

For the prevention of exacerbations bronchodilators and inhaled glucocorticoids are used in combination with long-acting β 2-adrenomimetics (severe and very severe COPD). Yearly influenza vaccination is highly recommended.

In conclusion, it should be noted that if the antibiotic therapy is chosen correctly for the individual, it reduces the duration of hospital stay and the costs associated with medical care.

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The Modification of the Serum Ascites Lymphatic Albumin Gradient in Liver Cirrhotic Decompensated Patients with Ascitic Syndrome

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Abstract

The study involved 23 patients with decompensated liver cirrhosis and ascitic syndrome. This trial was designed to determine the value of serum-ascites and lymphatic albumin gradients. We established diminution of the albumin ascites-lymphatic gradient in relationship with the evolution of the ascitic syndrome. We introduce the notion of serum/ascites/lymphatic albumin gradient and its significance on parameters of the evolution of the ascitic syndrome. It is required to validate the clinical application of the gradient in following studies.

Key words: ascitic syndrome, serum ascitic lymphatic albumin gradient.

Изменения альбуминового градиента (асцит, плазма, лимфа) у декомпенсированных больных циррозом печени и асцитическим синдромом

В настоящую работу включены 23 больных с декомпенсированным циррозом печени и асцитическим синдромом. Исследование было посвящено изучению и оценке альбуминового градиента (асцит, плазма, лимфа). Установлено уменьшение альбуминового градиента асцит-лимфа в соотношении с развитием асцитического синдрома. Впервые предложена терминология альбуминового градиента (асцит, плазма, лимфа), однако его значение, как критерия развития асцитического синдрома, требует уточнения в дальнейших исследованиях.

Ключевые слова: асцитический синдром, градиент концентрации альбумина сыворотка-асцит.

Introduction

According to literature data, 4-5% of the global population shows disturbances of liver functions, of which about 10-20% are caused by viral hepatitis, toxic hepatitis or ethanol alcohol, that within 10-20 years lead to the

evolution of cirrhosis liver [1], which inevitably leads to a high rate of complications such as variceal hemorrhage either cirrhogenous hypersplenism with coagulopathy in progress or ascitic syndrome. Thus, N. Fisher et al. notes that in Great Britain alone, during the years 1993-2000,

the mortality from complications of liver cirrhosis doubled from 6 x 105 in 1993 to 12.7 x 105 in 2000 [3].

In this context the problem of diagnosis, prophylaxis, and treatment of complications of cirrhotic portal hypertension is current and remains the focus of the medical community.

Ascitic syndrome, and especially in its advanced forms (with lack of response to diuretic therapy) is one of the most serious complications of liver cirrhosis, which according to different authors evolves in 50 percent of cases within 10 years of diagnosis of hepatic cirrhosis. More than that, statistics of randomized trials denote a rate of mortality within the limits of 60-70% of cases of these patients in terms of 24-36 months from the onset of resistant and refractory ascites (called in some publications as intractable ascites) [3, 4], which in our view is debatable.

Besides a reduced quality of life, in cases of medically or surgically uncontrolled evolution of ascitic syndrome, patients are at high risk of appearance of hepato-renal failure, due to the fact that in general, hepato-renal failure has 5-year incidence rate of 18-39% in cirrhotic patients primarily diagnosed, the prognosis being extremely poor [5-8], and as a "golden" therapeutic option only liver transplantation is being considered [9], which currently can not fully solve the problem because of the small number of organ donations.

Meanwhile, another major complication in advanced cirrhotic ascites is ascites fluid infection. The development of spontaneous bacterial peritonitis by intestinal flora translocation and bacteremia in the lymph nodes in turn contributes to deterioration of liver and kidney functions [6].

Thus, future research on the assessment of prognostic factors triggering spontaneous bacterial ascites-peritonitis, without the need for sophisticated laboratory tests, is reasonable and also useful to medical practitioners.

Over the past decades in order to differentiate and diagnose the etiology of ascites (portal hypertension, peritoneal carcinomatosis, tuberculous peritonitis, secondary bacterial or neoplastic), using concepts of exudative vs transudative properties, we studied the total protein concentration in ascitic fluid and serum. Conventionally, it was established that neoplastic ascites ("exudative theory") have a characteristic protein index of > 25 g/l, while in portal hypertension ("transudative conception") the value of protein concentration is < 25 g/l.

Later, a new biochemical criterion was proposed and namely - assessing the difference in serum albumin concentration and ascitic fluid, or the so-called gradient album serum/ascites (GASA), which proved to be a higher sensitivity compared to determination of the total concentration of proteins in ascitic and serum fluid [12]. Simultaneously, investigations indicate that the value (GASA) > 1.1 g/dl denotes ascitic syndrome in portal hypertension with an accuracy of 97% [12] while the value of the named gradient below 1.1 g/dl, is characteristic to "non-portal hypertension etiology" [13, 14, 15].

Also, no research literature exists regarding the role of the serum-ascites-lymph albumin gradient in evaluating the severity of cirrhotic syndrome.

Aim of the study - the analysis of albumin concentration,

serum and lymph in decompensated cirrhotic patient with ascitic syndrome, the serum-ascitic albumin gradient analysis, lymph and its variations depending on the stage of ascites and hepatic functional reserve.

Material and methods

This study included a prospective analysis of changes in the serum-ascitic-lymphatic albumin gradient in 23 cirrhotic patients with advanced cirrhosis with ascites (13 - resistant, 10 - refractory), surgically treated in the Surgery Clinic "Sfinta Treime" ("Holy Trinity") in the period 2008 - 2010.

The study group included 11 men and 12 women ranging in age limits of 45-58 years, etiology of liver cirrhosis was caused by viral hepatitis (HBV, HBV + HBV-HDV and HCV in 7, 6 and 10 cases respectively, confirmed by immunoserological investigations. Average Child-Pugh score was 10.4 ± 1.28 points. Patients were separated into previously described stages of ascites syndrome in accordance to criteria for classification of Ascites International Club (International Club of Ascites). We mention the fact that the patients with activation of cirrhotic process were not included in the research group. Additionally, perfusion conservative treatment with administration of albumin, plasma, etc. in terms of the previous three months was considered as a criterion of exclusion from the study.

The surgical treatment included the cervical decompression of the thoracic lymph duct, which in 6 cases was associated with paracentesis decompression, performed in patients with tense ascites and cardiopulmonary disturbances.

In order to standardize the research the biological substrate was investigated (serum, lymph and ascitic fluid) and was collected only intraoperative under sterile conditions, being collected 5.0 ml of serum and ascitic fluid obtained by paracentesis. Intraoperatively the thoracic lymph duct was punctured with SECALON catheter (Becton Dickinson Critical Care Systems, USA) and the lymph fluid was collected.

The collected biological fluids were subjected to laboratory research with clinical and general bacteriological proteino-gram assessment, and especially the measurement of albumin concentration. A general characteristic of patients included in the study is summarized in tab. 1.

Table 1

Structure of the study group (n = 23)

Ascites	Men / Women	Average age	Child Average Score
Resistant	7/6	42.6 ± 2.3	9.8 ± 0.35
Refractory	7/3	48.1 ± 2.5	10.6 ± 0.45
Total	14/9	45.8 ± 2.1	10.2 ± 0.15

Obtained results

The results of research conducted on a group of 23 patients with hepatic decompensate cirrhosis were estimated and analyzed according to the severity of the ascitic syndrome (resistant / refractory). It was found that the albumin concentration in serum, lymph and ascites did not differ statistically

or significantly in those groups. Serum albumin concentration in resistant as compared to refractory ascites was 2.65 ± 0.78 (gm/dl) and 2.45 ± 0.89 respectively. The corresponding lymph and ascites albumin concentrations in resistant ascites were 2.15 ± 0.88 and 1.01 ± 0.98 respectively, while in refractory ascites they were 1.87 ± 0.76 and 0.93 ± 0.66 , $p > 0.05$ (tab. 2).

Table 2

Profile of serum albumin, ascites and lymph to patients included in the study group (n = 23)

Index	Resistant ascites	Refractory ascites	p
Serum albumin concentration (gm/dl)	2.65 ± 0.78	2.45 ± 0.89	> 0.05
Lymph albumin concentration (gm/dl)	2.15 ± 0.88	1.87 ± 0.76	> 0.05
Ascites albumin concentration (gm/dl)	1.01 ± 0.98	0.93 ± 0.66	> 0.05

We conclude that in this study the quantitative assessment of albumin concentration in serum, ascitic fluid and lymph was not predictive of the development of complicated cirrhotic ascites in patients with decompensated cirrhosis.

Simultaneously, in both study groups, the albumin gradient of serum-ascites included higher values of 1.1 (gm/dl) in 100% cases confirming the value of this parameter as a characteristic sign of portal hypertension, justifying in this sense, the “transudative” hypothesis of differential diagnosis of ascites [12, 17, 20].

The analysis of albumin gradients in resistant and refractory ascites was, respectively 0.48 ± 0.09 and 0.51 ± 0.11 gm/dl for serum-lymph gradient, and 1.05 ± 0.20 and 0.89 ± 0.07 , for lymph-ascites gradient. Also we found, that ascites-lymph albumin gradient decreases during the evolution of lymph-ascitic syndrome, with a tendency to decrease with the progression of advanced forms, although these results were non-significant ($p > 0.05$)

Table 3

Changes in albumin gradient in the study group (n = 23)

Index	Resistant ascites	Refractory ascites	p
Albumin gradient Ser - ascites (gm/dl)	1.56 ± 0.64	1.49 ± 0.75	> 0.05
Albumin gradient Ser - Lymph (gm/dl)	0.48 ± 0.09	0.51 ± 0.11	> 0.05
Albumin gradient Lymph-ascites (gm/dl)	1.05 ± 0.20	0.89 ± 0.07	> 0.05
Albumin gradient Ser/ascites/Lymph *	-0.40 ± 0.05	-0.90 ± 0.10	< 0.01

* Negative values of the gradient

On further analysis of our data, we found that the albumin gradient in ser/ascites/lymph proved to be more sensitive in differentiating resistant vs refractory ascites as compared to the analysis of albumin concentration in each of the biological fluids analyzed separately or in pairs. This can be explained by the multiplicity and complexity of peritoneal absorption mechanisms, the phenomenon of “washing” of albumin in ascitic fluid, described by JH

Henriksen [16]. In this study we noted a statistically significant difference in the groups investigated for this index, namely a serum/ascites/lymph albumin gradient of -0.40 ± 0.05 in the resistant ascites group vs -0.90 ± 0.10 in the refractory ascites group ($p < 0.01$).

Table 3 summarizes research data of albumin gradients.

Discussions

The evolution of ascitic syndrome with advancing complications represents a difficult clinical problem, both medically and surgically [17]. Also, many randomized trials have evaluated various laboratory parameters of ascitic fluid, which would allow the differentiation of etiology, such as: proteinogram, cytology, albumin gradient serum/ascites, measurement of lactate hydrogenase concentration, amylase, adenosine deaminase, glucose, fibronectin level [18, 19].

It is known that, in peritoneal fluid of healthy individuals the physiological concentration of proteins exceeds the value of 4 g/dl, while in ascites, serum protein concentrations decrease to below 2.5 g/dl. This traditional concept is also debatable because patients with ascites are usually treated conservatively with diuretics and infusions of plasma or albumin, leading to increased protein concentration in ascitic fluid and thus decreasing the sensitivity of a low serum protein measurement [20].

Therefore a new criterion-gradient of album serum/ascites was proposed, which proved to have a higher sensitivity compared to determination of total protein concentration in ascitic fluid and serum [12]. This gradient is based not on a simple assessment of albumin concentration in the above-mentioned fluids, but serves as a reflection of portal pressure, being derived on the basis of oncotic and hydrostatic balance.

Thus, the research shows a direct connection between the serum/ascites albumin gradient and the degree of portal hypertension. This ratio is clearly superior compared to the overall concentration of proteins in serum and ascites [22, 23]. More than that, some authors recorded a direct connection between the value of portal pressure gradient GASA, as well as its complications, gastro-esophageal varices and ascitic syndrome [24, 26]. However, in this study we were unable to confirm a significant serum-ascites albumin gradient difference between patients with resistant and refractory ascites.

Investigations of lymph fluid components were started in the 60s, with achievements in clinical and experimental studies by several of the well-known men of science who were also the founders of this field, A. Dumont, 1960, H. Mayerson, 1963, M. Orloff, 1966, C. Witte, 1968 [27-29].

Meanwhile, in spite of a long period of time, available literature does not show any scientific works towards protein variations, especially albumin in serum, ascites and lymph appreciation of these gradients. This can be explained by deficiencies in obtaining lymph from lymph central collector (thoracic duct), as well as a relatively small number of men of science specialized in the field.

Conclusions

Quantitative assessment of albumin concentration in serum, ascitic fluid and lymph is not an index revealing the prognosis in terms of evolution of ascites to patients with cirrhotogenous decompensated cirrhosis. This study found that serum-ascites albumin gradient does not reveal a significant difference in the case of resistant and refractory ascites. Ascites albumin gradient decreases during the evolution of lymph and ascitic syndrome and has a tendency to decrease with the progression of advanced forms of ascitic syndrome. Implementation of the notion of serum-ascites-lymph albumin gradient and its significance as a criterion of evolution for ascitic syndrome requires further study and validation.

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The Impact of Long Term Medication Ramipril Versus Eprosartane on Renal Function and on Microalbuminuria in Patients with Essential Arterial Hypertension

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Abstract

This research presents the experience of the Arterial Hypertension Department in the treatment of patients with essential hypertension and microalbuminuria. The study focused on the analysis of clinical observation materials according to the protocol, established in a group of 100 patients, of whom 50 were treated with angiotensin II converting enzyme inhibitors Ramipril and 50 were treated with angiotensin II receptor antagonist Eprosartane. Both drugs have proven beneficial effect on renal function parameters, especially in microalbuminuria at all stages of control with a peak at the end of the follow-up period. However, the treatment with AT1-receptor antagonist Eprosartan has proven to be superior to angiotensin II in converting enzyme inhibitor Ramipril.

Key words: arterial hypertension, microalbuminuria, angiotensin II converting enzyme inhibitors, angiotensin II receptor antagonist.