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Bulletin de la Dialyse à Domicile

Peritoneal Dialysis Initiation to treat End Stage Kidney Disease during pregnancy. A report of 2 cases

(Initiation de dialyse péritonéale pour traiter l'insuffisance rénale terminale durant la grossesse : Un rapport de deux cas)

Lucas Jacobs[1], Saleh Kaysi[1], Maria Mesquita[1], Christelle Fosso[1], Andrew Carlin[3], Isabelle Brayer[2], Max Dratwa[1]

[1]Médecin [2]Infirmière
Service de Néphrologie-Dialyse, Département de Médecine Interne, CHU Brugmann, Université Libre de Bruxelles, Belgique
[3]Service de Gynécologie, CHU Brugmann, Université Libre de Bruxelles, Belgique

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Résumé

Malgré les preuves tangibles suggérant que la dialyse péritonéale (DP) est une technique comparable à l'hémodialyse (HD) de longue durée pour les femmes enceintes [11,12], peu de cas sont rapportés dans la littérature médicale actuelle.
De plus, démarrer la DP chez une femme enceinte ayant besoin d'épuration extra-rénale est rarement sinon pas décrit du tout. Dans cet article, nous présentons deux cas de patientes qui ont commencé la DP en étant déjà enceintes de plusieurs mois : la première il y a 14 ans, la seconde alors que nous écrivons cet article.
Nos deux patientes sont dans leur trentaine, étaient à respectivement 16 et 10 semaines de grossesse à leur admission et ont un historique de syndrome des anti-phospholipides. Il fut décidé de démarrer un programme de DP chez elles. Notre première patiente accoucha d'une fille de 2.5 kg et 45 cm en bonne santé malgré un épisode de péritonite et une adhésiolyse du cathéter de dialyse péritonéale. Notre deuxième patiente est actuellement dialysée, sans complication et en est à 28 semaines de grossesse.
Initier la DP chez une femme enceinte est un sujet qui n'a presque jamais été publié dans la littérature médicale actuelle. Avec de plus hauts taux de grossesses que jamais dans la population en insuffisance rénale terminale [31], nous suggérons d'évaluer les bénéfices de la DP via l'élaboration d'une étude prospective comparative entre la DP et l'HD de longue durée.

Mots clés : Anti-phospholipides ; Dialyse péritonéale ; Femme ; Grossesse ; Insuffisance rénale terminale

Summary

Despite strong evidence suggesting that peritoneal dialysis (PD) is a comparable technique to long-hour hemodialysis (HD) for pregnant patients [11,12], few cases are described in the current literature. Moreover, initiating PD in a pregnant woman needing extrarenal epuration is rarely described if at all.
In this article, we present two cases of patients who initiated PD while being already multiple month pregnant: the first one 14 years ago and the other today.
Our two patients are in their thirties, are respectively 16 and 10 weeks pregnant and have a history of anti-phospholipids syndrome. It was decided to start a PD program with both of them. Our first patient gave birth to a healthy 2.5 kg and 45 cm daughter despite an episode of peritonitis and the freeing of the peritoneal catheter from adherences. Our second patient is currently on dialysis without complications and is now 28 weeks pregnant with a healthy monitored child.
Initiating PD in a pregnant patient is a subject that has not yet been published in the current scientific literature. With higher pregnancy rates than ever in the end stage renal disease population [31], we suggest to assess the objective benefits of PD extrarenal epuration method by performing a prospective comparative study between PD and HD.

Key words : Anti-phospholipid; Female; Kidney Failure; Peritoneal Dialysis; Pregnancy

Correspondant : LucasMichelPierre.JACOBS@chu-brugmann.be
Dr. JACOBS Lucas LucasMichelPierre.JACOBS@chu-brugmann.be - +32(0)472.85.85.22
Dr. KAYSI Saleh [Saleh.KAYSI@chu-brugmann.be),
Dr. MESQUITA Maria [Maria.MESQUITA@chu-brugmann.be),
Dr. FOSSO Christelle [Christelle.FOSSO@chu-brugmann.be),
Mme BRAYER Isabelle, Infirmière [Isabelle.BRAYER@chu-brugmann.be),
Dr. DRATWA Max [Max.DRATWA@chu-brugmann.be)

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INTRODUCTION

Pregnant patients with ESRD are mostly managed with hemodialysis (HD). However, the literature contains rare cases of pregnant patients being managed with peritoneal dialysis (PD). Furthermore, PD initiation in an already pregnant woman is hardly described at all.

However, PD offers specific benefits in ESRD management throughout pregnancy, such as more continuous and gentle daily ultrafiltration, better metabolic balance without the fluctuations noted in intermittent therapies, less anemia, avoidance of systemic anticoagulation, and a more liberal diet for maintaining good maternal nutrition [1,2].

While more studies show increased rates of pregnancy and successful delivery in women undergoing dialysis [3], nephrologists rarely choose to initiate peritoneal dialysis as a method to substitute the renal function.

We herein describe two patients starting PD while being already pregnant. The first one 14 years ago, the second one nowadays.

Case report :

Our first patient, a 32 year old woman, in Belgium since two months, was transferred into our hospital in 2006 for the workup of her ESRD and chronic anemia. She was then 16 weeks pregnant and was primiparous (G1P0).

She complained of vomiting and a 16 kg weight loss since the start of her pregnancy. She had no gynecological follow-up. She had chronic low blood pressure, arthralgia, oral canker sores, fluctuating pyrexia and hair loss in plaques dating back to 2 years prior.

A biology workup showed serum potassium levels of 5.4 mEq/L, Creatinine: 4.6 mg/dl (404 μmol/l) and Urea: 92 mg/dl (32.8 mmol/l) and a calculated glomerular filtration rate of 12 ml/min (CKD-EPI). She had positive Antinuclear Antibodies with 1/320 titration, positive Anti-SSA antibodies. Kidney ultrasound showed a hyper-echogenic cortex with reduced cortico-medullar differentiation. A kidney biopsy showed signs of chronic pyelonephritis but also demonstrated a C3 presence indicating a possible immunological-mediated kidney disease. However, since the pathological lesions were advanced, it was impossible to determine the precise etiology of her ESRD.

Extra-renal epuration was indicated due to high serum urea levels (over 50 mmol/l) and, taking into account the frequent hypotension episodes, the patient chose peritoneal dialysis after having received complete information about dialysis modalities, and transplantation.

At 23 weeks pregnancy, a swan-neck coiled peritoneal catheter was inserted. Continuous ambulatory peritoneal dialysis (CAPD) was initiated a week later. A volume of 500 milliliters (ml) of Physioneal 1.36 % dialysate was infused and left for 2-3 hours during two days. Afterwards, volumes were increased up to 7 times 1300 ml + one time 1100 ml in 12 hours using an APD cycler with intraperitoneal pressure monitored to be around 9 cm of water. A fluctuating program was applied to lower abdominal and pelvic discomfort.

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A month later, tests showed that dialysis dose was inefficient, due to catheter misplacement causing alarms to ring constantly. After an unsuccessful passage through manual peritoneal dialysis, a complete epiploic adhesiolysis was performed and could restore a CAPD of 500 ml every 2 hours. The volumes were gradually increased. She was admitted to the hospital and received a week of intra-peritoneal empiric antibiotics (Ceftazidim 1g and Cefazolin 1g) for peritonitis suspicion (cloudy peritoneal fluid, white blood cell count (WBCC) 866/ μL but a negative bacterial culture). A fetal monitoring and obstetrical examination showed eutrophic fetus with good vitality. After hospital discharge, she was monitored weekly through biology workup and gynecologic consultations. We had to reduce PD volumes as the womb grew.

Besides, our patient's treatment consisted in Aspirin (80 mg per day), vitamin supplements (folic acid 4 mg per day, vitamins B,C and D) along with iron supplements (14 mg per day), calcium carbonate (2 g per day) and sodium bicarbonate (2g per day). Around the fifth month of pregnancy, our patient developed anemia with hemoglobin (Hb) at 9.3 g/dl and hematocrit (Hte) at 30 % and ferritine at 266 μg/dl. Therefore erythropoiesis stimulating agents were initiated. We started Aranesp 50 μg once a week. A month later we increased dosage to Aranesp 80 μg once a week because the Hb was at 8.1 g/dl and Hte at 25.6 %. From then on, Hb levels steadily increased, reaching 12.9 g/l on delivery date.

During her pregnancy, plasma Urea ranged between 66 mg/dl (23.5 mmol/l) and 100mg/dl (35.7 mmol/l) and Creatinine between 4.5 mg/dl (396 μmol/l and 5.4 mg/dl (475 μmol/l). We calculated a Kt/Vurea of 4.4. Intra-peritoneal pressure (PIP) did not exceed 15 cm of water. Her residual urine output was stable.

She finally gave birth to her female child at 38 weeks, two weeks prior to calculated term. It was a vaginal birth with no complication during delivery. Her child weighted 2.5 kg and was 45 cm tall. The patient could restart PD one day after giving birth.
Our second patient, presently under treatment, is 35 year old and is known to have chronic renal disease stage G4A1 (according to KDIGO) [4] of unknown origins, in association with a reduction of nephronic mass due to a right nephrectomy that was performed in Italy in 2013 for a reason which remains undefined.

Since the age of 28 years, she has been known for having an anti-phospholipid syndrome and systemic lupus erythematosus (Nuclear Antibodies at 1/80, positive anti-cardiolipin antibodies and positive anti-dsDNA antibodies in moderate titration) without rheumatological or dermatological signs. Lupus was diagnosed in the course of a severe pre-eclampsia during her first pregnancy and after a central retinal artery occlusion. Her first pregnancy ended in a medical abortion in Italy. She is treated with anti-vitamin K since then. She had high blood pressure since childhood, currently on quadruple therapy, and complicated with severe retinopathy without renal artery stenosis or adrenal nodule. Finally she has a microcytic anemia partly due to an iron deficiency, alpha thalassemia and her renal failure.

She was referred to the kidney-pregnancy consultations in our hospital while 10 weeks pregnant (G2P0). She had a plasmatic Urea around 50 mg/dl (17.8 mmol/l), Creatinine at 2.0 mg/dl (228 μmol/l) and glomerular filtration rate at 30 ml/min/1.73 m^2. She was prescribed 180 milligrams (mg) of Aspirin (up until the 36th week of pregnancy) and 40 mg of Low Molecular Weight Heparin sub-cutaneously since she has a high risk of pre-eclampsia.

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At 19 weeks of pregnancy, her biology showed blood Urea approaching 80 mg/dL Creatinine at 2.6 mg/dl and a glomerular filtration rate at 23 ml/min/1.73 m² (CKD-EPI formula). Dialysis was considered in order to reduce the urea level, and thus to improve the fetal and maternal prognosis. After having received information about dialysis modes, she opted for peritoneal dialysis. A peritoneal catheter was placed and peritoneal dialysis was initiated on the 23rd week of pregnancy. At present, her treatment consists in aspirin 160 mg and sub-cutaneous low molecular weight heparin 40 mg per day (for anti-phospholipids syndrome), folic acid supplements (4 mg per day), iron supplements (80 mg per day) and labetalol 400 mg 3 times a day for persistent high blood pressure. She does not require erythropoiesis stimulating agents at this point.

She is now 28 weeks pregnant and on daily 6days/7 CAPD, without vaginal discharge or contraction. Ultrasound and fetal monitoring are showing fetal wellness. She has a residual urine output of 2500 cc. And with that, her total weekly Kt/V urea is 3.74 and her total creatinine clearance reaches 147 L/week.

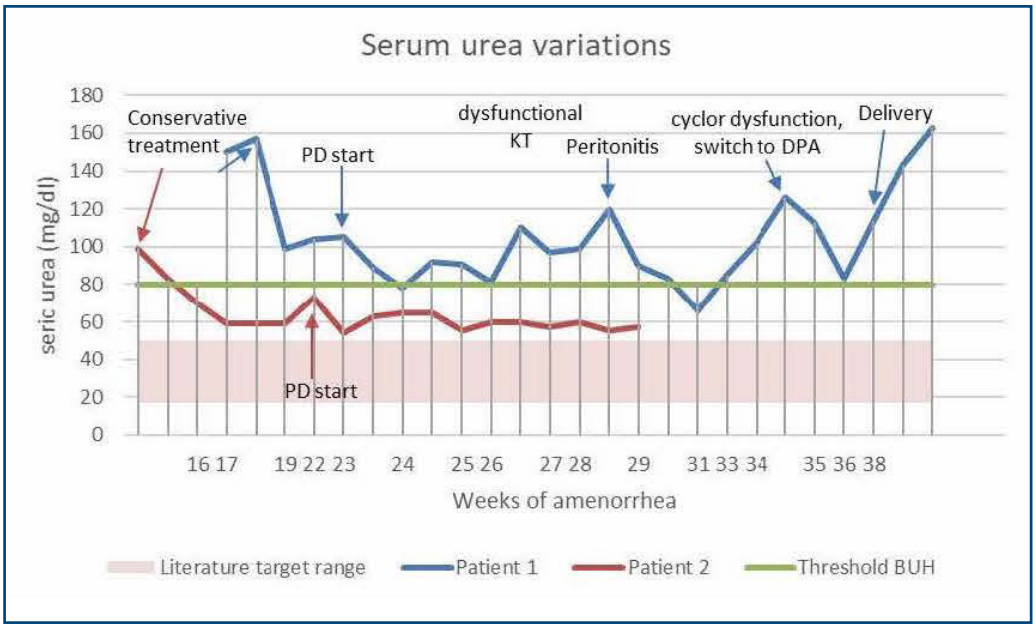

Figure 1. Serum urea variations during pregnancy

Note : Literature target range defined as the target cited in descriptive reports [18,30]; BUH : Brugmann University Hospital; BUH threshold of 80 mg/dl (28.5 mmol/l) defined as target of urea reduction; KT: catheter; PD : peritoneal dialysis; BUH : Brugmann University Hospital.

DISCUSSION

It is primordial to dialyze pregnant patients with ESRD. A recent systematic review of pregnancy outcomes in women with chronic kidney disease (CKD) not requiring dialysis compared with women not having CKD showed a doubled risk for adverse maternal outcomes. In addition, premature births in the CKD cohort were twice as frequent [5]. It is reasonable to think that terminal renal disease without dialysis treatment may represent an ever higher risk of adverse events during pregnancy.

Pregnancy on dialysis is now more conceivable than ever with a reported success rate being over 70–80 % in the last decades [3,6-13]. To date, the best results published regarding pregnancy in

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RRT were obtained with long-hour daily dialysis. Indeed, current medical literature recommends intensive hemodialysis (> 37 hours per week) as RRT [14]; therefore in their "Best practices on pregnancy on dialysis"[15], the Italian Study Group on Kidney and Pregnancy suggested considering this as first choice, when available, although there was no evidence suggesting that intensive PD may lead to different pregnancy-related outcomes [11,12]. Wiles et al even suggest PD patients switching to HD when getting pregnant. [15] Short-daily home hemodialysis using low dialyzate flow-rate has also been described as usable technique during pregnancy. The theoretical concept of low dialysate flow rate in PD is comparable in home dialysis and their feto-maternal outcomes could therefore be comparable. A recent observational study by Weinhandl et al [16] has even issued results in favor of home HD after comparison with PD. HHD was associated with lower mortality, lower hospitalization rate and less technique failure. Obviously certain data were not analyzed as the residual renal function, the frequency and duration of treatment. Recent case reports have since also described successful pregnancies in short daily home dialysis [17,18].

Fewer studies were done on PD as compared to HD during pregnancy. Conception rate is reported to be lower in PD patients [14] but the smaller number of cases reported for PD is also at least partly a reflection of the overall lower prevalence of this technique. Furthermore, the few PD patients included in case reports [5] are patients getting pregnant while on peritoneal dialysis prior to the conception and therefore continuing their dialysis mode.

Initiating PD in a pregnant patient needing extra renal epuration is hardly described at all in the current literature. And yet, compared with the dialysis patients who become pregnant while on long-standing dialysis, CKD patients who become pregnant and subsequently initiate PD (or HD) later in the pregnancy tend to experience better maternal and fetal outcomes [19,20]. That observation might suggest that the degree of residual kidney function (RKF) favorably affects pregnancy outcomes [1].

Furthermore, pregnant chronic dialysis women might have better hope for a successful pregnancy while on PD [21]. The reasons include a higher residual renal function, more stable metabolic milieu and the absence of intradialytic hypotension that could potentially cause intrauterine growth retardation and fetal death. A further issue may be the risk of rapid loss of residual renal function, which is expected to be higher with HD than with PD. In addition to those benefits of PD, the incidence of peritonitis is not reported as being higher than what is observed in patients who are not pregnant [22-26] But those potential benefits might be offset by uterine distention during the third trimester, which could complicate management of the pregnant patient on PD.

It has been suggested that the Kt/V for PD patients should be increased to the range of 2.2–2.4 for better pregnancy outcomes, but this remains to be proven. To achieve this Kt/V target, therapy volume of up to 20 L per day has been recommended [26]. Some publications propose starting dialysis at urea concentrations of 17 mmol/l (50 mg/dl) to avoid polyhydramnios besides correcting anemia and metabolic acidosis. [3,20,31] In our center, dialysis is considered in a pregnant patient as soon as her urea serum level reaches (or approache) 80 mg/dl (28.5 mmol/l). Although we could reduce urea levels by approximately 20 percent, the range of urea levels in our first patient still represented a significant uremic state.

Our first case of PD initiation in a pregnant woman showed great outcome with the child born almost on calculated term and vaginally without any delivery complication. The baby was, as

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expected, smaller. Indeed, many of the pregnancies are notable for lower birthweight infants [27]. The choice of dialysis mode fell on PD mainly because of her history of hypotension besides the increased evidence of maternal and infant wellness with PD emerging in literature. Of course, she needed special care, with attention set on Uremia, PIP, in-out peritoneal fluid balance, the replacement of catheter if needed, the treatment of infections, etc. As pregnancy advances in a woman on PD, the increasing abdominal girth necessitates a reduction in dwell volume. Thus the number of exchanges must be increased to ensure adequate clearance [2,21,28]. Despite her terminal renal failure at arrival, our patient kept her residual urine output. Over the last decade, multiple articles had stressed the importance of residual urine output with regards to successful pregnancy outcomes [14,29]

CONCLUSION

Initiating PD in a pregnant patient needing extra renal epuration is rare. Yet, nothing seems to suggest worse outcome in comparison with what is currently advised by the Good Practice Recommendation for pregnant patients: namely long-hour daily hemodialysis [14,15]. More so, one may think that PD offers a better outcome due to the more stable metabolic milieu and avoidance of per-dialytic hypotension.

With our first case reported in this article, we can pledge for good maternal and fetal outcome in a peritoneal dialysis program. PD is safe, however it requires close clinical and paraclinical monitoring. Adapting the technique modalities (CAPD or APD) allowed us to lead the pregnancy to term and to the birth of a healthy child (now 13 years old). This experience will undoubtedly help treating our current pregnant patient ho chose PD.

In order to finally assess the actual benefits of PD compared to HDD, this issue should be examined using a multicenter comparative prospective trial (perhaps under the auspices and among the centres of the RDPLF).

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

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