the exception of North American patients, for whom it appears to be worse (Level II).

Across all ages, the possible benefit of PD on survival could fade over time and reverse, but these data do not take into account new solutions used for PD.

The survival of diabetic chronic kidney disease patients is generally worse than that of non-diabetic patients, regardless of the technique chosen: HD or PD (level II).

V. COMPLICATIONS OF DIABETES IN PERITONEAL DIALYSIS:

a. Cardiovascular Morbimortality

In addition to cardiovascular risks, diabetes is an independent risk factor for stroke in the hemodialysis (HD) population [17]. Similarly, PD patients are at higher risk of cardiovascular death due to the inflammatory process, calcifications, malnutrition, and possibly endothelial dysfunction and oxidative stress associated with ESRD. The additional CV risks specific to PD are likely related to the glycemic load leading to insulin resistance and an increased atherogenic lipid profile. In addition, loss of residual renal function, peritoneal membrane failure, and ultrafiltration failure can induce overload, further increasing PD-related risk factors.

b. Foot ulcers

Diabetic patients on hemodialysis have a higher prevalence of ulceration (>4 times the risk of foot ulceration), infection, osteomyelitis, and ischemia requiring either amputation or revascularization, with a higher mortality rate [14,26,37,38]. Similarly, the presence of diabetic foot is a complication strongly associated with mortality in diabetic patients on peritoneal dialysis (PD) [7].

c. Health-related quality of life (HRQOL)

Diabetic patients on HD or PD have lower perceived health-related quality of life and poorer functional status than non-diabetic patients on dialysis, which is an independent predictor of morbidity and mortality [8]. Martinez Castelao et al. reported a strong relationship between perceived mental health during the first month of renal replacement therapy, particularly in diabetic patients on dialysis, and morbidity and mortality, regardless of comorbidity [8].

VI. MEASUREMENT OF GLYCEMIC CONTROL IN DIALYSIS PATIENTS:

Uremic status is associated with various laboratory abnormalities that can influence the accuracy of various measures used to assess medium- and long-term glycemic control, including glycated hemoglobin (HbA1c), fructosamine, and glycated albumin. Despite these limitations, the Kidney Disease Quality Outcomes Initiative (KDOQI) and Kidney Disease Improving Global Outcomes (KDIGO), as well as the clinical practice guidelines of the British Diabetes Societies, recommend routine measurement of long-term glycemic control using HbA1c in combination with home blood glucose monitoring as the basis for diabetes management in patients with CKD and ESRD [9,10].

1. Glycated hemoglobin (HbA1c)

HbA1c is the current standard for glycemic monitoring in the general population because it measures the circulating blood glucose concentration over the previous 120 days, which is the average lifespan of red blood cells [11]. HbA1c is formed by a non-enzymatic reaction between glucose and the beta chain of hemoglobin. The rate of hemoglobin glycation is influenced by various factors, including 1) duration of glucose exposure, 2) blood glucose, 3) hemoglobin level, 4) pH, and 5) temperature.

Therefore, numerous confounding factors related to ESRD can lead to abnormal HbA1c levels and make HbA1c testing less reproducible. Despite all the factors that influence HbA1c levels in dialysis, HbA1c is still recommended in all current guidelines as the primary biomarker for assessing glycemic control in dialysis patients. However, fructosamine and glycated albumin (GA) have been suggested as better surrogate markers of glycemic control in patients with ESRD. Glycation of these proteins is not affected by red blood cell lifespan or treatment with erythropoietin-stimulating agents.

2. Fructosamine

Fructosamine is a medium-term (i.e., 7–14 days) measure of blood glucose, a measure of ketoamines formed by non-enzymatic glycation of serum proteins [66]. Fructosamine may be a more accurate measure of glycemic control in dialysis patients than HbA1c, but it can also be confounded by many disorders, including dysproteinemias; Therefore, falsely low fructosamine levels may be observed in patients undergoing peritoneal dialysis or due to protein losses in the peritoneal dialysate and in patients with hypoalbuminemia due to protein-energy wasting [10]. Fructosamine has been shown to be a powerful predictor of cardiovascular morbidity (hospitalizations and infections) and mortality (hospitalization with sepsis) in diabetic patients on dialysis.

3. Glycated Albumin

Glycated albumin can assess glycemic control over a short period (7 to 14 days) and with greater accuracy in diabetic patients on hemodialysis [9,12]. While fructosamine is a measure of all glycated serum proteins, glycated albumin is a non-enzymatic reaction between blood glucose and albumin. Fructosamine concentration is strongly influenced by serum protein concentrations and low-molecular-weight molecules such as urea and uric acid.

However, glycated albumin (GA) is not affected by serum albumin or urea levels like fructosamine, nor by hemoglobin levels or erythropoietin injection like HbA1C; therefore, it may be superior to fructosamine as a measure of glycemic control in patients with advanced ESRD [9,12]. Furthermore, elevated glycated albumin levels have been associated with adverse cardiovascular outcomes such as

increased arterial stiffness and vascular calcification, which are associated with poor prognosis in dialysis patients [12,13].

4. Self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGMS)

The use of self-monitoring of blood glucose (SMBG) using repeated finger-prick blood glucose (PPG) remains the cornerstone for assessing glycemic control in diabetic patients on dialysis [9]. The accuracy of CGMS may be limited by the precision of blood glucose meters, the age of the strips used, the timing of measurement with medications and food, and the expertise of the person performing the test [13]. CGMS results may also be affected by hemolysis, anticoagulation, hyperlipidemia, and metabolic acidosis. Other potential interferences: Factors include environmental factors (strips should not be exposed to air, humidity, temperature, and altitude), sample volume, use of generic test strips, and strip reuse [9]. CGMS accuracy is instrument and user dependent, so it is important to evaluate each patient's monitoring technique at regular intervals.

In contrast, continuous glucose monitoring (CGMS) can provide an accurate assessment of glycemic control in diabetics on dialysis; however, its use is limited by technical issues related to device calibration (less of an issue with 3rd generation devices), which must be considered for accurate data interpretation [13,14]. Unlike HbA1c, CGMS can reveal short-term glycemic changes at the time of dialysis with results that are unaffected by urea nitrogen level, red blood cell lifespan, and red blood cell manufacturing [52]. Of particular importance for patients receiving peritoneal dialysis is the finding that some glucometers (those using the enzyme glucose dehydrogenase pyrroloquinoline quinone [GDH-PQQ]) will give falsely elevated readings in patients using icodextrin in peritoneal dialysis fluids. This may overestimate blood glucose readings and may lead to a risk of "missing" hypoglycemic episodes [15,16]. Therefore, blood glucose measurements in patients receiving icodextrin should be performed with a glucose-specific method to avoid interference from maltose, which is a metabolite of icodextrin. This effect can persist for two weeks after discontinuation of icodextrin [17].

VII. ADVANTAGES OF PERITONEAL DIALYSIS IN DIABETICS

- Better preservation of residual renal function
- Fewer unnecessary subcutaneous punctures
- Better hemodynamic stability, leading to a reduction in cardiac and cerebrovascular complications
- No need for vascular access
- No need for anticoagulants
- The only out-of-center method free from technical complications involving immediate life-threatening risks

VIII. DISADVANTAGES OF PERITONEAL DIALYSIS (PD) IN DIABETIC PATIENTS:

- Potentially increased risk of peritoneal infection
- Protein loss and increased malnutrition
- Clinical and metabolic consequences of continuous absorption of glucose and the dialysate solution

- The progressive loss over time of the peritoneal membrane's ability to remove water and salt can lead to the insidious development of subdialysis, requiring transfer to hemodialysis

IX. CHOICE OF DIALYSE IN DIABETIC PATIENTS

While glucose has been proven to be an effective osmotic agent for ultrafiltration during peritoneal dialysis, diabetic patients nevertheless absorb an average of 150 to 300 g of glucose per day when using conventional solutions.

1. Icodextrin Solution (Extraneal): Glucose Polymer:

This colloid-type osmotic agent advantageously replaces conventional glucose solutions to improve UF volume during periods of long stasis. In addition, icodextrin helps reduce glucose absorption.

Mistry et al [18], in a randomized multicenter study comparing iso-osmolar icodextrin to plasma with hyperosmolar glucose solutions in CAPD, observed a mean absorption of 29±5g when using icodextrin versus a mean absorption of 62±5g of 3.86% glucose (p<0.01) after 8 hours of stasis when using conventional solutions in 18 patients. Carbohydrate-sparing PD regimens include: A) Icodextrin, in which carbohydrate absorption is equivalent to a 2.5% dextrose bag, but is combined with ultrafiltration of a 4.25% dextrose bag; and B) amino acid (AA) dialysate solutions. As part of a glucose-sparing policy, the use of 1 bag of icodextrin or amino acid (AA) dialysate solution daily can reduce glucose load by 15–30%. In addition, the AA-containing dialysate should serve as a source of both protein and calories [15,16,17].

Other authors have reported a reduced rate of glucose breakdown products (GBPs) production compared to conventional glucose solutions and a low potential for advanced glycation end products (AGEs) formation when using this solution. Replacing a conventional glucose solution with icodextrin may require adjustment of insulin doses. Blood glucose measurement must be performed using a specific method to avoid interference with maltose.

2.Amino acid solution:

Completely glucose-free and therefore PDG-free, it helps reduce amino acid and protein loss and is necessary to improve the nutritional status of malnourished patients. However, international guidelines currently recommend amino acid-rich solutions as a glucose-sparing solution rather than a nutrient solution.

3. Biocompatible solutions:

Several studies have shown that neutral pH solutions, bicarbonate/lactate buffer or pure bicarbonate, with low PDG content and therefore low AGE formation, have improved biocompatibility indicators in in vitro studies compared to lactate-buffered solutions. They preserve RRF longer than standard solutions.

X. THERAPEUTIC OBJECTIVES

Target HbA1c levels for diabetic patients on dialysis have not yet been identified. A moderate HbA1c range (less stringent than the levels suggested for diabetic patients without CKD) is probably associated with greater survival in dialysis patients. It should be individualized for each patient.

Currently, the KDOQI and KDIGO clinical practice guidelines recommend a higher HbA1c target (e.g., <7.5% or <8.0%) in patients with multiple comorbidities, limited life expectancy, and those at risk of hypoglycemia, which almost certainly includes dialysis patients [10,19]. The Joint British Diabetes Societies guidelines recommended an HbA1c target for diabetic patients on dialysis of between 7.5 and 8.5%. Hypoglycemic patients should have their doses reduced if HbA1c is <7.5% to avoid the risk of hypoglycemia [9]. The National Institute for Health and Clinical Excellence (NICE) recommends HbA1C targets between 6.5% and 7% in all diabetic patients, but has not specified a target for the dialysis population [20]. In contrast, Berns et al. recommend an HbA1C target of 7–8% for dialysis patients and the specific target should be individualized according to the risk of hypoglycemia and comorbidities. For example, for younger patients (under 50 years) and without significant comorbidities, the HbA1C target should be close to 7% (7–7.5%), while higher HbA1c (7.5–8%) should be aimed at in older dialysis patients with multiple comorbidities [15].

XI. MANAGEMENT OF HYPOGLYCEMIC THERAPY IN PD

A. Non-pharmacological Therapy

The management of diabetic patients on dialysis requires a multidisciplinary approach. Here, we detail some general advice based on international recommendations.

a. Dietary Recommendations and Education

Dietary advice should include information on diabetes and the specific renal dietary requirements. Each dialysis unit should have appropriate dietary expertise ready to provide a tailored approach to each diabetic patient on dialysis. They provide professional and comprehensive support for patient adherence to their prescribed diet. The nutritional management of diabetic patients on dialysis should consider energy, protein, phosphate, potassium, salt, fluids, and vitamins.

Nutritional Status:

Regardless of the dialysis method used, patients are generally malnourished. Several factors contribute to this: inadequate protein intake, gastroparesis, enteropathy, metabolic stress, to which may be added intercurrent pathology, in particular peritoneal infection. Particular effort must be made to limit sugar and unsaturated fat intake. It is therefore recommended that patients have an intake of 140 to 160 g of carbohydrates and a protein intake of around 1.5 g/kg of body weight per day. In these patients, nutrition can be improved by the use of an IP exchange per day of a 1.1% amino-acid-rich solution, preferably administered during the best meal. The dose of dialysis delivered also plays an important role in nutritional status. Currently, the recommended dose of dialysis delivered per week corresponds to a KT /V urea of 1.7 and a total creatinine clearance of 50 L/week/1.73 m². These targets do not differ from those of the non-diabetic population.

According to the NKF KDOQI guidelines, total energy should consist of 50–60% carbohydrates, <30% fat, and at least 15% protein. Fruits, vegetables, and low-potassium carbohydrates with a low-moderate glycemic index should be encouraged to achieve the recommended "5 a day" servings of fruits and vegetables [21]. Salt intake <6 g/day is recommended and should be emphasized as part of fluid management. Nasogastric feeding or gastrostomy feeding may be necessary for some patients if oral nutrition is insufficient [9].

PD may offer greater lifestyle benefits than hemodialysis, with fewer dietary restrictions and better preservation of residual renal function; however, one of the major problems of PD in diabetics is the increasing risk of peritoneal fibrosis. Diabetic patients have a thicker and poorly vascularized peritoneal membrane even before starting PD; this, in addition to recurrent peritonitis and the use of conventional high-glucose PD solutions, are all implicated in functional changes leading to peritoneal membrane failure [22, 23].

Recommendations:

- Therapeutic education
- Dietary advice
- Oral nutritional supplementation
- IP nutrition during long exchanges
- Reduced carbohydrate intake
- Glucose-sparing strategies
- Regular exercise
- Regular and meticulous glycemic control

b. Active exercise and weight control

A higher BMI should predict a lower mortality rate in dialysis patients because it determines a better status compared to malnutrition and reduced albumin levels, which are independent predictors of mortality [24]. However, overweight and obese patients considering kidney transplantation should be encouraged to lose weight to reduce surgical complications and improve patient and allograft survival post-transplant.

B. Pharmacologic Therapy

1. Insulin Therapy:

According to the KDOQI guidelines, insulin use should be encouraged in dialysis patients, particularly those whose properties are similar to human insulin physiology. Some oral agents should either be used with caution or not at all in dialysis patients [24]. Dialysis patients may require either basal insulin alone or basal insulin as part of multiple daily injections [25,26]. It is recommended that the initial insulin dose be reduced to approximately 50% of that of pre-dialysis patients, and the dose may be increased based on daily glycemic monitoring of CGMS and HbA1c levels [27,28,29].

Patients starting peritoneal dialysis may continue treatment if their blood glucose is controlled; however, insulin may be introduced to maintain glycemic targets.

In PD, insulin can be administered either subcutaneously or intraperitoneally; the intraperitoneal (IP) route has a more favorable effect on glycemic control. Insulin is instilled directly into an empty abdominal cavity before infusion of the dialysis solution into this cavity. It is physiologically delivered directly to the liver via the portal circulation. As a result, peripheral insulin action is minimized, resulting in better insulin sensitivity. The IP route requires higher doses of insulin because the dialysate adsorbs and insulin comes into contact with the superficial plastic of the dialysate solution [30]. Studies have shown that insulin dose requirements could be twice that of the subcutaneous route [31]. In addition, intraperitoneal insulin administration is associated with an increased risk of

bacterial infections, fibroblast proliferation, and hepatic subcapsular steatonecrosis [10, 32]. Another disadvantage of intraperitoneal administration is dose fluctuation [33].

Determining the daily dose:

▪ Add the total insulin dose administered pre-dialysis, then multiply by 2 to obtain the initial daily insulin dose.

▪ Gradually adjust the dose based on glycemic control.

▪ The final dose is usually 3 times the NPH dose + the usual dose.

2. Oral Hypoglycemic Drugs

The medications used to treat diabetes mellitus have expanded over the last decade. However, many hypoglycemic drugs contain active metabolites that are metabolized and excreted by the kidneys; thus, they require dose adjustment or avoidance in dialysis patients . Oral agents can also be used in dialysis patients.

1. First-generation sulfonamides, including acetohexamide, tolbutamide, chlorpropamide, and tolazamide, are not recommended because they have a longer half-life and an increased risk of hypoglycemia. It is recommended to use a second-generation sulfonylurea such as gliclazide, which is metabolized by the liver and is associated with a reduced risk of hypoglycemia [34,35].

2. Glinides: Repaglinide is the preferred agent in this class because it is metabolized by the liver; the inactive metabolites are excreted in the urine. It is therefore associated with a lower risk of hypoglycemia. Nateglinide is less preferred because the metabolites are active, unlike repaglinide; therefore, there is an increased risk of hypoglycemia [27,35].

3. Thiazolidinediones (TZDs). TZDs are metabolized by the liver, and neither the drug nor its metabolites are excreted by the kidneys. The main side effect of TZDs is fluid retention in dialysis patients, which is associated with a lower risk of hypoglycemia, improved lipid profiles, and reduced inflammation [36].

4. Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors).

DPP4 inhibitors are generally safe in dialysis patients. Some doses of certain molecules may need to be adjusted in patients with CKD and dialysis.

5. GLP-1 analogs:

Delay gastric emptying and promote early satiety and weight loss.[27] Exenatide and lixisenatide are excreted by the kidneys and are not recommended for GFR <30/mL/min/1.73 m2. Liraglutide is not metabolized or eliminated by the kidney; however, there are limited data on the use of liraglutide in dialysis patients. Manufacturers caution against administration in moderate to severe renal dysfunction; however, few authors suggest that no dose adjustment is necessary in patients with ESRD [37,38]. Dulaglutide is a long-acting GLP1 analogue that is administered once weekly. In the AWARD 7 trial, dulaglutide was compared with insulin, and it showed fewer hypoglycemic events and renal benefits without compromising glycemic control. Manufacturers recommend use up to CKD stage 4 and with caution in CKD stage 5 without dose adjustment [39]. The effect of dulaglutide on

renal function was evaluated in a study by Tuttle et al. who analyzed the effects of dulaglutide on renal function in phase I and II trials. The authors concluded that dulaglutide did not affect eGFR and slightly decreased albuminuria [40].

6. AGIs (alpha glucosidase inhibitors). Alpha-glucosidase inhibitors (acarbose, miglitol) are primarily renally excreted and should be avoided.

7. SGLT2 inhibitors. The use of SGLT2 inhibitors has been associated with significant cardiovascular and renal benefits, however. The 2022 KDIGO guidelines for diabetes in CKD recommend the use of SGLT2 inhibitors for patients with EGFR >20 mL/min per 1.73 m2 but not below, as there is a lack of evidence of benefit and safety. The guidelines also recommended that patients already on SGLT2-i may continue the drug until dialysis. These recommendations are likely to be revised pending the results of ongoing clinical trials [41].

## XII. CLINICAL CASE OF A DIABETIC PERSON ON PD

54-year-old patient on peritoneal dialysis, BMI 28 kg/m2, weight 87 kg, height 177 cm, BP 17/8 cmHg, Hb at 9.3 g/dL, HbA1c 9.5%, hypercholesterolemia 2.4 g/L, LDL 1.4 g/L, and TG 2.8 g/L with a UFT of 800 ml and urine output of 200 ml/day

Patient Concerns

• Increased HbA1c and weight

• Hypoglycemia +++

• OMI and dyspnea due to fluid and salt overload

• Chest X-ray reveals a sulcus with moderately abundant pleurisy

• Self-monitoring of blood glucose levels reveals the following values:

Finger-stick blood glucose (FBG)	D1	D2	D3	D4	D5
Fasting blood glucose (FBG) (mg/dl)	2.8	3	2.7	3.2	3.6
Pre-lunch blood glucose (mg/dl)	1.6	1.8	1,8	1.6	1.6
Pre-dinner blood glucose (mg/dl)	2.3	2	3	2	3.2

Continuous Glucose Monitoring System (CGMS)
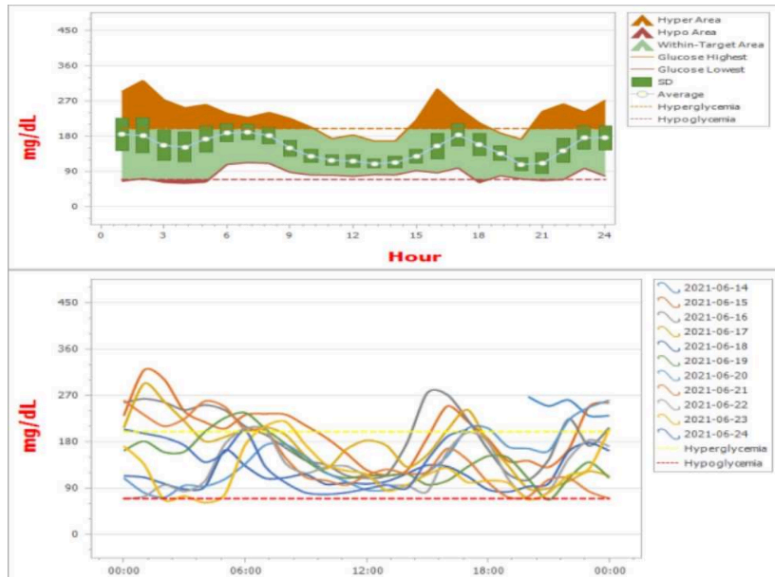
CGMS Comment:

A Time in Range < 70% with ART > 40% with several clinically asymptomatic hypoglycemic episodes

and a coefficient of variability > 36% (normal < 36%)

The patient received 3 bags: two 1.36% glucose isotonic and one 2.5% glucose bag in the evening with :

Novomix 30: 28 IU in the morning and 16 IU in the evening

Atorvastatin 10 mg/day,Lasilix 250 mg/day, Amlodipine 5 mg/day, Kardegic 75 mg/day,Calcium Element 1.5 g/day, Darbapotine 50 μg/week

Our management aims to reduce weight gain and episodes of excursion glycemic, asymptomatic hypoglycemia, for glucose saving and to improve ultrafiltration since the patient presented signs of overload with OMI, pleurisy and HBP. We opted for

- 3 PD exchanges: 2 iso 1.36% bags and one icodextrin bag in the evening on a full stomach
- With a basal-bolus regimen: based on GLARGINE U300 "TOUJEO": 30 IU in the evening combined with rapid-acting insulin "Novorapid": 8 IU-8 IU-6 IU
- Increased atorvastatin doses to 20 mg/day
- Discontinued amlodipine due to an improvement in UF to 1500 ml and normalization of BP to 132/82 mmHg

The outcome was marked by improved glycemic figures (as shown below in the CGMS figures) with less hyperglycemia and fewer hypoglycemic episodes, and especially glucose sparing with improved ultrafiltrate.
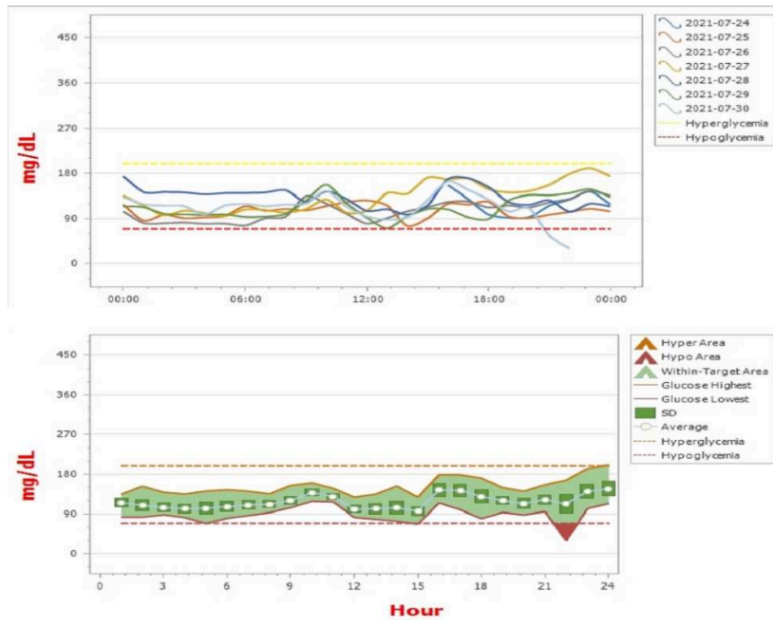
CGMS Commentary:

TIR >90%, rare hypoglycemic episodes, and coefficient of variability <36%

XIII. CONCLUSION

The management of diabetic patients on dialysis is a real challenge and requires a multidisciplinary approach. Ideally, treatment should be individualized for each diabetic patient on dialysis to reduce diabetes-related complications, minimize adverse events, and increase survival rates. This requires continuous, effective glycemic assessment tailored to peritoneal dialysis patients, particularly continuous interstitial glucose monitoring (CGMS), which, in our clinical case, demonstrated an ease in achieving therapeutic targets with fewer complications and greater sensitivity to glycemic variations. Above all, it enabled accurate interpretation of clinical and biological data, allowing for profile-dependent therapeutic adaptation.

Kidney transplantation with or without simultaneous pancreas transplantation remains the primary replacement therapy for diabetics with ESRD. It improves the patient's quality of life compared to dialysis. However, this is often difficult with the presence of multiple comorbidities and reduced availability of donor organs.

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