Advances in the diagnosis and therapy of liver cirrhosis: a systematic review

Avanços no diagnóstico e terapia da cirrose hepática: uma revisão sistemática

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ABSTRACT
Hepatic cirrhosis (HC) is a diffuse pathophysiological state of the liver considered to be the end-stage of several liver injuries. It is essential to highlight the need to implement new diagnostic and treatment methods to contain subsequent damage to liver cirrhosis, so that we can better understand the pathophysiological process of the disease and obtain better therapeutic results. Thus, this study aimed to identify advances in diagnostic methods and treatments for liver cirrhosis. This is a systematic literature review study, conducted by searching the descriptors “Liver cirrhosis”, “Alcoholic liver cirrhosis”, “Liver fibrosis” and “Liver”, in the databases: Scielo- Scientific Electronic Library Online, Lilacs - Latin American and Caribbean Center on Health Sciences Information, NIH-NCBI-Pubmed- National Center for Biotechnological Information – National Library of Medicine, following a search strategy according to descriptors in Portuguese and English, years 2015 to 2021. At the end of the search with the descriptors, 835 articles were found in the databases, of which 88 were in the Scielo platform, 286 in Lilacs and
461 in Pubmed. After the three selection steps, 811 articles were excluded and 23 articles that met the inclusion and exclusion criteria were selected for analysis. Based on this systematic review, it is pointed out that there has been a lot of development regarding the diagnosis and treatment of cirrhosis that, for many years, required scientific evidence to combat morbidity and mortality and reverse the condition of liver cirrhosis.

**Keywords:** Liver cirrhosis, Alcoholic Liver Cirrhosis, Liver fibrosis and Liver.

**RESUMO**

A cirrose hepática (HC) é um estado fisiopatológico difuso do fígado, considerado o estágio final de várias lesões hepáticas. É imprescindível destacar a necessidade de implantação de novos métodos diagnósticos e terapêuticos para conter os danos subsequentes à cirrose hepática, para que possamos melhor compreender o processo fisiopatológico da doença e obter melhores resultados terapêuticos. Assim, este estudo teve como objetivo identificar avanços nos métodos de diagnóstico e tratamento da cirrose hepática. Trata-se de um estudo de revisão sistemática da literatura, realizado por meio da busca dos descritores “Liver cirrhosis”, “Alcoholic liver cirrhosis”, “Liver fibrosis” e “Liver”, nas bases de dados: Scielo- Scientific Electronic Library Online, Lilacs - Latin American and Caribbean Center on Health Sciences Information, NIH-NCBI-Pubmed- National Center for Biotechnological Information - National Library of Medicine, seguindo uma estratégia de busca segundo descritores em português e inglês, anos 2015 a 2021. Ao final da busca com os descritores, foram encontrados 835 artigos nas bases de dados, sendo 88 na plataforma Scielo, 286 no Lilacs e 461 no Pubmed. Após as três etapas de seleção, 811 artigos foram excluídos e 23 artigos que atenderam aos critérios de inclusão e exclusão foram selecionados para análise. Com base nesta revisão sistemática, aponta-se que houve uma grande evolução no diagnóstico e tratamento da cirrose que, por muitos anos, exigiu evidências científicas para combater a morbimortalidade e reverter o quadro da cirrose hepática.

**Palavras-chave:** Cirrose Hepática, Cirrose Hepática Alcoólica, Fibrose Hepática e Fígado.

**1 INTRODUCTION**

Liver cirrhosis (LC) is a diffuse pathophysiological state of the liver considered the final stage of several liver lesions, characterized by chronic necroinflammatory and fibrogenetic processes, with subsequent conversion of normal liver architecture into structurally abnormal nodules, dense fibrotic septa, concomitant parenchyma exhaustion, and collapse of liver tissue (BARNETT, 2018). Alcoholic liver disease and chronic hepatitis B virus (HBV) and/or hepatitis C virus (HCV) infections are the main causes of liver cirrhosis worldwide (GOMES; TORRES, 2020).

LC is an increasing cause of morbidity and mortality in more developed countries, being the fourteenth most common cause of death worldwide, with about 1.3 million deaths per year. It is the fourth leading cause of death in Central Europe with about
170,000 a year in Europe and 33,539 per year in the United States of America. Liver disease is the main indication for 5,500 liver transplants each year in Europe (TSOCHATZIS et al., 2014). In Brazil, according to Melo et al. (2017) CH is considered the main chronic liver disease, which was responsible in 2015 for 18,923 deaths related to alcohol use alone.

This pathology is divided into two symptomatological conditions. The compensated is characterized by being the initial phase, does not present major problems for the patient, because it is in the asymptomatic form (AYDIN; AKÇALI, 2018). And decompensated, also called terminal liver disease when the clinical manifestations of liver cirrhosis appear. After the first decompensation event, cirrhosis becomes a systemic disease, with potential dysfunction of multiple organs and systems (SOUZA, 2019).

Most chronic liver diseases are notoriously asymptomatic until cirrhosis occurs with clinical decompensation (SMITH et al., 2019). Decompensating events include ascites, sepsis, varicose vein bleeding, encephalopathy, and non-obstructive jaundice. Ultrasound, computed tomography or magnetic resonance imaging of an irregular and nodular liver, together with impaired synthetic liver function, are sufficient for the diagnosis of cirrhosis (COSTA et al., 2016).

In this context, in advanced-stage patients, liver transplantation is adopted, the recommended treatment of which is recommended for both people in adult backgrounds and also for children. After surgery, care should be taken and cautioned with any risk, to avoid possible complications or rejection (JUNG; YIM, 2017). The categories of liver transplantation are: deceased donor transplantation, Split transplant, intervivas transplantation (ABTO, 2021). The new concept in the management of patients with cirrhosis should be prevention and early intervention to stabilize disease progression and prevent or delay clinical decompensation and the need for liver transplantation (MANSOUR; MCPHERSON, 2018).

According to Bernardi and Caraceni (2018) in a study on the nursing process applied to patients with liver cirrhosis, in addition to describing the need for pathophysiological care, they identified the need for care in relation to psychological and social status. In a way, the best way to prevent CH is to avoid the abusive use of alcoholic beverages, use condoms in sexual intercourse, hepatitis B vaccine, avoid caloric foods, excessive medications and self-medication (GOMES; TORRES, 2020).

Therefore, the prognosis of liver cirrhosis is highly variable and influenced by several issues such as etiology, severity of liver disease, presence of complications and
comorbidities. In advanced cirrhosis, survival decreases to one or two years. Correct advanced diagnosis and selected treatment with different molecules may help to understand the mechanisms of fibrogenesis, the driving forces of the pathogenesis of cirrhosis and the cautious approach of more effective therapeutic procedures (SANTOS et al., 2016).

Prevention of fibrosis with further deterioration of liver function by specific treatments is always necessary by removing the underlying causes of liver disease. Advanced liver disease, with subsequent complications, requires targeted treatment. It is essential to highlight the need to implement new methods of diagnosis and treatment to contain subsequent damage to liver cirrhosis in order to better understand the pathophysiological process of CH and obtain better therapeutic results. Thus, the aim of this study is to identify advances in diagnostic methods and treatments for liver cirrhosis.

2 METHODS

This is a literature review study, with descriptive and comparative procedure, using as a data source the bibliography on recent advances in diagnosis and treatment for the scope of liver cirrhosis.

The study was conducted through a research of the descriptors "Liver", "Liver Cirrhosis", "Alcoholic Liver Cirrhosis" and "Hepatic Fibrosis" in the following databases: Scielo- Scientific Electronic Library Online, Lilacs- Latin American and Caribbean Center for Information in Health Sciences, NIH-NCBI-Pubmed- National Center for Biotechnological Information - National Library of Medicine, following a search strategy according to the descriptors. For the fulfillment of this research, articles published in indexed journals and available online were selected that offered information on the descriptors in the years 2015 to 2021, aiming at a search for current studies.

The crossings of these descriptors were performed in English and Portuguese according to the table below (Chart 1).
The exclusion of the papers occurred in the absence of the full versions, as well as studies of the type: manuals, abstracts of congress annais, articles without abstract or without methodology, literature reviews, repeated and those performed outside the established period.

For the extraction of data from selected publications, a standardized and previously tested form was used and contains the following fields: authors, year of publication, publication category, language, geographic location, study design, sample design, evaluated populations, age group, gender, resources and diagnostic and therapeutic criteria for liver cirrhosis. The included publications were organized in tables, following the order of the year of publication of the study.

3 RESULTS

At the end of the research with the descriptors, 835 articles were found in the databases, of which 88 were on the Scielo platform, 286 in Lilacs and 461 in Pubmed. After the three selection stages, 812 articles were excluded and 23 articles that met the inclusion and exclusion criteria were selected for analysis, 10 articles are included in the table on diagnosis (Tables 1) and 13 are included in the treatment table (Table 2). The flowchart is organized according to the criteria described in the methodology and illustrates how the studies were successively excluded (Figure 2).
Figure 1: Systematic research flowchart.

Selection Criteria:
Complete papers, available online, published from 2015 to 2021 on the diagnosis and treatment of liver cirrhosis in the Portuguese English languages.

Publications
SCIELO - 88
LILACS - 286
PUBMED - 461
Total 835

Deleted 812

Selected Publications
SCIELO - 8
LILACS - 0
PUBMED - 15
Total 23

Source: Prepared by the authors, 2021.
Table 1: Articles selected and analyzed for advances in the diagnosis of liver cirrhosis.

<table>
<thead>
<tr>
<th>Autor e Ano</th>
<th>Título do artigo</th>
<th>Objetivo</th>
<th>Tipo de Estudo</th>
<th>População estudada</th>
<th>Tipo de terapia utilizada</th>
<th>Intervalo e Duração da terapia</th>
<th>Resultados</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Chalasani et al (2020)</td>
<td>Effects of Belapectin, an Inhibitor of Galectin-3, in Patients With Nonalcoholic Steatohepatitis With Cirrhosis and Portal Hypertension</td>
<td>Report phase 2b of safety in patients with NASH, cirrhosis and portal hypertension.</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>162 Patients with NASH cirrhosis and portal hypertension</td>
<td>Two doses of belapectin (2 mg/kg and 8 mg/kg) and placebo</td>
<td>Fortnightly for 52 weeks</td>
<td>2 mg/kg Belapectina reduziu a pressão venosa hepática</td>
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<tr>
<td>2 Anstee et al (2020)</td>
<td>Cenicriviroc for the treatment of liver fibrosis in adults with nonalcoholic steatohepatitis: AURORA Phase 3 study design</td>
<td>Evaluate the efficacy and safety of Cenicriviroc for the treatment of hepatic fibrosis in adults with NASH.</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>1,200 Patients with NASH and Fibrosis in stage F2 or F3.</td>
<td>150mg of CVC orally or placebo.</td>
<td>60 months</td>
<td>Decreased activity in NASH, predict the clinical benefit in the prevention of cirrhosis and death.</td>
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<td>3 Kimer et al (2020)</td>
<td>Atorvastatin for prevention of disease progression and hospitalisation in liver cirrhosis: protocol for a randomised, double-blind, placebo-controlled trial</td>
<td>investigate whether atorvastatin improves survival or delays the onset of systemic inflammation and decompensation in cirrhosis</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>225 people with liver cirrhosis.</td>
<td>atorvastatin 10–20 mg per day or placebo.</td>
<td>68 weeks, after 4 weeks.</td>
<td>A beneficial effect of atorvastatin on the clinical findings of cirrhosis will provide a cheap and effective causal treatment for chronic liver disease.</td>
</tr>
<tr>
<td>4 Nishikawa et al (2018)</td>
<td>Wnt/β-Catenin Signaling as a Potential Target for the Treatment of Liver Cirrhosis Using Antifibrotic Drugs</td>
<td>Report the correlation between Wnt/β-catenin and hepatic fibrosis and the antifibrotic effects of the binding protein.</td>
<td>Single-center, open-stage, phase I and II clinical trial</td>
<td>284 patients with advanced myeloid malignancies, advanced solid tumors, advanced pancreatic cancer.</td>
<td>PRI-724 doses of 10 mg / m² / day and 40 mg / m² / day, and the wnt / β-catenin route</td>
<td>12 weeks.</td>
<td>PRI-724 shows great potential as a therapeutic agent of hepatic fibrosis.</td>
</tr>
<tr>
<td>5 Curry et al (2015)</td>
<td>Sofosbuvir and Velpatasvir for HCV in Conduct an open phase 3 study</td>
<td>Sofosbuvir nucleotide and ns5a velpatasvir</td>
<td>Randomized, double-blind,</td>
<td>267 patients</td>
<td>High sustained virologic response rates in patients</td>
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<tr>
<td></td>
<td>Authors</td>
<td>Study Title</td>
<td>Study Design</td>
<td>Eligibility Criteria</td>
<td>Intervention</td>
<td>Comparator</td>
<td>Outcomes</td>
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<td>6</td>
<td>Xia et al. (2018)</td>
<td>Role of probiotics in the treatment of minimal hepatic encephalopathy in patients with HbV-induced liver cirrhosis.</td>
<td>Randomized assay analyzed using biology technique of recommended systems</td>
<td>67 consecutive patients with HBV-induced cirrhosis without reported hepatic encephalopathy</td>
<td>Clostridium cluster I and Bifidobacterium</td>
<td>Antibiotics, albumin (1.5 g/kg in inclusion [day 1] and 1 g/kg on day 3) albumin group plus antibiotics, n = 61</td>
<td>Probiotics improved the results of psychometric tests for MHE. Predominant bacteria (Clostridium cluster I and Bifidobacterium) were enriched in the probiotic-treated group, while Enterococcus and Enterobacteriaceae decreased.</td>
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<td>7</td>
<td>Fernández et al. (2019)</td>
<td>Effect of albumin treatment on portal and systemic hemodynamics and systemic inflammation in patients with decompensated cirrhosis.</td>
<td>Randomized, double-blind, placebo-controlled trial</td>
<td>136 patients with decompensated cirrhosis</td>
<td>Antibiotics, albumin (1.5 g/kg in inclusion [day 1] and 1 g/kg on day 3) albumin group plus antibiotics, n = 61</td>
<td>1 g/kg every 2 weeks for 12 weeks.</td>
<td>Evaluate the effects of long-term treatment with low doses and high doses of albumin in albumin serum, plasma rein, cardiocirculatory function, portal pressure and plasma cytokine levels.</td>
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<td>8</td>
<td>Bajaj et al. (2019)</td>
<td>Long-term results of faecal microbiota transplantation in patients with cirrhosis</td>
<td>Randomized clinical trial of FMT after antibiotics in cirrhosis and HS.</td>
<td>A healthy 37-year-old man whose material was used by at least 280 patients for the treatment of recurrent Ciprofloxacin, 500 mg orally 2 times a day, amoxicilline 500 mg orally 3 times a day and metronidazole 500 mg/day</td>
<td>Lactulose, rifaximine and proton pump inhibitors (PPIs) improves in the prevention of HE recurrence and liver-related hospitalizations.</td>
<td>Monitor all participants for at least 12 months after enrollment in both groups after their initial</td>
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<tr>
<td></td>
<td>Authors</td>
<td>Title</td>
<td>Study Design and Details</td>
<td>Result/suggestion</td>
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<td>9</td>
<td>Moreau et al (2018)</td>
<td>Effects of Long-term Norfloxacin Therapy in Patients With Q1 Advanced Cirrhosis.</td>
<td>Report a randomized clinical trial on the effects of long-term oral fluoroquinolone therapy in patients with advanced cirrhosis.</td>
<td>291 patients with Child-Pugh class C cirrhosis who did not receive recent fluoroquinolone therapy. Norfloxacin did not reduce mortality by 6 months, estimated by the Kaplan-Meier method, however, seems to increase the survival of patients with low protein concentrations in ascites fluid.</td>
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<td>10</td>
<td>Takehara et al (2018)</td>
<td>Efficacy and safety of sofosbuvir–velpatasvir with or without ribavirin in HCV-infected Japanese patients with decompensated cirrhosis: an open-label phase 3 trial</td>
<td>Report a randomized trial stratified by class and genotype on the effects of sofosbuvir-velpatasvir therapy with or without ribavirin.</td>
<td>102 patients with any HCV genotype and decompensated cirrhosis. Sofosbuvir-velpatasvir 400/100 mg. Ribavirin (REBETOL) was based on body weight. SVR12 rates were 92% (47/51) in each group. Sofosbuvir-velpatasvir for 12 weeks provides a highly effective and well tolerated therapy for Japanese patients.</td>
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<td>11</td>
<td>Bureau et al (2016)</td>
<td>Transjugular Intrahepatic Portosystemic Shunts With Covered Stents Increase Transplant-free Survival of Patients With Cirrhosis and Recurrent Ascites.</td>
<td>Compare efficacy of covered TIPS for high-volume paracentesis + albumin infusion (LVP + A) in terms of liver transplant-free survival (STF).</td>
<td>62 patients with liver cirrhosis and tense ascites in patients allocated to TIPS 6 7 8 9 10. TIPS coverage of 10 mm. The stent was used with dilation of 8 or 10 mmHg according to hemodynamic response. 12 meses. Stents covered for TIPS to increase the proportion of patients with cirrhosis and recurrent ascites who survive without transplantation for 1 year compared to patients who received LVP+ A.</td>
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<td>12</td>
<td>Guimaraes Et al (2020)</td>
<td>Peripheral blood endotoxin levels are not associated with small intestinal bacterial diseasesC. Difficile.</td>
<td>Determine the relationship between SIBO and serum endotoxin levels with the clinical, General biochemical evaluation, expired H2 test with Patients older than 18 years and with histological diagnosis of For the treatment of SBI use metronidazole 250 mg for 8/8 hours, for cases of 10 days for each case.</td>
<td>The values of endotoxin before and after treatment with antibiotics did not differ, even in the paired analysis, suggesting</td>
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<td>13</td>
<td>Vilela et al (2018)</td>
<td>Evaluation of the behavior of levels of hmgb1 and il6 as predictors of infection, acute kidney injury and mortality in cirrhotic patients with variceal bleeding</td>
<td>To evaluate the potential role of HMGB1 (High Mobility Group Box 1) and IL-6 (Interleukin-6) biomarkers as predictors of infection.</td>
<td>It is a prospective and observational study controlled by placebo.</td>
<td>32 cirrhotic patients with varicose vein bleeding.</td>
<td>HMGB1 were 1487 pg/mL (0.1 to 8593.1) and the average seeric level of IL-6 was 62.1 pg/mL (0.1 to 1102.4).</td>
<td>5-17 weeks.</td>
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4 DISCUSSION

According to the selected studies we can establish that hepatic fibrosis is a dynamic process and that early cirrhosis can be reversible. When clinical signs, symptoms, or abnormal liver function tests are discovered, an additional evaluation should be performed immediately. The most common causes of cirrhosis are viral hepatitis, alcoholic liver disease and nonalcoholic steatohepatitis (Bureau et al., 2016; FEDRIZZI et al., 2020; GUIMARAES et al., 2020; TAKEHARA et al., 2018; VILELA et al., 2018). Also, according to the articles, it was possible to describe two chapters, one on recent diseases in the diagnosis of liver cirrhosis and another on the new therapies used for the work and reversal of the clinical picture of the disease.

4.1 RECENT ADVANCES IN THE DIAGNOSIS OF LIVER CIRRHOSIS

Generally speaking, initial investigation for the diagnosis of liver cirrhosis includes serologies for viral hepatitis, ferritin, transferrin saturation and abdominal ultrasound, as well as complete blood count, liver function tests, and international normalized prothrombin time/ratio, if not yet requested. Additional tests are based on demographic data and risk factors (BARBUTI et al., 2020; FU et al., 2017; JIŘÍ et al., 2016; LURIE et al., 2015; MACHADO et al., 2020).

Common serum and ultrasound screening tests to assess fibrosis include score of the ratio index of aspartate transaminase for platelets, fibrosis score 4, FibroTest/FibroSure, nonalcoholic fatty liver fibrosis score, standard ultrasound, and transient elastography. Generally, noninvasive tests are more useful in identifying patients with fibrosis of no to minimal or advanced fibrosis. The management of chronic liver disease includes targeted counseling, laboratory tests and ultrasound monitoring (GUERRA et al., 2015; HONAR et al., 2015; RAMALHO et al., 2017; SCHMILLEVITCH et al., 2016).

In this context, Jiří et al. (2016) reported the early diagnosis of liver cirrhosis and treatment with appropriate systemic measures, studying 2,000 individuals with liver diseases of various etiologies and concluded that early diagnosis on regular ultrasound examination of the liver is recommended 6 months apart.

Fu et al. (2017) evaluated whether quantitative measurement of 90alpha thermal shock protein (Hsp90α) in plasma can improve the accuracy of the diagnosis by utilizing plasma Hsp90α by ELISA, the results conclusively demonstrate that Hsp90α plasma is a much better diagnostic biomarker than HCC AFP.
Yoav et al. (2015) analyzed biomarkers and noninvasive diagnostic tools in 1842 patients with hepatic fibrosis and non-inflammation and cytolysis, in the noninvasive diagnoses were used Fibrotest, Fibrometer, Cirrometer, Diffusion Weighted Magnetic Resonance and Magnetic Resonance Weighted Susceptibility -Fibro CT and came to the conclusion that they are diagnostic methods that may have the same efficacy as biopsy.

Machado et al. (2020) evaluated the use of Stroop EncephalApp for diagnosis and evaluation of minimal hepatic encephalopathy (EM) in a cross-sectional observational study, evaluating 99 patients with Liver Encephalopathy Psychometric Score (PHES), the current gold standard for the diagnosis of HmS, and later the Stroop EncephalApp. And they have come to the conclusion that Stroop EncephalApp is a viable tool with good sensitivity for EHM screening.

Guerra et al. (2015) evaluated the sensitivity and specificity of sonoelastography compared to liver biopsy in an observational study with 24 patients with chronic hepatitis C and non-alcoholic fatty liver disease. And they came to the conclusion that sonoelastography is an effective method to differentiate advanced fibrosis from early fibrosis and can replace liver biopsy most of the time.

Honar et al. (2015) in a study verified the diagnostic accuracy of the leukocyte esterase strip test for the diagnosis of spontaneous bacterial peritonitis in a cross-sectional study with 150 patients (children) with liver cirrhosis and ascites using abdominal paracentesis and concluded that the leukocytes esterase strip test can be used as a rapid test for diagnosis of spontaneous bacterial peritonitis, due to its high diagnostic validity. Ramalho et al. (2017) describe the imaging findings auxiliary for the diagnosis of hepatocellular carcinoma in observational and analytical carcinoma of 72 patients and concluded that magnetic resonance imaging proved to be superior to computerized tomography, not only in the diagnosis of liver cirrhosis, but also in the evaluation of tumor response after therapy.

Schmillevitch et al. (2016) evaluated liver elasticity after transplantation by means of a noninvasive examination using ARFI elastography in a cross-sectional study with 33 consecutively operated patients between 2002 and 2010. A cutoff point of 1.29 m/s was identified that sequesters patients with or without significant fibrosis.

Fredizzi et al. (2020) evaluated the profile of patients with IAR seen in a reference center in southern Brazil and verified factors related to treatment response. This was a retrospective cohort study that analyzed demographic, epidemiological and clinical data. In liver biopsies, the degree of fibrosis, histological activity, the presence of rosettes,
plasmocytic infiltrate and confluent necrosis were evaluated. And they concluded that most patients were young at the time of diagnosis and female. Association with extrahepatic autoimmune diseases and cirrhosis at presentation was seen in a considerable portion of cases. The treatment was effective, but there were no clinical, histological or serological parameters capable of predicting the response to treatment.

4.2 RECENT ADVANCES IN THE TREATMENT OF LIVER CIRRHOSIS

The goals of treatment are to prevent cirrhosis, decompensation and death. Varicose veins are monitored with endoscopy and often require prophylaxis with non-selective beta-blockers. Treatment of ascites includes diuresis, salt restriction, and antibiotic prophylaxis for spontaneous bacterial peritonitis, when indicated. Hepatic encephalopathy is treated with lifestyle and nutritional changes and, as needed, with lactulose and rifaximine. Screening for hepatocellular carcinoma includes ultrasound screening every six months for patients with cirrhosis (ANSTEE et al., 2020; BAJAJ et al., 2019; Bureau et al., 2016; CHALASANI et al., 2020; CURRY et al., 2015; FEDRIZZI et al., 2020; FERNÁNDEZ et al., 2019; GUIMARAES et al., 2020; KIMER et al., 2020; KOJI et al., 2018; MOREAU et al., 2018; SMITH et al., 2019; TAKEHARA et al., 2018; VILELA et al., 2018 XIAOXUE et al., 2018).

Chalasani et al. (2020) reported phase 2b safety in patients with nonalcoholic hepatic steatosis, cirrhosis and portal hypertension in a randomized, double-blind, placebo-controlled trial with 162 patients using two doses of belapectine (2 mg/kg and 8 mg/kg) and placebo fortnightly for 52 weeks and concluded that 2 mg/kg Belapectin reduces hepatic venous pressure.

Anstee et al. (2020) evaluated the efficacy and safety of Cenicriviroc (CVC) for the treatment of hepatic fibrosis in adults with non-alcoholic hepatic steatosis in a randomized, double-blind, placebo-controlled trial in 1,200 patients using 150mg of oral or placebo CVC for 60 months and found that there was decreased activity in non-alcoholic hepatic steatosis, preventing cirrhosis and death.

Kimer et al. (2020) investigated whether atorvastatin improves survival or delays the onset of systemic inflammation and decompensation in cirrhosis in a randomized double-blind, placebo-controlled trial in 225 people with liver cirrhosis using atorvastatin 10–20 mg per day or placebo for 68 weeks, and it has been observed that there is a beneficial effect of atorvastatin on clinical results of cirrhosis will provide a costly and effective causal treatment for chronic liver disease.
Nishikawa et al. (2018) report the correlation between Wnt/β-catenin and hepatic fibrosis and the effects of binding protein antifibrotics in a phase I and II single-center open clinical trial in 284 pri-724 doses of 10 mg and 40 mg per day, and wnt/β-catenin for 12 weeks and concluded that PRI-724 shows great potential as a therapeutic agent of hepatic fibrosis.

Curry et al. (2015) conducted an open phase 3 study involving HCV genotypes with sofosbuvir-velpatasvir or without ribavirin involving patients who developed decompensated cirrhosis. The study involved 267 patients using the drugs for 12 and 24 weeks and had reached the conclusion that there are high rates of sustained virologic response in patients with HCV infection and decompensated cirrhosis.

Guimarães et al. (2020) determined the relationship between BIS and serum endotoxin levels in non-cirrhotic patients with NAFLD, with the clinical, laboratory and histopathological aspects of the disease and the relationship between BIS and serum endotoxin levels before and after antibiotic treatment. This study included patients older than 18 years and with histological diagnosis of NAFLD, without cirrhosis. For the treatment of SBI we used metronidazole 250 mg for 8/8 hours for 10 days and ciprofloxacin 500 mg of 12/12 days was used for the cases of retreatment. And they came to the conclusion that serum endotoxin levels did not differ between patients with and without BIS, and that these levels did not change after drug treatment of bacterial proliferation, practically excluding the possibility that elevated endotoxemia levels are related to BIS.

Moreau et al. (2018) reported a randomized clinical trial on the effects of long-term oral fluoroquinolone therapy in patients with advanced cirrhosis in a randomized, double-blind, placebo-controlled trial with the participation of 291 patients with Child-Pugh class C cirrhosis who did not receive recent fluoroquinolone therapy. For treatment, 400 mg of norfloxacin (n 1/4 144) or placebo (n 1/4 147) was used once daily for 12 months and concluded that norfloxacin did not reduce mortality by 6 months, estimated by the Kaplan-Meier method, however, it seems to increase the survival of patients with low protein concentrations in ascites fluid.

5 FINAL CONSIDERATIONS

Based on this systematic review, it is noted that there was a lot of development about the diagnosis and treatment of cirrhosis that for many years required scientific evidence to combat morbidity and mortality and reverse the picture of liver cirrhosis.
Among the articles selected for diagnosis were serologies tests for viral hepatitis, ferritin, transferrin saturation and abdominal ultrasound, as well as complete blood count, liver function tests and prothrombin time, as well as common serum and ultrasound screening tests to assess fibrosis include the score of the rate of proportion of aspartate transaminase for platelets, fibrosis score 4, FibroTest/FibroSure, nonalcoholic fatty liver fibrosis score, standard ultrasound and transient elastography.

Antibiotics, probiotics, genetic markers and proteins were presented for treatment as satisfactory results for the reversal of the clinical picture and.
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