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FUNGAL PERITONITIS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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Summary: Fungal peritonitis represents one of the most serious complications in patients on peritoneal dialysis (CAPD). The therapy often consists of peritoneal catheter extraction and patient recruitment to hemodialysis. For some of the patients the peritoneal dialysis is the only way of dialysis, due to inability to perform a permanent vascular access.
In this study we present 13 patients with fungal peritonitis on CAPD in the last five years. Three patients (all of them diabetics on insulin therapy, and hypoalbuminemic) died in the course of fungal peritonitis or immediately after. Seven patients were transferred to hemodialysis, and five continued on CAPD, two of them with reimplanted peritoneal catheter.
Low incidence (2.6%) of fungal peritonitis in our patients on CAPD could be attributed to the strict intrahospital treatment of every bacterial peritonitis episode and no preventive antibiotic usage.

Key words: Fungal peritonitis, peritoneal dialysis, CAPD, therapy, antimycotics

Introduction

Fungal peritonitis is relatively uncommon complication on continuous ambulatory peritoneal dialysis (CAPD), but it accounts for significant morbidity and mortality. Its incidence varies from 1.5–10% of all peritonitis episodes on CAPD (1) in Europe and as high as 15% in the Far East. Fungal peritonitis usually follows the episode of bacterial peritonitis treated with antibiotics. The most common causative agent for fungal peritonitis is Candida species. Controversy still exists about the way fungal infection in peritoneum begins and persists. Antimicrobial therapy causes alteration of fecal flora, transmigration into the peritoneal cavity and, particulary in the immunocompromised host, growth of fungi. The fungus colonizes the peritoneal catheter and is embedded in the amorphous matrix on the surface of the catheter (1). Early catheter extraction and transfer to hemodialysis (2) is supposed to bring rapid relief of symptoms and is still the cornerstone of fungal peritonitis treatment.

For some of the patients the peritoneal dialysis is the ultimate choice. When such a patient suffers a fungal peritonitis episode, the therapy with antimycotics and temporary discontinuation of CAPD, reinsertion of a new peritoneal catheter and recommencement of dialysis could be the effective therapy.

Patients and Methods

From 1991 to 1995 13 patients with fungal peritonitis were treated in Institute of Nephrology and Hemodialysis in Niš. The patients' characteristics were shown in Table 1.

The duration of dialysis treatment before the episode of fungal peritonitis was as follows: eight patients (62%) were on CAPD up to one year, three patients (23%) up to 2 years, and two patients (15%) spent on CAPD more than three years.

The previous episodes of peritonitis were absent in four patients (30%), and three of them were diabetics. In the same number of patients (30%) the episode of fungal peritonitis follows 4 or more episodes of bacterial peritonitis.

Previous antibiotic therapy was undertaken in four patients, i.e. three patients were treated with Vancomycin 1g intraperitonealy due to bacterial peritonitis for the past two weeks, and one patient was treated with Cefuroxime 1g i.v. for seven days due to serious respiratory infection.

Four out of 13 patients with fungal peritonitis were diabetics, age above 60, on insulin therapy.

None of the patients was previously treated with corticosteroids or other immunosuppressive drugs.

On admission to the hospital, the specimens of the peritoneal fluid were taken for estimation of number of leukocytes in mm^3, Gram stain, and culture.

Table 1. Patients characteristics

Age	male	female
>65 yrs	1	2
55–64 yrs	2	5
45–54 yrs		1
35–44 yrs		1
<35 yrs		1
Previous dialysis treatment		
<1 year	8 (62%)	
<2 yrs	3 (23%)	
>3 yrs	2 (15%)	
Previous episod. of peritonitis		
none	4 (30%)	
one	1 (8%)	
2–3 episod.	4 (31%)	
>4 episod.	4 (30%)	
Diabetics	4 (30%)	

Results

Overall peritonitis rate in our patients during observation period was 0.15peritonitis/pts/mth.

Incidence of fungal peritonitis from 1991 through 1995 is presented in Fig. 1.

Clinical presentation of fungal peritonitis

Fungal peritonitis presented with abdominal pain, fever and cloudy peritoneal effluent. In 46% patients the number of leukocytes in peritoneal effluent was below 500/mm^3. Only in four patients the number of leukocytes was above 2000/mm^3.

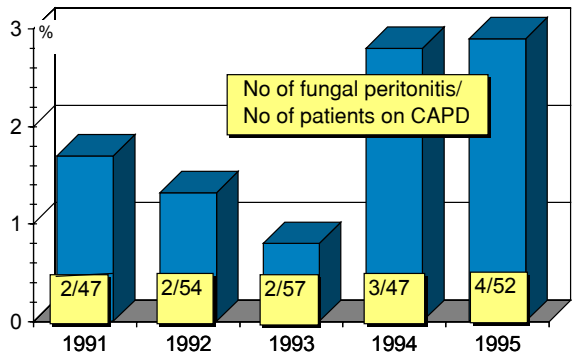

Fig 1. Incidence of fungal peritonitis on CAPD

None of the Gram stain revealed yeast, so the beginning of the antimycotic therapy was postponed until arrival of a positive culture. In the meantime all patients were treated as having a bacterial peritonitis with negative Gram stain. The therapy consisted of i.p. Vancomycin a 1g on the beginning and after 7 days, and trimethoprim–sulfamethoxazole 200/40mg, respectively in every exchange during 7 days.

The culture of dialysis fluid is shown in Table 2. The most common fungus isolated was Candida albicans in 69% patients. Aspergillus species was isolated in two patients (14%).

Therapy of fungal peritonitis

1) Antimycotics

All patients with positive culture for yeast were started immediately with antimycotic therapy. In the period from 1991 to 1994 the antimycotic drugs used were: ketoconazole 400mg a day given orally during three weeks, or miconazole 600mg twice a day for 10 days. In 1995 we started antimycotic therapy according to the recommendations of the Ad Hoc committee for treatment of peritonitis in 1993. The patients were given flucytozine 2000mg on the first day, and than maintaining dose of 1000mg a day orally. Another antimycotic agent given was fluconazole in a dose of 150mg every other day. Antimycotic therapy was continued for 3–4 weeks. Side effects of antimicotic therapy were recorded in two patients, during the course of treatment, related to the use of flucytozine. The elevated liver enzymes gradually fell to the normal levels after the discontinuation of the drug.

Table 2. Isolated yeast in patients with fungal peritonitis

Isolated yeast	Number of patients
Candida albicans	9 (69%)
Alternaria	1
Aspergillus	2 (14%)
Blastospore	1

2) Transfer to hemodialysis

In seven patients the peritoneal catheter was removed and after creating a permanent vascular access they were transferred to hemodialysis.

3) Peritoneal catheter outcome

In seven out of 13 patients peritoneal catheter was removed, and patients were transferred to hemodialysis. In two of them peritoneal catheter was reimplanted after a successful treatment of fungal peritonitis for a month. One of those two patients is still on CAPD treatment, and the second was transferred to hemodialysis due to early catheter malfunction.

Five patients continued with intermittent peritoneal dialysis. The reason for such a treatment was inability to create a permanent vascular access. In two of them, after the course of

antimycotic therapy peritoneal catheter was removed and a new one was implanted in a new site.

One patient died before the definite diagnosis was obtained.

4) Patients outcome

At the end of 1996 only three patients survived an episode of fungal peritonitis. None of the patients with preserved peritoneal catheter survived. None of the diabetics survived. All the survivors went on hemodialysis, one of them only temporary and continued peritoneal dialysis (CAPD) through new catheter.

Discussion

The incidence of fungal peritonitis in literature data is 3 to 15% (1), significantly higher than in our patients (up to 3%). Reasons for a low incidence of fungal peritonitis in our patient population could be attributed to the intrahospital treatment of peritonitis episodes, and to no use of preventive antibiotic treatment.

Up to the end of 1993 patients with bacterial peritonitis were treated with antibiotics on the Penicillin basis, Pyranosids, Sulfonamides, and Aminoglicosids, and only severe bacterial infections of the peritoneum were treated with Cephalosporins. The incidence of fungal peritonitis in that period was below 2%.

1993 coincides with overt antibiotic shortage, but the incidence of fungal peritonitis was minimal.

After beginning with the protocol according to the Ad Hoc Committee in 1994 we recorded a slight increase in the incidence of fungal peritonitis. Similar trend was observed in 1995.

The definite diagnosis of fungal peritonitis was made 7–15 days late, since Gram stain in all patients was inconclusive. All patients were, in the meantime, given antibiotics as in the case of negative Gram stain results.

The results of peritoneal fluid cultures are in agreement with those in literature data (3,4,5). The most frequent yeast isolated was Candida albicans.

The optimum therapy for fungal peritonitis is still controversial. Early peritoneal catheter removal, with or without antifungal drugs, antifungal therapy alone with catheter preservation, or instillation of antimycotics into the catheter are possible therapic alternatives (3,4,6,7). According to the recommendations of the Ad Hoc Committee on Peritonitis Management (2), the crucial therapic measures include antifungal therapy and/or removal of the catheter.

In our study antimycotics were given to all pa–tients with positive dialysate culture for fungi. The duration of the antimycotic therapy was at least 3 weeks. All antimycotics used (in 1993 ketoconazole and miconazole, in 1994 and 1995 flucytozine and fluconazole) were safe in prolonged therapy in the majority of patients with very few side effects (elevated liver enzymes) in only two patients. Side effects were reversible.

The golden standard for the treatment of fungal peritonitis is the removal of peritoneal catheter early in the course of the disease (1,2,5). In seven of our patients peritoneal catheter was removed and were transferred to hemodialysis. Five patients continued on CAPD due to inability for creation a permanent vascular access. One patient died before the diagnosis of fungal peritonitis was made.

Therapy of fungal peritonitis is very important because the disease causes relatively high mortality rate up to 25% (1).

In our study three patients died, one in the course, and two patients after the episode of fungal peritonitis. All were diabetics on insulin therapy with low plasma albumin levels (below 25g/L). In these patients' cultures of peritoneal fluid were positive for Candida albicans. All were treated with antimycotics, the catheter was removed, and were transferred to hemodialysis.

After the treatment of fungal peritonitis 62% of the patients continued on hemodialysis, and 32% on peritoneal dialysis (CAPD).

Conclusion

Taking into account our results, it is mandatory to reduce the time for making the definite diagnosis of fungal peritonitis; this would make previous antibiotic treatment unnecessary.

It is obvious that antibiotic protocols should be carefully evaluated and applied only if indicated.

Diabetics, as a high risk population for fungal peritonitis and dubious outcome, should be given antimycotics even if fungal peritonitis is suspected.

New antimycotic drugs used in the treatment of fungal peritonitis seem to be effective and safe in recommended doses with only few side effects. Caution should be paid to patients with impaired liver function or cirrhosis.

Besides antimycotic therapy, discontinuation of peritoneal dialysis, removal of peritoneal catheter and subsequent transfer to hemodialysis is obligatory. Whether decision is made in favor of continuation of hemodialysis or peritoneal dialysis, peritoneal catheter should be removed. The timing of new peritoneal catheter implantation is dictated

by clinical recovery of fungal peritonitis and usually takes at least one month. Preservation of an old catheter and intermittent interruption of peritoneal dialysis should be reserved for patients with no other choice.

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GLJIVIČNI PERITONITIS NA KONTINUIRANOJ AMBULATORNOJ PERITONEALNOJ DIJALIZI

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Kratak sadržaj: Gljivični peritonitis pretstavlja jednu od najozbiljnijih komplikacija kod pacijenata na peritonealnoj dijalizi (CAPD). Terapija se obično zasnova na ekstrakciji peritonealnog katetera i prevođenju pacijenta na lečenje hemodijalizom. Za pojedine pacijente peritonealna dijaliza je i jedini mogući način aktivnog lečenja, jer ne postoji mogućnost postavljanja trajnog pristupa za lečenje hemodijalizom.
U našoj studiji prikazali smo 13 pacijenata sa gljivičnim peritonitisom na CAPD u poslednjih 5 godina. Tri pacijenta (svi dijabetičari na insulinskoj terapiji i sa hipoalbuminemijom) umrli su u toku ili odmah nakon gljivičnog peritonitisa. Sedam pacijenata je prevedeno na hemodijalizu, a petoro je ostalo na CAPD (dva pacijenata sa reimplantiranim peritonealnim kateterom).
Niska incidenca (2.6%) gljiivčnih peritonitisa na CAPD može se pripisati isključivo intrahospitalnom lečenju svake epizode gljivičnog peritonitisa i ne davanju antibiotika u preventivne svrhe.

Ključne reči: Gljivični peritonitis, peritonealna dijaliza, CAPD, terapija, antimikotici

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