Peritoneal Dialysis is a Valuable Solution for Fluid Removal in Cardiorenal Patients Type 2

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INTRODUCTION

CRS (Cardiorenal Syndrome): the interaction between kidney and CV systems where acute or chronic changes in one organ leads to adaptive (or maladaptive) changes in the other organ system. The term cardiorenal syndrome (CRS) has been used in the medical literature to describe the hemodynamic and neurohormonal connection that exists between the heart and kidneys[1]. This syndrome can be defined as a clinical situation in which both cardiac function and renal function are simultaneously compromised, with progressive damage to both organs[2]. CRS has been classified into several different types1,2 based on the primary organ affected and a clinical or acute progression of disease:

1. Acute CRS type I: acute deterioration of cardiac function, inducing acute renal failure.
2. Chronic CRS type II: chronic heart failure (HF) associated with chronic kidney disease (CKD) or contributing to its progression.
3. Acute CRS type III: sharp deterioration in renal function, producing acute heart damage.
4. Chronic CRS type IV: defined as CKD that contributes to decreased cardiac function, cardiomegaly, and increased cardiovascular risk.
5. Secondary CRS type V: systemic pathology that causes renal and cardiac damage simultaneously. For example: systemic lupus erythematosus, amyloidosis, and diabetes mellitus.

PATHOPHYSIOLOGY

Regarding CRS Type 2, chronic Heart failure even systolic or diastolic dysfunction. lead to increase sympathetic activity lead to peripheral Vasocontraction also, also lead to release of RAAS (Renin- Angiotensin-Aldosterone system) which lead to Glomerular efferent arteiroles vasocontraction lead to more decrease in GFR(Glomerular filtration Rate), also increase RAAS vactivities lead to release endothelium and vasopressin which cause further asocontraction and further kidney injury and water retention which lead finally to decrease perfusion to kidney lead to acute kidney Injury. (increase serum creatinine 26 umol), and by time these Multiple attacks will cause permeant chronic damage in the Kidneys. Heart tries to compensate by secret BNP to cause vasodilatation and naturesis but if pervious pathophysiology persist will lead to heart failure which lead to BNP resistance by the time. And impair Right ventricular function also can cause decrease GFR by decreasing renal perfusion due to low cardiac output due to venous congestion (High Preload)

We are Focusing here on CRS type II (chronic HF), this important cause of morbidity, mortality, and hospitalizations can produce chronic deterioration of renal failure in 36%-50% of patients[3].which in turn can lead to fluid overload, resistance to the diuretics effect, and even HF refractory to normal treatment; this then leads to terminal HF, such that patients that are no longer candidates for heart transplantation and are placed on palliative treatment[3]or newer alternatives, such as vasopressin receptor antagonists, natriuretic peptide, adenosine receptor blockers, and ultrafiltration (UF) techniques, with an active role of the nephrologist in these last few options[3]. In this manner, UF using peritoneal dialysis (PD) may offer certain advantages over hemodialysis (HD) in the treatment of these cases by improving the preservation of residual renal function (RRF), hemodynamic stability, continuous UF etc[3,4].

The Main Causes of Diuretics Resistance in this type of patients are due to Multiple factors Like: Intestinal Edema lead to Decrease absorption of oral Diuretics, Inadequate does due to renal impairment (renal impairment lead to less Loop Diuretics filtered to tubular cell), Low albumin (Lasix Carried by Albumin in Plasma) due to chronic inflammation, patient noncompliance to Salt restriction[5], using medication that can cause Salt retention like NSAID, post diuretics sodium retention due to distal tubule hyperplasia from chronic use of Loop Diuretics) and finally but not Common patients use drugs interfere with tubular secretion of Loop Diuretics like, probenecid, sulfonamide, beta lactam , Methotrexate , cimetidine)

CASE REPORT

75 Years old Male patient.

His Past Medical History:

- Stage III chronic kidney disease with mild proteinuria attributed to hypertension, cardiorenal syndrome, diabetes and atherosclerosis.
- Heart failure
- Hypertension.
- Type 2 diabetes.
- Peripheral vascular disease.
- Pulmonary hypertension.
- COPD.
- Atrial fibrillation.
- Aortic stenosis.
- Sciatica.
- Rheumatoid arthritis.
- NASH/hep A.

CARDIAC STATUS

Heart failure with severe diastolic dysfunction and pulmonary hypertension, mild degenerative aortic valve disease. The left ventricle is normal in size. There is mild concentric left ventricular hypertrophy. The left ventricle is hyperdynamic. Ejection Fraction = >70%. The right ventricle is mildly dilated. The right ventricular systolic function

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is reduced. There is mild mitral regurgitation[6,7].

Calcified aortic cusps with mild to moderate valvular aortic stenosis and mild aortic regurgitation. There is mild tricuspid regurgitation. Severely elevated pulmonary pressure estimate - The right ventricular systolic pressure is estimated at 90-95mmHg according to last ECHO before his referral to PD clinic. Followed by cardiology and according to his General status its Contraindications for heart-lung transplantation.

The clinical situation of the patient included continuous Hospitalizations and Cardiology and Nephrology clinic visits Since 2018 due to severe CHF decompensations (NYHA class IV), with basal dyspnea at rest and during minimal exertion, paroxysmal nocturnal dyspnea, and orthopnea. Restricted to bed/chair. His Wife mentioned that he is almost Bed bound last two Years.

During his last Combined Nephrology Cardiology Clinic on Jan 2021, he clearly was an increasingly difficult therapeutic challenge. He is currently on 400 mg of Lasix per day IV coupled with 5 mg twice a day metolazone. He still has severe congestive syndrome. JVP is elevated all the way to his jaw. He has gross ascites. Blood pressure is 155/69, pulse rate 54 beats per minute, despite his best efforts at salt and water restriction. He still has very poor quality of life and is NYHA class III/IV. Currently, his serum creatinine is relatively stable at 262 micromoles per liter with a potassium of 3.6 mmol/L. The Team Have discussed with him the Another non-pharmacological Options and There is very little left to be done in terms of pharmacological interventions at that time his diuretic (Lasix) dose Titrated up to 250 mg iv bid (through PiCC line) with Metolazone 5 mg oral Bid. then the Medical Team Consulted Us in regard to consider peritoneal ultrafiltration for nonpharmacological removal of fluid and salt. in light of the previous mentioned symptoms, and the progressive deterioration of CKD and resistance to normal treatment for CHF, in addition to progressively worsening renal failure, with progressive oligoanuria[8].

So, We Saw the Patient in Our PD clinic end of Jan 2021 to assess him for PD catheter. At the date of his visit to Our PD unit he came with his Wife, he showed his interest to do the PD at home with Support from His Wife. A physical examination revealed poor general state of health, he has marked restriction of his daily activities due to Shortness of breath at-rest that was aggravated with tachypnoea upon minimal exertion, and severe jugular venous distension, but no cyanosis peripherally or centrally. Pulmonary auscultation revealed a complete absence of vesicular breathing sounds in both lung base, with basal crackles in both lung fields also[9]. Cardiac auscultation revealed weak regular peripheral pulses and with systolic Murmur at apex radiate to Pulmonary Area. An abdominal examination revealed signs of ascites, with painful hepatomegaly and edema in the abdominal wall. We also observed edema in lower limp extend to his abdomen with vascular trophic disorders in his lower limps, but no signs of venous thrombosis. Blood pressure was 139/75, pulse was 54 bpm, and O2 Sat was 89% on room Air but 96% on 2 L oxygen through the Nasal cannula, His Abdomen was distended, large ascites with No previous Major Abdominal Surgeries, the patient was Able to lay flat on the Bed but he needs 2-3L oxygen through Nasal Cannula. So, we have discussed the risks and benefits of the procedure and the patient is agreeable to proceed with percutaneous insertion. The patient has signed the consent form.

BLOOD WORKS AND IMAGING

Blood analyses: hemoglobin: 119 g/dl; hematocrit: 37 %; leukocytes: 6.6; platelets: 146 000; glucose: 7mmol\L; urea: 43.2mmol\L; creatinine: 283mmol\ L ; ALT 24 mmol\L lactate-dehydrogenase (LDH): 130U/l; Na:136mEq/l; K 3.6mEq/l; Ca: 2.29 mmol\L ; total protein: 6.9g/l; pH: 7.45; pCO2: 42; HCO3: 30 ALP 130 mmol\L , Anion Gap 14 mmol\L Mg 1.03 , Bilirubin 16 umol\L Urate 488 umol\L. .Electrocardiogram: Low voltage QRS Nonspecific ST abnormality Abnormal ECG .chest x-ray: notable cardiomegaly and bilateral pleural effusion. . Abdominal ultrasound: The liver is echogenic and slightly heterogeneous; the appearances would be in keeping with fatty infiltration. No focal liver lesion is seen. The liver measures 13.5 cm in the midclavicular line. The tail the pancreas is not well seen. The gallbladder is normal[10]. The common bile duct measures 0.3 cm. The spleen measures 10.8 cm. The kidneys and aorta normal. Echocardiography 2019: The left ventricle is normal in size. There is mild concentric left ventricular hypertrophy. The left ventricle is hyperdynamic. Ejection Fraction = >70%. The right ventricle is mildly dilated. The right ventricular systolic function is reduced. There is mild mitral regurgitation. Calcified aortic cusps with mild to moderate valvular aortic stenosis and mild aortic regurgitation. There is mild tricuspid regurgitation. Severely elevated pulmonary pressure estimate - The right ventricular systolic pressure is estimated at 90-95mmHg.

TREATMENT AND CLINICAL COURSE OF THE PATIENT TILL THE TIME PRESENT

Initially, the patient's medical treatment was intensified to include renin-angiotensin-aldosterone system (RAAS) blockers, beta blockers but stopped because of his recent worsening of his kidney function and persist low Blood pressure and baseline low heart rate, and conventional diuretics (loop diuretics and thiazide like medication). This treatment was not effective: the symptoms persisted, and the patient's general state of health continued to deteriorate, in addition to progression of renal failure due to progressive oligoanuria with an acute superimposed component of CKD due to HF decompensations and long-standing DM. Given the situation of refractory heart failure (RHF)[10], we decided to procced with insertion of PD catheter under Fluoroscopy for Ultrafiltration. The urgency of the situation required an Extra step during the insertion procedure (applying Deep Purse string suture below the Deep Cuff of PD catheter with Rectus Muscle Sheath in order to help decrease the risk of Leaking).

So, On Feb 5th/2021 His Weight was 99 kg and Blood pressure 135/85 otherwise Vitally stable, patient had Successful Fluoroscopic Insertion of PD catheter in his Right Lower. At the date of procedure, a total of 4 L Ascites Fluid Drained. The patient tolerated the procedure well and sent to Recovery Unit for couple of Hours then Discharged home on stable condition[11].

The patient after that underwent several sessions with normal hemodynamic tolerance, weight loss, and stabilization (Table 1), with recovery of diuresis and mild improved and Stabilization of his renal function, after his clinical improving the patient Diuretics regimen decreased from IV to oral Medication (his current regimes are Bumetanide 5 mg oral BID, Spirolactone 25 mg oral daily and finally Metolazone 5 mg oral daily), The patient physical daily activities at home markedly improved without any restriction**.**

DISCUSSION

Chronic HF that induces a chronic deterioration of renal function has been labelled as CRS type II. Several different mechanisms can be involved in the coexistence of these two entities, contributing to a progressive deterioration of both conditions and an increase in the rate of progression of atherosclerosis, altered regulation of intravascular volume, and inadequate compensation of regulatory mechanisms, which finally leads to a global increase in morbidity and mortality rates[3]. As Montejo et al. described, the pathophysiological mechanisms

Date	Initial Drain (Ascites)	Program of PD	Bp and Pulse	Weight	Serum Cr
05/02/2021	4L fluid Drained	Only Drain no cycling	132/71, 52 bpm	99 kg	283
08/02/2021	3L Fluid Drained	Only Drain no cycling	137/75, 58 bpm	94 kg	231
10/002/2021	1L Fluid Drained	On Cycler total UF 812ml	123/53, 58 bmp	95.4 kg	175
12/02/2021	1.166ml Drained	On Cycler Total UF 372ml	133/59, 49 bpm	94 kg	n\a
13/02/2021 patient had leak so cycler PD stopped for a week then the patient started on program of (3 days per week on a cycler and the rest of days of week on Single ICO 7.5% 1L.					
23/02/2021	560 ml drained	On Cycler Total UF 1193ml	125/60, 55 bpm	92 kg	183
24/02/2021	260 ml drained	On Cycler total UF 1200ml	114/56, 59 bpm	88.5 kg	n\a
25/02/2021	210 ml drained	On Cycler total UF 1100ml	123/59, 58 bpm	87.5 kg	193
03/03/2021	200 ml drained	On Cycler total UF 1323ml	118/51, 55 bpm	83.8 kg	217
04/03/2021	100 ml drained	On Cycler total UF 1100ml	120/54,58 bpm	83 kg	n\a
05/03/2021	70 ml drained	On Cycler Total UF 1300ml	120/52,57 bpm	82.7 kg	232
Then after that the patient started only on single ICO 7.5% 1L was Ultra filtrating from 500-1000ml per day till his Weight on 23/03/2021 was 74.4 kg.					Stable 261

BP: Blood Pressure, UF **Ultrafiltration**, Cycler: NIPD 4-5 exchanges fill Volume 1100-1500 ml per Exchange, **Serum Cr**: Serum Creatinine mmol\L**. n\a**: Not Available.

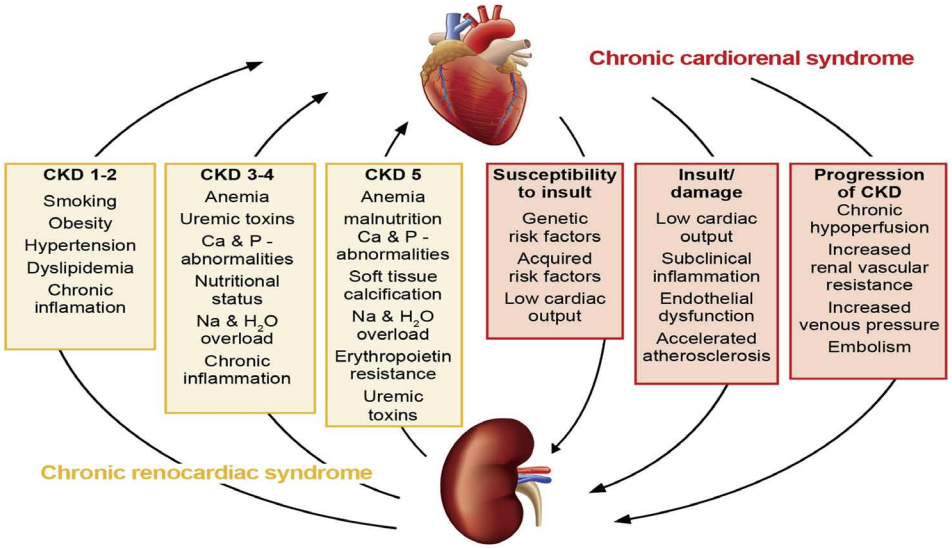

Figure 1: Determining factors the vicious circle between cardiac dysfunction and renal dysfunction

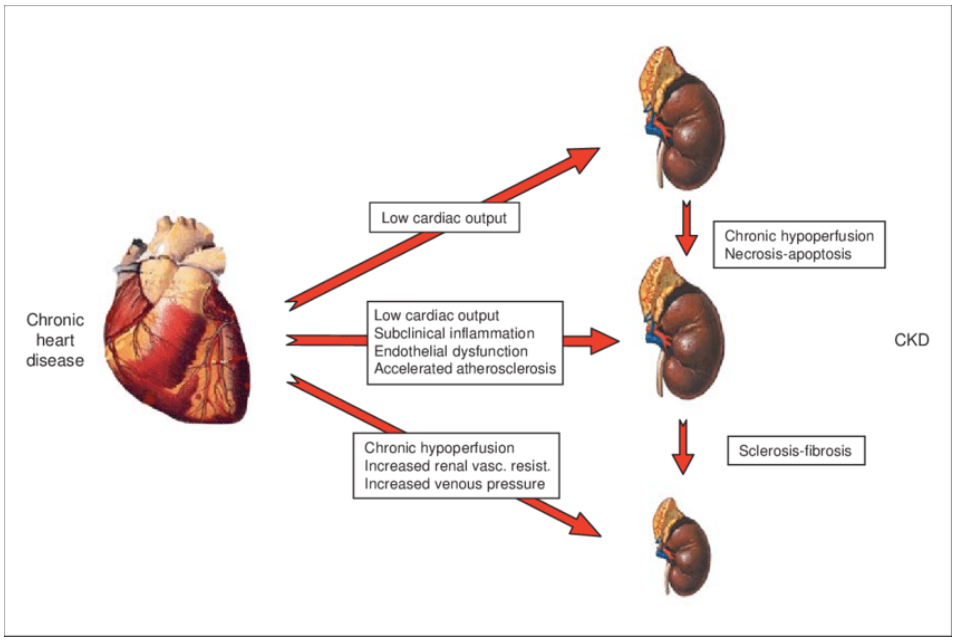

Figure 2: Pathophysiological interactions between the heart and kidneys in cardiorenal syndrome type II

implied in this process are precipitated by low cardiac output, which induces activation of the RAAS and sympathetic nervous system, altered nitric oxide balance, and anti-diuretic hormone release. This produces systemic vasoconstriction and water and salt retention. This mechanism will lead to in turn causes progressive volume overload and worsening of symptoms, hospitalizations, progression of HF and decrease the survival[12]. Another important factor is raised in right pulmonary pressure, some Lectures said increase in right side pressure associated with more worsening of renal function compare with decreased in cardiac index alone so finally in regards to kidney function, low cardiac output and raised RA pressure produce renal hypoperfusion, which can deteriorate renal function, even more so if other factors are added such as the use of diuretics and RAAS inhibitors, especially during episodes of cardiac decompensation or in cases of prior renal dysfunction (Figure 1)[13].The final result, to which several different inflammatory factors also contribute, is progressive deterioration of renal and cardiac tissues(Figure 2), and the end result of most of patient are persist fluid overload, resistance to diuretic treatment, and finally refractory HF and progressive renal impartment. one of biggest dilemma in treating these patients is when they are become diuretics resistance over the time due to worsening of volume overload, worsening of kidney function and other factors mentioned previously and they have contraindication to heart transplantation due to their clinical situation, using peritoneal dialysis in these patients can be valuable option for fluid removal and improve their clinical status and decrease hospitalization like our case. With using the fluoroscopic technique for insertion, the patient can have their pd catheter inserted and used urgently for ultrafiltration if their have PD program in their hospital. The advantages of using PD here are simple, cost effective, gentile ultrafiltration and less stress on the heart and finally improve clinical status.

Key's concept:

- Heart failure that is refractory to normal treatment is common, but implies high rates of morbidity and mortality, with substantial associated health costs.
- Renal failure is a common complication in these patients, and even when only moderate in severity, this can substantially worsen patient prognosis.
- PD has been shown to improve quality of life, functional class of HF, and rate of hospitalizations.
- PD can be a very cost-effective treatment in these patients.
- PD solutions with icodextrin allow for long dwells on dialysis, and facilitate treatment with a single exchange per day, greatly simplifying treatment.
- Some patient showed better response to Oral Diuretics after initiate of PD and lower their weight.

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