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Review Article

Bacterial infections and hepatic encephalopathy in liver cirrhosis–prophylaxis and treatment

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ABSTRACT

Infections are common among patients with liver cirrhosis. They occur more often in cirrhotic patient groups than in the general population and result in higher mortality. One reason for this phenomenon is bacterial translocation from the intestinal lumen that occurs as a consequence of intestinal bacterial overgrowth, increased permeability and decreased motility. The most common infections in cirrhotic patients are spontaneous bacterial peritonitis and urinary tract infections, followed by pneumonia, skin and soft tissue infections. Intestinal bacterial overgrowth is also responsible for hyperammonemia, which leads to hepatic encephalopathy. All of these complications make this group of patients at high risk for mortality. The role of antibiotics in liver cirrhosis is to treat and in some cases to prevent the development of infectious complications. Based on our current knowledge, antibiotic prophylaxis should be administered to patients with gastrointestinal hemorrhage, low ascitic fluid protein concentration combined with liver or renal failure, and spontaneous bacterial peritonitis as a secondary prophylaxis, as well as after hepatic encephalopathy episodes (also as a secondary prophylaxis). In some cases, the use of non-antibiotic prophylaxis can also be considered. Current knowledge of the treatment of infections allows the choice of a preferred antibiotic for empiric therapy depending on the infection location and whether the source of the disease is nosocomial or community-acquired.

Contents

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Core tips: This paper is an assembly of current knowledge regarding bacterial infections and other complications of liver cirrhosis such as hepatic encephalopathy. It consists of previously performed studies on the most common infections in the course of end-stage liver fibrosis. The article presents a summary of the epidemiological studies results from different countries. It also includes guidelines for current indications for antimicrobial prophylaxis. There has been discussed the current guidelines for empiric treatment of bacterial infections, that coexist with the liver cirrhosis.

1. Introduction

The human gastrointestinal tract is the largest surface covered by the epithelium in the body [1]. This surface is exposed to multiple microorganisms, including intestinal bacteria, archaea, viruses and others such as protozoa [2]. The endogenous intestinal microbiota creates an ecological system that plays roles in vitamin production, bile acid degradation, digestion, and immunity (both local and general [3]), and together with the intestinal mucosa forms a barrier against pathogens [4]. There is a relationship between the gut and the liver: blood with its intestinal content flows through the portal system and activates liver functions, while the liver produces the bile that is secreted into the gut to make fat digestion possible.

Liver damage may be caused by various factors including but not limited to viral infections, toxic damage and metabolic diseases. Changes in the intestinal microbiota may induce or worsen liver damage [5]. Liver cirrhosis is the tenth most common cause of death in the Western world, and infections are among the causes of acute decompensation of liver disease [6–8].

This paper is a summary of the current knowledge of the prophylaxis and treatment of bacterial infections in patients with liver cirrhosis and other complications of liver disease, such as hepatic encephalopathy (HE) [9].

2. Materials and methods

2.1. Search strategy

A broad search of the relevant literature for this topic was conducted. Searches in PubMed, Embase, and the Web of Science included but was not limited to the following search terms: “liver cirrhosis AND prophylaxis”, “liver cirrhosis AND SBP”, “liver cirrhosis AND infections”, “liver cirrhosis AND antibiotics”, “SBP prophylaxis”, “spontaneous bacteremia AND liver AND prophylaxis OR treatment”, “intestinal flora AND cirrhosis”, “norfloxacin AND prophylaxis”, “ciprofloxacin AND prophylaxis”, and “rifaximine AND liver cirrhosis”, “hepatic encephalopathy AND treatment”, “hepatic encephalopathy AND prophylaxis”, “bacterial translocation”, “gut microbiota”, “TLR AND cirrhosis”, “bacterial infection AND cirrhosis AND prevention”, “infection diagnosis AND cirrhosis”. The articles that were found had been published between 1994 and 2016. The inclusion and exclusion criteria were set “a priori” (see below).

2.2. Inclusion and exclusion criteria

There were selected studies that matched following criteria: observational or case-control studies, meta-analyses published in a peer-reviewed journal regarding the influence presence of liver cirrhosis and its association with bacterial infections. The duplicates were excluded; the excess of animal model studies were excluded if there were available studies regarding the same issue performed on humans.

Fig. 1 shows that there were found 120 full-text original articles. Five studies were excluded because they were duplicates. Low clinical relevance to date was the reason for excluding another 22 studies. Finally, 19 articles were excluded due to not evaluable data. Finally there have been selected 74 original articles [10].

3. Review: The influence of the microbiota on liver disease: pathomechanisms of the microbiota

The microbiota that can be found in the human gastrointestinal tract plays a pivotal role in maintaining the health of the host [2], including but not limited to processing food, synthesizing vitamins, digesting indigestible polysaccharides [9,11,12] and secreting bioactive metabolites that may affect the host's metabolism [12]. These organisms may also play a significant role in the pathogenesis of liver disease [2]. One possible complication is small intestinal bacterial overgrowth (IBO). While pathogenesis associated with the intestinal microbiota has not been clearly demonstrated, there is some evidence that alcohol metabolites and pro-inflammatory cytokines allow the overgrowth of intestinal flora [13–16]. Alcohol results on qualitative change of the microbiota (in humans [17,18] and in animal models [19–21]). Other factors that contribute to bacterial overgrowth include the modulation of gastric acid secretion, decrease of intestinal motility, lack of bile constituents, antimicrobial peptides, and portal hypertension [15,19,22]. Changes in intestinal microbial composition may also have an influence on homeostasis. Among the factors that affect intestinal microbiota, environmental and genetic should be mentioned [23]. The microbial inhabitants from populations with similar cultural factors like hygiene, exposure to antibiotics, chemicals, and diet are more similar than populations in different countries [24]. Bacteria gain energy from the diet. There are also observations that microbiota can regulate nutrient harvest. Increase in *Firmicutes* and decrease in *Bacteroides* were associated with an intensified energy harvest [23]. Alcohol also results in

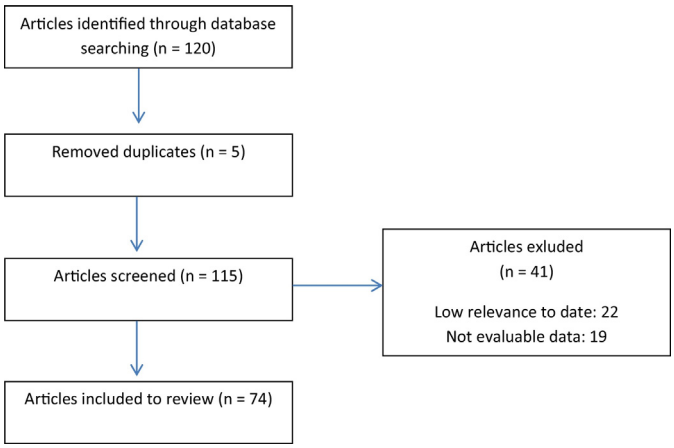

Fig. 1. PRISMA 2009 flow diagram [10].