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Bulletin de la Dialyse à Domicile

Seasonal variations of enteric peritonitis in Belgium and France : from RDPLF data

(Variation saisonnière des péritonites entériques en Belgique et France : d'après les données du RDPLF)

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Summary

Little information is available on the seasonal ecology of germs responsible for peritoneal dialysis peritonitis. We performed a retrospective study based on RDPLF data covering the last 20 years and 20411 episodes of peritonitis.

We show that the percentage of enteric peritonitis is highest in summer, lowest in winter and identical in spring and autumn. This higher proportion of organisms of enteric origin in summer has itself tended to increase in recent years.

We postulate that a food contamination by enteric germs associated with an increased bacterial translocation at the level of the digestive tract itself favoured by constipation, as well as changes of the food nature could be responsible for this phenomenon.

These seasonal variations may suggest that probabilistic initial antibiotic therapy should be adapted in cases of suspected peritonitis before the results of bacteriological analysis.

Key words : peritoneal dialysis, seasonal variation, peritonitis, enteric peritonitis

Résumé

Peu d'informations sont disponibles sur l'écologie saisonnière des germes responsables des péritonites en dialyse péritonéale. Nous avons réalisé une étude rétrospective à partir de la base de données du RDPLF portant sur les 20 dernières années et 20411 épisodes de péritonites.

Nous montrons une proportion de péritonites à germes entériques plus élevée en été, la plus faible en hiver et identique au printemps et en automne. Cette proportion de germes d'origine entérique plus élevée en été a elle même tendance à augmenter ces dernières années.

Nous postulons qu'une contamination alimentaire par des germes entériques associée à une translocation bactérienne accrue au niveau du tube digestif, elle-même favorisée par la constipation et des changements saisonniers d'alimentation pourrait être responsable de ce phénomène.

Ces variations saisonnières pourraient suggérer d'adapter l'antibiothérapie probabiliste lors d'une suspicion de péritonite, avant les résultats de l'analyse bactériologique.

Mots clés : dialyse péritonéale, variation saisonnière, péritonite, péritonite entérique

INTRODUCTION

Peritonitis related to peritoneal dialysis has long been considered as the Achilles heel of peritoneal dialysis. Today, they represent 14% and 26% of the causes of transfer to hemodialysis centers in France and Belgium respectively, and 3% and 2% of deaths [1]. Moreover, the identification of the causative organism varies from 10% to 50% from one center to another [2]. The ISPD has published a recommendation on the first choice of antibiotic before knowing the organism [3], recently synthesized by Taghavi and Dratwa [4]. However, these recommendations do not take into account the time of year of peritonitis occurrence. For example, we do not know whether the epidemics of gastroenteritis each year have an influence on the ecology of peritonitis, and therefore whether the choice of probabilistic antibiotic therapy depending on the time of year should vary. There are previous studies of seasonal variations in peritoneal dialysis-related peritonitis, but these are generally small series from a single center with limited numbers of patients over short periods of time. The RDPLF has been recording peritonitis in French-speaking countries for more than 30 years. Our objective is therefore to evaluate, over a long period of time, the seasonal variations of bacterial ecology during peritoneal dialysis-related peritonitis in Belgium and France, with a particular analysis of seasonal variations of organisms known to be of enteric origin.

PATIENTS AND METHODS

We performed an observational cohort study to measure variations in the bacterial ecology of peritonitis in peritoneal dialysis in metropolitan France and Belgium in the French Language Peritoneal Dialysis Registry (RDPLF). The RDPLF database is declared to the Commission Nationale de L'Information et des Libertés under the number: 11950164795. The data were exported to an independent file after total and irreversible anonymization. As the data were retrospective from a registry, the written consent of the patients was not necessary for the study. The design and functioning of the RDPLF have been described elsewhere [1].

The variable of interest in this study is the germ responsible for peritonitis in peritoneal dialysis, as recorded by the nurses and physicians of the participating centers, based on the results of their respective bacteriology laboratory.

We selected from the RDPLF database the centers in Belgium and France, which have similar climatic conditions; the French-speaking regions in the south were excluded because of very different climatic conditions. We studied all reported peritonitis from 2000 to 2019.

The description of treatment is not available in the database, but we postulated that the average treatment duration is 2 weeks. As the ISPD definition of recurrence [3] is the occurrence of peritonitis within 4 weeks of stopping treatment we defined as recurrence any peritonitis with the same germ occurring within 6 weeks of the date of the previous episode.

In order to keep only the germs clearly identified according to their seasonal frequencies, we deleted the episodes of cloudy fluid related to a hemoperitoneum, an eosinophilic reaction, aseptic chylous peritonitis, peritonitis without identified germ, and recurrences. In total we retained 20411 episodes.

We classified the germs as enteric or not following the classification previously described [5]. The season of reporting of the infections was calculated according to their dates and classified as winter, spring, summer, autumn. The percentages of peritonitis related to the same type of germ were calculated for each season by dividing the number of germs of a given type by the total number of germs encountered during each season.

Patients were grouped according to age (<44 years, 45-64 years, 65-84 years, 85 years and older), type of peritonitis (enteric and non-enteric), modified Charlson score (<4, 4-8, >8) [6], diabetic status, and causative germ (*E. coli*, enterococcus). In each category the seasonality of enteric peritonitis was studied.

Statistics:

Results are presented as percentages of peritonitis by season. The chi2 test was applied to the observed numbers of peritonitis. A $p < .05$ was considered statistically significant. Tests performed on Medcalc Statistical Software.

Similar results being observed over the last 20 years and the last 10 years, we limited the study in groups of patients to this second period for which we have the Charlson score of the patients.

RESULTS

Over the 10 as well as the last 20 years, the percentage of enteric peritonitis is lowest in winter, identical in autumn and spring and highest in summer: winter 25%, spring 27%, summer 29%, autumn 27% ($\chi^2=24.1$; $p < 0.001$). Seasonal differences were as follows: fall-winter, $p=0.016$; fall-spring, NS; fall-summer, $p=0.009$; winter-spring, $p=0.043$, winter-summer, $p < .001$; spring-summer, $p=0.008$.

Figure 1 shows the seasonal variations of enteric peritonitis by 2-year periods for the last 20 years, showing that the rate of enteric peritonitis is always the highest in summer except for the period 2004-2005.

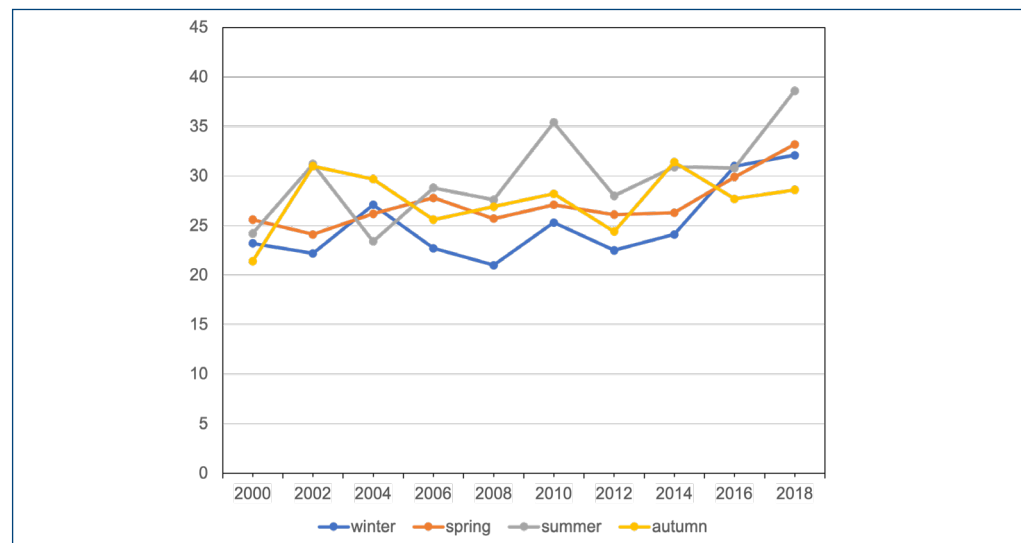


Figure1. Seasonal peritonitis percentages per period of two years from 2000 – 2020. The highest summer values were observed for years 2004 and 2006

Study in subgroups of patients over the last 10 years:

Effect of age:

Seasonality is found in the youngest (<44years, $\chi^2=10$, $p<.02$) and 65-84 ($\chi^2=12.4$ $p<.01$) but not in the 45-64 group ($\chi^2=5.8$ NS) nor in patients >85 ($\chi^2=6.7$ NS)

Effect of comorbidities:

Charlson score does not influence the epidemiology of enteric peritonitis, none of the groups are significant (<4, 4-7, >7)

Effect of diabetes:

Seasonality is found in non-diabetics ($\chi^2=14.4$ $p<.001$) but not in diabetics ($\chi^2=5.75$, NS)

Responsible germ:

No seasonality is demonstrated for E Coli and Enterobacter

DISCUSSION

The data in the literature are poor concerning the seasonal variations of peritonitis in patients treated with peritoneal dialysis. We therefore conducted a retrospective registry study in order to shed more light on this subject, which, to our knowledge, is the first study of this type carried out in European countries.

The data in the literature concerning seasonal variations in peritonitis are quite divergent. Cho Y et al (8), in their multicenter study conducted in Australia, did not show any seasonal variation in peritonitis, even if they concluded that there was a seasonal effect of certain germs in the occurrence of peritonitis; for example, a peak of gram-negative germs in peritonitis in summer. But they do not specify the type of germ in question in their finding and we know that enterobacteria (gram negative) are one of the causes of peritonitis in summer. Furthermore, we must also keep in mind that the Australian climate is considered a tropical climate where the separation between seasons can be difficult. Núñez-Moral M et al (9) obtained similar results in their single-center study conducted in Spain.

Other investigators such as Kim et al (3) and Szeto et al (10) have demonstrated a significant seasonal variation in peritonitis with a high incidence during the hot and humid months of the year. They further advocate that maintaining a dry environment can help avoid peritoneal dialysis treatment failures in tropical climates. Zeng Y et al (11) confirm the data expressed by the others above and demonstrate the higher incidence of PE in summer but fail to reach a statistically significant threshold because of the small size of their cohort.

Our study is in agreement with the results of Zeng Y et al, and confirms the seasonality of peritonitis. The peak incidence of peritonitis was observed in summer and then a stabilization was noticed during the fall and spring seasons. Finally, a significant decline in peritonitis frequencies was observed in winter. When comparing the different seasons, we did not find a statistically significant difference between autumn and spring while it remained significant for the other seasons. On the other hand, the difference was highly significant between summer and winter.

We note that during the second decade of the XXI century, Europe has experienced a real climatic change with well-defined separations between the seasons. Hot summer seasons with multiple heat waves and cold winters leading to a change in the lifestyle of patients. This results in a higher consumption of cold and raw food during the summer months, thus favoring intestinal infections during this period of the year (10). One explanation for the increase in peritonitis during the summer may be higher episodes of gastroenteritis with diarrhea (12). This finding is also put forward by other authors such as Elshafie et al (13) who consider diarrhea as an important source of peritonitis in PD patients.

In addition, CKD patients treated with dialysis are considered to be immunocompromised. A state of undernutrition, such as that caused by vomiting and diarrhea during episodes of gastroenteritis, further weakens the defense of these patients against pathogenic bacteria and thus may facilitate their passage to the peritoneal cavity. Szeto et al (14) and Shu et al (15) show that a hypokalemic state associated with undernutrition in these patients leads to excessive proliferation and stasis of enterobacteria in the intestines. A state of hypokalemia can also lead to a slowing of intestinal peristalsis and constipation, thus facilitating the migration of these enteric germs towards the peritoneum.

Guo, Qunying et al (16) highlight the important role of hypervolemia on the increased incidence of peritonitis in patients treated by PD. It is well known that dialysis patients, treated by PD or hemodialysis, are frequently in a state of fluid overload and this is even more so during the summer when fluid intake increases for everyone. Our results support these explanations by showing a higher incidence of peritonitis in summer. However, we cannot confirm the hypothesis of greater hypervolemia in summer without studying other parameters such as bioimpedancemetry, episodes of dyspnea, edema or cardiac decompensation in these patients. Experimental studies also point to the hypothesis of translocation of enteric germs in the absence of abdominal pathology (17-18).

Enteric germs can be divided into two large families: enterococci, gram positive, whose most frequent germs are *Enterococcus faecalis* and *Enterococcus faecium*, and enterobacteria, gram negative, characterized mainly by *Escherichia Coli* (*E. Coli*) and *Klebsiella Pneumoniae* in peritonitis (11-19-20). Some authors have established the seasonal character of gram-negative enterobacteria with a peak of infection observed in summer (8-11) while other researchers such as Buttigieg J et al (21) do not obtain the same results.

The evaluation of germs in our study did not show any seasonality for peritonitis. But we are forced to mention that contrary to other authors our research was essentially focused on enterococci and *Escherichia coli*. In our understanding this result is logical because the incidence of gram-positive peritonitis has been decreasing in the last years due to better connection systems and therapeutic education programs for patients and health professionals (12-22). Bronikowski et al (23) demonstrate that the ideal temperature for in vitro multiplication of *E. Coli* is 35-36°C, but in Europe and more specifically in the regions considered in our study, these temperatures are rarely reached even in summer, except during heat waves.

Some authors consider diabetes as an independent risk factor for peritonitis and poor prognosis in patients treated by peritoneal dialysis (24-25). In our study, the seasonality of peritonitis is found in non-diabetic patients with a higher incidence in summer. This is not surprising because

we know that diabetics are more likely to have gram-positive peritonitis, especially with *Staphylococcus*, whereas non-diabetics are more likely to have gram-negative peritonitis such as *E. Coli* (26). The prevalence of *E. Coli* increases strongly during the months of the year when temperatures are high.

Similarly, our results also show a seasonal influence of *E. coli* in young patients with an age < 44 years. This could be explained by the fact that compared to elderly patients, they pay less attention to their food hygiene and therefore would more easily consume food contaminated by enteric germs. Another explanation may be that younger patients are more independent and therefore more likely to enjoy swimming in summer when we know that the prevalence of enteric germs such as *E. Coli* increases.

Strengths and weaknesses

This is a registry study over a long period of time and a large number of peritonitis but other studies are necessary to confirm certain hypotheses such as hypervolemia and intra-abdominal translocation of germs in order to elucidate their exact role in the physiopathology of enteric peritonitis.

CONCLUSION

The frequency of enteric peritonitis varies according to the seasons in the French-speaking regions of Western Europe, with a higher incidence in summer and a lower incidence in winter. The incidence of enteric peritonitis is similar in autumn and spring. We postulate that food contamination by enteric germs associated with increased bacterial translocation in the gastrointestinal tract favored by constipation is responsible for this phenomenon. These seasonal variations may suggest that probabilistic initial antibiotic therapy should be adapted to season in cases of suspected peritonitis before the results of bacteriological analysis.

Declaration of interest

The authors declare that they have no conflict of interest in this article.

Role de chaque auteur

PB : rédaction de l'article ; EM : lecture critique, conseils et hypothèses bactériologique, FC : analyse statistique, CV : conception de l'étude, extraction des données et rédaction des méthodes.

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