Prognostic significance of hemoperitoneum in peritoneal dialysis

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SUMMARY

According to previous reviews, hemoperitoneum episodes appear in 6.1-8.4% of the peritoneal dialysis patients, and they are severe in a 20% of them. Due to the absence of severe hemoperitoneum in our peritoneal dialysis program, we retrospectively reviewed hemoperitoneum non-related with abdominal surgery or catheter placing. We analyzed its incidence, etiology, prognostic and clinical outcome, as well as the possible effect of recurrent hemoperitoneum on peritoneal function. A total of 132 patients were treated in our centre during a period of 173 months. Mean age at the beginning of peritoneal dialysis was 59 ± 17.1 years, 43.2% were females, and 22.8% of them were menstruating women. Twenty-two patients had at least one hemoperitoneum episode during follow-up, with an incidence of 17%. The mean time interval between the start of peritoneal dialysis and the first hemoperitoneum episode was 0,66 ± 0,94 years (range: 0.01-3.20 years). 73% were women. Most cases (59%) were due to menstruation. Remarkably, all the menstruating women presented hemoperitoneum at least once with a high incidence of recurrent episodes. The other hemoperitoneum episodes were mainly of unknown etiology (32% of patients), being this one the main cause in males. We only observed two more cases: a male who presented hemoperitoneum related to dicumarinic overdose and a female who presented hemoperitoneum due to mesenteric ischemia. All the 22 patients had a favourable outcome, except for the woman with mesenteric ischemia, what represented an incidence of 4.5% of severe hemoperitoneum. No significant association was found between episodes of hemoperitoneum and aspirin treatment, dicumarinic treatment or the presence of coagulopathy. There was no association either between recurrent hemoperitoneum and the number of peritonitis episodes, peritoneal function or technique survival. In conclusion, hemoperitoneum is a common and usually benign problem in peritoneal dialysis patients, frequently due to retrograde menstruation, and no deleterious long-term effects were found in patients with recurrent hemoperitoneum.

Key words: *Hemoperitoneum. Hemorrhagic peritoneal fluid. Peritoneal dialysis complications.*

RESUMEN

Según revisiones previas, entre el 6,1 y el 8,4% de los pacientes en diálisis peritoneal presentan episodios de hemoperitoneo y su pronóstico es grave hasta en un 20% de casos. Ante la ausencia de hemoperitoneos graves en nuestro programa de diálisis peritoneal, decidimos revisar retrospectivamente los hemoperitoneos no relacionados con la cirugía abdominal ni con la colocación del catéter. Analizamos su incidencia, etiología, pronóstico y evolución, así como el efecto del hemoperitoneo recurrente sobre la función peritoneal en 132 pacientes con edad media al iniciar diálisis peritoneal de 59 ± 17,1 años, de los que el 43,2% eran mujeres y, de éstas, un 22,8% tenían la menstruación. Durante el seguimiento, 22 pacientes tuvieron al menos un episodio de hemoperitoneo, con una incidencia del 17% y un tiempo medio en diálisis peritoneal hasta el primer episodio de hemoperitoneo de 0,66 ± 0,94 años (rango: 0,01-3,20 años). El 73% eran mujeres. La menstruación fue la causa del 59% de los hemoperitoneos. El 32% fueron de etiología desconocida, siendo ésta la causa más frecuente en varones. Únicamente un varón presentó hemoperitoneo en relación a sobredosis de dicumarínicos y una mujer presentó hemoperitoneo secundario a una isquemia intestinal. La evolución fue favorable en todos ellos a excepción de la paciente con isquemia mesentérica, lo que supuso una incidencia de hemoperitoneos graves del 4,5%. El tratamiento antiagregante o anticoagulante y la presencia de coagulopatía no se relacionaron con la aparición de hemoperitoneo. Tampoco hubo relación entre el hemoperitoneo recurrente y el número de peritonitis, el deterioro de la función peritoneal y la supervivencia de la técnica. En conclusión, el hemoperitoneo es un problema frecuente en diálisis peritoneal y generalmente benigno, a menudo asociado a la menstruación, y sin efectos negativos a largo plazo en los pacientes con hemoperitoneo recurrente.

Palabras clave: Hemoperitoneo. Líquido peritoneal hemático. Complicaciones en diálisis peritoneal.

INTRODUCTION

Hemoperitoneum (HP) during peritoneal dialysis (PD) is a complication with an incidence ranging 6.1%-8.4%, according to previous reviews.[1-3] The characteristics of the peritoneal fluid may vary from a pinkish to bright red coloration, causing in the latter case big alarm in both the patient and the health care personnel. Most of the PD clinical guidelines clas-

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sify HP as mild, moderate, and severe.[4] Most of the patients are childbearing-aged women, and are related to menstruation or ovulation.[5-6] The course is asymptomatic with a benign prognosis. However, in the classical study by Greenberg et al. published in 1921, 10% of the cases were moderate with longer duration and higher severity of the hemorrhage, and up to 20% of the HP episodes were classified as severe producing hemodynamic instability, requiring transfusions, complex complementary examinations, or urgent surgical interventions. Moderate and severe HP tends to be secondary to intra-abdominal pathology such as rupture of follicular ovarian cysts, liver or kidney cysts, liver tumors, aneurisms of the intra-abdominal arteries, spleen rupture, pancreatitis, radiotherapy, mechanical trauma related to the catheter,[3,6-18] or sclerosing peritonitis.[19]

Independently of the etiology and prognosis of HP, the presence of blood within the abdominal cavity may have implications on survival of the dialysis technique due to the inflammatory and fibrotic effect of blood itself,[20] even more considering that the most frequent and recurrent HP episodes are those related with menstruation.[1-2,5-6] In this sense, in 2002, Tse et al. revised the prognostic value of recurrent HP, and they could not find any relationship with worsening of the peritoneal transport or technique survival.[2]

From the onset of our PD program, HP episodes have been rare. For this reason, we decided to retrospectively review HP episodes detected for the last 14 years in order to study their frequency, etiology, severity, management and course, and analyze the influence of recurrent HP on peritoneal function and technique survival.

MATERIAL AND METHODS

We have retrospectively reviewed HP episodes not related with placement of peritoneal catheter or with abdominal surgery occurring at our PD program from September of 1991 to February of 2006.

The following demographical and clinical data were gathered: etiology of renal failure; personal history of diabetes mellitus, diverticulosis, coagulation impairments, or abdominal surgery; anti-aggregant or anti-coagulant therapy; peritoneal balance test (PBT) at the beginning and the end of the follow-up; time on PD; transfer to hemodialysis (HD) and reason for it; and cause of death, if it happened. About HP episodes, we have studied their number, severity, time elapsed from the beginning of PD, diagnostic examinations carried out, management, and course. Recurrent HP has been defined as the existence of more than one episode.

The data have been analyzed by using the statistical software SPSS for Windows, version 11.5, using the appropriate non-parametric tests (Mann-Whitney U test, and Fisher's exact test) to compare the patients with recurrent HP with those having never had HP.

RESULTS

During the 14 years and 5 months of the study period, a total of 132 patients were treated with PD, with a mean age at the treatment beginning of 59.0 ± 17.1 years and mean follow-up time of 1.95 ± 1.78 years (range: 0.01-7.26 years). 43.2% of the patients were women, 29.8% younger than 50 years, and of them, 76.5% were menstruating. Nine percent of the patients (n = 12) were on PD for more than 5 years. Among the causes of primary kidney disease, the most common ones were diabetic nephropathy (22.7%), polycystic renal disease (6.1%), and systemic amiloidosis (8.3%).

Twenty-two patients had at least one HP episode, which represented an incidence of 17%. The mean time from the beginning of PD to the first HP episode was 0.66 ± 0.94 years (range: 0-3.20 years). A clear predominance of the female gender was observed: there were 16 women (73%) and 6 men (27%).

The etiology was different according to sex. In 11 out of the 16 women, the HP episode was attributed to backwards menstruation, in 2 to ovulation, and in 2 the etiology was unknown, and one was associated to mesenteric ischemia. In six patients with HP, 5 were of unknown origin and one was due to overdose of dicoumarin agents.

All the HP episodes, but one female patient dying of mesenteric ischemia, had a favorable course. So that, only 4.5% of the patients with HP and 0.9% of all HP episodes observed had an unfavorable course and could be classified as severe.

About diagnostic examinations, cell counts were commonly done, and cultures of the peritoneal fluid and plain abdomen X-ray films were occasionally carried out; in just one case abdominal ultrasound was performed.

About management, only 3 out of 22 patients required peritoneal lavage and administration of intraperitoneal heparin. None of them required blood transfusions, arteriography, or urgent surgery.

Table I shows the incidence of HP in relation to the presence of possible promoting factors, such as anti-aggregant therapy, anti-coagulation, and the presence of coagulopathy, diverticulosis, or other abdominal pathologies. None of them showed any significant association with HP occurrence.

HP was recurrent (range: 2-15 episodes) in 16 out of 22 patients (73%) (table II). Thirteen were childbearing-aged women, HP being attributed to menstruation or ovulation. There also were two men with two episodes each, and an old lady with three episodes, all of them of unknown origin. In 10 patients (10 women, 9 with HP attributable to menstruation) in whom we have valid initial and final PBT, we have not observed significant changes in peritoneal transport (fig. 1). Those patients with recurrent HP did not show a higher rate of peritonitis or higher risk for transfer to HD. Besides, and according to their younger age, these patients received more renal transplants and died less (table III).

DISCUSSION

When comparing our data to other published series, the higher incidence of HP (17% *vs* 6-8%) in our program is striking, in spite of the older age of our patients [1] and the fact of having excluded HPs secondary to surgery or other procedures, which have been included in previous publications.[1-2] A likely explanation is that in the review by Greenberg[1] only 15% of the childbearing-aged women had menstruations, whereas in our series 76.5% still had it, similar to the series by Holley et al.[21] Virtually all women with regular menstruation in our PD

Table I. Possible factors promoting HP

	Total: 132	No HP: 110	Single HP: 6	Recurrent HP: 16	P*
Anti-coagulation	10 (7.6%)	8 (7.3%)	1 (16.7%)	1 (6.3%)	NS
Anti-aggregation	31 (23.5%)	27 (24.5%)	2 (33.3%)	2 (12.5%)	NS
Coagulopathies	2 (1.5%)	2 (1.8%)	0 (0%)	0 (0%)	NS
Diverticulosis	6 (4.5%)	4 (3.6%)	0 (0%)	2 (12.5%)	NS
Previous abdominal surgery	30 (22.7%)	27 (24.5%)	1 (16.7%)	2 (12.5%)	NS
Severe abdominal pathology in PD	8 (6.1%)	8 (7.3%)	0 (0%)	0 (0%)	NS

Fisher's exact test* for comparison of patients having never presented HP and those having recurrent HP.
(HP = hemoperitoneum, PD = Peritoneal dialysis, NS = not statistically significant [P > 0.05]).

Table II. Baseline characteristics of the patients by absence of HP, one HP episode, or recurrent HP

	Total: 132	No HP: 110	Single HP: 6	Recurrent HP: 16	P
Women (%)	57 (43.2%)	41 (37.3%)	2 (33.3%)	14 (87.5%)	< 0.001*
Age of PD onset (years)	59.0 ± 17.1	61.3 ± 16.0	63.2 ± 14.2	41.5 ± 16.4	< 0.001**
Time on PD (years)	1.95 ± 1.78	1.82 ± 1.66	2.07 ± 2.44	2.88 ± 2.10	0.02**
Time on PD until first HP episode (years)	–	–	1.27 ± 1.24	0.41 ± 0.70	-
Diabetes (%)	42 (31.8%)	37 (33.6%)	3 (50%)	2 (12.5%)	NS*
Poliycystic renal disease (%)	8 (6.1%)	4 (3.6%)	1 (16.7%)	3 (18.8%)	0.04*
Amiloidosis (%)	11 (8.3%)	9 (8.2%)	1 (16.7%)	1 (6.3%)	NS*

Fisher's exact test* or Mann-Whitney U test** for comparison of patients having never presented HP and those having recurrent HP.
(PD = peritoneal dialysis, HP = hemoperitoneum, NS = not statistically significant [P > 0.05]).
The data are presented as mean ± SD or N (%), depending on the cases.

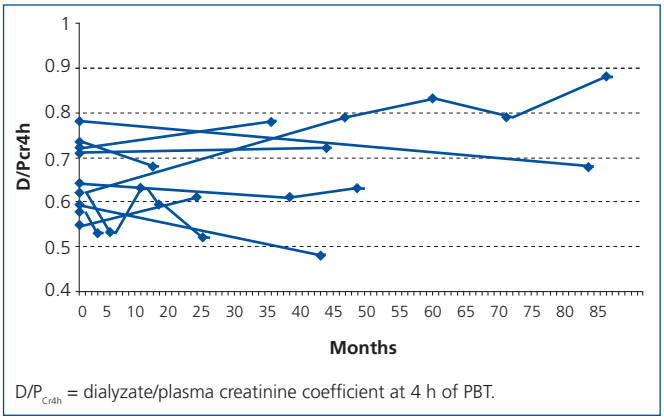

Figure 1. Evolution of creatinine peritoneal transport in patients with recurrent hemoperitoneum.

program presented recurrent HP throughout the follow-up period. It is likely that the technical advances in dialysis and the introduction of erythropoiesis-stimulating factors may explain the higher percentage of women with regular menstruation currently.[22]

In spite of the fact that backwards menstruation is the most common etiology of HP in PD, other possible causes are described in the literature among childbearing-aged women, such as endometriosis or rupture of a follicular cyst.[6-8] We have observed no case of that.

Most HP cases in men are idiopathic. The hypothesis that they might be caused by damage to the venules within the epiploon secondary to catheter-related trauma,[2] which rarely may be severe,[18] has been postulated.

It was very significant that 8 patients were diagnosed with severe intra-abdominal pathology while on PD program (1 pancreatitis, 3 mesenteric ischemia episodes, 1 liver carcinoma, and 3 intestinal perforations), some of which died, none of them with HP. One patient was diagnosed with sclerosing peritonitis one year after being transferred to HD after 4.5 years on PD due to associated clinical pathology, the first symptom being the presence of ascites that was never hematic. Thus, although severe abdominal pathology is relatively common among PD patients, it is not so common that it clinically manifests as HP. It is also interesting to underline that none of the two patients with severe coagulation impairments (hemophilia) presented HP. Supporting this finding, we cite the experience by Bajo et al.[23] that treated with PD and no re-

Table III. Influence of HP occurrence on the course of the patient on PD

	Total: 132	No HP: 110	Single HP: 6	Recurrent HP: 16	P*
Transfer to HD	41 (31.1%)	36 (32.7%)	2 (33.3%)	3 (18.8%)	NS*
Deaths in PD	50 (37.9%)	45 (40.9%)	3 (50%)	2 (12.5%)	0.03*
Renal transplant	30 (22.7%)	23 (20.9%)	0 (0%)	7 (43.8%)	0.06*
Peritonitis/patient-year	0.80 ± 1.84	0.84 ± 1.98	0.48 ± 0.56	0.64 ± 1.00	NS**

Fisher's exact test* or Mann-Whitney U test** for comparison of patients having never presented HP and those having recurrent HP.
(HD = hemodialysis, PD = peritoneal dialysis, HP = hemoperitoneum, NS = not statistically significant [P > 0.05]).

levant complications three patients with hereditary coagulopathies. We have not observed an increase in the incidence of HP with the use of dicoumarin agents or aspirin either.

To assess HP, in virtually all the cases only anamnesis, physical examination, and assessment of the severity of the HP episode, as well as cellular count of the peritoneal fluid were used. Performance of other complementary examinations was exceptional. In most of the cases, the episodes were self-limited, and few patients required peritoneal lavage, arteriography, or surgery.

About the severity, only one HP episode had a fatal course: this was a case of acute abdomen secondary to mesenteric ischemia where HP was an epiphenomenon of little relevance due to its mild intensity. Some observations suggest a relationship between late-onset HP during PD (more than 5 years) and sclerosing peritonitis.[1,19] In our series, all HP episodes have occurred before 3.5 years from the beginning of PD and most of them have been mild considering the intensity of the hemorrhage, the absence of abdominal symptoms, and their short duration.

Similarly to Tse et al.[2] we have not observed repercussions of HP on the technique survival, the peritoneal transport, or peritonitis rates, although the mean time on PD in our series was shorter.

To conclude and based on our experience, HP during PD is a common problem with a good prognosis, being more common in young women and almost always related to menstruation, whereas in men the etiology is usually unknown and its incidence is smaller. Anyhow, we have not observed a 20%-rate of severe HP as described in the literature.

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