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Peritoneal Dialysis Adequacy During the r-Hu EPO Treatment

Adekwatność dializy otrzewnowej w czasie leczenie erytropoetyną (r-Hu EPO)

The dialysis adequacy was considered as the treatment method which eradicated the symptoms and signs of uremia and led to the full rehabilitation of treated patients (37). The chronic renal failure patients substitutional treatment using both peritoneal dialysis and hemodialysis assures correction of biochemical disturbances but only 33% of dialyzed patients are fully rehabilitated (16). Such situation is caused by the uremic anemia (12).

The erythropoietin deficit is the main reason of the uremic anemia (15). The clinical effects of the erythropoietin treatment in hemodialyzed, peritoneal dialyzed and predialyzed patients were proved (6, 13, 14, 31).

The erythrocytes increment to the normal or almost normal levels may caused the dialysis kinetics changes. During the r-Hu EPO treatment in both hemodialyzed (2, 4, 9) and peritoneal dialyzed (19, 21, 30, 38) patients the dialysis effectiveness changes occurred.

The dialysotherapy adequacy is mainly caused by the dialysis efficiency and additionally by the residual renal function and metabolism state (37).

Taking into account own peritoneal dialysis kinetics parameters research results during the r-Hu EPO treatment (20) the dialysis adequacy was evaluated.

The aim of this study was the optimal dialysis scheme definition when the peritoneal transfer changes occurred as the r-Hu EPO treatment effect.

MATERIAL AND METHODS

Seven patients undergoing the intermittent peritoneal dialysis (IPD) were studied. In the group of patients were 6 males and 1 female in the age range 31-63 years (average 49.6 $\pm$9.6). The primary renal diseases were glomerulonephritis (5 patients) and obstructive nephropathy (2 patients).

The stable dialysis patients without specific complaints and peritoneal episodes were examined in this study. Their dietary compliance was adequate. The protein intake was maintained stable at 1.2 g/kg/day. Under this protein intake and absence of any catabolic state the urea average

concentration TAC (mg/dl BUN) (40) was not higher than 70 mg/dl. The patients were dialyzed three times per week, the dialysis time was calculated by the standard procedure according to Twardowski's equilibration test, body mass and residual renal function (36).

The r-Hu EPO was injected intravenously 3 times per week, with a starting dose 50 U/kg of body mass. The target Hb level was 10-12 g/dl and the desired increment rate was 1 g/month, otherwise Ht target level was 30-33% (max 36%) (13).

Before and during the r-Hu EPO treatment, when Ht exceeded 30% level the Peritoneal Equilibration Test (PET) at 1, 2, 4, 8 hours was carried out. The dialysis solution in the quantity of two liters per dwell containing sodium (132 mmol/l), calcium (1.75 mmol/l), magnesium (0.25 mmol/l), chloride (101 mmol/l), acetate (35 mmol/l), glucose (15 g/l) was used in this study.

SELECTED DIALYSIS ADEQUACY CRITERIA

1. D/P (dialysate/plasma) and D/Do (dialysate/dialysate) mean values courses comparison by the PET classification.

2. Optimal total weekly drainage assuring adequate weekly creatinine clearance using creatinine equilibration curves before and after the anemia correction drew up for the examined patients (37):

$$K_{Cr} = \frac{D}{P_{Cr}} V_d;\ K_{Cr_{optimal}} \approx 50 \text{ (l/week)}$$

where V_d – total weekly drainage dialysate volume, D/P = f(t), t – dwell time

3. Optimal total weekly drainage per 1 kg of ideal body weight (IBW) assuring peritoneal dialysis KT/V = 2.29 (34):

$$\frac{KT}{V_{weekly}} = \frac{D/P_{Ur}\ V_d}{0.6\ IBW} \approx 2.29\ (-)$$

4. Ultrafiltration adequacy evaluated as the ultrafiltration volume (UFV = f(t) per 1 g of absorbed glucose (B_{Glu} = f(t)) (37):

5. Total weekly dialysate drainage volume estimated as the dialysis index DI (33):

$$DI = \frac{V_d}{V_{rx}} \geq 1$$

$$V_{rx} = 0.23\ IBW - (2.6 + 1.44\ K_r)$$

where: V_{rx} – prescribed total dialysate volume to obtain BUN = 70 mg/dl, K_r – residual renal function

RESULTS

All patients responded to the r-Hu EPO treatment with 50-75 U/kg doses given intravenously three times per week. The hemoglobin and hematocrite increased significantly ($p < 0.001$), reaching the target level Hb 10-12 g/dl and Hct 30-36% within 8-12 weeks.

DIALYSIS ADEQUACY CRITERIA

1. Equilibration test: The mean values of D/P and D/D_0 parameters before the r-Hu EPO treatment were comprised in the high peritoneal transfer efficiency partition. After the r-Hu EPO treatment and the anemia normalization in the same group of patients the equilibration test curves changed its partitions attachments from higher to lower efficiency for 8-hour dwells, otherwise for short (1 and 2 hour) dwells the efficiency increment occurred (Figs. 1-3).

2. The weekly total mean drainage dialyzate volume assuring the weekly creatinine clearance $C_{Cr} = 50$ l/week is shown in the Fig. 4. The weekly drainage values after the anemia correction can be lower than before the r-Hu EPO treatment especially for 1 and 2 hours dwells. Continuous peritoneal dialysis using 8-hour dwells should be joined with the higher drainage volume and/or shorten dwells time.

3. The mean total weekly dialysate drainage per 1 kg of ideal body weight (IBW) assuring peritoneal dialysis $KT/V = 2.29$ is shown in Fig. 5. Using long time dwells (4, 6, 8 hours) the higher total weekly dialysate drainage volumes and/or shorten dwells time after the r-Hu EPO treatment are necessary.

4. The ultrafiltration volume per 1 g of absorbed glucose shows Fig. 6. The ultrafiltration for 1, 2, 4-hour dwells using 1.5 g/l glucose concentration solute before and after the r-Hu EPO treatment fulfills adequate dialysis ultrafiltration criterion. After the anemia correction the ultrafiltration efficiency decreased especially for 1 and 2-hour dwells which was closely connected with the glucose PET curve, presenting glucose transfer increment (Fig. 3).

5. Dialysis index DI is unsuitable to scheme dialysis treatment definition during the r-Hu EPO treatment. DI can precisely describe weekly total dialysate drainage volume for 4 and 8-hour dwells before EPO treatment only, when $D/P_{Ur} = 1$. For short dwells and after EPO treatment for 4, 8-hour dwells urea equilibrium level was not reached (Fig. 2). This is the reason DI is not useful to adequate dialyze procedure prescription.

DISCUSSION

The r-Hu EPO treatment and anemia correction influence on the peritoneal transfer kinetics are not univocally described in the literature (19, 21, 30, 38). Various peritoneal transfer research methods such as shortened PET and 4-hour dwells evaluation, hyperosmotic glucose concentration in dialyzate solution could be the reasons.

Own r-Hu EPO treated patients research results proved transfer increment as follows: creatinine – 40% (1 h dwells), 13% (2 h); phosphate – 72% (1 h), 35% (2 h); glucose – 23% (2 h). Transfer decrement occurred for 8-hour dwells as follows: creatinine 26%, phosphate 35%, sodium 10%, potassium 14%, glucose 22%, total protein 12% (20).

Increment of peritoneal transfer for 1 and 2 h dwells can be achieved by:

– augmented mesenteric blood flow which was stimulated by greater quantity

of glucose absorption, moving water into mesenteric capillaries which caused extension of capillary lumen and growth of endothelial connection diameters; maybe such effect was dependent on natriuretic factor, insulin or glucagon action (Maher's explanation of glucose influence on peritoneal transfer increment, (24))

– raised peritoneal permeability cuased by better hydration of interstitium and water channels extension (Wayland's theory (39))

– changed osmotic gradient between dialyzate solution and plasma (23, 35)

– mesothelium permeability changes caused by dehydration of mesothelium cell (greater quantity of absorbed glucose) and intracellular connections of mesothelium extension; urea as a smaller than creatinine and phosphate is transported intercellularly and transcellularly (Knapowski and Breborowicz's theory (5))

– increment in mesenteric perfusion by improved cardiac function (1, 3, 7, 22, 29)

– mesenteric blood flow changes caused by the capillaries fenestrating (25)

– change of mesenteric blood flow caused by plasma platelet mediator (serotonin, tromboxan B_2) (11, 32)

– blood water reduction that occurs at high Hct may have an impact on stagnant fluid film in capillary and changes dialysate clearance (1, 25)

– increment of oxygen supply to peritoneal tissue (26, 27).

No information is available on the effect of anemia correction on peritoneal lymphatic absorption and osmotic gradient. More effective glucose absorption during 1h and 2h dwells and faster osmotic equilibrium after r-Hu EPO treatment may have caused the stronger influence of lymphatic flow at 8h dwells and net peritoneal transfer (peritoneum oedema protection mechanism described by Guyton (17, 18)).

It seemed to be especially important to repeat PET during the anemia correction by the r-Hu EPO treatment. It will allow to define new, actual dialysis scheme and adequate dialysis performance. On the basis of PET results the weekly total drainage volume can be evaluated in order to obtain weekly total creatinine clearance an weekly KT/V in adequacy area (34). The creatinine blood concentration could not exceed 12-14 mg/dl, BUN should be lower than 70 mg/dl, stable protein intake 1.2 g/kg/day (10).

Total weekly drainage increment should be joined with dwells time decrement, avoiding higher than 2 l solute volumes per dwell. The intraabdominal pressure increment caused by the higher dialyzate volume stimulates the lymphatic flow, decreasing dialysis effectiveness (17, 25).

There are not in clinical practice medicines limiting the lymphatic flow in peritoneal dialysis, because of cholinergic crises risk after neostigminum and other cholinergic drugs (23) and not clear effect of phosphatydylocholine action (8, 28).

The current view of CAPD adequacy is based mainly on the clinical grounds, the patient's feeling of well-being, and the survival date (10). It is very important to apply some dialysis parameters optimizing dialysis scheme to avoid non-adequate treatment and uremia.

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STRESZCZENIE

Powtarzanie otrzewnowowego testu ekwilibracji (PET) w czasie leczenia erytropoetyną umożliwia określanie nowego, aktualnego schematu dializy. Na podstawie wyników testu możliwe jest obliczenie całkowitego tygodniowego drenażu płynu dializacyjnego, zapewniającego optymalny tygodniowy klirens kreatyniny oraz optymalną wartość wskaźnika Kt/V.

LIST OF FIGURES

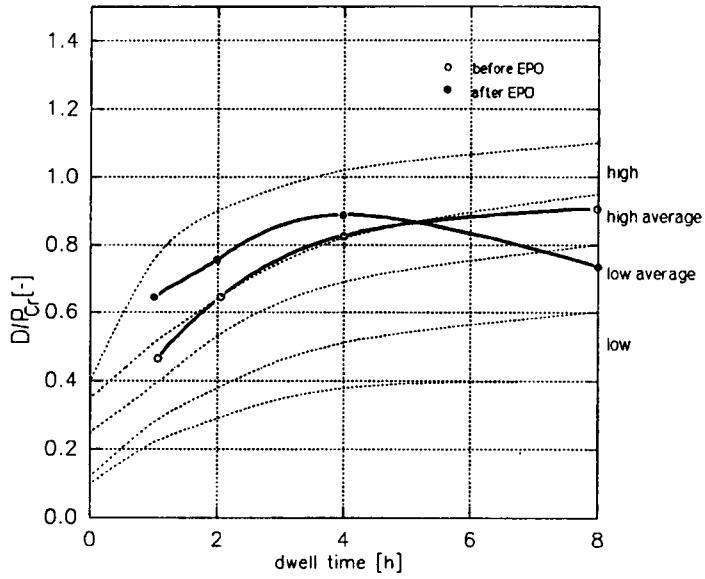

Fig. 1. Peritoneal equilibrium test for creatinine

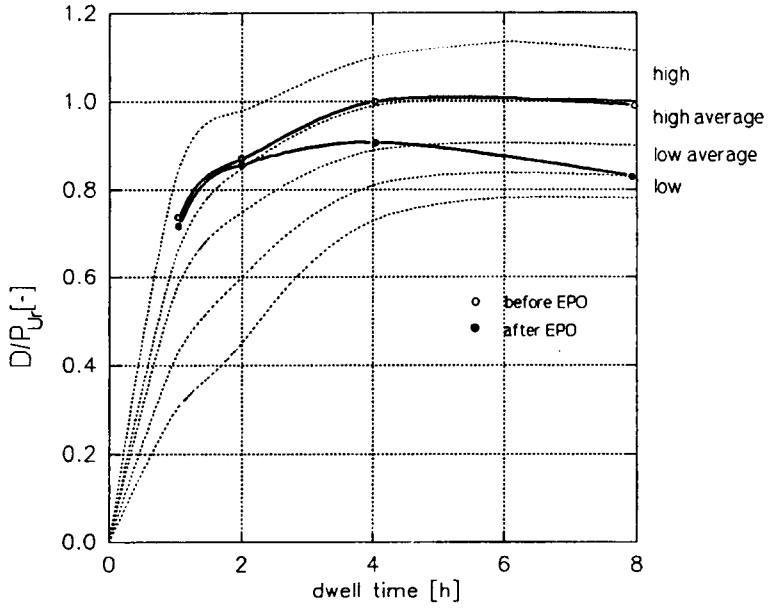

Fig. 2. Peritoneal equilibrium test for urea

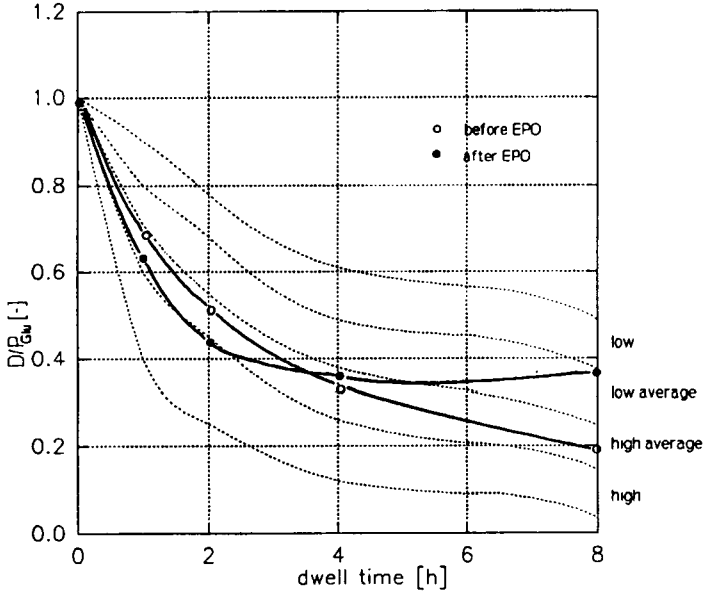

Fig. 3. Peritoneal equilibrium test for glucose

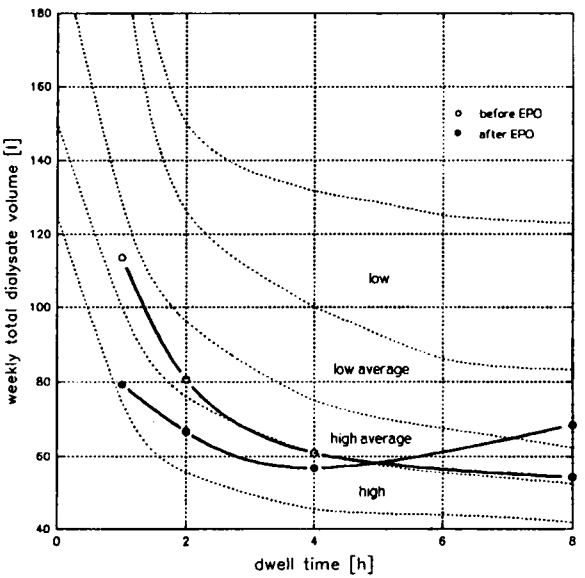

Fig. 4. Total weekly drainage assuring adequate weekly creatinine clearance

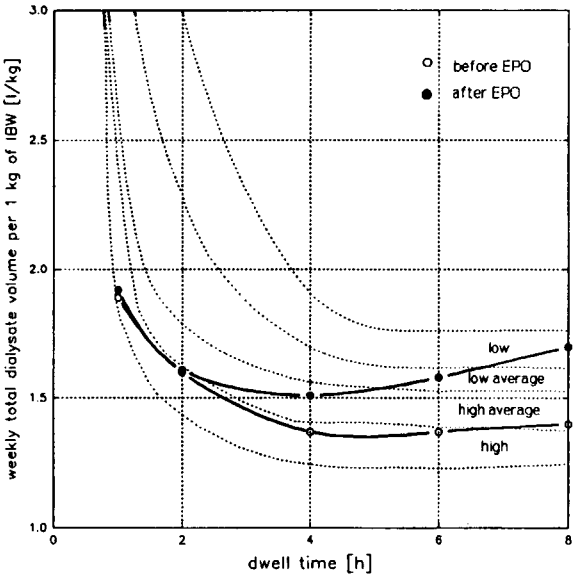

Fig. 5. Total weekly drainage per 1 kg of IBW assuring ideal peritoneal dialysis KT/V = 2.29

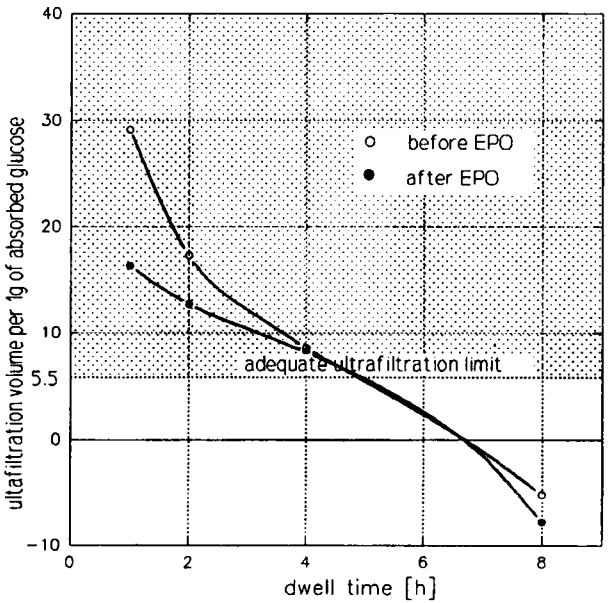

Fig. 6. Ultrafiltration adequacy