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Dental considerations in patients with liver disease

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Abstract

Introduction: Liver diseases are very common, and the main underlying causes are viral infections, alcohol abuse and lipid and carbohydrate metabolic disorders. The liver has a broad range of functions in maintaining homeostasis and health, and moreover metabolizes many drug substances. Objective: An update is provided on the oral manifestations seen in patients with viral hepatitis, alcoholic and non-alcoholic liver disease, cirrhosis and hepatocellular carcinoma, and on the dental management of such patients. Material and methods: A Medline-PubMed search was conducted of the literature over the last 15 years using the keywords: “hepatitis”, “alcoholic hepatitis”, “fatty liver”, “cirrhosis” and “hepatocellular carcinoma”. A total of 28 articles were reviewed, comprising 20 literature reviews, a clinical guide, three clinical trials and four case series. Results: Oral clinical manifestations can be observed reflecting liver dysfunction, such as bleeding disorders, jaundice, foetor hepaticus, cheilitis, smooth tongue, xerostomia, bruxism and crusted perioral rash. In the case of infection caused by hepatitis C virus (HCV), the most frequent extrahepatic manifestations mostly affect the oral region in the form of lichen planus, xerostomia, Sjögren’s syndrome and sialadenitis. The main complications of the patient with liver disease are risk of contagion (for healthcare personnel and other patients), the risk of bleeding and the risk of toxicity due to alteration of the metabolism of certain drugs.

Key words: *Hepatitis, alcoholic hepatitis, fatty liver, cirrosis, hepatocellular carcinoma.*

Introduction

Liver diseases are very common and can be classified as *acute* (characterized by rapid resolution and complete restitution of organ structure and function once the underlying cause has been eliminated) or *chronic* (characterized by persistent damage, with progressively impaired organ function secondary to the increase in liver cell damage). Based on the extent and origin of the damage, chronic liver disease ranges from steatosis or fatty liver to hepatocellular carcinoma, and includes hepatitis, fibrosis and cirrhosis. Liver diseases can also be classified as *infectious* (hepatitis A, B, C, D and E viruses, infectious mononucleosis, or secondary syphilis and tuberculosis) or *non-infectious* (substance abuse such as alcohol and drugs, e.g., paracetamol, halothane, ketoconazole, methyldopa and methotrexate) (1).

The liver has a broad range of functions in maintaining homeostasis and health: it synthesizes most essential serum proteins (albumin, transporter proteins, blood coagulation factors V, VII, IX and X, prothrombin and fibrinogen (1), as well as many hormone and growth factors), produces bile and its transporters (bile acids, cholesterol, lecithin, phospholipids), intervenes in the regulation of nutrients (glucose, glycogen, lipids, cholesterol, amino acids), and metabolizes and conjugates lipophilic compounds (bilirubin, cations, drugs) to facilitate their excretion in bile or urine. Liver dysfunction alters the metabolism of carbohydrates, lipids, proteins, drugs, bilirubin and hormones (2). Accordingly, liver disease is characterized by a series of aspects that must be taken into account in the context of medical and dental care (3).

Since many drug substances are metabolized in the liver, it is essential for the clinician to compile a complete medical history, evaluating all body systems and the medication used by the patient. The patient drug metabolizing capacity can be evaluated based on the analysis of enzymes such as alanine aminotransferase (ALT) or aspartate aminotransferase (AST), and other liver function tests (2, 4).

In situations of advanced liver disease, the vitamin K levels can be significantly lowered, thus giving rise to a reduction in the production of blood coagulation factors. In addition, portal hypertension can scavenge platelets formed in the spleen, thus giving rise to thrombocytopenia. This in turn can lead to an excessive bleeding tendency, which is one of the main adverse effects seen during the treatment of patients with impaired liver function (4).

Dentists are particularly at risk of hepatitis B and C contagion, due to the transmission routes of these viruses, since these professionals are exposed to the blood and oral secretions of potentially infected individuals (5) – particularly in the case of accidents with sharp or cutting instruments.

VIRAL HEPATITIS

Hepatitis of viral origin comprises a heterogeneous group of diseases caused by at least 6 different types of viruses: A, B, C, D, E and G (2).

Five million new cases of viral hepatitis are documented each year throughout the world, and a study published by Chandler-Gutiérrez et al. (6) estimates the prevalence in Spain to be 3.7%.

- *Hepatitis A*

Hepatitis A is caused by the hepatitis A virus (HAV), an RNA picornavirus (3) endemic in many developing countries. Its estimated prevalence is 1.1% (6). This virus is transmitted via the enteral (oral-fecal) route (5), as a result of the ingestion of contaminated water or food (mollusks), though intrafamilial contagion has also been described, as well as contagion in closed institutions and secondary to sexual intercourse.

The disease is typically mild and self-limiting, and is characterized by the sudden onset of nonspecific symptoms. There is no carrier state. In children or young individuals the disease tends to be asymptomatic, while adults typically present fever, fatigue, abdominal discomfort, diarrhea, nausea and/or jaundice. The patient is able to transmit the infection during the incubation period (2-6 weeks) and until the appearance of symptoms.

The diagnosis is based on the signs and symptoms and on serological testing for anti-HAV IgM and IgG antibodies (3). Host response in the form of anti-HAV antibodies affords lifelong immunity, protecting the patient against future HAV infection.

The risk of nosocomial contagion among healthcare personnel is quite low (3). Vaccines are available that offer immunity against HAV (Havrix®, Vaqta®) for people at risk (i.e., subjects traveling to endemic areas, drug abusers, patients with chronic liver disease and subjects with occupational risk factors) (2, 3).

- *Hepatitis B*

The hepatitis B virus (HBV) is an encapsulated DNA virus that replicates within the hepatocyte (3). Hepatitis B is a worldwide health problem, with an estimated 400 million carriers of the virus (5). It has been calculated that 1.53% of all patients reporting to the dental clinic are HBV carriers (6).

The transmission routes comprise sexual contact, intravenous drug use and blood transfusions. In Asia perinatal transmission is common (3). An important consideration among dental professionals is the risk of percutaneous transmission through punctures or cuts with instruments infected from HBV-positive patients, or absorption through the mucosal surfaces (eyes, oral cavity). Transmission through saliva can occur as a result of absorption from mucosal surfaces (2). Some studies have reported the presence of HBsAg in saliva and crevicular fluid of HBV-positive patients. Dental professionals, particularly those dedicated to oral surgery (7), have a

three- to four-fold greater risk of HBV infection than the general population (3), though vaccines and barrier methods have contributed to lessen the risk (2, 7). Following inoculation, the seroconversion risk is 30% (8). The incubation period lasts 2-6 months. Over 50% of all infections are subclinical and are not associated with jaundice. In this context, since the disease may prove asymptomatic, many people are unaware that they have suffered the infection in the past (5). Approximately 90% of all HBV-infected adults show complete healing, but 5-10% develop chronic hepatitis with complications in the form of cirrhosis and hepatocellular carcinoma (3, 4), resulting in 5000-6000 deaths a year due to liver failure (4).

The disease is diagnosed by quantifying the levels of HBV DNA, HBsAg and the antigen / antibody ratio.

Vaccines have been developed that induce an effective immune response against the virus in most patients. If a non-immunized individual becomes exposed to HBV, immunoglobulin can be administered to afford protection after exposure. The current management protocols include HBV immunization as part of the pediatric vaccination program (3).

- *Hepatitis C*

Hepatitis C virus (HCV) infection is the main cause of chronic liver disease (9, 10) and of liver-related morbidity and mortality worldwide (9). It has been estimated that 8000 to 10,000 deaths a year are attributable to HCV (4), and the latter represents the main indication for liver transplantation in Europe and the United States (9). The estimated global prevalence of the disease is 2.2%, representing approximately 130 million infected individuals in the world (10). Great geographical variability is observed (9), possibly as a result of immunogenetic factors. The lowest prevalences are found in the United Kingdom and Scandinavia, and the highest in Egypt (11).

HCV is an RNA virus mainly transmitted via the parenteral route from infected blood (3, 9, 12). The sources of contagion include blood transfusion (although the risk has been minimized since donor blood tests and controls are made (12)), percutaneous exposure through contaminated instruments, and occupational exposure to blood (9). The individuals at greatest risk are hemophiliacs, patients on dialysis and parenteral drug abusers. Other transmission routes are sexual contact and perinatal and idiopathic contagion (3). The prevalence of the infection among dental professionals is similar to that found in the general population, though epidemiological studies suggest that dentists constitute a risk group for HCV infection (12).

Following inoculation, the estimated seroconversion risk is 1.8% (8). The incubation period is long (up to three months), and 85% of all patients with HCV infection develop chronic hepatitis. In those cases where symptoms are observed, these tend to be mild, and most subjects remain relatively asymptomatic during the first two decades after infection with the virus (4).

The morbidity associated to HCV infection is due not only to the consequences of chronic liver disease but also to the extrahepatic manifestations (11). The best documented condition associated to hepatitis C is cryoglubulinemia, a multisystemic disorder often characterized by purpura, weakness and joint pain, and which may precede the development of B-cell non-Hodgkin lymphoma or membrane proliferative glomerulonephritis (12). Other related disorders are porphyria cutanea tarda, lichen planus, sialadenitis, thyroid gland dysfunction, diabetes mellitus and peripheral neuropathy (11). Over 74% of all HCV-infected patients ultimately develop extrahepatic manifestations in the course of the infection (10).

Different enzyme-linked immunosorbent assay (ELISA) and recombinant immunoblot assay (RIBA) techniques have been developed for the diagnosis of HCV infection, though the diagnostic gold standard remains detection of the viral genome using real time polymerase chain reaction (RT-PCR) technology (3, 12).

No effective vaccine against HCV has yet been developed, and spontaneous resolution is unusual (12). The existing therapy comprises combination treatment with interferon and ribavirin, which offers a sustained response rate of 30-40% (3).

CHRONIC HEPATITIS

Chronic hepatitis is a diffuse inflammatory disorder of the liver with a duration of over 6 months in which the underlying cause can be infectious (mainly hepatitis C virus and, to a lesser extent, hepatitis B and D viruses), pharmacological or immunological.

The disease can develop in the absence of symptoms or with nonspecific manifestations such as fatigue, nausea or abdominal pain. The course is normally slow and progressive, and symptoms typically do not manifest until years after the initial causal event (e.g., infection). Some patients develop the disorder without significant liver damage, while others rapidly progress towards cirrhosis and possible hepatocarcinoma. Chronic hepatitis due to HCV infection is the principal cause of cirrhosis and hepatocellular carcinoma (3).

ALCOHOLIC LIVER DISEASE

Alcoholic liver disease is one of the 10 most common causes of death in the industrialized world, and is responsible for 3% of all fatalities. The epidemiological data indicate a threshold of 80 g of alcohol in males and 20 g in females, consumed on a daily basis during 10-12 years, in order to cause the corresponding liver damage. Ten grams of pure ethanol are equivalent to a glass of wine or a beer, while a glass of whiskey doubles that amount. Factors such as chronic hepatitis C infection, obesity and genetic factors can accelerate the develop-

ment of alcoholic liver disease even with smaller doses of alcohol.

Alcoholism is characterized by physical dependency that includes great tolerance of large amounts of alcohol in blood, a strong urge to drink, difficulty controlling consumption (13), progressive abandonment of usual daily life activities, and persistence of the habit despite its consequences. Alcoholism in turn leads to malnutrition, anemias, diminished immune function and important drug interactions.

The clinical spectrum of alcoholic liver disease ranges from simple liver steatosis (fatty liver) with alcoholic (toxic) hepatitis to more severe steatohepatitis or cirrhosis. *Simple steatosis* is the most common presentation, is found in 90% of all heavy drinkers, and proves reversible upon abandoning the habit. *Alcoholic hepatitis* is observed in over 35% of all heavy drinkers and tends to be a precursor of *cirrhosis*. The condition ranges from asymptomatic forms to liver failure and life-threatening situations, and is usually accompanied by febricula, jaundice, leukocytosis and liver enzyme elevations.

NON-ALCOHOLIC FATTY LIVER

Non-alcoholic fatty liver is defined as the accumulation of fat (mainly triglycerides) in the liver, representing over 5% of the weight of the organ (5), in the absence of alcohol consumption in excess of 10 g a day (15).

The observed liver damage ranges greatly from simple *steatosis* (accumulation of fat in the liver) to *steatohepatitis* (fat accumulation with added inflammation), advanced *fibrosis* and *cirrhosis* (16).

This disorder is mainly associated to obesity, diabetes, hyperlipidemia and insulin resistance. There is a strong correlation between insulin resistance and excessive triglyceride accumulation within the liver cells (15). However, 16.4% of all patients with non-alcoholic fatty liver present none of these predisposing factors (17). The condition is potentially reversible after eliminating or minimizing the aforementioned causal factors (14).

No clear treatments have been established to date for non-alcoholic fatty liver, though interventions such as bariatric surgery (in the case of obese individuals) and oral antidiabetic drugs (glitazones) in patients with type 2 diabetes have shown encouraging results (15).

CIRRHOSIS

Liver cirrhosis is very common in our setting, with well defined morphopathological characteristics that lead to destruction of the liver parenchyma. The disease is accompanied by a series of extrahepatic manifestations in other body organs and system (18). Liver cirrhosis is irreversible, and is characterized by the formation of fibrous scarring in the liver, with the formation of regeneration nodules that increase resistance to blood flow through the organ. The resulting deficient liver perfusion damages vital structures in the organ and adversely affects its physiological functions (19). The main causes of liver cirrhosis are hepatitis B and C infection and alcohol abuse. Other potential causes are non-alcoholic steatohepatitis, genetic alterations and autoimmune disorders (3).

The main complications of cirrhosis are portal hypertension, hepatocellular carcinoma and organ function loss. Cirrhosis in itself constitutes a risk factor for the development of hepatocellular carcinoma (16).

The treatment options comprise suppression of the causal stimulus, antiviral therapy and liver transplantation in the end stages of cirrhotic disease (3).

HEPATOCELLULAR CARCINOMA

Hepatocellular carcinoma is the fifth most frequent cancer worldwide (16). As such, it constitutes an important public health problem, and is one of the most common and life-threatening malignancies in the world – with a survival rate after two years of only about 2% (3).

It has been estimated that HBV and HCV are responsible for over 80% of all hepatocarcinomas. The other causes are alcoholic and non-alcoholic steatohepatitis. Most patients with hepatocellular carcinoma have a history of cirrhosis, which in itself constitutes a preneoplastic condition (12, 16).

Liver cirrhosis has a prolonged natural course, and produces symptoms only in the advanced stages of the disease, when no healing treatment options are available. The main treatment for hepatocellular carcinoma is surgery (in those cases where the tumor proves resectable), though unfortunately many cases are non-operable due to the proximity of vital structures, the presence of metastases, or other comorbidities (3).

Objectives

The present study offers a literature review of the oral manifestations that can be found in patients with viral hepatitis, alcoholic and non-alcoholic liver disease, cirrhosis and hepatocellular carcinoma, and the dental management of patients with these liver disorders.

Material and Methods

A literature search was made of the articles indexed in the PubMed – Medline database, using the following MeSH validated key words: hepatitis, alcoholic hepatitis, fatty liver, cirrhosis and hepatocellular carcinoma. The search was limited to articles in English or Spanish published over the last 15 years. A total of 28 articles were reviewed, comprising 20 literature reviews, a clinical guide, three clinical trials and four case series.

Results

1. ORAL CLINICAL MANIFESTATIONS

The oral cavity can reflect liver dysfunction in the form of mucosal membrane jaundice, bleeding disorders, petechiae, increased vulnerability to bruising, gingivitis, gingival bleeding (even in response to minimum trau-

ma) (3, 19), *foetor hepaticus* (a characteristic odor of advanced liver disease), cheilitis, smooth and atrophic tongue, xerostomia, bruxism and crusted perioral rash (1). In these patients, chronic periodontal disease is a common finding.

Patients with alcoholic hepatitis can present glossitis, angle cheilitis and gingivitis, particularly in combination with nutritional deficiencies (3, 20). Some patients who consume large amounts of alcohol for prolonged periods of time can develop sialadenosis. As commented by Friedlander (20), this is believed to be the result of ethanol-induced peripheral autonomic neuropathy giving rise to alterations in salivary metabolism and secretion.

Patients with advanced cirrhosis tend to present deficient oral hygiene, particularly in those cases where the liver impairment is associated to alcohol abuse. Bagán et al. (18) reported worsened dental conditions in patients with liver cirrhosis, in coincidence with other authors such as Novacek et al. (21), who considered that due to the severity and characteristics of cirrhosis, patients tend to neglect care of the oral cavity (18).

In a recent study, Grossmann et al (9). found many patients with HCV infection to present poor dental health – a situation that contributes to worsen their quality of life. Extrahepatic manifestations have been reported in 74% of all HCV-infected individuals (19), and some of these conditions predominantly or exclusively affect the oral region (10). The main disorders associated with HCV infection are xerostomia, Sjögren's syndrome (SS), sialadenitis and particularly lichen planus (LP) (9).

Xerostomia increases patient vulnerability to caries and oral soft tissue disorders (9) which, in combination with deficient hygiene, in turn facilitate the development of candidiasis.

It has not yet been demonstrated whether HCV infection causes disease similar to primary Sjögren's syndrome or whether it is directly responsible for development of Sjögren's syndrome in certain types of patients. However, it is notorious that some subjects can present a triple association of HCV infection, Sjögren's syndrome and sialadenitis or salivary gland lymphoma (10).

Although bacteria are the main cause of sialadenitis, viruses such as HCV have been implicated as causes of sialadenitis associated to xerostomia (19).

Epidemiological evidence suggests that lichen planus may be significantly associated to HCV infection, though the existing data are controversial (22). This association appears to be dependent upon the geographical setting, being more common in Mediterranean countries and in Japan (22). Bagán et al. (23) found the prevalence of HCV infection to be greater in patients with oral lichen planus (OLP) than in the control group. Although further studies are needed, recent data suggest that patients are most likely first infected with HCV and posteriorly develop lichen planus (24) – though the way in which this occurs is not known.

2. DENTAL MANAGEMENT

Liver disease has important implications for patients receiving dental treatment (3). The most frequent problems associated with liver disease in clinical practice refer to the risk of viral contagion on the part of the dental professionals and rest of patients (cross-infection), the risk of bleeding in patients with serious liver disease, and alterations in the metabolism of certain drug substances (1) – which increases the risk of toxicity.

HCV has been detected on different surfaces within the dental clinic after treating patients with hepatitis C, and the virus moreover is able to remain stable at room temperature for over 5 days (12). Strict sterilization measures are therefore required, since deficient sterilization can expose both the dentist and other patients to hepatitis infection (5). The universal protective measures are applicable in order to prevent cross-infection, i.e., the use of barrier methods, with correct sterilization and disinfection measures (1). It has been demonstrated that conventional sterilization techniques eliminate specific proteins and nucleic acids (HBV DNA and HCV RNA) from dental instruments previously infected with HBV and HCV. Although there are no data confirming their efficacy in lessening the risk of contagion, the measures recommended in the case of accidental perforation of the skin with instruments or needles comprise careful washing of the wound (without rubbing, as this may inoculate the virus into deeper tissues) for several minutes with soap and water, or using a disinfectant of established efficacy against the virus (iodine solutions or chlorine formulations). In turn, pressure should be applied beneath the level of the wound in order to induce bleeding and thus help evacuate any possible infectious material. If exposure through some mucosal membrane has occurred, abundant irrigation with tap water, sterile saline solution or sterile water is advised, for several minutes. The rationale behind these measures is to reduce the number of viral units to below the threshold count needed to cause infection (i.e., the infectious dose). In this sense, dilution with water may lower the viral count to below this threshold (8). Whenever possible, the hepatitis antigen status of the patient should be determined. In the event of parenteral exposure to hepatitis virus-positive antigens, the dentist should receive treatment with anti-hepatitis B immunoglobulin (5). Table 1 offers a schematic description of the steps to be followed.

The compilation of a *detailed clinical history* is essential before dental treatment in order to identify patients posing possible risks (5), together with a thorough oral exploration. *Interconsultation* with the patient physician or specialist is advisable in order to establish a safe and adequate treatment plan adapted to the medical condition of the patient (3), considering the degree of liver functional impairment involved (1). Exploration of the

PROCEDURE AFTER ACCIDENTAL INJURY	
Puncture/Cut	**Mucosal surface contact**
1. Careful washing of the wound, without rubbing, for several minutes with soap and water or a disinfectant.	Abundant irrigation with water or saline solution for several minutes.
2. Pressure applied beneath the level of the wound to induce bleeding.	
Determine the hepatitis antigen status of the patient	
Parenteral exposure to hepatitis virus-positive antigens ⇨ anti-hepatitis B immunoglobulin	

Table 1. *Procedure to be followed after accidental exposure to infected blood.*

oral cavity should assess any signs alerting to the existence of systemic disease. The patient should receive an explanation of the risks associated with treatment, and informed consent is to be obtained.

In patients with acute-phase *viral hepatitis*, only emergency treatment should be considered. In subjects with *chronic hepatitis* it is important to determine the possible existence of associated disorders (autoimmune processes, diabetes, etc.) in order to prevent their direct complications and problems derived from specific medication use (corticosteroids and/or immune suppressors). Evaluation is also required of the possible medical conditions associated to HCV contagion, fundamentally blood transmitted infections (HIV, HBV).

It also must be taken into account that liver disease is often associated with a decrease in plasma coagulation factor concentrations (2, 3). In a patient with liver disease, the surgical risk is related to the severity of the disease, the type of surgery planned, and the presence of comorbidities. Surgery is contraindicated in patients with certain conditions such as acute hepatitis, acute liver failure or alcoholic hepatitis (25). If invasive measures are required, prior coagulation and hemostasis tests are required: complete blood count, bleeding time, prothrombin time / international normalized ratio (INR), thrombin time, thromboplastin time and liver biochemistry (GOT, GPT and GGT) (1, 26). Table 2 reports the normal coagulation test values. In the event altered test values are detected, the hematologist or liver specialist should be consulted (3), with the postponement of elective treatment. Any emergency treatments should be provided in the hospital setting (4). In the event of surgery, trauma should be minimized (3) in order to optimize hemostasis, with a careful surgical technique, applying pressure to control bleeding and using hemostatic agents (2). Based on the laboratory test findings and the treatment to be carried out, local hemostatic agents may be advisable (oxidized and regenerated cellulose), as well as antifibrinolytic agents (tranexamic acid), fresh plasma, platelets and vitamin K (1, 26). Antibiotic prophylaxis is suggested, since liver dysfunction is associated to diminished immune competence (2).

Liver disease may result in alterations in the metabolism of certain drugs. The physician treating the patient therefore should be consulted in order to establish which drugs are used, their doses and possible interactions (3). The administration of certain analgesics, antibiotics and local anesthetics is generally well tolerated by patients with mild to moderate liver dysfunction, though modifications may prove necessary in individuals with advanced stage liver disease (2). In this context, drugs metabolized in the liver may have to be used with cau-

Test	Normal values
Bleeding time	1-3 minutes
Prothrombin time	11-15 seconds
Thrombin time	15-20 seconds
Thromboplastin time	25-35 seconds
Platelet count	150.000-400.000/mm3 < 50.000/mm^3: bleeding
INR	0,9-1,1

Table 2. *Normal coagulation test values.*

Drugs metabolized mainly in the liver	
Local anesthetics	Lidocaine
	Prilocaine
	Mepivacaine
	Bupivacaine
Analgesics	Aspirin
	Acetaminophen (Paracetamol)
	Ibuprofen
	Codeine
	Meperidine
Sedatives	Diazepam
	Barbiturates
Antibiotics	Erythromycin
	Clindamycin
	Tetracycline
Antifungals	Ketoconazole
	Fluconazole

Table 3. *Drugs metabolized mainly in the liver (3).*

tion or their doses reduced (1, 26) (Table 3), and certain substances such as erythromycin, metronidazole or tetracyclines must be avoided entirely (3). Most of the antibiotics prescribed for oral and maxillofacial infections can be used in patients with chronic liver disease, and in general the beta-lactams can be administered. Aminoglycosides can increase the risk of liver toxicity in patients with liver disease, and so should be avoided. The metabolism of clindamycin in turn is prolonged in such patients, and different studies suggest that it contributes to liver degeneration (27). Nonsteroidal antiinflammatory drugs (NSAIDs) should be used with caution or avoided, due to the risk of gastrointestinal bleeding and gastritis usually associated to liver disease. Prophylaxis can be provided in the form of antacids or histamine receptor antagonists (2, 3). Acetaminophen (paracetamol) is to be avoided in patients with serious liver disease (4), and aspirin and NSAIDs are not indicated in patients with altered hemostasis (4). Authors such as Douglas et al. (27) describe acetaminophen as a safe alternative to aspirin or NSAIDs that can be administered at doses of up to 4 g/day during two weeks without adverse liver effects, warning patients to avoid alcohol consumption while receiving treatment with the drug. In patients using benzodiazepines, the dose should be lowered, with prolongation of the interval between doses. Local anesthetics are generally safe provided the total dosage does not exceed 7 mg/kg, combined with epinephrine (27). Table 4 shows the drugs that are contraindicated and those that can be used with caution. Although some of these substances are metabolized in the liver, the doses at which they are used in dental practice are considered to be acceptable – unless the patient suffers very severe liver dysfunction.

Patients with alcoholic cirrhosis show increased tolerance of anesthetics, sedatives and hypnotic agents; as a result, the anesthesia doses should be increased. The safety and efficacy of many drug substances are influenced by concomitant alcohol consumption. Concern is greatest regarding the effects of combining alcohol and central nervous system depressors, and the complex effects of alcohol upon the capacity of the liver to metabolize drug substances (20). Paracetamol combined with alcohol can prove particularly dangerous, since the metabolism of both substances involves the same enzyme (isoenzyme CYP2E1 of the P-450 cytochrome system) (28), and care is required not to prescribe alcohol-containing rinses among patients recovering from alcohol abuse (1).

Lastly, preventive oral hygiene measures are indicated to lessen the need for dental surgical treatments (12).

	CONTRAINDICATED	RECOMMENDED
Anesthetics	Halothane Thiopentone	Isoflurane Nitrous Oxide Local anesthetics
Analgesics	Acetylsalicylic acid Codeine Indomethacin Mefenamic Acid Ibuprofen	Nitrous Oxide
Antibiotics	Tetracycline Erythromycin estolate Metronidazole	Local anesthetics
CNS depressants	Opioids	Benzodiazepines
Corticosteroids	Prednisone	Prednisolone

***Table 4**. Management of the different drugs in patients with liver disease.*

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