



Determination of prevalence, symptoms, signs, complications and mortality rate in patients with encapsulating peritoneal sclerosis in Iran

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ABSTRACT

Introduction: Patients suffering from chronic peritoneal dialysis (PD) encapsulating peritoneal sclerosis (EPS) are more likely to have a small bowel obstruction, sepsis, and death.

Objectives: This study was conducted to investigate how the EPS is prevalent in Iranian patients suffering from continuous chronic PD. It was also tried to detect risk factors, clinical symptoms, signs, complications and mortality rate.

Patients and Methods: The study population consisted of all incident patients undergoing PD for more than 6 months from 1994 until 2015. The criterion to detect EPS was either positive radiological or surgical results in terms of the clinical short bowel obstruction (SBO) or a thickened peritoneum in the absence of an alternative etiology. Control groups were non-EPS patients that were twice the EPS patients. These patients were being followed up for at least 6 months after the end of PD.

Results: This study showed that in people with EPS, 58.3% were women. The mean age was 47 years. The duration of treatment with PD in these patients was 58 months. Mortality rate in patients with EPS was 61.1 percent.

Conclusion: It is advisable that individuals should be treated with chronic PD for a maximum period of three to 4 years.

Implication for health policy/practice/research/medical education:

Encapsulating peritoneal sclerosis (EPS) is a grave and life-threatening side effect of peritoneal dialysis (PD). The early clinical symptoms and signs are directly associated with disturbances in gastrointestinal transit. The most common findings are abdominal pain, nausea, vomiting, anorexia, abdominal mass and significant protein loss that leads to malnutrition, and incomplete or complete small-bowel obstruction. Though the observed findings may be powerfully indicative of EPS, radiologic examination is required to confirm a clinical diagnosis of EPS. Not infrequently, laparotomy or laparoscopy is required to establish the diagnosis. The main elements in conservative management are early diagnosis, cessation of PD with transfer to hemodialysis, continued bowel rest with total parenteral nutrition, and corticosteroids. If conservative treatment does not ameliorate the symptoms of EPS, surgical treatment should be envisaged. By definition, EPS refers merely to the encapsulating and ileus stages of the disease. However, the early identification should be recognized before the symptoms of ileus occur. Hence, an effort to cure the illness with medical treatment can be conducted. Further studies concerning prevention, early detection, and treatment of EPS are also necessary.

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Introduction

One of the challenges of chronic peritoneal dialysis (PD) therapy is encapsulating peritoneal sclerosis (EPS). It involves a gradual progressive inflammation that influences the peritoneum diffusely; consequently, the

small bowel obstruction (SBO) may occur because of adhesions or mural fibrosis from the adjacent sclerotic peritoneum. In the end, the peritoneum is substituted with thickened vascularized sclerotic tissue that looks like an "abdominal cocoon" (1,2). Ultrafiltration failure (UFF)

is the result of the peritoneum vascularization (3,4). EPS can develop gradually and remain asymptomatic for a long-time. The first symptoms may appear as early as one year after the start of PD or years after transplantation or transfer to hemodialysis (1,5-8).

Several studies have reported that EPS has a high mortality rate ranging from 24 to 54.5% (1,9). The overall prevalence within the PD population is less than 2%, which is not high (1,9,10). Studies show that extended PD leads to increased incidence of EPS, which is not frequent among patients undergoing treatment with PD for less than two years (7,8,11). Data on the pathogenesis of EPS is scarce. Nevertheless, several risk factors have been suggested including PD duration. Other risk factors that have variably been associated with the risk of EPS include bio-incompatible dialysate, administration of beta blocker drugs, severe chemical or infective peritonitis, and genetic factors (3,4,9,10,12,13).

The criterion to detect EPS was either positive radiological or surgical results such as clinical short bowel obstruction (SBO) or a thickened peritoneum in the absence of an alternative etiology (1,7,8,11).

Objectives

Data on EPS in Iranian PD individuals is scarce. The aim of the present study was to determine the rates of EPS in the target PD population. It was also tried to evaluate the risk factors, clinical presentation, diagnosis, control, and results of affected individuals.

Patients and Methods

Study population and research design

Our research is a cross-sectional study that was conducted in all centers of PD in Iran. The study protocol was approved by the ethics committee of Tehran University of medical sciences. The study population consisted of all incident patients undergoing PD for more than 6 months from 1994 until 2015. All individuals used Baxter PD systems and followed lactate-based fluid regimes. The criterion to detect EPS was either positive radiological or surgical results regarding clinical SBO or a thickened peritoneum in the absence of an alternative etiology (1,7,8,11). Control groups were non-EPS patients that were twice as many as EPS patients. These patients were being followed up for at least 6 months after the end of PD. All Iranian centers of PD provided the present study with patients' demographic and clinical data, which featured the following items; prevalence of EPS, age, gender, administration of beta blockers, duration of PD, UFF, peritoneal equilibrium test (PET), peritonitis frequency, imaging finding, relevant surgical results, and patient's outcome.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. Informed consents were obtained from all patients. The study was approved by the ethical committee

of Tehran University of Medical Sciences. This paper is part of Fellowship thesis of Farnaz Tavakoli, in Department of Nephrology, Tehran University of Medical Sciences. The study was supported by a grant from Tehran University of Medical Sciences (#9211402001).

Statistical analysis

Collected data were analyzed using the SPSS software (statistical package for the social sciences version 21.0 SPSS Inc., Chicago Ill, USA). Quantitative variables were expressed as mean, standard deviation or median and qualitative variables were expressed as count and percentage. The independent-sample *t* test or the Mann Whitney U test was used to compare quantitative variables in EPS and control groups. The chi-square and Fisher exact test were used to compare qualitative variables in two groups. The Pearson's correlation coefficient test was used to evaluate the significant correlations between the quantitative parameters within each group. Additionally *P* values less than 0.05 were considered significant.

Results

According to our investigation, 3800 patients underwent PD treatment since 1994 until 2015 in Iran. A prevalence rate of 0.94% was observed among 36 cases of EPS; 11 patients (30.5%) were suffering from EPS after modality of renal replacement therapy was changed (2 cases after renal transplantation were done successfully and 9 cases after hemodialysis were started). EPS patients had a mean age of 47 years. Affected patients had longer median PD duration in comparison with the unaffected patients, but it was not significant (58 months versus 48 months; $P = 0.279$). Around 41.7% and 58.3% of the EPS patients were men (15 individuals) and women (21 individuals) respectively (in comparison with the unaffected PD population that were 59.5% male and 40.5% female). EPS was observed in one patient within the first year of PD treatment.

The frequency of clinical symptoms and signs of SBO in EPS patients versus control group were (91.7% versus 8.9%; $P < 0.001$), recurrent positive culture peritonitis (>1 year) (91% versus 25.3%; $P < 0.001$), recurrent negative culture peritonitis (>1 year) 36.1% versus 8.9%; $P < 0.001$), abdominal mass (16.7% versus 0%; $P < 0.001$), weight loss (77.8% versus 3.8%; $P < 0.001$), bloody effluent (38.9% versus 0%; $P < 0.001$), UFF (97.2% versus 22.8%; $P < 0.001$), administration of beta blockers (52.8% versus 26.9%; $P = 0.007$) and administration of PD solutions with high glucose content (86.1% versus 22.8%; $P < 0.001$) (Table 1). PET in EPS patients were low in 2.85%, below average in 0%, high in 80% and above average in 17.15% whereas in control groups were 16.5%, 19%, 13.9% and 50.6% respectively ($P < 0.001$).

Around 33 patients with EPS underwent abdominal imaging (radiography, US, CT scanning). The results confirmed the clinical suspicion of EPS in 23 cases (69.7%). Laparotomy and omental resection was

Table 1. Comparison of clinical parameters and risk factors in EPS group and control group

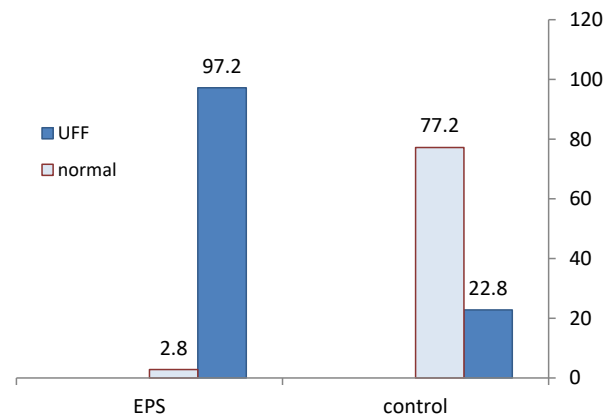
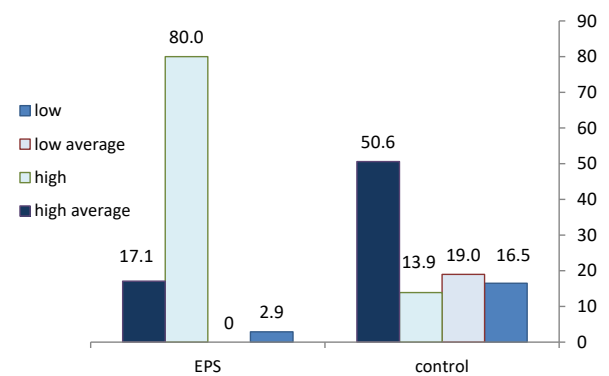
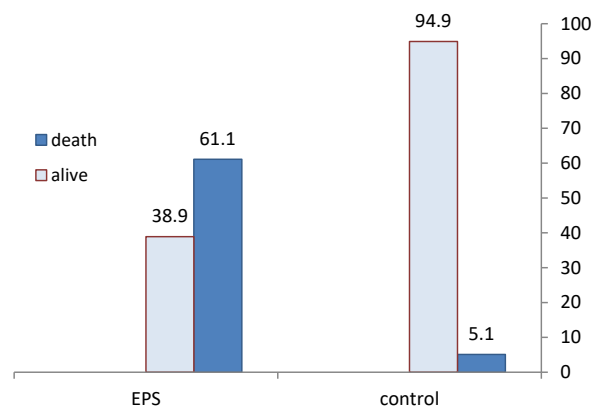
| Parameter | EPS group | Control group | P value |
|--|-----------|---------------|---------|
| Median duration of PD | 58 months | 48 months | 0.279 |
| Clinical SBO | 91.7 | 8.9 | <0.001 |
| Recurrent peritonitis (positive culture) | 91 | 25.3 | <0.001 |
| Recurrent peritonitis (negative culture) | 36.1 | 8.9 | <0.001 |
| Abdominal mass | 16.7 | 0 | <0.001 |
| Weight loss | 77.8 | 3.8 | <0.001 |
| Bloody effluent | 38.9 | 0 | <0.001 |
| UFF | 97.2 | 22.8 | <0.001 |
| Use of beta blockers | 52.8 | 26.9 | 0.007 |
| Use of PD solution with high glucose content | 86.1 | 22.8 | <0.001 |

Abbreviations: SBO, Short bowel obstruction; UFF, ultrafiltration failure; PD, peritoneal dialysis.

performed on seven patients with EPS. Thickened peritoneum, encapsulated collection with cocooned bowel and bloody effluent were observed in all cases with laparotomy findings of EPS. Three patients undergoing the aforementioned operation are alive (42%). The peritoneal biopsy of these patients confirmed the classic pathologic features of EPS. According to chronic PD complications and EPS, 22 patients died. Thus, mortality rate reached 61.1%. About 5.06% patients died because of chronic PD complications in control groups ($P < 0.001$). Ten individuals were diagnosed with EPS shortly prior to death. All individuals died because of sepsis brought about by SBO (Table 1) (Figures 1 to 3).

Discussion

According to the results of the present study, it could be interpreted that EPS has a 0.94% prevalence in Iran, which was reported by other studies as well (1,5,6,9,10,14). As in other investigations, the impact of duration of PD on the development of EPS was shown in our research. Following the switch to hemodialysis or receiving a kidney transplant, EPS was observed in 30% of individuals. This result is consistent with other studies (5,6,8). We believe that the occurrence of EPS after transplantation could be associated with the proportion of immunosuppression. Nevertheless, it is likely that ceasing the PD provides fibrin, pro-inflammatory, and pro-fibrotic mediators with the opportunity for proliferation in the peritoneal space that leads to sclerosis peritonitis progression and worsening the condition (15). The relationship between repeated episodes of peritonitis more than one year and the following development of EPS was also investigated in this study. We believe that chemical or infectious peritonitis might mediate EPS too (15,16). It was shown that EPS group had a high rate of recurrent peritonitis. In general, high rate of bowel obstruction was diagnosed late in the patients under study and thus, the prognosis

**Figure 1.** Comparison of ultrafiltration failure (UFF) in EPS group and control group.**Figure 2.** Comparison of peritoneal equilibration test (PET) in EPS group and control group.**Figure 3.** Comparison of mortality in EPS group and control group.

was poor. Defining EPS at an early stage before severe peritoneal involvement has happened to constitute a challenge. In most of our patients, the classic finding of EPS has been confirmed by CT scanning, although the scans were conducted when peritoneal sclerosis was well

developed. Thus, when EPS is suspected, CT scanning will be performed as an early procedure to detect potential early cases (17). In terms of managing the modalities, the mainstay of patients' handling was satisfactory at our center. Changing the dialysis modality and supplying parenteral nutrition in most of the individuals were our main procedures. Successful results were observed in three individuals who underwent omental resection and adhesion lysis. They had no relapse of symptoms and no long-lasting nutritional difficulties. With regard to history, surgical intervention did not bring about significant results because of high rates of complications consisting sepsis (18,19). Kawanishi et al studied fifty individuals suffering from EPS. Their encapsulating membrane was removed by surgery. Two patients died due to surgical complications but the remaining patients all had a successful outcome (14). EPS is the complication of prolonged PD therapy. PD therapy increases the risk of EPS that is correlated with the duration of PD therapy (7,20-22). It has been shown in several studies that patients with EPS have high mortality rate and poor outcome, thus early diagnosis of EPS is very important. Physicians must be conscious of the symptoms and signs of EPS, especially in patients with long-term PD who have gastrointestinal symptoms and signs (7,11).

Conclusion

EPS is a grave and serious complication of PD. The early clinical symptoms and signs are directly associated with disturbances in gastrointestinal transit. The extremely common findings are abdominal pain, nausea, abdominal mass, vomiting, anorexia, and significant protein loss that lead to malnutrition, and incomplete or complete small-bowel obstruction. Though the detected findings may be strongly suggestive of EPS, radiologic examination is required to confirm a clinical diagnosis of EPS. Not infrequently, laparotomy or laparoscopy is essential to establish the diagnosis. The key elements in conservative treatment are early diagnosis, cessation of PD with transfer to hemodialysis, continued bowel rest with total parenteral nutrition, and corticosteroids. If conservative treatment does not ameliorate the symptoms of EPS, surgical treatment should be envisaged. By definition, EPS refers merely to the encapsulation and ileus stages of illness. However, the early identification should be determined before the symptoms of ileus appear. Further studies concerning prevention, early detection, and treatment of EPS are also necessary.

Limitations of the study

This study has a number of limitations. First, retrospective studies are prone to inherent weaknesses. In addition, the first delayed diagnosis after starting our PD program would suggest that some cases might have been missed. Nevertheless, the rates of EPS presented in this study are consistent with other studies. Since the beginning of our program, a low rate of EPS, consistent with other reports,

have been observed at our centers. The relationship between duration on PD and EPS has been highlighted by the present study. It is worth noting that the mortality rate was high in our study, but surgical techniques could bring about desirable outcomes even in the severely affected cases.

Authors' contribution

FT was the principal investigators of the study. FT and FY participated in preparing the concept of design. FT and DB revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revisited the manuscript, and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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