"Dental considerations for patients with hepatic dysfunction"

Dr. A. Balatandayoudam, R. Karthigeyan, R. Sathyanarayanan, B. Saravana Kumar, R. Selvakumar,

Corresponding author

Dr. A. Balatandayoudam MDS, Associate Professor
Department of Oral & Maxillofacial Surgery
Adhi Parasakthi Dental College & Hospital
Melmaruvathur 603 319

Abstract:

Liver is a vital organ that metabolizes drugs and endogenous substances and contributes to the excretion of the body. It is also essential for the synthesis of plasma proteins, vitamin B12 and in the production of clotting factors for normal haemostatic function. Disorders of liver have now become very common, and the causes are mainly viral infections, alcohol abuse, and lipid and carbohydrate metabolic disorders. We have provided the current perspective in the oral manifestations seen in patients with viral hepatitis, alcoholic and non-alcoholic liver disease, cirrhosis and hepatocellular carcinoma, and the dental management of such patients.

Introduction:

Liver dysfunction has many implications on patients receiving dental treatment; they can be classified as acute or chronic. Based on the extent and origin of the damage, liver diseases can be categorized into hepatitis, (hepatitis A, B, C, D and E viruses) infectious mononucleosis, or secondary syphilis and tuberculosis cirrhosis, steatosis or fatty liver to hepatocellular carcinoma or non-infectious (substance abuse such as alcohol and drugs ketoconazole, methyldopa and methotrexate).1

The liver has many essential functions. Liver is essential for the production of serum proteins like albumin, transporter proteins, blood coagulation factors V, VII, IX and X, prothrombin and fibrinogen,1 as well as many hormone and metabolism of drugs. The patient’s 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

In liver disease, the vitamin K levels become significantly lowered, leading to
reduction in the production of vitamin K depended blood coagulation factors. In addition, portal hypertension can scavenge platelets formed in the spleen, thus giving rise to thrombocytopenia. This in turn causes an excessive bleeding tendency, which is one of the main adverse effects seen during the treatment of patients with impaired liver function.³

Hepatitis

Hepatitis has a number of potential causes, both infectious and non-infectious. Alcohol, drug intoxication, and drug abuse are predominant noninfectious causes, while viruses and bacteria are important infectious etiologic factors. Viral and drug induced hepatitis are examples of primary hepatitis. Secondary hepatitis may occur as a sequela of other disease entities such as mononucleosis, syphilis, and tuberculosis.⁴ viral hepatitis is clearly of importance to the dentist. 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, according to a study published by Chandler-Gutierrez et al. Hepatitis A is caused by the hepatitis A virus (HAV), an RNA picornavirus endemic in many developing countries. It is estimated that the prevalence is 1.1%, ⁵ this virus is transmitted via orofecal route. More than 350 million people worldwide and 1.25 million people in the United States are chronically infected with hepatitis B virus (HBV). ⁶ It is an encapsulated DNA virus that replicates within the hepatocytes. Transmission routes comprises of sexual contact, intravenous drug use and blood transfusions. In Asia perinatal transmission is common. 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.

Hepatitis C virus (HCV) infection is the main cause of chronic liver disease, an estimated 170 million people worldwide and 1.6% of the United States populations are chronically infected with hepatitis C virus (HCV).⁷ HCV is an RNA virus mainly transmitted via the parenteral route from infected blood. The prevalence of the infection among dental professionals is similar to that of general population, though epidemiological studies suggest that dentists constitute a major risk group for HCV infection, because no effective vaccine against HCV has been developed, and spontaneous resolution is unusual.

Hepatitis D virus (HDV, delta agent) is a defective RNA virus that uses the HBV surface antigen as a viral envelope. HDV can occur as a co-infection or superinfection in individuals infected with HBV, which may then progress to severe fulminant infections. Transmission of HDV can occur via infected blood or blood products and is primarily seen in intravenous drug users and hemophiliacs. HDV may also be transmitted through sexual activities. There is no HDV vaccine available, and treatment is palliative.

Hepatitis G virus (HGV) is caused by two isolated viruses that appear almost
identical. They are single-stranded, positive-sense RNA viruses similar to HCV. HGV is transmitted through blood and blood products, sexual activities, and perinatal contact. The rate of remission is low, little evidence exist that HGV cause significant liver damage.

Liver cirrhosis

Cirrhosis is irreversible, end result of fibrous scarring and architectural changes in normal hepatic cell with interconnecting bands of fibrous tissue.

Nodules that increase resistance to blood flow through the organ, which results in deficient liver perfusion leading to damage of vital structures in the organ and adversely affecting its physiological functions. The etiologic factors resulting in cirrhosis are Hepatitis B, Hepatitis C, and chronic alcoholism. Other causative factors are immune-mediated damages, genetic abnormalities, and nonalcoholic steatohepatitis. Complications of cirrhosis are portal hypertension, hepatocellular carcinoma and functional loss. The treatment option comprises suppression of the causal stimulus, antiviral therapy and liver transplantation in the end stages of cirrhotic disease.

Hepatocellular carcinoma

It is the most common primary cancer of the liver, the fifth most common cancer in men, and the eleventh most common cancer in women in the United States. Common etiological factors in hepatocellular carcinoma are HBV and HCV (80%). In this condition, alpha fetoprotein levels may be elevated. Incidence of hepatocellular carcinoma is rising, and this trend is expected to continue for years. The treatment for hepatocellular carcinoma is surgery for those cases where the tumor proves resectable, but unfortunately many cases are non-operable due to the proximity to vital structures, the presence of metastases, or other co morbidities.

Alcoholic liver

It is one of the 10 most common causes of death in the industrialized world, and responsible for 3% of total fatalities. The epidemiological data indicates 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 development of liver dysfunction, which in turn leads to malnutrition, anemia, and diminished immunity and also leads to drug interactions. Clinical spectrum of alcoholic liver disease ranges from simple liver steatosis (fatty liver) with alcoholic (toxic) hepatitis to more severe steatohepatitis or cirrhosis.

Implications of liver disorder

- Unpredictable hepatic metabolism of administered drugs
- Defective haemostatic cascade due to either thrombocytopenia or reduced hepatic production of coagulation factors.
Increased risk of infection.

Oral manifestations

The oral cavity may show evidence of liver dysfunction with the presence of

- Petechiae,
- Hematoma,
- Jaundiced mucosal tissues,
- Gingival bleeding,
- Icteric mucosal changes.
- HCV has been linked to the onset of Sjogren’s syndrome
- Chronic hepatitis have been associated with lichen planus
- Glossitis may be seen with alcoholic hepatitis,
- Parotid gland enlargement is evident.

Dental management

We should be aware of the most frequent problems associated with liver disease in clinical practice. There are risks of viral contamination 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 leading to drug toxicity. A thorough medical and dental history is mandatory, regarding hepatitis, jaundice, cancer, autoimmune disorders, HIV/AIDS, surgeries, family history, medications, alcohol intake, recreational drug usage, sexual history, and bleeding tendencies. Consultation with the patient’s physician is essential for proper management of the dental patient with liver diseases. Cross-infection can be prevented by the use of proper barrier methods, effective sterilization and disinfection techniques. Liver disease is often associated with a decrease in plasma coagulation factor concentration and thrombocytopenia. Blood investigations to be done prior to the treatment are;

- Complete blood count with differential count (CBC)
- Prothrombin time
- Partial thromboplastin time
- International normalized ratio (INR)
- Bleeding time
- Liver function tests

Consultation with a hematologist and hepatologist are suggested before beginning dental treatment when any abnormal levels are discovered; special attention should be emphasized in minimization of trauma to the patient during any minor oral surgical procedures. If the risk of bleeding increases, local hemostatic agents may be advised (oxidized and regenerated cellulose), as well as antifibrinolytic agents (tranexamic acid), and vitamin K. Infusion of fresh frozen plasma and platelets may be indicated in rare cases. All oral surgical procedures with potential tend to cause bleeding when performed on a patient with multiple or a severe single coagulopathy are to be hospitalized prior to the procedure.
Patients with liver disease may show a significant decrease in hepatic drug metabolism, resulting in an increased or unpredictable effect at normal doses. Dental clinician should avoid or reduce the use of drugs metabolized by liver.\textsuperscript{2, 14} (Table I). It has also been suggested that patients with liver dysfunction should be given only half the initial dose of an oxidized drug (e.g., drugs that would be inactivated by a normal microsomal enzyme system) and adjustment should be made according to therapeutic response or side effects.

**Drugs use in patients with liver diseases: table1.**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Use in patients with liver disorder</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Yes with modifications</td>
<td>To be given in divided doses &lt; 4.0 gm per day for up to 2 weeks without adverse hepatic effects.</td>
</tr>
<tr>
<td>Amide local anesthetics (lido &amp; mepivacaine)</td>
<td>Yes with caution</td>
<td>Lidocaine has a large and rapid volume distribution. Only 6% of injected volume is present in blood and minimal elevation of peak blood concentration occurs after single dose which is clinically insignificant.</td>
</tr>
<tr>
<td>Aspirin and NSAIDs</td>
<td>Avoid</td>
<td>A decreased serum protein levels cause increased toxicity of drug as they are protein bound causing more free drug availability</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Yes with modifications</td>
<td>Decreased metabolism causes increased sedation also receptors in brain are more sensitive. Dosage to be reduced with less frequent intervals. Use drug without active metabolite (e.g., alprazolam, lorazepam) rater than with active metabolite (e.g., diazepam)</td>
</tr>
<tr>
<td>Beta lactam antibiotics (penicillin, amoxicillin)</td>
<td>Yes</td>
<td>Elimination of drug is mainly by renal filtration and tubular excretion. Penicillin, ampicillin, amoxicillin, cepalexin, and cefazolin are well tolerated.</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Avoid</td>
<td>It causes progressive liver disease causing more damage.</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Avoid</td>
<td>It is principally eliminated by liver, so to be</td>
</tr>
</tbody>
</table>
Clarithromycin | Yes with cautions | Concentration with mild to moderate liver disease does not differ from those in patients with normal hepatic function.

Erythromycin | Avoid | Half life has been increased in patients with impaired hepatic function.

Metronidazole | Yes with caution | Dose of 500 mg be given on a 12 hourly

Codeine | Yes with modifications | Codeine is rapidly distributed to spleen, kidney, and liver. Its derivatives e.g., oxycodone can be used in liver disease but with increased dosage interval.

Benzodiazepines’, barbiturates and general anesthetics (halothane) impairs detoxification in hepatic diseases and should be used cautiously. Brain metabolism may be altered, and sensitivity to medications may also increase. Encephalopathy can be triggered by sedatives and opioids. Caution must be taken in prescribing medications metabolized in the liver, such as methyldopa, acetaminophen, nonsteroidal anti-inflammatory agents (NSAIDs), phenytoin, phenobarbitones, and some sulfonamides. Local anesthetics should be administered cautiously in hepatic impairment. Most amides are primarily metabolized in the liver and therefore may reach toxic levels with lower doses of anesthetic. Articaine (plasma) and prilocaine (partly in lungs), however, have other sites of metabolism. Drug dosages and possible interactions should be discussed with a treating physician. In some cases, lower drug dosages are required; some drugs (erythromycin, metronidazole, tetracyclines) should be avoided completely. Nonsteroidal anti-inflammatory agents should be used cautiously or avoided due to an increased risk of gastrointestinal bleeding and interference with fluid balance.

Conclusion:

Day to day dental practice involves administration of common drugs irrespective of the patient’s health status. Extreme caution and modifications are to be given paramount importance while dealing with patients with hepatic disorders.

References


