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Review Article

Risk in Liver Disorders

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Abstract

Liver disease or dysfunction can be due to numerous causes or factors, such as acquired infections, congenital pathologies, or drug abuse. When this liver dysfunction and damage continue over time, it can lead to liver cirrhosis, which is irreversible and leads to jaundice, ascites, and portal hypertension. There are multiple complications that can occur in patients with liver damage and dental procedures must be very careful when paying attention to these patients. Therefore, an exhaustive bibliographical review was carried out about the main risks and complications in liver disease.

Keywords: Liver; Disorders; Risk; cirrhosis

Introduction

The two most frequent liver pathologies and main causes of cirrhosis are hepatitis or liver inflammation, which can be due to numerous factors, the most frequent being virus infections, and alcoholic liver disease, caused by continued alcohol abuse for a long time. a long period of time. The dental management of a patient with liver disorders is a real challenge, since the liver plays a vital role in many metabolic functions, such as bile secretion or bilirubin excretion from hemoglobin metabolism. A failure in liver function can lead to alterations in the metabolism of amino acids, ammonia, proteins, carbohydrates and triglycerides. A patient with liver disease will have an altered metabolism of numerous drugs commonly used by the dentist, will have a greater risk of bleeding due to abnormalities in the synthesis of different coagulation factors, and is also a patient at greater risk of infections.

Other important functions that can be affected when there is a liver disorder are those involved in the synthesis of coagulation factors and the metabolism of certain drugs. This fact will greatly condition the dental treatment of these patients, since it must be taken into account that there may be a greater risk of bleeding and that when using certain drugs their effect may be prolonged or altered [1,2].

Objective

Deepen and discuss the main risks of liver disorder in dental treatments.

Analysis strategy

The search was based solely on liver disease conditions of the buccomaxillofacial complex

Developing.

Given the repercussions of liver disease and the dental risks that it entails, it is important to understand the liver as an organ from the morphofunctional point of view in a general way, in order to have an idea of its functioning under normal and disease conditions. The liver. Morphofunctional characteristics. Situation. The normal liver occupies the right upper quadrant of the abdomen and extends from the fifth intercostal space in the midclavicular line to the right costal margin. The lower border of this organ descends below the costal margin during inspiration. Weight. On average, it weighs 1800 g in men and 1400 g in women; although in carcasses it weighs 1500 g. It represents 1.5 to 2.5% of lean body mass.

Dimensions. It is the largest organ in the body. It measures about 28 cm transversely, 16 cm anteroposteriorly, and 8 cm thick in the most voluminous area of its right lobe. Consistency. It is firm but friable and fragile, it allows itself to be depressed by the neighboring organs; It's dark red. External configuration and relations. The surface is smooth, it has two faces, one diaphragmatic and the other visceral, as well as a well-defined border between them, the lower border; in addition, a posterosuperior border and a posteroinferior border. Diaphragmatic face. The diaphragmatic face of the liver is convex, smooth and regular, and is oriented at the same time superior, anterior, posterior and to the right, since it adapts to the inferior face of the diaphragm, determining four portions: superior, anterior, right and right. later [1,3].

The diaphragmatic surface is divided into two lobes, one right and one left, by a peritoneal fold known as the falciform ligament, which extends from the diaphragmatic surface of the liver to the di-

aphragm. The right lobe is very convex, the left one is much smaller than the right, it is flatter and presents its middle part, inferior to the tendinous center of the diaphragm and, through it, in front of the pericardium, a slight concavity called cardiac impression, It is determined by the heart. The diaphragmatic surface of the liver conforms to the concavity of the diaphragm. Its right portion is almost covered by the thoracic layer and rises, like the diaphragm, up to the fourth intercostal space, at the level of the right mammillary line. From the anterior perspective, the diaphragmatic face comes into contact with the anterior abdominal wall, along the costal arch of the right hemithorax, to a near extension to 1 cm [4].

These relationships with the wall are much more extensive in the region of the infrasternal angle. The posterior portion of the diaphragmatic face of the liver is vertical and presents a very pronounced transverse concavity, which conforms to the projection formed by the vertebral column. Its most superior part is located to the right of the inferior vena cava; from here its height decreases towards the ends. It consists of two main lobes, the right and the left, which are divided by a ligament, called the falciform ligament, and the round ligament. The left lobe has two small lobes: the quadrate and the caudate. The liver has a dual blood supply, receiving blood from the right and left hepatic arteries (15%) and from the portal vein (85%). Blood leaves the hepatic veins, which drain into the inferior vena cava. The liver has different types of cells: a) Kupffer cells: They are macrophages and are located within the liver sinusoid. These cells are involved in the processing of microbial organisms, enzymes, tumor cells, antigens, and immune complexes. They are the main site of elimination of endotoxins. b) Stellar cells: Also known as Ito cells, vitamin A storage cells, fat storage cells, and lipocytes, they are located between the endothelium and hepatocytes (Disse spaces). When there is chronic damage, these cells are activated by the loss of retinoids, and loss of regulation of the synthesis of the extracellular matrix and collagen, this being the main event of fibrosis. c) Endothelial cells: These cells have receptors that allow the endocytosis of substances such as LDL and hyaluronic acid.

They also produce vasoactive mediators, endothelin 1, and cytokines. d) Hepatocytes: 60% of the cells in the liver are hepatocytes and are arranged in trabeculae or lamellae constituting the hepatic lobule. Depending on their location within the lobule, they display different structural, histochemical, and biochemical properties. They have an enormous regenerative capacity. Hepatocytes are organized as follows: Classic hepatic lobule: It is the structural unit of the liver. It is organized around a central vein from which the trabeculae of hepatocytes extend radially, bordering the sinusoids. It is hexagonal in shape and on the periphery are the portal spaces. In these portal spaces are branches of the portal vein and hepatic artery located in the periphery, the blood goes to the sinusoids. Hepatic acinus: is the functional structural unit of the liver. It has a rhomboid shape in the central part of which are a ductulus and small terminal branches of the portal vein and the hepatic artery. It has 3 metabolically active zones [5].

The vascular and lymphatic systems of the liver The liver has a high blood flow and low vascular resistance. Every minute about 1100 mL of blood reaches the liver from the portal vein. It also receives another 300 mL/min through the hepatic artery, so that the total flow is about 1400 mL/min, that is, 27% of the cardiac output. Under normal conditions, resistance to blood flow through the liver is low, as evidenced by the 9 mm Hg drop from the portal vein (mean pressure, 9 mm Hg) to the vena cava (mean pressure, 0 mm Hg).. In certain pathological conditions, such as cirrhosis (formation of fibrous tissue in the liver) or when there are clots in the portal vein, blood flow through the liver is greatly impeded. Elevated vascular resistance in the liver can produce a increased capillary pressure in the splanchnic circulation, causing significant fluid loss from the intestinal capillaries, ascites, and probably death. The liver has a very high lymphatic flow. The pores of the hepatic sinusoids are highly permeable, which facilitates the passage of fluids and proteins into the lymphatic system. The protein concentration of the lymph draining the liver is approximately 6g/dL, slightly less than the protein concentration in the plasma. The enormous permeability of the sinusoidal epithelium of the liver allows the exit of a large quantity of proteins, which implies the high formation of lymph. Almost half of the lymph in the body at rest is formed in the liver. Elevation of hepatic pressure (due to cirrhosis or congestive heart failure) produces the consequent elevation of lymphatic flow in the liver. An increase in vena cava pressure from 0 to 15 mm Hg can increase lymphatic flow from the liver up to 20-fold.

Under certain pathological conditions, the excess lymph thus formed can “bleed” through the external hepatic surface directly into the abdominal cavity, producing ascites. The basic functions of the liver are as follows

- Filtration and storage of blood.
- Metabolism of carbohydrates, fats, proteins, hormones and strange chemical compounds.
- Formation and excretion of bile.
- Storage of vitamins and iron.
- Formation of coagulation factors.

The liver makes bile, stores glycogen, iron, copper, vitamin A, many of the B vitamins, and vitamin D. It synthesizes albumin and other proteins, many of which are essential for normal blood clotting (prothrombin and fibrinogen) and an anticoagulant substance that is heparin. The most important functions are: a) Elaboration of Bile: Produces between 600 and 1200 ml. per day.

It is made up mainly of water, but it also contains bile salts (bile acids), bilirubin glucuronate, phospholipids, lecithin, electrolytes (Na+ and HCO3), cholesterol, and IgA. b) Degradation of hormones: The hepatocytes endocytose and degrade the hormones and, later

without being modified, they move them to the bile canaliculus. They then reach the lumen of the digestive tract and are digested. c) Detoxification of toxins and drugs: The liver purifies many drugs and secretes bilirubin (product of the degradation of hemoglobin). In the smooth endoplasmic reticulum of hepatocytes there is a mixed-acting enzyme called oxidase. This methylates, conjugates or oxidizes different drugs and toxins, thus inactivating them. d) Storage of vitamins: The liver acts as the main store of vitamin A. It also stores (although in smaller quantities) vitamin B12 and vitamin D, being able to prevent its deficiency for 12 and 4 months respectively. e) Carbohydrate metabolism: Hepatocytes are permeable to glucose, so insulin has no effect on glucose uptake in this organ. These can store glucose as glycogen. This process acts as a metabolic regulator [6,7].

Glycogen is hydrolyzed (glycogenolysis) by hepatocytes in the event that glucose levels fall below normal (hypoglycemia). Another process that hepatocytes can carry out is gluconeogenesis, which consists of synthesizing glucose from amino acids. f) Metabolism of proteins: The liver also breaks down amino acids (AA). Glucogenic amino acids are transformed into pyruvate or intermediates in the tricarboxylic acid cycle. In contrast, ketogenic AAs are converted to ketone bodies. The urea cycle is also carried out in the liver, in which the body disposes of the excess nitrogen that comes from AA. Ammonia, which is a toxic product derived from bacterial action in the digestive tract, is converted by the hepatocyte into urea and eliminated in the urine. g).

Lipid metabolism: Free fatty acids are used by the liver to synthesize triacylglycerols which are finally stored in adipose tissue as energy reserves. Phospholipids, cholesterol, and ketone bodies are stored in hepatocytes until they are released. This process begins when the chylomicrons reach the liver. Hepatocytes are responsible for breaking them down into fatty acids and glycerol. Fatty acids are used to synthesize phospholipids and cholesterol. The liver also produces very low density lipoproteins. metabolic functions of the liver Taken together, liver cells constitute a large chemical laboratory that shares substrates and energy with a myriad of metabolic systems.

The liver processes and synthesizes many substances that are transported to and from other regions of the body. Carbohydrate metabolism. In the metabolism of carbohydrates, the liver carries out the following: following functions

- Stores large amounts of glycogen.
- Converts galactose and fructose to glucose.
- It is the primary site of gluconeogenesis.
- Synthesizes compounds from intermediate products of carbohydrate metabolism.

One of the main functions of the liver in the metabolism of carbohydrates is the maintenance of the normal concentration of glucose in the blood. The liver can remove excess glucose from the blood and store it as glycogen. When the glucose concentration decreases, the liver can again form glucose from glycogen; this is known as the glucose buffering function of the liver. When the blood glucose concentration falls below normal, the liver begins to convert amino acids and glycerol into glucose through gluconeogenesis, to try to maintain the normal blood glucose concentration. Fat metabolism. Although almost all cells in the body metabolize fat, some aspects of fat metabolism occur primarily in the liver:

- The b-oxidation of fats to acetyl-CoA occurs very quickly in the liver. Excess acetyl-CoA is converted to acetoacetic acid, a highly soluble molecule that can be transported to other tissues, where it can be reconverted to acetyl-CoA and used for energy [8,9].

- The liver synthesizes large amounts of cholesterol, phospholipids and lipoproteins. About 80% of the cholesterol synthesized in the liver is converted to bile salts; the remainder is transported by lipoproteins to other body tissues. Phospholipids are also transported in the blood by lipoproteins. Both cholesterol and phospholipids are used by the body's cells to form membranes and intracellular structures.
- Almost all lipid synthesis from carbohydrates and proteins takes place in the liver. The fat synthesized in this way is transported by lipoproteins to adipose tissue for storage. Protein metabolism. The body cannot dispense with the functions of the liver in protein metabolism beyond a few days without death. The most important functions of the liver in the metabolism of proteins are the following:
- Deamination of amino acids, necessary so that they can be used for energy or converted into carbohydrates or fats. Almost all amino acid deamination takes place in the liver.
- Formation of urea, which removes ammonia from body fluids. The deamination process and the action of bacteria in the digestive tract form large amounts of ammonia. If the liver does not carry out this function, the concentration of ammonia in the plasma can increase rapidly.
- Formation of plasma proteins; plasma proteins are formed mainly in the liver (with the exception of gamma globulins, which are formed in lymphoid tissues).
- Interconversion of the different amino acids and synthesis of other compounds from the amino acids; An important liver function is its ability to synthesize non-essential amino acids and to convert amino acids into other metabolically important compounds. Miscellaneous metabolic functions of the liver Storage of vitamins and iron.

Liver tends to accumulate vitamins and iron; stores enough vitamin D to prevent deficiency for 4 months, enough vitamin A for 10 months, and enough vitamin B 12 for one year. When the body has extraordinary amounts of iron, it combines it with the protein apoferritin to form ferritin and it is stored in this form in the liver

cells. Formation of coagulation factors. The liver forms the following substances, necessary in the coagulation process: fibrinogen, prothrombin, accelerating globulin and factor VII; therefore, liver dysfunction can lead to blood coagulation abnormalities.

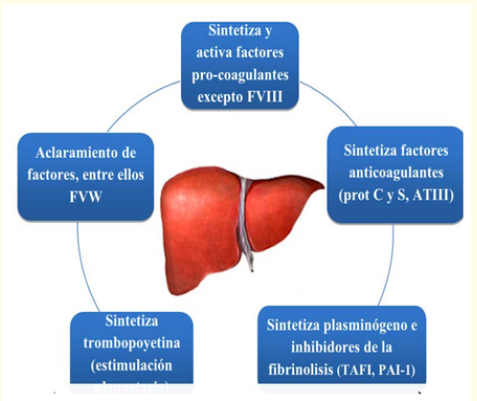

Figure 1

Prothrombin is a plasmatic protein that is continuously formed in the liver and is used continuously throughout the economy to coagulate blood. If the liver does not produce prothrombin, its concentration in the plasma decreases within 24 hours to values that are too low to ensure proper blood coagulation. The liver needs vitamin K to normally form prothrombin, so that a lack of vitamin K or the existence of a liver disease where the normal formation of prothrombin is compromised decreases its blood concentration, with a tendency to produce bleeding [9,10].

Fibrinogen is a protein present in the plasma produced by the liver and therefore, as a consequence of liver diseases, there is a decrease in the total amount of circulating fibrinogen. However, due to its high molecular weight, fibrinogen does not escape in significant amounts into the interstitial tissues. Metabolism of hormones and other foreign substances. The liver's ability to clear or eliminate many drugs and hormones, such as estrogen, cortisol, and aldosterone, is well known. Liver damage can cause the accumulation of drugs and hormones in the body. Formation and excretion of bilirubin in the liver Bilirubin is an end product of the metabolism of hemoglobin, which is excreted in the bile. When the heme portion of hemoglobin is metabolized, a substance called biliverdin is formed; this substance is rapidly reduced to bilirubin, which immediately combines with plasma albumin. This combination of plasma albumin and bilirubin is called free bilirubin. Free bilirubin is absorbed by liver cells, where it is released from plasma albumin and conjugated with glucuronic acid to form bilirubin glucuronide or with sulfuric acid to form bilirubin sulfate. The conjugated forms of bilirubin are excreted in the bile in the intestine, where they are converted to urobilinogen by bacterial action. Urobilinogen is highly soluble; part is reabsorbed into the blood in the intestinal mucosa. About 5% of the urobilinogen thus reabsorbed is excreted in the urine in the kidneys. The rest is eliminated again by the liver. Jaundice is an excess of bilirubin, free or conjugated, in extracellular fluids. Jaundice may be caused by: a) increased destruction of red blood cells (hemolytic jaundice), or b) obstruction of the bile ducts or damage to liver cells so that bilirubin cannot be removed from the digestive tract (jaundice). obstructive). In hemolytic jaundice, the excretory function of the liver is not impaired, but red blood cells are destroyed so rapidly that hepatocytes cannot clear bilirubin at the same rate.

The concentration of free bilirubin in the plasma rises well above normal values. In obstructive jaundice the bile ducts may be blocked by a gallstone or by cancer, or the liver cells may be damaged, as in hepatitis. The rate of bilirubin formation and its conjugation by the liver are nearly normal, but the conjugated bilirubin cannot pass into the intestine. In obstructive jaundice, the concentration of conjugated bilirubin in the blood is increased, so that most of the plasmatic bilirubin is conjugated, rather than free.

Warfarin and liver function

When a coumarin such as warfarin is administered, the plasma values of prothrombin and factors VII, IX and X formed entirely by the liver begin to decrease, thus indicating that warfarin has an intense depressant effect on the hepatic formation of all these compounds. . Warfarin acts like this by competing with vitamin K at the level of reaction sites in the intermediate process of prothrombin formation, and the other 3 procoagulants, thus blocking the action of vitamin K. After an effective dose of warfarin is administered, the coagulant activity of the blood decreases to approximately 50% of normal within 12 hours, and reaches approximately 20% of normal within 24 hours.

In other words, the coagulation process is not blocked immediately, but must wait for the prothrombin and other factors already in the plasma to be consumed. Coagulation normalizes one to three days after stopping treatment. There are several types of liver disease, including: - Intrahepatic and extrahepatic cholestasis - Acute and chronic hepatocellular failure - Hepatic encephalopathy - Portal hypertension - Hepatic steatosis - Alcoholic liver disease - Acute alcoholic hepatitis - Autoimmune hepatitis - Acute and chronic viral hepatitis. - Hepatic cirrhosis - Hepatocellular carcinoma - Cirrhotic ascites Cholestasis: alkaline phosphatase and gamma-GT enzymes are elevated. However, these are not specific for cholestasis since they may be altered by other causes. Alkaline phosphatase may be elevated during body growth and due to bone lesions; gamma-GT is inducible by drugs or alcohol. Another enzyme that more sensitively reflects cholestasis is 5' nucleotidase. This is exclusively of hepatic origin and its concentration does not increase with bone disease and it is not inducible by drugs or alcohol. During cholestasis due to extrahepatic obstruction of the bile ducts in the absence of liver failure, parenteral administration of vitamin K corrects pro-

thrombin time (Quick's time), this vitamin has no effect on Quick's time in acute or chronic hepatocellular failure. This is explained by the following: in cholestasis due to extrahepatic bile duct obstruction, coagulation disorders are due to a defect in the absorption of a fat-soluble vitamin, vitamin K, essential for the synthesis of factors II, VII, IX and X [11].

On the other hand, the synthesis of coagulation factors is exclusively hepatic and does not depend on vitamin K: these are factors I (fibrinogen), II (prothrombin), V (proacelerin), VII (proconvertin); VIII (antihemophilic factor A), and factor X (Stuart factor). In chronic hepatocellular insufficiency, the synthesis of factors of hepatic origin is decreased, which results in a lengthening of the Quick time.

Factor V is always decreased in liver failure and normal or increased in extrahepatic cholestasis, so its measurement is a good diagnostic measure in cases of liver failure and as a prognostic factor in the evolution of severe liver failure, as is the case. of acute fulminant hepatitis. Albumin is synthesized exclusively in the liver. It also synthesizes some essential proteins for the coagulation process. That is why when there is chronic deficiency in the functional capacity of the liver, plasma albumin levels are reduced and prothrombin time is prolonged. These two tests are used to estimate the degree of liver failure on the Child-Pugh scale. However, these tests are not specific to liver function: prothrombin time may be altered by impaired vitamin K absorption in cholestasis and prolonged fasting, and hypoalbuminemia may be seen in cases of insufficient protein intake, wasting enteropathy. of protein and proteinuria due to renal failure. Acute and chronic hepatocellular failure Acute liver failure: Characterized by a severe and progressive deficit of hepatocellular function in a patient without previous liver disease. It is associated with significant coagulopathy defined by a prothrombin time or factor V less than 50% above the normal value. It is called severe liver failure when encephalopathy develops.

Based on the interval between the onset of jaundice and the presentation of encephalopathy O'Grady., *et al*. in 1999 they classified acute liver failure into: a.- Hyperacute liver failure: Interval between jaundice and the onset of encephalopathy less than 7 days. b.- Acute liver failure: Between 8 and 28 days. c.- Subacute liver failure: Between 4 and 12 weeks. Main alterations to take into account from the stomatological point of view - Hematological: coagulopathy (due to decreased synthesis of coagulation factors, Disseminated Intravascular Coagulation DIC) - Infectious: seen in 90% of patients, especially by gram+ and fungal organisms. Chronic liver failure: There is no conceptual definition for chronic liver failure. Liver cirrhosis is considered the extreme of liver disease and the final path of clinical manifestations secondary to portal hypertension in the cirrhotic patient. Any chronic liver damage can lead to associated chronic liver disease that can progress to cirrhosis. There are numerous pathophysiological mechanisms of damage, but a single final common pathway that results in liver parenchymal fibrosis.

It has been determined that the destruction of 80 to 90% of the liver parenchyma is necessary for liver failure to manifest clinically as ascites, malnutrition, hepatic encephalopathy, esophagogastric varices, and risk of hepatocarcinoma. Hematologic disorders of chronic liver failure Anemia is multifactorial; contributing factors: chronic gastrointestinal losses, folate deficiency, direct alcohol toxicity, hypersplenism, bone marrow suppression, anemia of chronic disease (inflammation), hemolysis. Thrombocytopenia: due to splenomegaly caused by portal hypertension, it can sequester up to 90% of circulating platelets, rarely <50,000 [12].

- **Leukopenia and neutropenia:** Due to hypersplenism with splenic migration. Coagulopathy: correlates with the severity of liver failure. Deficiency of coagulation factors, they can develop disseminated intravascular coagulation (CIV), fibrinolysis, vitamin K deficiency, dysfibrinogenemia, thrombocytopenia. Susceptibility to infections in cirrhotic patients is well recognized; an incidence of bacterial infections in hospitalized cirrhotic patients between 15 and 47% has been reported. Hepatic encephalopathy: is a syndrome encompassing a spectrum of potentially reversible neuropsychiatric abnormalities seen in patients with liver failure, excluding unrelated metabolic and/or neurological causes. It implies that the cerebral alteration is due to metabolic alterations, which occur as a consequence of liver failure. Complete recovery of symptoms after improvement in liver function is direct evidence of this causal relationship.
- **Portal hypertension:** Defined as the presence of a pressure gradient in suprahepatic veins (HPVP) > 5 mmHg, or the presence of clinical complications derived from it, such as ascites, hepatic encephalopathy, esophageal varices, or hepatorenal syndrome. Ascites: the presence of serofibrinous fluid in the peritoneal cavity. It can be clinically detected when the amount of fluid exceeds 2.5 liters. In most cases, ascites is caused by cirrhosis of the liver. alcoholic liver disease It has been shown that alcohol is hepatotoxic, and its metabolite, acetaldehyde, fibrinogenic, so the consumption of large amounts of alcohol for a long time contributes to liver damage and disease. Although the amount and duration in terms of alcohol intake necessary to produce cirrhosis is not clear, the profile of the patient with alcoholic liver cirrhosis is usually that of a man with prolonged alcoholism for at least 10 years, who ingests large amounts of alcohol daily. . However, only 10-15% of alcoholics end up developing cirrhosis, which explains that, in addition to alcohol intake, other hereditary factors or nutrition have a great influence. Alcohol induces a flow of endotoxins (lipopolysaccharides) within the hepatic portal circulation, ultimately responsible for the release of chemokines, which directly and indirectly are responsible for damage to hepatocytes.

The pathological effects of alcohol on the liver manifest in the form of three pathological entities, which can appear alone or in combination: Acute alcoholic hepatitis: it is a progressive syndrome of inflammatory lesion associated with chronic and excessive intake of ethanol. Patients with severe conditions present symptoms such as fever, hepatomegaly, leukocytosis, and intrinsic liver function problems (jaundice, coagulopathies) together with manifestations of portal hypertension (ascites, hepatic encephalopathy, bleeding esophageal varices). It is a diffuse inflammatory alteration present in 10-35% of cases of alcoholic liver disease [13].

It is characterized by the appearance of different pathological changes such as cellular damage to hepatocytes, inflammatory infiltrate (predominance of neutrophils), fibrosis (mesh image). of wire) and other additional histological characteristics such as the presence of Mallory bodies, steatotic changes or proliferation of bile ducts. Hepatic steatosis: it is the abnormal accumulation of fatty acids and triglycerides in the hepatocytes. This accumulation is presented in the form of vesicles of which two types are recognized: microvesicular steatosis and macrovesicular steatosis. Currently, the importance of hepatic steatosis lies in the fact that it is considered the precursor lesion of non-alcoholic liver disease (NASH) that includes steatohepatitis. The accumulation of fat in the hepatocytes can lead to liver inflammation, with the possibility of developing fibrosis and finally ending in chronic liver damage (hepatic cirrhosis). Serum albumin levels and prothrombin time are normal unless the patient has cirrhosis and portal hypertension. It is the earliest alteration derived from the effect of alcohol on the liver and occurs in up to 90% of cases. It is characterized by a fatty infiltrate in the hepatocytes, which causes their distension and consequently leads to hepatomegaly. Cirrhosis: it is a chronic and diffuse disease of the liver characterized by changes in its histological structure, which include death of hepatocytes and their replacement by bands of fibrosis; retraction and occlusion of the venous sinusoids, damage and occlusion of the cholangioles are observed. Once this picture is established, the disease is irreversible. Cirrhosis of the liver, which occurs in 10-20% of cases of chronic liver disease, is the final stage of all progressive chronic liver diseases. It is a diffuse histopathological alteration of the liver characterized by loss of the liver parenchyma, formation of fibrous septa and structurally abnormal regenerative nodules, giving rise to a distortion of the normal liver architecture and an alteration of the anatomy of the hepatic vasculature. and microcirculation. Approximately 90% of the causes of liver cirrhosis in Western countries are alcohol abuse, non-alcoholic fatty liver disease (NAFLD) and chronic viral hepatitis.

Its natural history is characterized by an asymptomatic phase, called compensated cirrhosis, of variable duration. As the disease progresses with the development of greater portal hypertension and further deterioration of liver function, the complications of so-called decompensated cirrhosis appear, such as ascites, variceal bleeding, hepatic encephalopathy, or jaundice. Clinical manifestations of alcoholic liver disease The effects of alcohol will depend on the amount ingested, its plasma concentration, the concomitant use of certain drugs or other medical problems present in the individual. Its prolonged intake can cause cognitive deterioration even when the person is sober, in addition to other psychiatric problems such as anxiety, antisocial behavior, irritability or memory and learning difficulties [14].

Clinically, with the exception of liver enlargement, there are no visible manifestations of fatty liver and the diagnosis is usually made incidentally by evaluating other pathology. On the other hand, the clinical presentation of alcoholic hepatitis is often nonspecific and may include signs and symptoms such as nausea, vomiting, anorexia, malaise, weight loss, and fever. More specific findings include hepatomegaly, splenomegaly, jaundice, ascites, ankle edema, and spider angiomas. Alcoholic cirrhosis may remain asymptomatic for many years until sufficient destruction of the liver parenchyma has occurred to produce clinical evidence of liver failure. Ascites, spider angiomas, ankle edema, and jaundice may be the first manifestations, but bleeding from esophageal varices is often the primary sign. Other less specific signs of alcoholic liver disease include anemia purpura, ecchymosis, gingival bleeding, palmar erythema, nail abnormalities, and parotid sialodenosis.

Dental management of patients with alcoholic liver disease In a patient with alcoholic liver disease we have to have three main considerations: - Increased risk of bleeding due to impaired synthesis of coagulation factors: Bleeding tendencies are a significant feature in advanced liver disease. The basis of the diathesis is a deficiency of coagulation factors, especially the prothrombin group (factors II,VII, IX and X). All of these factors depend on vitamin K as a precursor for production. In addition to these deficiencies, thrombocytopenia can be caused by hypersplenism secondary to portal hypertension and bone marrow depression. Anemia and leukopenia can also be caused by the toxic effects of alcohol on the bone marrow and nutritional deficiencies. - Alteration in the metabolism of certain drugs. - Increased risk of infection: Kupffer cells, which account for more than 80% of tissue macrophages in the body, are impaired by continued exposure of the liver sinusoids to alcohol. Alcohol-induced impairment of Kupffer cell function and T cell responses results in increased risk of infection. As a general rule, a patient with alcoholic liver disease who is not treated should be immediately referred to a specialist doctor, avoiding any dental treatment. Once the patient is stable and under medical control, treatment can be carried out.

If a patient has a history of chronic liver disease or alcohol abuse, their doctor should be consulted if their current condition allows treatment. If the case of a patient with alcoholic liver disease who has not been reviewed in recent months is presented, a complete blood test should be requested that includes platelet count, leuko-

cyte count and coagulation tests (with determination of bleeding time, thrombin time and prothrombin). It must always be borne in mind that when surgery is to be performed on these patients or any treatment that involves bleeding, hemostatic measures such as those discussed in the section on viral hepatitis must be taken care of: topical hemostatics (oxidized and regenerated cellulose), agents antifibrinolytics (tranexamic acid), fresh plasma, platelets and vitamin K. As in the patient with viral hepatitis, the metabolism of different drugs will be altered. In these patients, there is a greater tolerance to local anesthetics and sedative or hypnotic drugs, so the use of higher than usual doses will be required to obtain the desired effects [15].

On the other hand, in cases where there is more advanced liver destruction, the metabolism of some drugs will be decreased, thus increasing their effects, so in many cases we will have to reduce the dose. The dentist should be especially careful in alcoholic patients when prescribing some drugs such as paracetamol, aspirin or metronidazole. There is a series of data that will suggest that drug metabolism will be affected: aminotransferase levels increased more than four times the normal value, serum bilirubin levels above 35 mM/L, serum albumin level less than 35g/L, signs of ascites and encephalopathy.

On the other hand, in these patients there is an increased risk of infection due to the passage of oral microorganisms into the blood circulation, mainly in surgical procedures and trauma, due to presenting a functional alteration of the mononuclear phagocytic system (Kupffer cells). Therefore, in cases of patients with uncontrolled liver dysfunction who strictly need to perform a procedure with a high risk of infection such as grafts, tumor and bone surgery (as in orthopedic and trauma surgery), as well as periapical surgery and dental inclusions, it will be necessary to carry out antibiotic prophylaxis (Amoxicillin 2g PO or IV or Clindamycin 600 mg PO prior to surgery as a general rule). Patients with alcoholic liver disease and cirrhosis tend to have more plaque and calculus, mainly related to poor oral hygiene, and therefore are patients at increased risk of caries and periodontal disease. No complex dental treatment should be carried out on these patients until they show a greater interest in their oral health, since any treatment that is not accompanied by a change in hygiene habits and lifestyle will fail. In addition, the nutritional deficiencies that usually accompany these patients can lead to the appearance of glossitis, tongue depapilation, cheilitis or candidiasis and, on the other hand, portal hypertension and coagulation disorders can cause spontaneous gingival bleeding and ecchymosis and petechiae. level of the oral mucosa. It is also common in patients with liver disease to find parotid sialodenosis.

Finally, the dentist must bear in mind that these patients with alcoholic liver disease, in addition to being heavy drinkers, most of them also consume large amounts of tobacco daily, so they are patients with a high risk of developing oral carcinoma and, therefore, Therefore, special attention must be paid to the appearance of potentially malignant lesions and any lesion suspected of malignancy must be carefully monitored. As part of the dental treatment, the patient should be insisted on the need to immediately reduce the consumption of alcohol and tobacco and on the importance of proper oral hygiene and acquiring healthy lifestyle habits. Oral manifestations in the cirrhotic patient The presence of oral manifestations in patients with cirrhosis such as the appearance of hemorrhages, petechiae, bruising, mucosal jaundice, gingival bleeding, glossitis and sialadenosis may be concomitant with the appearance of other signs and symptoms of liver dysfunction and their detection could indicate decompensation of cirrhosis [16].

On the other hand, treatment with diuretics causes a decrease in the amount of saliva or hyposialia, with the consequent risk of caries, gingival inflammation and candidiasis. In addition, there are indications obtained from animal experimentation that in cirrhosis there may be a delay in healing and in the formation of spongy bone after simple or surgical extractions. Regarding the differential diagnosis of oral neoplasms, oral carcinoma should be included. Squamous cell tumor (OSCC), which has been related to alcoholic cirrhosis, and the possibility of oral metastasis from hepatocellular carcinoma, since the risk of the appearance of this type of tumor is high in patients with cirrhosis.

Risk of infection in the cirrhotic patient. Prophylaxis and treatment The probability of the appearance of infections is higher in cirrhotic patients due to their state of immunosuppression, greater or lesser depending on the stage of the disease, which increases the susceptibility to suffering systemic infections. Dental infections constitute a local infectious focus that can cause the passage of bacteria and toxins into the blood, resulting in an increase in the state of systemic inflammation. In a healthy organism these small bacteraemias are neutralized by the components of the immune system; however, in cirrhosis there is a reduction in the clearance of circulating endotoxins, bacteria and inflammatory mediators due to the existence of a state of liver dysfunction. The influence of oral infections on the progression of cirrhosis has been extensively studied in the last decade [17].

The presence of teeth in need of dental treatment (apical periodontitis, pockets greater than 6 mm, root remains or great loss of bone support) has been positively correlated in some with the presence of more advanced stages of cirrhosis, with greater urgency. liver transplantation and with alcoholic cirrhosis, although a cause-effect relationship between the severity of dental disease and liver disease has not been demonstrated. In turn, alcohol is a substance that interferes with protein metabolism and tissue healing, both processes related to periodontal disease. In addition, patients with cirrhosis, especially of the alcoholic type, have high levels of serum cytokines also involved in the process of inflammation and

periodontal destruction, so in these patients the prevalence and severity of periodontitis could be higher. In patients with cirrhosis, regular visits to the dentist are advisable in order to maintain a good state of oral hygiene, thus preventing the appearance of oral infections and avoiding invasive treatments. Dental treatment in cirrhotic patients, especially that which involves bleeding, requires prior consideration of the stage of the disease and the need for antibiotic prophylaxis in order to reduce complications derived from bacterial dissemination, especially in patients with advanced cirrhosis. In addition, an increased risk of bacterial endocarditis has been found in patients with liver cirrhosis, especially in those with heart defects, drug abuse, and chronic renal failure, which justifies the need to administer antibiotics prior to surgery, notwithstanding , there is no clear evidence to recommend its administration 600 mg clindamycin in case of allergy to penicillin, one hour before the procedure [1,2].

Regarding the groups of antibiotics most used in dentistry, we will highlight penicillins-cephalosporins, clindamycin, macrolides and quinolones. Penicillins and derivatives very rarely cause liver damage, and it is usually asymptomatic. Both pencicillin G, penicillin V, ampicillin and amoxicillin are drugs with very few reported cases of hepatotoxicity. For this reason, its use as single-dose prophylaxis in patients With advanced cirrhosis and risk of sepsis, administering 2 g amoxicillin alone, or combined with 500 mg metronidazole one hour before the procedure, could offer a favorable benefit-risk ratio, which would explain its almost general administration in most invasive dental procedures. However, cases of hepatotoxicity due to amoxicillin-clavulanate have been widely reported and it is considered responsible for between 13 and 23% of cases of drug-induced hepatotoxicity, especially in patients older than 65 years, sex female and after repeated prescriptions, generally over 2 weeks of treatment. Clavulanic acid seems to be responsible for the marked increase in cases of hepatotoxicity. The liver damage produced by this component can appear up to 2 weeks after the end of the treatment, and it is advisable to dispense with the use of beta-lactamase inhibitors due to the risk of liver damage that they can generate.

Cephalosporins have rarely been implicated in cases of cholestatic hepatitis, assuming a hypersensitivity mechanism similar to that of penicillins. Macrolides have also been implicated as possible producers of liver damage. Cases of hepatotoxicity have been reported with erythromycin, sometimes occurring up to 2 weeks after the end of treatment. Azithromycin has been considered responsible for some pictures of cholestasis, like clarithromycin, especially in patients taking them in high doses. Clarithromycin, erythromycin and especially telithromycin have been associated with cases of acute liver failure and death. For all these reasons, the use of macrolides in advanced cirrhotic patients should be avoided. Liver damage as a consequence of the use of clindamycin is exceptional. However, its use, as occurs with macrolides, should be avoided or used at lower doses in advanced cirrhotic patients, especially if more effective treatment alternatives are available. Despite this, clindamycin is the antibiotic of choice for antibiotic prophylaxis in cirrhotic patients allergic to penicillin (single dose of 600 mg clindamycin in case of allergy to penicillin, one hour before the procedure). Cases of quinolone hepatotoxicity are rare, although cases of hypertransaminasaemia with hepatocellular damage, cholestasis, and acute liver failure resulting in death have been reported involving ciprofloxacin. In any case, its use in cirrhotic patients is very common, and it constitutes a fairly safe option. In addition, they do not usually require dose adjustment for this reason, although dose adjustment should be made in case of renal failure. Considerations in the management of hemostatic alterations in the cirrhotic patient [17,18].

The liver plays a very important role in the coagulation system, because it is the site where all the hemostatic factors (except von Willebrand factor) are produced, most of the regulatory proteins of the coagulation system, and the components of the fibrinolytic system. In addition, the liver is the major organ where activated hemostatic factors and plasminogen activators are cleared from the circulation. Although both hemostatic and antihemostatic factors are affected in liver disease, most diseases are related to alterations in primary and secondary hemostasis, therefore, in liver disease, the most frequent and lethal alteration of the coagulation system is hemorrhage. This can manifest as epistaxis, gingival bleeding, ecchymosis, gastrointestinal bleeding in any of the two large groups of liver pathologies: acute and fulminant hepatitis and chronic hepatocellular disease.

Alterations in the coagulation system in liver patients are due to thrombocytopenia and platelet function abnormalities, abnormal fibrinogen synthesis, disseminated intravascular coagulation (DIC), hyperfibrinolysis, and defects in the production of vitamin K-dependent factors. Spontaneous bleeding is rare in these patients, however, they can present with mild to moderate thrombocytopenia. In fact, this is the main hemostatic disorder in these patients. Its pathogenesis includes: hypersplenism; poor production possibly secondary to invasion of megakaryocytes by the virus, direct cytopathic effect on platelets, autoimmune destruction mediated by antibodies initially directed against the virus and in the most severe cases, due to DIC; and decreased platelet half-life. Occasionally, severe thrombocytopenia may occur and sometimes this may be the prelude to aplastic anemia secondary to this type of virus. Multiple alterations in platelet function have been described in acute hepatitis: decreased clot retraction, decreased platelet aggregation induced by ADP, collagen, or ristocetin, and ultrastructural platelet abnormalities. However, the mechanisms causing these abnormalities are still unknown. The most common of them in the fluid phase of coagulation is the lengthening of the prothrombin time (PT), which correlates quite well with the severity of the disease, so much so that it may be a better prognostic factor than any

of the other death tests. hepatic. The dependent K factors decrease significantly, but FVII does so before the others. Another factor that is reduced in acute hepatitis is FV and although it has been suggested that it may be an important marker of liver damage, the results are still not completely convincing. Although contact phase factors may be significantly decreased in this pathology, their clinical significance is uncertain. FVIII and fibrinogen levels are normal or elevated. However, levels of the former rise and those of the latter fall in patients with fulminant hepatitis.

Finally, there may be dysfibrinogenemia, especially in cases with fulminant hepatitis, although the real contribution of this last alteration in the hemorrhage of the liver disease patient is unknown. Most patients with fulminant hepatitis meet the criteria to be considered carriers of DIC. The appearance of the latter is due to the release of procoagulants by damaged hepatocytes, virus-induced expression of tissue factor by monocytes or endothelial cells, endotoxin, inflammatory mediators, and accumulation of activated factors in the portal flow. This DIC is magnified by decreased clearance of activated factors by the liver and by decreased plasma concentrations of natural anticoagulants. Lastly, it has been shown that patients with acute hepatitis may experience increased fibrinolysis, although this condition is much more frequent in fulminant failure.

Chronic hepatocellular disease Mild to moderate thrombocytopenia is a common finding in both liver cirrhosis and chronic hepatitis. In the bone marrow, megakaryocytes are normal or increased. The main mechanism to explain this thrombocytopenia is hypersplenism because between 60 and 90% of the total platelets of an individual with cirrhosis may be housed in the spleen. Other mechanisms may be an increase in platelet turnover, autoimmune destruction, folic acid deficiency, and a direct effect of ethanol on platelets or megakaryocytes. There are several alterations in platelet function in these patients: decreased adhesiveness, malaggregation induced by ADP, epinephrine, thrombin, ristocetin, and abnormal clot retraction. These alterations have been attributed to the inhibitory effect of the fibrinogen degradation products (PDF) present in the plasma of these patients, to ethanol and to the presence of high concentrations of high-density lipoproteins, and to alterations in the transmembrane signal transmission mechanisms in the plasma. platelet. The progressive loss of the liver parenchyma is proportionally reflected in its inability to produce proteins. Therefore, the plasma concentration of all hemostatic factors, except FVIII, decreases. The decrease in factors II, VII and X is proportional to liver failure. Frequently, a proportional decrease in FV is also found and, according to some studies, it seems to be a more reliable parameter of liver damage [19].

The FVIII is slightly elevated and the vWF may be functionally abnormal. Fibrinogen is normal or increased in patients with stable disease, but as the disease progresses, the level of this protein decreases proportionally. Dysfibrinogenemia characterized by inadequate fibrin polymerization is a common finding. It is postulated that some degree of low intensity DIC exists and that it may contribute to the mild decrease in fibrinogen and some other factors during the disease. The origin of this DIC is the release of procoagulants into the circulation, procoagulant endotoxins from the portal vein, decreased clearance of tissue factor and activated factors, and decreased concentration of natural anticoagulants. Finally, chronic liver disease patients have hyperfibrinolysis, which is evidenced by a shortening of the euglobulin lysis time, an increase in PDF and tissue plasminogen activator, decreased clearance of activated profibrinolytics, and a drop in the production of profibrinolytics. fibrinolytic regulators, specifically, tissue plasminogen activator inhibitor. It is known that there is a decrease in the intrinsic fibrinolytic mechanisms, which limits the extent of the degree of total fibrinolysis. The increase in fibrinolysis in liver cirrhosis may be, in part, conditioned by DIC because the problem partially reverses with the application of heparin. Preoperative management requires analyzing the patient's clinical history as well as evaluating the dental treatment to be performed and the history of bleeding from other previous procedures, since this last premise is an important indicator of coagulation disorders. In case of doubt, it is advisable to consult with the specialist doctor in order to know the degree of severity of the disease. The surgical risk of cirrhotic patients depends on the degree of liver dysfunction, portal hypertension, type of procedure to be performed, and presence of comorbidities [1,2].

The MELD and Child-Pugh scales, along with quantifying the severity of liver disease, may be useful in defining who could access elective surgery. Thus, patients with Child-Pugh A or MELD scores less than 10 points, in general, do not have a surgical contraindication; those with Child-Pugh B or MELD between 10 and 15 points have a relative contraindication, and finally, those with Child-Pugh C or MELD greater than 15 have a contraindication for elective surgery, so they should be accessed only in case of vital emergency. . Cirrhosis can result in depressed plasmatic levels of coagulation factors since the absorption and use of vitamin K will not be adequate, affecting the synthesis of factors II, VII, IX and X. Due to this, before a dental procedure that involves bleeding, it is recommended to perform an evaluation of hemostasis that includes a complete blood count with platelet count, prothrombin time, activated partial thromboplastin time, international normalized ratio (INR) and liver function test (transaminase levels, bilirubin level and albumin level). The INR alone does not always accurately predict the risk of postoperative bleeding.

Postoperatory, like the aforementioned laboratory tests. However, it is associated with the degree of liver dysfunction and its progression. Thrombocytopenia or platelet dysfunction suggest an increased risk of postoperative bleeding, even more so if this is found together with a high INR. A platelet level ≥ 100,000 is recommended for dental surgical procedures with increased risk of

bleeding, such as bone surgery, large flaps, or multiple extractions, and a minimum level of 50,000-55,000 for lower-risk surgical procedures, such as simple extractions or flaps. small in size [20].

Antifibrinolytic agents such as epsilon aminocaproic acid (EACA) or tranexamic acid inhibit fibrinolysis. For this reason, the use of these drugs to control bleeding after simple exodontia, as well as the intranasal administration of desmopressin (1-acid-8-D-arginine vasopressin, DDAVP), which increases the synthesis of factor VIII and stimulates the Von Willebrand factor generation can be a good alternative in those patients with platelet counts between 30,000-50,000 and INR values between 2-3, in whom platelet transfusion seems inadequate. Depending on the type of surgery and the risk of bleeding, antifibrinolytics can be used orally preoperatively, or in the form of rinses postoperatively. However, good control of post-extraction haemorrhage has been described in patients undergoing liver transplantation only with compression maneuvers of the surgical wound with gauze, provided that the INR values were equal to or less than 2.5 and platelets were below above 30,000, previously making sure that there are no other coagulopathies, diseases or drug use that affect hemostasis. Regarding laboratory analytical parameters, it has been described that low hematocrit levels (below 25%) correlate with a greater increase in bleeding time, even in patients with normal platelet counts. Similarly, the determination of fibrinogen values in blood and its replacement when its figures are less than 120 mg/dl is a parameter to take into account.

On the other hand, it must not be forgotten that the increased risk of bleeding in cirrhotic patients is also due to the presence of ectasias and varicosities in the gastroesophageal, pharyngeal, and oral mucosa, and that certain invasive procedures on these areas may cause a profuse bleeding, especially if there is also a significant compromise of the patient's haemostatic parameters, so it is also important to carry out careful handling of the tissues, avoiding excessive traumatization. American Society of Anesthesiologists (ASA) III compensated cirrhotic patients may be able to be treated at an outpatient level as long as the previously described premises and haemostasis parameters are within the previously described ranges, and the dental operative procedures are susceptible to performed under these conditions. On the contrary, ASA IV or ASA III cirrhotic patients in whom the hemostatic alterations are severe, coexist with another pathology associated with the patient, or there is a high risk of complications derived from complex dental treatment, dental treatment with hospital means would be recommended 1 , assessing an interconsultation with the hematology or digestive medicine specialist, especially when they are susceptible to being transfused with blood products or the administration of unconventional hemostatic agents such as intravenous DDAVP is required.

Drugs for dental use in cirrhotic patients Although there is no reliable parameter related to liver function that allows us to adjust drug doses, the recommendations are based especially on the Child-Pugh and MELD classification that correlate the degree of dysfunction as a consequence of Cirrhosis and survival. In patients with compensated liver disease, drug metabolism is similar to that of the general population; on the contrary, in cirrhotic patients with high MELD and Child-Pugh scores, it is recommended to use drugs at higher doses. small and spaced for short periods of time to avoid its accumulation and its potential adverse effects. The complications that can appear in these patients after drug administration are: acute liver failure, hepatic encephalopathy, acute renal failure and gastrointestinal bleeding. Local anesthetics should be administered with caution, as amides are metabolized by the liver and toxic reactions may occur with lower than expected doses of local anesthetics. Some of them, such as articaine, are extensively metabolized in plasma, while prilocaine is partially metabolized in the lungs, therefore, since they are not so dependent on hepatic metabolism, their possible toxic effects will be less [20].

Regarding analgesic drugs, most dental procedures require drugs from the first and second steps of WHO analgesia, that is, the use of non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol and minor opioids. The use of major opioids (third step of the WHO) or adjuvants is not usually required, and if required, their use should be considered after prior consultation with the specialist. Paracetamol can be safely prescribed in cirrhotic patients in small doses of 2 or 3g per day, even for long periods, due to the absence of sedation and nephrotoxicity and is recommended as first-line pain treatment, even in patients with alcoholic cirrhosis in whom this drug has an increased risk of toxicity. Good tolerance of up to 4g of paracetamol per day for short periods of time has been described, even in patients with cirrhosis who consume alcohol, although it is advisable not to exceed 2g per day in these cases. NSAIDs, despite the fact that they could be tolerated in patients with moderate liver disease, should be avoided or used with great caution in cirrhotic patients because they increase the risk of gastrointestinal bleeding due to their antiaggregant effect, which is added to the hemostatic alterations and thrombocytopenia that these patients frequently present. This risk is further increased in those subjects with varices and gastroesophageal ectasias or portal hypertension. Another reason why their use should be avoided is due to the cases of hepatotoxicity with acute hepatic decompensation associated with NSAIDs and the potential renal failure that all of them can cause.

In addition, many of them depend on transport by means of proteins, so that in cirrhotic patients with hypoproteinemia the free drug levels in serum are increased, which is why, if prescribed, it would be necessary to do so in lower doses than usual. There is still little experience in the use of coxibs in these patients. They seem to be effective in pain control and could be better tolerated as they do not interfere with platelet and renal metabolism, although their use is also recommended with caution. Regarding minor opi-

oids, their use is recommended with caution, since their toxicity increases in cases of hypoalbuminemia associated with cirrhosis. They should also be administered together with laxatives to prevent constipation and the development of encephalopathy.

Due to the marked bioaccumulation of these drugs, it is recommended to reduce the doses administered to these patients after prior consultation with the specialist. On the other hand, an erratic analgesic power has been described in the case of codeine and tramadol, since by reducing the hepatic passage, adequate biotransformation of these drugs into their active metabolites is not produced. However, low-dose tramadol can be considered a second-line analgesic for pain management in cirrhotic patients when the use of paracetamol is insufficient for pain control, although caution is recommended in its administration to patients with epilepsy. due to the risk of producing seizures and adjusting the dose on suspicion of renal dysfunction in cirrhotic patients. Considerations on the surgical management of the cirrhotic patient Surgical risk assessment in patients with liver cirrhosis is based on 3 main factors: assessment of liver function, urgency of the procedure, and type of procedure. Cirrhotic patients have a high surgical risk not only due to cirrhosis itself but also due to the presence of coagulopathy, malnutrition, immune dysfunction, cirrhotic cardiomyopathy, pulmonary and renal disorders.

Additionally, in the most important American study regarding surgical risk in elective procedures, it was possible to determine that the presence of clinically significant portal hypertension (esophageal varices, ascites, encephalopathy) is the primary factor related to mortality, morbidity, hospital stay, and costs. It is considered that there is a contraindication for surgery if the patient has acute hepatitis, especially if it is severe (international normalized ratio [INR] >1.5); alcoholic hepatitis; or acute liver failure, in which mortality of 10% to 50% has been described. Regarding the urgency of the procedure, it has been determined that when major emergency surgery (ASA V) is necessary, mortality is 50% to 100%, with great differences when compared to elective procedures, so it should be It should be discussed with the patient, the family and the surgical team if the risk of urgent intervention is assumed taking into account these poor results. CTP C cirrhotic patients have a contraindication for any major surgical procedure. The pre-surgical evaluation should include the American Society of Anesthesiology (ASA) classification.

Compensated cirrhotic patients are classified as ASA III and decompensated patients are classified as ASA IV, for which reason the surgical risk is considerable from the start. Bleeding: Patients with end-stage liver disease may experience severe bleeding. Prothrombin time and bleeding time data should always be available. Additionally, these patients might need vitamin K and/or platelet or coagulation factor replacement. Blood pressure: Blood pressure in patients with liver disease can increase significantly due to portal hypertension and cause bleeding. Emergencies and Urgent Care: For patients with severe liver disease who require urgent care, treatment in a special care clinic or hospital should be considered. Limited care should be provided only for pain control, treatment of acute infection, or control of bleeding until the condition improves [20].

Follow-up: It is important to follow up with the post-operative patient to be sure that there are no complications. 1. Correct anamnesis to inquire about antecedents such as: o Consumption of alcohol, tobacco or drugs. o Currently pharmacological treatment. o Concomitant diseases. o Anticoagulant/antiplatelet drugs: consult with the specialist and assess hospital treatment. 2. If you have moderate liver dysfunction/cirrhosis (ASA II/ASA III): Blood test: o Complete blood count: or Platelets >50,000/µl. o For procedures with a high risk of bleeding 100,000/µl. or INR < 2. o If the INR is > 2, platelets < 50,000/µl or the patient has known coagulopathies, consult the hematologist for the dental procedure to be performed and assess the administration of DDAVP in the hospital setting. Indicator parameters of liver dysfunction.

If the parameters are far from the normal range, interconsultation to assess hospital treatment. o History of previous dental treatment.

EACA or oral preoperative tranexamic acid (Administer depending on the risk of bleeding and the state of hepatic decompensation) o Antibiotic prophylaxis: or Amoxicillin 2g p.o. one hour before the procedure (600mg clindamycin p.o. one hour before the procedure in case of allergy to penicillin. o Careful handling of the tissues during the intervention. Avoid osteotomy and tearing of the flaps. or Suture. If extraction has been performed, placement of hemostatic material in the alveolus. o EACA or postoperative tranexamic acid in rinses and/or topical application through gauze. o Postoperative follow-up. If the bleeding does not stop, go to the emergency room. o Review at 48h: o Check the healing status and assess the establishment of rinses with 0.12% chlorhexidine 2 v/d for a week. 3. Advanced cirrhosis (ASA IV): Presence of esophageal varices, spontaneous bacterial peritonitis, portal hypertension, ascites, encephalopathy, or other complications derived from advanced cirrhosis [1,2].

Hospital treatment must be carried out by the Maxillofacial Surgeon with the prior interconsultation of your primary care physician. ASA: American Society of Anesthesiologists (ASA); EACA: Epsilon Aminocaproic Acid; DDAVP: Desmopressin. Considerations on the use of antibiotics and analgesics in patients with liver disease in Dentistry (ASA II and III) Mild liver dysfunction (ASA II): Use of antibiotic therapy: o First choice: Phenoxymethylpenicillin: 500-800 mg./8 h. VO. Or: amoxicillin: 500-1000 mg/8 h./PO. o In those allergic to beta-lactams: clindamycin: 150-450 mg./6 h. o Reserve the use of quinolones and cephalosporins for specialized

care. Limit or dispense with the use of macrolides and beta-lactamase inhibitors. o In the case of complex and extensive infections with lack of response or ASA IV patients: refer to specialized care for assessment. o Antibiotics: Antibiotic prophylaxis is not recommended as usual, although it should be noted that patients who have severe liver disease may be more susceptible to infection. The use of metronidazole and vancomycin should be avoided.

Use of analgesia. Dental procedures likely to cause mild musculoskeletal pain (VAS<3) and Drugs for dental use in cirrhotic patients Considerations on the surgical management of the cirrhotic patient Indicator parameters of liver dysfunction. Considerations on the use of antibiotics and analgesics in patients with liver disease in Dentistry (ASA II and III) Use of analgesia. Dental procedures likely to cause mild musculoskeletal and visceral pain (VAS<3). visceral There is the possibility of outpatient pain management by the dentist: o Dipyrone: 500 mg every 8 h PO with a duration adjusted to the period of pain, avoiding its unnecessarily prolonged prescription. o Paracetamol: 2-3 g/24 h. in 3-4 doses/VO. Duration adjusted to the period of pain, trying to avoid unnecessarily long treatments. Dental procedures likely to cause moderate musculoskeletal and visceral pain (VAS 3-7). There is the possibility of outpatient pain management by the dentist

- **Dipyrone:** Same regimen as above + tramadol 25-50 mg./8 h./PO or at the lowest possible dose for effective pain control. o Paracetamol: same regimen as above + tramadol 25-50 mg./8 h./PO or at the lowest possible dose for effective pain control. Procedures likely to cause severe pain (VAS >7): musculoskeletal and visceral.

It is advisable to refer for treatment to specialized care. Moderate liver dysfunction/cirrhosis (ASA III): Use of antibiotic therapy: o First choice: Phenoxymethylpenicillin: 500-800 mg./8 h. VO. Or: amoxicillin: 500-1000 mg/8 h./PO.

In those allergic to beta-lactams: clindamycin: 150-450 mg./6 h. o Reserve the use of quinolones and cephalosporins for specialized care. Limit or dispense with the use of macrolides and beta-lactamase inhibitors. o In the case of complex and extensive infections with lack of response or ASA IV patients: refer to specialized care for assessment. Use of analgesia. Dental procedures likely to cause mild musculoskeletal and visceral pain (VAS<3). There is the possibility of outpatient pain management by the dentist: o Dipyrone: 500 mg every 8 h PO with a duration adjusted to the period of pain, avoiding its unnecessarily prolonged prescription. o Paracetamol: 2-3g/24 h. in 3-4 doses/VO. Duration adjusted to the period of pain, trying to avoid unnecessarily long treatments. Dental procedures likely to cause moderate musculoskeletal and visceral pain (VAS 3-7).

There is the possibility of outpatient pain management by the dentist as long as there is adequate follow-up and monitoring of the patient at the outpatient level: o Dipyrone: same regimen as above + tramadol 25-50 mg./8h./PO or at the lowest possible dose for effective pain control + laxatives o Paracetamol: same regimen as above + tramadol 25-50 mg./8 h./PO or at the lowest possible dose for effective pain control + laxatives. Procedures likely to cause severe pain (VAS >7): musculoskeletal and visceral.

Referral to specialized care for treatment is recommended. Advanced cirrhosis (ASA IV): o Specialized care management. Avoid the use of NSAIDs and powerful opioids in ASA II, III and IV. Drugs: Because many drugs are metabolized in the liver, it may be necessary to avoid or reduce the dose of certain drugs. AVA: Visual Analogue Scale (pain). Hepatitis The WHO (world health organization) defines hepatitis as an inflammatory disease of the liver, which can be caused by viruses, bacteria, trauma, autoimmune processes, hereditary disorders or toxins (for example alcohol and some medications).

It is a fairly common disease. Approximately one third of the world's population is affected by hepatitis. For this reason it is important to know it, and to know how it can affect us in our day to day and more specifically at the level of dental treatment. It can have an acute or chronic course or evolution. In acute hepatitis, the disease appears suddenly and disappears in a matter of weeks or months. In chronic hepatitis, the disease persists beyond six months, and finally liver inflammation may persist but with proper functioning of the liver lobes (persistent chronic hepatitis, scarring) or in the worst case, lead to liver cirrhosis, in which liver tissue is progressively destroyed, with the corresponding failure of its functions, or liver cancer. Clinical manifestations Once contagion with the virus has occurred, an incubation period takes place, which is variable depending on the type of virus.

During this phase, the virus is detectable in the blood, but the serum bilirubin and aminotransferase are normal, and antibodies to the virus are not detected. After this first phase, the prodromal or pre-icteric period begins, the duration of which can be 10-15 days. It usually begins with asthenia, anorexia, followed by nausea and vague pain, which can be confused with a flu process (runny nose, cold, runny nose...) or even in some cases, developing a depressive picture. At this stage, specific antibodies against the virus are detected and serum aminotransferase levels are increased. When dark urine (coluric urine) begins to appear due to the increase in bilirubin in the blood due to obstruction of the hepatic bile ducts derived from inflammation, we know that we are in the so-called jaundiced period. This period, which usually lasts 1 to 3 weeks, may be accompanied by fatigue and more intense nausea, anorexia, or dysgeusia. In severe cases we can observe hepatomegaly and splenomegaly. In addition to increasing bilirubin levels, serum aminotransferase is increased up to 10 times its normal value, while serum and hepatic levels of the virus decrease. After this period, the recovery or convalescence stage begins, in which the

patient begins to feel better and recovers his appetite, the levels of bilirubin and serum aminotransferase normalize, the highest levels of antibodies are detected, and the virus clearance.

The most frequent complications of acute hepatitis are divided into hepatic and extrahepatic complications. Among the first are some such as jaundice, which is produced by an accumulation of bilirubin in plasma, epithelium and urine, clinically observed when plasma bilirubin levels are 2.5mg/100ml, the chronification of hepatitis, that inflammation of the liver lasting at least 6 months, acute or fulminant liver failure or the development of cholestatic hepatitis, interruption of bile flow in the liver, leading to leakage of bile and the development of prolonged fluctuating jaundice. Regarding extrahepatic complications, depression can be distinguished, the most common extrahepatic complication, manifesting in up to 25% of patients with hepatitis, Diabetes Mellitus type II, proving that its prevalence is higher in patients with hepatitis (15%).

Hepatitis B: The hepatitis B virus (HBV) belongs to the hepadnavirus family and the natural reservoir of HBV is man and it is transmitted parenterally. The virus is not spread by feces, contaminated food, water, insects, nor by to breast milk. Only vaginal and menstrual fluids, blood, and semen have proven to be infectious.

Four routes of transmission are known: - Parenteral: through syringes and infected blood products. - Sexual - Perinatal or vertical: from infected mother to child at the time of delivery. If the pregnant mother is a carrier of HBV and is also HB-Ag positive, her child will have a 90% chance of becoming infected and being a carrier, while if the mother is only a carrier of HBsAg, the infection occurs in about 10% of newborns. born. - Horizontal: through contact with infected people. The virus can remain stable for up to 7 days on different surfaces in the environment and, as a consequence, spread through contaminated objects such as toothbrushes, baby bottles, toys, cutlery or sanitary equipment, by contact with mucous membranes or open wounds. Hepatitis D: It is still a health problem, however its prevalence has decreased significantly. Its transmission can be through individuals using IV drugs. Blood transfusion is not a frequent mechanism since HBsAg was tested. HDV infection can take place in two scenarios: in the first, the patient is infected with HBV and HDV at the same time; this is known as a coinfection.

The patient presents acute hepatitis that ranges from mild to severe or fulminant and that in most cases is self-limited and is indistinguishable from hepatitis B. The second scenario is that in which the virus infects a person who is already a carrier of HBsAg , this is known as superinfection. The patient presents acute hepatitis in the case of the unknown HBsAg carrier or as an exacerbation of chronic hepatitis in a patient already known to have HBV. These usually present as severe or fulminant hepatitis. In superinfection it is also common for it to present as active chronic hepatitis. HDV is capable of producing cirrhosis in up to 70% of cases, and coinfection with HDV increases the risk of hepatocellular carcinoma and death.

Late-onset fulminant hepatic failure (>4 months) has also been reported. Individuals at risk based on the modes of transmission of the B and Delta virus There are groups among the general population with greater susceptibility to becoming infected and becoming chronic: patients with congenital or acquired immunodeficiency (HIV), immunosuppressed patients or patients on hemodialysis. There are also groups at high risk of contracting the infection such as: - Children of infected mothers. - Young children who attend nurseries or boarding schools in endemic areas. - Cohabiting family members and sexual partners of infected people. - Patients and employees of hemodialysis centers. - People addicted to intravenous drugs and who share syringes. - People who use non-sterile medical or dental material. - Patients who perform acupuncturist treatment or tattoos. - People who live or have to travel to endemic areas. - Homosexual couples or with multiple sexual partners. Hepatitis C: is caused by a single-stranded RNA virus belonging to the Hepacivirus genus, within the Flavivridae family, to which other viruses such as yellow fever (YFV) and Dengue virus belong. The main target cells are hepatocytes and B lymphocytes. One of the main characteristics of the hepatitis C virus (HCV) is its great genetic variability. Among the risk factors recorded in most of the studies are: blood transfusion or organ transplantation, use of illegal intravenous drugs, multiple sexual partners (subjects with >50 partners have a HCV prevalence of 9%), exposure to blood products in health personnel, perinatal infection, patients with human immunodeficiency virus (HIV) or hemodialysis.

Other attributed risk factors include a history of acupuncture, tattoos, or skin piercing. Breastfeeding is not a risk factor for HCV transmission except for the mother having cracked or bleeding nipples.

Autoimmune hepatitis: it is known as lupus hepatitis or chronic active hepatitis. It is characterized by being a predominantly periportal inflammatory disease, associated with hypergammaglobulinemia, frequently with detectable autoantibodies and a good response to immunosuppressive treatment. The cause of autoimmune hepatitis is not known, however, it is known that there is a certain genetic predisposition to develop this disease, as occurs with other autoimmune diseases.

Sometimes it is possible to identify an infectious trigger factor that initiates the hepatic inflammatory process and that can persist even after the infection is eliminated, as occasionally occurs with hepatitis A virus infection. Certain medications such as nitrofurantoin and minocycline can trigger an autoimmune hepatitis. Autoimmune hepatitis is classified into: Type 1: It is the most common form and can be seen at any age. It usually presents with anti-nuclear (ANA) or anti-smooth muscle (ASMA) antibodies. Type 2: It occurs in children and adolescents. Its most characteristic marker

is the presence of liver-kidney microsomal antibodies (LKM-1). Laboratory findings include variable elevations in transaminases (SGOT/AST and SGPT/ALT) with normal or slightly elevated alkaline phosphatase and gamma glutamyl transpeptidase (GGT) values.

There may be elevated bilirubin, decreased albumin, and prolonged prothrombin time. Immunoglobulin G (IgG) levels are characteristically elevated. oral manifestations of hepatitis The main problem associated with chronic hepatitis and prolonged liver damage (cirrhosis) is abnormal bleeding, due to alterations in the synthesis of coagulation factors, alterations in fibrin formation, excessive fibrinolysis or thrombocytopenia associated with splenomegaly. that can accompany chronic liver disease. Although it is very rare, it should be known that in patients who develop hepatocellular carcinoma, metastases may appear at the mandibular level, preferentially located at the premolar level and the mandibular ramus. Finally, we must bear in mind that in patients with advanced hepatitis there will be an alteration in the immune system, so there will be an increased risk of infection. The main oral manifestations of this disease are: xerostomia, gingival diseases, bad breath, jaundice of the mucous membranes, perioral eruptions, petechiae or small hemorrhages in the oral mucosa.

They are patients with a greater tendency to bleeding in surgeries or dental extractions, so before taking any action, the prothrombin time must be determined, which must be less than twice the normal value. (normal is 11 to 12 seconds). In addition, it must be taken into account that due to liver damage, these patients will have greater sensitivity to certain medications. Dental management in patients with hepatitis. Patient with Active Hepatitis: No non-emergency dental treatment should be performed on a patient with active hepatitis. According to the American Society of Anesthesiology, these patients are classified as ASA IV, patients with severe uncontrolled systemic disease who require imminent medical treatment, putting their lives in danger. If it were an emergency, the treatment must be carried out inside an isolated cabinet and following strict compliance with the regulations and safety precautions to avoid contagion. Aerosols should be minimized and drugs metabolized in the liver should be avoided as much as possible [1,2].

If it is necessary to perform any surgical intervention, tests should be requested to assess possible coagulation disorders: complete blood analysis, bleeding time, prothrombin time, thrombin time, liver biochemistry (GOT, GPT and GGT), and analyze the results by making an interconsultation with the specialist doctor to assess whether or not surgery is possible. Depending on the laboratory data and treatment to be performed, consider the possibility of using topical hemostatics (oxidized and regenerated cellulose), antifibrinolytic agents (tranexamic acid), fresh plasma, platelets, and vitamin K. In the case of patients with active hepatitis with marked liver dysfunction, it will be necessary to carry out antibiotic prophylaxis if a procedure with a high risk of infection is to be performed. It should be taken into account that the dentist must always refer a patient with acute hepatitis for diagnosis and medical treatment.

- **Patients with a history of hepatitis:** Most hepatitis carriers do not know that they have had the disease, this is because it is often asymptomatic and anicteric. Therefore, the only method of protection against a possible infection associated with people with undiagnosed hepatitis or with other undetected infectious diseases is to adopt a strict program of clinical asepsis for all patients, vaccination against HB being highly recommended. . For those patients who provide a positive history of hepatitis, it is recommended to send laboratory tests to detect the presence of the surface antigen for HB (HBsAg) or the antibody with HCV (anti-HCV) and to be able to recognize what type of hepatitis they suffered , since on many occasions the patient's information is not entirely reliable. Patients at high risk of HBV or HCV infection: In patients considered a risk population whose infection is not confirmed, it is recommended to test for the presence of HBsAg and anti-HCV. If it is discovered that the patient is a carrier, it would not be necessary to modify the therapeutic approach, but it would be necessary to take anti-contagion measures to the extreme at all times. In addition, the patient could have undetected active chronic hepatitis, which could lead to bleeding complications or drug metabolism problems. If a needle stick or other previously used material were to occur in one of these patients, it is vitally important to know if the patient was positive for HBsAg or anti-HCV, and thus be able to determine the need for antibody treatment, vaccination, and follow-up. doctor. Patients who are carriers of hepatitis: If a patient is a carrier of HB (HBsAg positive) or has a history of HC, standard precautions should be followed to prevent transmission of the infection. Some hepatitis carriers may have chronic active hepatitis, with the consequences that have already been discussed. Consultation with a doctor and a laboratory test are advised to assess liver function and thus determine the current state of the disease.
- **Patients with signs or symptoms of hepatitis:** Any patient who has signs or symptoms suggestive of hepatitis should not receive dental treatment and should be referred immediately to a physician. If an emergency intervention is needed, anti-contagion measures must be extreme at all times. As they are therefore patients with very possible uncontrolled active hepatitis, they are also classified as ASA IV. In the dental clinic we can be presented with different types of patients with hepatitis: Patients with a history of hepatitis: the level of liver damage that the patient has must be assessed with the specialist, since when undergoing dental treatment, we must limit the doses of medications with hepatic metabolism to

a minimum, such as , local anesthetics with lidocaine, (local anesthetics such as lidocaine and mepivacaine, paracetamol, ibuprofen, tetracyclines...etc) [1,2,20].

- **Patients with active hepatitis:** All non-emergency dental treatment should be postponed until the patient recovers. Virus carriers: in these cases, it is very likely that we do not know that the patient carries the virus, and may not even know it himself. In reality, it is very difficult to determine, due to the absence of early clinical signs of this disease, who has or does not have the virus in their body, so at least, in terms of avoiding the risk of contagion, any patient who enters the consultation dental should be treated as if it were a carrier. These are the basic general considerations that we must take when a patient with hepatitis (not in the acute phase) requires dental treatment: 1. The dentist and auxiliary personnel must be immunized and preferably dressed in disposable clothing. 2. Likewise, we will use the largest possible amount of disposable material in the intervention, and we will use the rubber dam in the treatments in which it is possible. 3. Appoint the patient at times of little activity in the dental clinic, or even at the end of the day, so that subsequent disinfection measures are fully complied with. 4. Reduce the number of appointments as much as possible, scheduling the greatest number of treatments per dental visit. 5. Carry out the necessary prior analyzes in terms of coagulation time, prothrombin time, etc., before performing extractions or other surgeries. We must emphasize the importance of these patients undergoing regular oral check-ups, as they are more likely to have oral health problems. In addition, it is well known that oral diseases can worsen other systemic diseases, in this case hepatitis, aggravating the symptoms and worsening the general state of health. That is why, the dentist, in constant contact with the hepatologist, will plan in the most appropriate way for each specific case, the treatments or prevention guidelines that each patient needs.
- **Hepatocellular carcinoma:** Usually composed of well-differentiated hepatocytes, which are prone to vascular invasion that can invade the portal vein or inferior vena cava, with extension to the right side. Hepatocellular carcinoma can range from well-differentiated to undifferentiated anaplastic lesions. In the moderately and well differentiated cell, the cells are arranged in a trabecular pattern, which is the most common; acinar or pseudo glandular, with changes in poorly differentiated forms may take on a pleomorphic appearance with numerous giant cells. Clinical-dental management of the liver patient Interconsultation with a specialist doctor: Current status of the disease, possible alterations secondary to liver disease (immunodeficiency, renal failure and bleeding), his medication and possible interaction with dental drugs.
- **Prevention of cross infection:** Vaccine for health personnel, barrier methods and disinfection and sterilization. Disposable material. Sterilization: - autoclave: manual cleaning. - disinfection. - ultrasonic cleaning. - bagged. - autoclave 121º 20min, 135º 5min. - dry heat: 160º 2h, 170º 1h. - Disinfection: phenolic gluteraldehyde 2% 15min, g. alkaline 3.2% 60 min. - Disinfected prosthetic impressions. - Rotating instruments: manual cleaning, autoclaving, greasing, packaging. Drug prescription: Unpredictable metabolism. Greater tolerance to local and general anesthesia, sedatives and hypnotics. Increase the dose of anesthesia. Alcoholics: Toxicity of paracetamol: 4gr+alcohol, lethal! Alcoholics in rehabilitation: Beware of elixirs and drugs with alcohol. Prevention of bleeding risk: Complete blood count and coagulation tests. Preoperative administration of platelets (TH>20´), antifibrinolytic agents p.o. (EACA, Tranexamic Acid), plasma or vitamin K i.m. may be necessary. Previous systemic antifibrinolytics: Ác. Epsilon-aminocaproic acid (25-50 mg/kg every 6h, 6-10 days) and Ac. Tranexamic (12-25 mg/kg every 8h, 6-10 days). Patients with viral hepatitis: In the active phase, no treatment, only emergencies.
- **Accidental inoculation by puncture or cut of carrier:** -Let the wound bleed, wash and apply povidone-iodine or another disinfectant. -Determine if the exposed person is vaccinated or not and their immunity status: If not vaccinated: dose of IgHB (antihepatitis B immunoglobulin) within the first 48 hours and vaccination will begin.

If she is vaccinated and the Ab count is >10mIU/ml, do nothing. If vaccinated and anti-HBs Ab count <10mIU/ml: HBIG dose and a booster dose of the vaccine. General dental treatment: Chemical and mechanical plaque control: fluoride and chlorhexidine in cycles (3 months fluoride, 15 days chlorhexidine). Xerostomia: Salivary substitutes, hydration, mechanical stimulation. Candidiasis: nystatin or miconazole solutions/gels/ovules. Increased risk of oral cancer: control prosthesis stability, regularize cusps. Delayed healing: antibiotic (amoxicillin, clindamycin).

Conclusion

The main complications and risks of liver disease in dental care are the risk of infection, contamination, and intraoperative and postoperative bleeding.

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