Efficeint Administration of Human Albumin in Clostridium Difficile Infection

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Albumin is the most important protean component of the plasma. Human albumin is a concentrate of plasmatic proteins from the blood with multiple therapy uses. The study aims to highlights the efficient administration of human albumin i.v. in hypoalbuminemia due to diarrhea with Clostridium difficile. Administering human albumin i.v. in symptomatic hypoalbuminemia manifested by the occurrence of edemas was followed by symptoms remission and ensured a favorable evolution.

Keywords: human albumin, Clostridium difficile

Antibiotherapy, included in therapy along with the discovery of penicillin has, in addition to healthy effects, and adverse reactions among which is the interruption of microbial ecology and the occurrence of dismicrobism.

Infection with Clostridium difficile (CDI), one of the causes that lead to the occurrence of colitis related to antibiotherapy has known, a high incidence from the 21th century; moreover, the severity of the cases, especially in elderly people, has increased alarmingly [1]. Although, the classic infection with Clostridium difficile is related to hospitalization, in the last years there have also been community cases on people previously considered minor risk cases. In the past 10 years, CDI incidence increased in most European countries reaching in 2011-2012 an estimated level of 124000 cases with a mortality of 3-30% [2]. The hypervirulent strains which belong to the ribotype determined through the protein chain reaction method (PCR), 027 and in a small number to ribotype 078 determined epidemics with severe forms of disease in all European countries [2-3]. In Romania, the dominant ribotype is 027, (fig. 1).

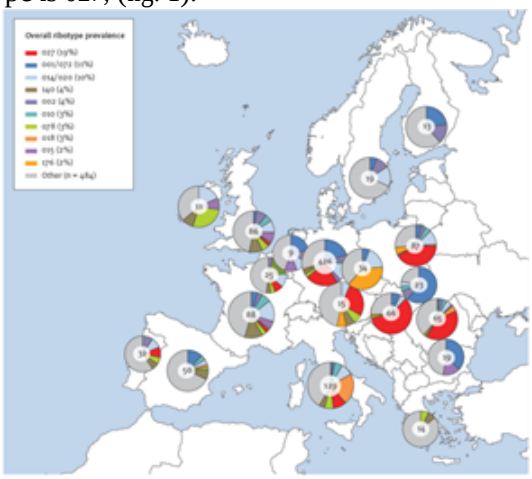

Fig. 1 Clostridium difficile ribotypes chart (source: EUCLID European, multicenter, prospective, biannual, point-prevalence study of Clostridium difficile infection in hospitalized patients with diarrhea)

The usual clinical manifestations of the infection include diarrhea, fever, abdominal pain and hyperleukocytosis; occasionally there have been cases of hypoalbuminemia [4-5]. The positive diagnosis is based on the detection of toxins A and B in the patient's ejection through immunoenzymatic methods. The biological election treatment of CDI includes oral administration of metronidazole, with healing rates of 94-95% and relapses signaled in 5-16% of the cases [4]. Vancomycin may be administered orally, 125 mg x 4 administrations/day in patients who do not tolerate metronidazole or for patients with relapses. Severe cases or relapses related to hypoalbuminemia may be associated with pathogenic therapy by administering albumin iv. Albumin is a non-glycosylated protein and is the most ample circulant protein representing 50-60% of the total of plasmatic proteins. Albumin has a tridimensional structure with three binding fields (I-III), each field is divided in two subfields (A and B); the center of the molecule is formed of hydrophobic radicals – binding locations for many ligands – and the exterior parts of the molecule are hydrophilic. Albumin is synthesized in the liver 12-25 g/day, but it is not stored hepatic, there are no albumin reserves [6]. Albumin is the most important protein component of the plasma, cephalo-rahidian liquid and urine.

In the plasma, albumin is responsible mainly for keeping the oncotic pressure and is involved in the transport of different composites (free fatty acids, bilirubin, hormones, metal ions and medication). The albumin levels below 2.0-2.5 g/dL (normal values 3.5-5.2 g/dL) related to nephritic syndromes, hepatic cirrhosis or enteropathies with protein loss may determine the occurrence of edemas [7].

Experimental part

This work presents our experience regarding the occurrence of hypoalbuminemia with clinical significance in diarrhea related to *Clostridium difficile* infection and the therapy effects of administering human albumin iv.

Following the ascending trend reported in Europe [1], the CDI cases of patients admitted in our hospital in the past three years increased, beginning with 5 cases diagnosed in 2013, 135 cases in 2014 and 227 cases in 2015, (fig. 2). Between 1.01.2016-30.10.2016, 256 patients diagnosed with enteritis with *Clostridium difficile* have been admitted.

The diagnosis of the disease was based on the clinical symptomatology with fluid ejections, many elements of specific epidemiology such as the recent intake of antibiotics or surgical intervention and the etiologic diagnosis was diagnosed by detecting toxins A and B in the patients' ejection using the immunochromatographic

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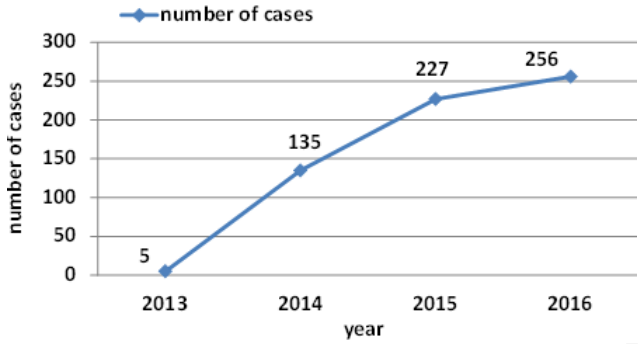

Fig. 2 Number of Clostridium difficile infections admissions in terms of years

Table 1

PATIENTS CHARACTERISTICS

Patient category	Gender		Provenience		Age (years)	Albumin values (g/dl) Mean	Associated co-morbidities with hypo-albuminemia (%)	Average hospitalization (days)	Relapse illness (%)
	Male (%)	Fem. (%)	Urban (%)	Rural (%)					
Lot patients	48	52	56	44	64.6	Not determ.	13.5%	14.8	13%
Patients with edemas	0	100	90	10	74.8	1.66 (2.1-1.9)	100 %	15.6	0 %

method. The colorimetric method with bromcresol green was used for albumin dosing.

Results and discussions

The demographic characteristics of the patients admitted are presented in table 1. They were mostly from the urban environment (56%), mostly female gender (52%), with age average 69.6 years old, 13% were relapses after a first disease episode.

Although asymptomatic albuminemia < 3.5g/dL was reported in a significant rate (79%) in patients from a study performed in the western part of the country [5], the standard investigation of the lot of patients did not include the determination of albuminemia, this was imposed by the occurrence of gambian edemas in admitted patients. From the 256 patients, only 19% (5 patients) have had a clinical expression of hypoalbuminemia expressed by the occurrence of Gambian edema; they occurred in a variable period of 4-7 days (average 5.2 days) after admission. The values acquired by determining the serum albumin in patients with diarrhea with *Clostridium difficile* and edemas was below the critical threshold of 2.5-2.1g/dL, average 1.66 g/dL [5]. Patients with edemas had the following characteristics: all patients were females, 90% from the urban environment, with the average age of 74.8 years old. None of the patients presented the relapse form of the disease, but all the patients were related to clinical cases which are regularly accompanied by hypoalbuminemia: renal insufficiency with proteinuria, colonic neoplasm, pulmonary tuberculosis, all the patients were under combined etiologic treatment: metronidazole and vancomycin orally. The characteristics of the two categories of patients are presented in table 1.

The occurrence of edemas and the biochemical confirmation of hypoalbuminemia imposed the provision of pathogenic correction treatment by administering slow endovenous perfusion of human albumin 20%, 1 bottle of 50 mL/day (daily dosage 10g) for a period no longer than 3 days; the administration period was limited to the disappearance of edemas and the evolution of all cases was favorable. Hypoalbuminemia was not a regular manifestation of colitis with *Clostridium difficile*, being rarely reported in literature, fact also confirmed by our study. Less than 2% of the patients had suggestive symptomatology for hypoalbuminemia represented by the presence of gambian edemas. The determined values of serum albumin in patients with diarrhea associated to CDI and edemas were below the levels considered for determining clinical expression (2.5-2.1g/dL), reaching the critical threshold of <1.5g/dL [7]. Although hypoalbuminemia represents an independent risk factor for death [7] in hospitalized elders, its quick correction by administering human albumin iv has had a positive effect on the clinical evolution. Although all female patients have had co-morbidities which are accompanied by hypoalbuminemia and the determined values of the serum albumin have had significantly low levels, the clinical manifestations were discrete, represented by modest gambial edemas.

Due to the low prevalence of symptomatic hypoalbuminemia, reported in literature and also highlighted in our study, regular determination of serum albumin in diarrhea caused by Clostridium difficile does not seem to bring any clinical-evolution or therapy benefit; however, if the disease occurs in elderly people with co-morbidities which induce hypoalbuminemia, the evolution of the serum albumin values from hospital admission may influence therapy prescription. In such cases, correcting hypoalbuminemia may be made before clinical manifestation with total dosage of low administration, with practical benefits: decreasing the theoretical risk of side and emotional effects represented by anxiety determined by the occurrence of new symptomatology represented by the occurrence of edemas.

Conclusions

Symptomatic hypoalbuminemia is rare in enteritis determined by *Clostridium difficile*.

Hypoalbuminemia has become clinically obvious through the appearance of edemas in patients with known co-morbidities which determine the decrease of serum albumin. For this category of patients, the dosing of serum

albumin may be made before the occurrence of clinical signs, immediately after admission(hospitalization).

Administering human albumin 200g/L iv determined the disappearance of clinical signs of hypoalbuminemia and positively influenced the evolution of the disease.

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