Management of Medical Emergencies in Dental Practice
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Chronic Hepatic Dysfunction

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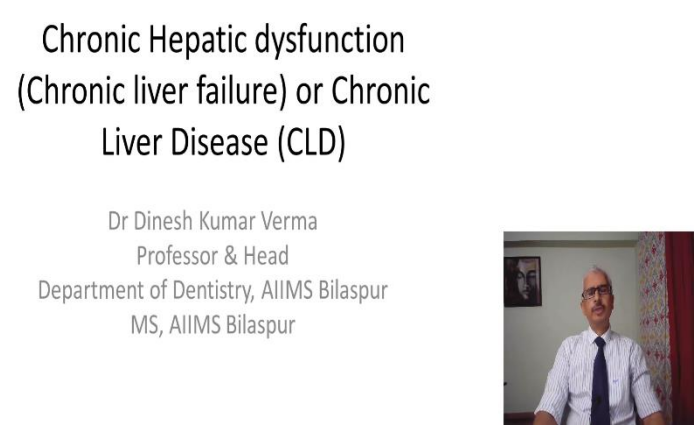

Hello friends. In this lecture series on medically compromised patients, today we will be talking about the chronic hepatic dysfunction also called as chronic liver failure or chronic liver disease.

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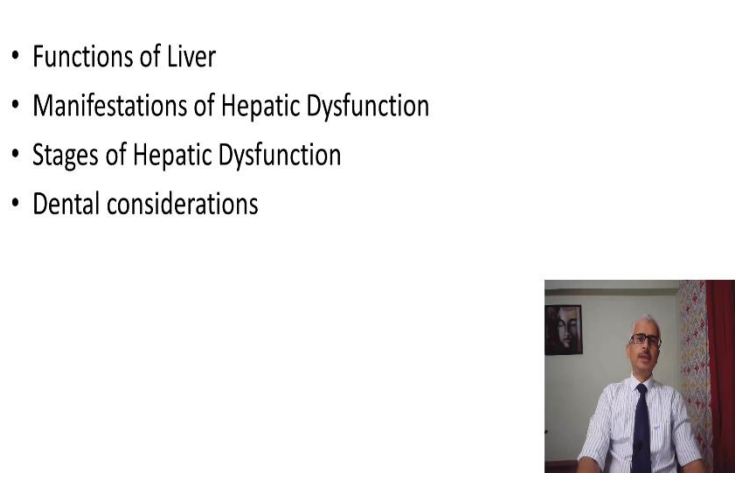

At the end of this discussion, we should be able to talk about the functions of liver, the manifestations of hepatic dysfunction, stages of hepatic dysfunction and dental considerations in these patients.

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Now, chronic liver disease is a progressive loss of liver function over a period of 6 months. CLD is a continuous process of inflammation this is followed by destruction and this is followed by regeneration of the liver (())(1:01).

Now, this repeated process of inflammation, destruction and regeneration leads to fibrosis of the liver and reduction in the parenchymal elements of the liver and this causes reduced function. Now, cirrhosis is the end stage of CLD. So, when the patient reaches the state of cirrhosis most of the liver function is lost.

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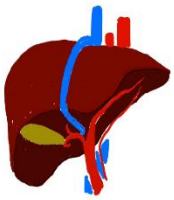
Functions of liver

- ***Part of lymphoreticular system*** – capturing microbes, cellular debri
- ***Carbohydrate, protein and fat metabolism*** – glucose to glycogen and reverse, excess carbs & proteins to fat
- ***Protein synthesis*** – Albumin, coagulation factors(I, II, VII, IX, X, XI), immunoglobulins
- ***Bile production*** – aids Vit A, D, E, K absorption



Now, since we have seen in the definition of CLD, that it is a loss of function, let us look at some of the important functions of Liver. Liver has a very important protective role. It is a

part of lymphoreticular system, it helps by capturing microbes and cellular debri. Now, liver is also a very important site for carbohydrate, protein and fat metabolism. Here glucose is converted to glycogen as a storage form and whenever required, glycogen is converted back to glucose. Now, excessive carbohydrates and protein taken in the diet is converted to fat in liver.

One of the most important functions of liver is protein synthesis. One of the important proteins responsible for maintaining the blood osmolarity is albumin which is synthesized in liver. In addition to this coagulation factors I, II, VII, IX, X and XI are also synthesized in liver. So, we can see that because of its effect because of its ability to synthesize the coagulation factor, it plays a very important role in the coagulation cascade. In addition to that, the proteins are important for the body immunity that is immunoglobulins are also synthesised in Liver.

Liver also produces the bile, the bile salts and the bile juice. Now, this bile helps in absorption of fats from intestines. Now, in addition to absorption of fat, it helps in absorption of fat soluble vitamins like vitamin A, D, E and K, their absorption and their storage.

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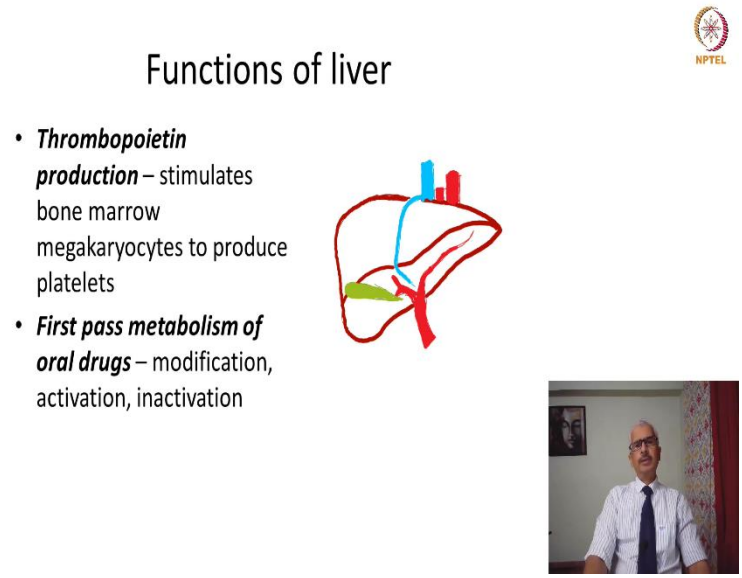

Now, we have seen that liver plays a very important role in the coagulation cascade. It has effect on blood clotting by controlling the production of platelets. Thrombopoietin is produce in liver, this thrombopoietin stimulates the bone marrow megakaryocytes to produce platelets. Now, liver is one of the most important sites for metabolism of various drugs. In addition to that, the first pass metabolism, the first pass metabolism of oral drugs also happen in liver where they are either, modified, activated or inactivated.

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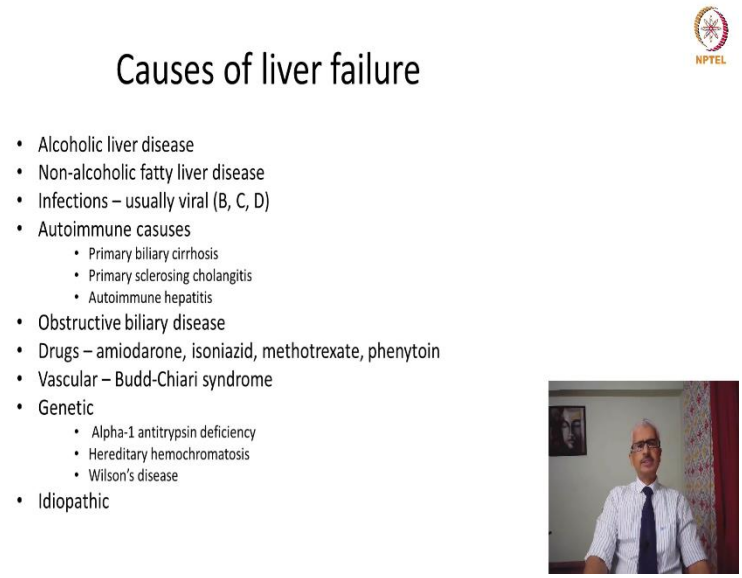

Now, the various causes of liver failure, the most common cause all over the world is considered to be alcoholic liver disease. Now, chronic alcoholism is associated in the end stage with liver failure.

Another rising cause of liver failure is now which is associated with metabolic syndrome is non-alcoholic fatty liver disease or NAFLD. It has now been recognized as a separate clinical entity. Its association with the metabolic syndrome is association with diabetes, obesity, and hyperlipidemia. A many of these patients have stiffness hepatitis. So, when there is stiffness hepatitis, there is inflammation of the liver and this progresses to fibrosis of the liver leading to loss of liver function.

Now, in Asian countries and sub Saharan countries, one of the leading causes of liver failure is viral infections. That is Hepatitis B, C and D infection. Some of the autoimmune causes for liver failure are primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune hepatitis. Obstructive biliary disease are another cause for liver failure where due to the outflow of suction there is back pressure in the liver leading to damage the liver parenchyma. Hepatotoxic drugs like amiodarone, isoniazid, methotrexate and phenytoin also cause liver failure.

Now, vascular cause like Budd-Chiari syndrome, have the venous drainage of suction. So, because of the venous drainage of suction there is back pressure effect and there is congestion and inflammation and increase in the size of liver. This causes over a period of time, damage to the liver parenchyma.

Some of the genetic causes for liver failure are alpha-1 antitrypsin deficiency, hereditary hemochromatosis and Wilson's disease. Out of these, the leading cause is alpha-1 antitrypsin deficiency. Hereditary hemochromatosis is excessive absorption of iron which leads to formation of hydroxyl radicals which cause organ fibrosis including liver fibrosis. Wilson's disease is parenchymal damage due to copper deposits in the liver. Now, around 15 percent of liver failure patients, the exact etiology is never known. These patients are grouped in the idiopathic causes of liver failure.

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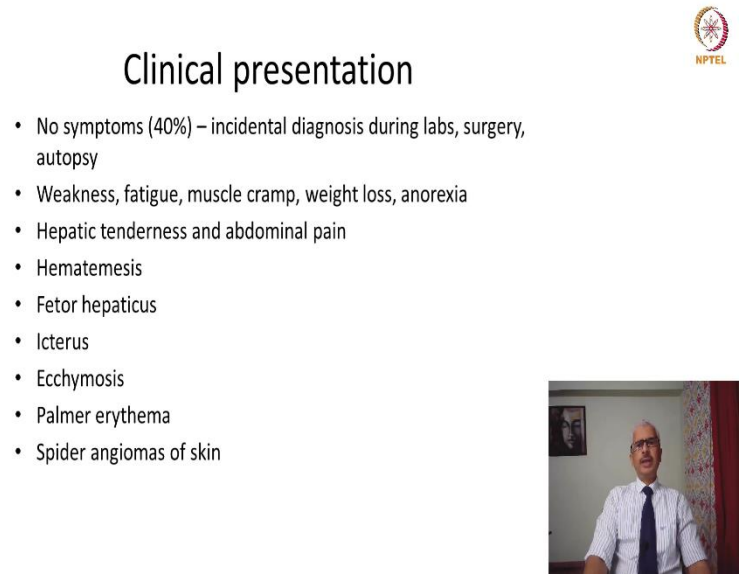

Many of these patients approximately 40 percent, they are asymptomatic. They present to us without any symptoms and they are incidentally diagnosed during labs or surgery or autopsy. Many of these patients have non-specific symptoms like weakness, fatigue, muscle cramps, weight loss and anorexia. Otherwise, they may present with hepatic tenderness, abdominal pain, hematemesis, fetor hepaticus, icterus, ecchymosis, palmer erythema and spider angiomas of skin.

Hematemesis is primarily due to the gastroesophageal arises due to portal hypertension. The fetor hepaticus is due to production of the mercaptans by the GI bacteria and shunting of the portal blood to the systemic circulation. Now, icterus is due to accumulation of the bile pigments. Now, this icterus or Jaundice has a very good correlation with the severity of the liver failure. So, more is the icterus more likely is the severity of the liver failure.

Now, we have seen that liver is an important site of synthesis of the coagulation proteins, the proteins responsible for coagulation cascade and production of platelets. So, one of the clinical features is ecchymosis. Now, palmer erythema is usually seen in alcoholic liver

disease patients. This is due to local vasodilation. The spider angiomas of skin is due to altered metabolism of estrogen.

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- Hypogonadism, gynaecomastia
- Skin pigmentation
- Xanthomas
- Muehrcke lines
- Hepatomegaly with blunt/nodular edge
- Ascitis
- Dialated superficial veins of abdomen/thorax

The levels of estrogen are raised and this can also cause hypogonadism and gynecomastia. In addition to this, patients may also present with skin pigmentation, xanthomas, Muehrcke's lines, hepatomegaly with blunt and nodular edge, ascites and dilated superficial veins of abdomen or thorax. Xanthomas is deposition of the fat under the skin which presents clinically as yellow, small yellow nodules. Muehrcke lines are parallel lines of the nails which do not change position with the growth of nails. Now, hepatomegaly, ascitis and dilated superficial veins are due to protal hypertension.

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Investigations

Raised	*Reduced*
Aspartate aminotransferase (AST)	Albumin
Alanine aminotransferase (ALT)	Hb
Serum lactate dehydrogenase	Platelets
Serum alpha-fetoprotein due to fibrosis	
Alkaline phosphatase	
Plasma conjugated bilirubin	
PT	

Now, when we do the labs, we see raised AST, ALT, serum lactate dehydrogenase, serum alpha-fetoprotein, alkaline phosphatase, plasma conjugated bilirubin and raised prothrombin time. On the other hand, the albumin, haemoglobin and platelets are usually reduced.

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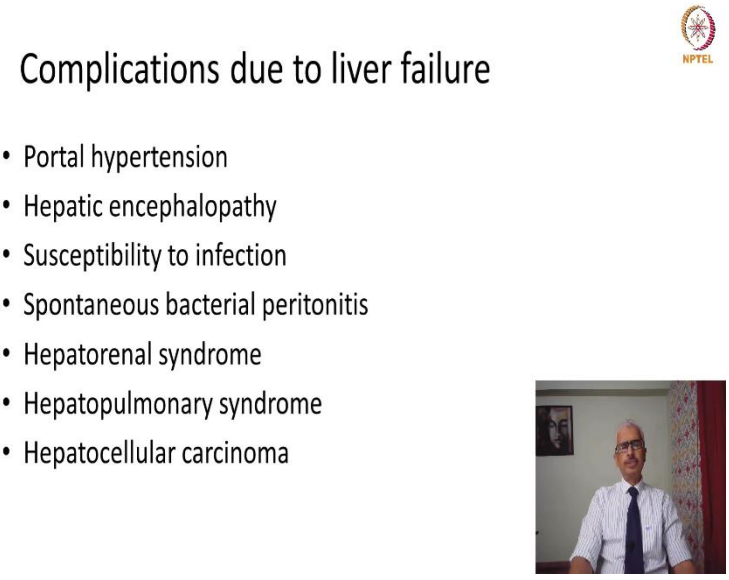

Now, patients may also present with various complications due to liver failure like portal hypertension, hepatic encephalopathy, susceptibility to infection, spontaneous bacterial peritonitis, hepatorenal syndrome, hepatopulmonary syndrome and hepatocellular carcinoma. The hepatorenal syndrome is renal failure due to the hepatic failure. Similarly, the hepatopulmonary syndrome is pulmonary failure due to hepatic failure.

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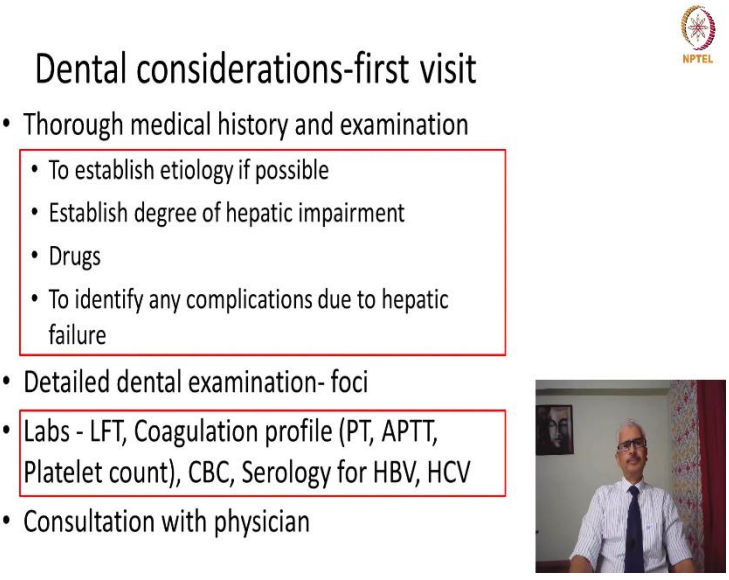

Now, when such a patient visits us the first time what should we do? So, we have to take a thorough medical history and conduct a detailed examination. This is done to establish the etiology, if possible, to establish the degree of hepatic impairment, to check what drugs patient might be taking and to identify any complications due to the hepatic failure. Now, we have seen that we have discussed earlier that these patients may have increased susceptibility to infection and therefore, a detailed dental examination becomes a very, very important. So, this is done from the point of identifying any present and future foci of infection.

Now, these foci of infection may later be a significant cause of morbidity and mortality due to spread of infection locally and systemically. The advice labs are LFT that is Liver Function Test, Coagulation Profile, CBC that is Complete Blood Count and Serology for HBV and HCV as one of the main one of the significant causes of liver failure is presence of hepatitis chronic, hepatitis B and C infections.

And that is why we have to know the status of these patients whether they are hepatitis B or C positive as this adds to the risk to the doctor also contracting infection from them and transferring the infection from one patient to another in the dentist clinic. Whenever we plan to conduct any procedure, we should consult the physician regarding the general status of the patient and his fitness to undergo any procedure.

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Now, before we take up any procedure, we have to keep some of the important things in mind. We have to remember that the liver is one of the most important sites of metabolism of many drugs. So, because of liver failure, these patients have unpredictable hepatic

metabolism of drugs. And therefore, we have to assess which drugs we should not give at all, which drugs require reduction in the dose and which drugs can be given safely.

Similarly, these patients have a high risk of bleeding and infection. Now, in addition to that, there is a risk of contracting hepatitis B, or C infection to the doctor and cross infecting the other patients in the clinic.

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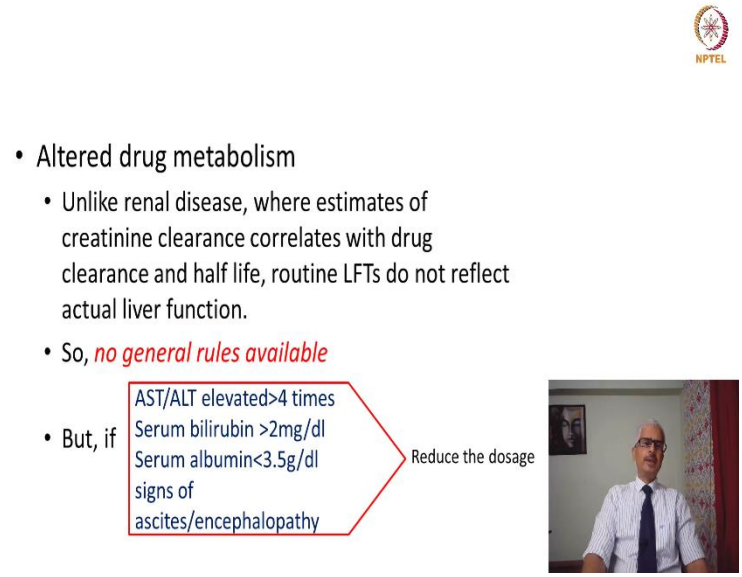

Now, let us look at the drug metabolism in a little bit more detail. Now, when compared to the renal disease, where the estimate of Creatinine clearance correlates the drug clearance in half life, routine LFTs do not reflect actual liver function. What does it mean? So, when we have a patient of liver, the renal failure and when we ask for the Creatinine values, we get a fair idea of how the drug is going to be eliminated. And similarly, and therefore, we can take fairly accurate decision on the amount of drug that has to be given.

When compared to that in liver failure, the values actually do not give the actual level of liver function. So, it does not correlate very well with liver function. However, we have certain indicators that can tell us to reduce the dose. So, if there is elevated AST, ALT which is more than four times, if the serum bilirubin is more than 2 milligrams per deciliter, if the serum albumin is less than 3.5 grams per deciliter and if there are signs of a situs or encephalopathy in all these cases, we should reduce the dose of drug we plan to administer.

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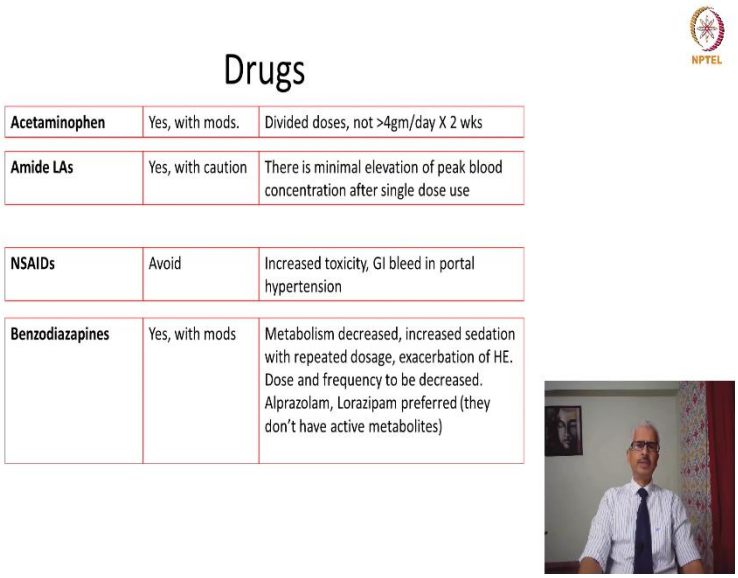

Now, let us look at some of the common drugs used in dentistry whether it is safe to give them or if they require any modifications. Acetaminophen, yes, it can be given but it has to be given in divided doses and you should not give more than 4 grams in a day and not more than continuously not more than 2 weeks.

The Amite local anesthetics can be given however we have to be careful that we do not give excessive dose and we avoid intravascular injection of amide local anesthetic agents. It has been shown that there is only minimal elevation of the peak blood concentration after a single dose use. So, it is fairly safe to use amide local anesthetic agents in CLD patients.

NSAIDs on the other hand should be completely avoided because of their increased toxicity and because of the high chance of GI bleed in portal hypertension patients. Benzodiazepines yes, they can be used. However, we have to remember that they are metabolism is decreased and there is increased sedation with repeated doses.

And in patients who are having hepatic encephalopathy, there is likelihood of exacerbation of hepatic and encephalopathy. And therefore, the dose and frequency needs to be decreased. When compared to diazepam, alprazolam and Lorazepam are preferred because they do not have active metabolites. So, the possibility of increased sedation and exacerbation of hepatic encephalopathy is relatively less when compared to diazepam.

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Clindamycin	Avoid	Delayed metabolism, role in liver damage
Azithromycin	Yes, with caution	Elimination delayed
Clarithromycin	Yes, with caution	Can be used ***unless renal failure also present***
Erythromycin	Yes, with caution	Reduced elimination. Can cause hepatic dysfunction

Clindamycin should be avoided as it has delayed metabolism and it has been implicated in liver damage. Azithromycin can be given, however, the dose should be removed, the dose should be reduced as the elimination of azithromycin is delayed in CLD patients. Clarithromycin can be used however, if the patient is also having renal failure in that case, it should be avoided. Erythromycin can be used but we should use the dose as it has reduced elimination and in some cases has been implicated in hepatic dysfunction.

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Metronidazole	Yes, with mods.	Metabolism affected more by obstructive casues than hepatocellular disease. BD instead of TDS
Narcotic analgesics	Yes, with mods	May worsen HE. Reduce frequency, avoid chronic use.
Clavulanic acid	Yes, with mods	Reports of hepatotoxicity
Penicillins	Yes	Predominantly renal elimination

Metronidazole is considered safe but we may have to reduce the dose as metabolism is affected by obstructive causes rather than hepatocellular disease. Therefore, if the emphatic

failure is due to obstructive causes, in those cases, daily dose or twice daily dose maybe required instead of 3 times a daily 3 times a day dose.

Then narcotic analgesics can be used but in reduced dosage as it may worsen hepatic encephalopathy. So, reduce frequency and avoiding chronic use is the caution for narcotic analgesics. Clavulanic acid, yes, it can be used only some cases in some cases, there have been reports of hepatotoxicity due to clavulanic acid however, in general it is considered to be a very safe drug that can be given in CLD patients. Penicillins are considered to be safe, and it can be given in CLD patients and has predominantly renal elimination.

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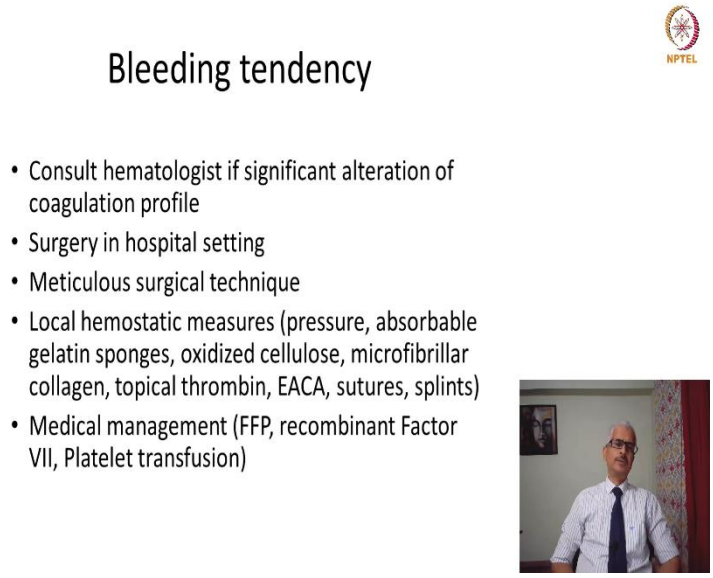

Now, these patients, the next significant problem, we encounter is the bleeding tendency. Therefore, we must consult haematologist, if we have significant alteration of coagulation profile. If we choose to do any surgery it should be done in a hospital setting and medical surgical techniques should be employed to reduce any trauma and any chance of bleeding intraoperative or post operative.

After surgery, we should use local anesthetic measures like pressure anesthetics like absorbable gelatin sponges, oxidized cellulose microfibrillar collagen, topical thrombin, epsilon aminocaproic acid in addition to sutures and splints. Sometimes, medical management may be required with fresh frozen plasma, recombinant factor VII and platelet transfusion.

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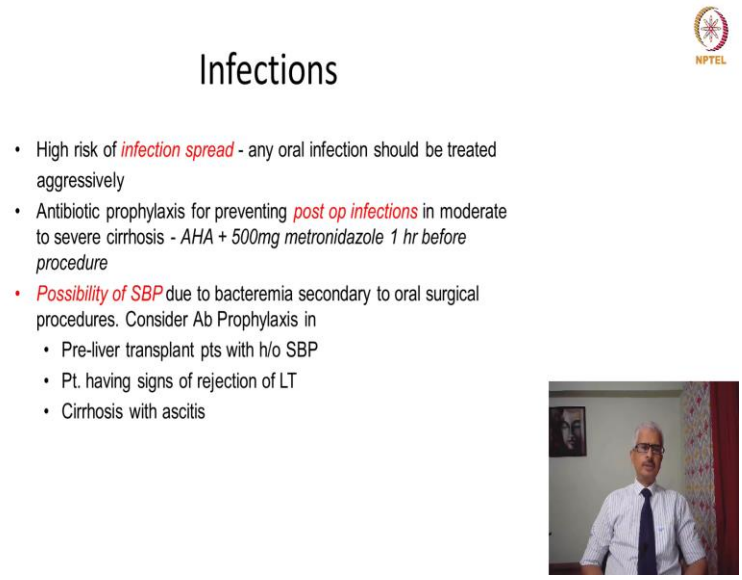

Now, we must remember that these patients not only have a high risk of local infections but they have a high risk of spread of infection from local to system. So, any oral infection should be treated aggressively and therefore, antibiotic prophylaxis is also recommended for these patients in moderate to severe cirrhosis cases. The prophylaxis is same as the American Heart Association prophylaxis for bacterial endocarditis along with 500 milligrams of metronidazole given 1 hour before the procedure.

Now, because of their increased susceptibility to infection, these patients have a high possibility of spontaneous bacterial peritonitis due to bacteremia. And this can be secondary to the oral procedures, oral surgical procedures or any oral procedures that can then those are invasive.

And therefore, antibiotic prophylaxis should be considered in these patients who are pre-liver transplantation with history of the spontaneous bacterial peritonitis, patients having signs of rejection of liver transplant and cirrhosis patients with ascitis. So, let me stress this again. These patients are very prone for infection and therefore, we must aggressively take care of any oral foci of infection.

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Now, the other considerations in patients who are having CLD, these patients frequently have ascites and therefore they find it difficult to lie down in the dental chair. And therefore, an upright or semi reclined position may be better for these patients and short appointments should be given to these patients.

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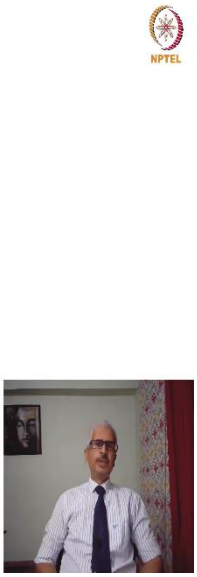

Now, as liver transplant is becoming more and more successful all over the world, more and more of these patients, liver transplant patients are actually visiting the clinic for taking care of their dental needs. Now, two category of patients may land in the dental clinic. One is pre-transplant patients who are scheduled to go for liver transplant in a few months and post-transplant patients who have already had transplant done.

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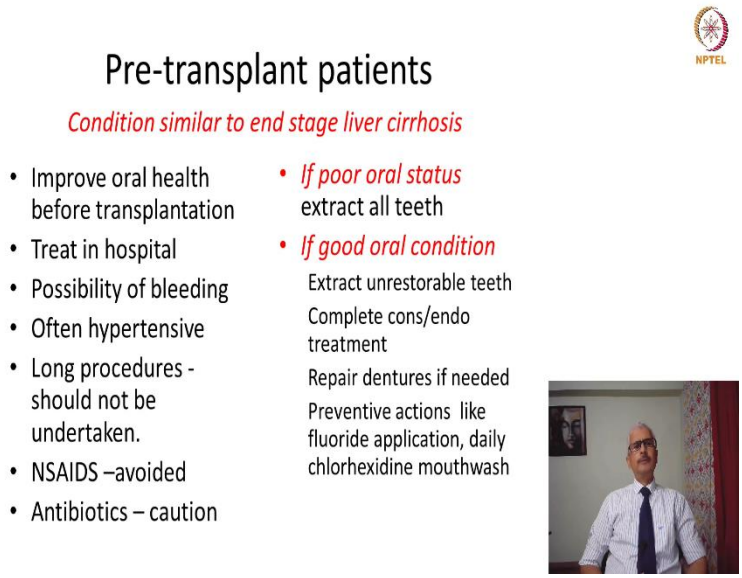

Now, when a pre-transplant patient visits us, their condition is their general condition is not very good. They are very similar to the end stage liver cirrhosis patients. Our primary aim is to improve the oral health before transplantation. Now, again, this is extremely important because if oral health is not taken care of, then even a small foci of infection in the oral cavity may later cause systemic infection and infection of the liver transplant and that can cause failure of the liver transplant. So, this is our primary aim, the primary aim is to improve the oral health before transplantation.

These patients should be treated in hospitals because their condition is not good. Then have a high possibility of bleeding, these patients are often hypertensive. Long procedures should be avoided and NSAIDs should be avoided and antibiotics should be given with caution. In general, all the drugs should be given with great caution. Now, if the general oral health status is poor and we expect that this patient may not be able to maintain good oral hygiene postoperatively, I mean after liver transplant in that case, we have to elect to extract all the teeth.

On the other hand, if the general oral health is good and if we think that if we assess that the patient will be able to maintain oral hygiene properly, will be able to follow the instructions properly after transplant. In that case, we extract only unrestorable teeth and we restored all the teeth where we can give a fair prognosis. Then we undertake repair of dentures because dentures can cause tissue trauma and infection. Then we take preventive actions like to fluoride application and daily chlorhexidine mouthwash.

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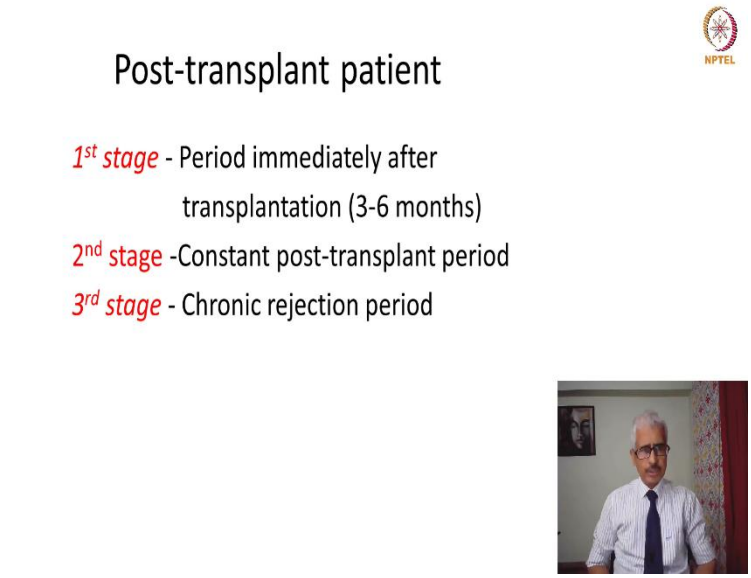

The post-transplant patient may present to us in either first stage or second stage or third stage. The first stage is the period immediately after transplantation that is the first 3 to 6 months. The second stage is the constant post-transplant period. Now, this is the period where patient is considered to be relatively stable, the transplant appears to have been taken up and patient is not showing signs of rejection. On the other hand, the third stage is chronic rejection period, where the patient is showing signs of rejection of the transplant.

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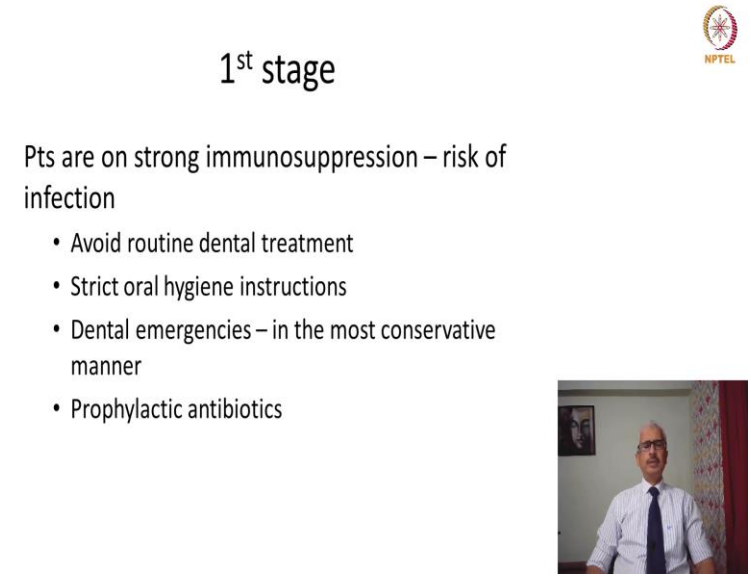

Now, when the patient presents to us in the first stage, the most important and the single most important factor to consider is immunosuppression. Now, these patients for the first 6 months, they are on strong immunosuppression and therefore, they are at a very high risk of

infection. Therefore, we avoid any routine treatment and we reinforce oral hygiene instructions, if there is a dental emergency, then it is dealt with in the most conservative manner.

And if any procedure is undertaken, any invasive procedure is undertaken in that case, prophylactic antibiotics must be given as they have a high risk of infection and an oral procedure can cause rejection of the graft.

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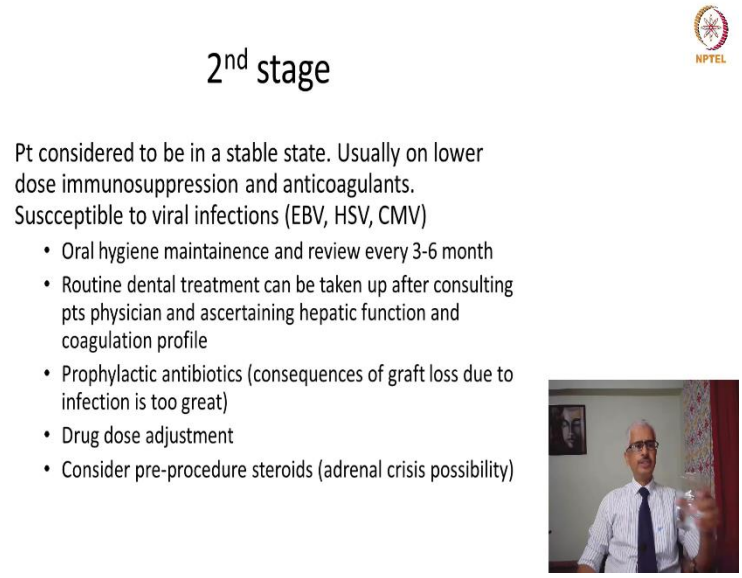

When compared to that, if the patient presents in the second stage, here the patient is considered to be in a stable state. Now, in this the patient is on lower dose of immunosuppressants and anticoagulants. However, these patients are susceptible to viral infections like Epstein Barr Virus, herpes simplex virus and cytomegalovirus. Again, the mainstay of frequent is oral hygiene maintenance and strict review protocol every 3 to 6 months. Routine dental treatment can be taken up after consulting the patient's physician and ascertaining hepatic function and coagulation profile.

Prophylactic antibiotic as we have stressed earlier should be given. The reason for this is even though the level of immunosuppression has been reduced, however still the consequences of graft loss due to infection is simply too great and therefore, we cannot take the risk of graft loss. Therefore, we advise prophylactic antibiotics.

Now, as we have seen in other cases, drug dose whatever drugs we are giving, we have to adjust the dose, adjust the drugs and we have to completely avoid hepatotoxic drugs. Now, since these patients are on immunosuppression, one of the components one of the component

drugs of immunosuppression is steroid. Therefore, these patients have adrenal cortical suppression. And therefore, we therefore, it is advised to give a double dose of steroid before procedure.

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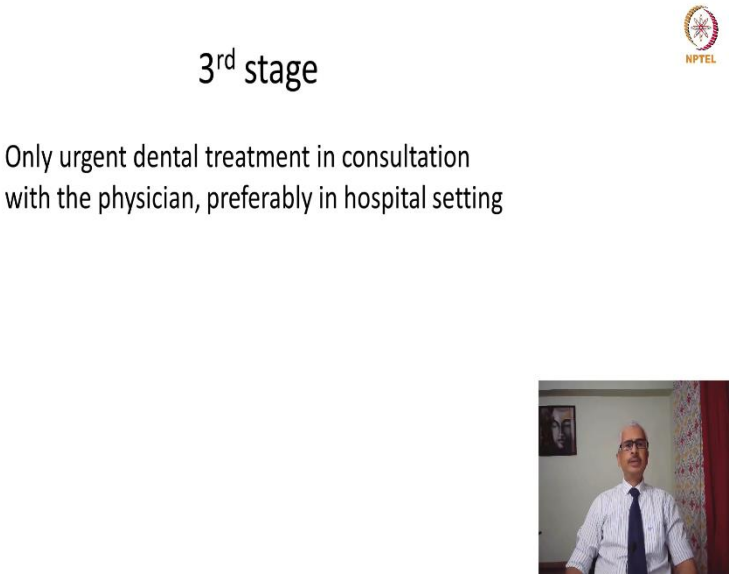

Now, in the third stage, only urgent dental treatment in consultation with the physician and preferably in a hospital setting should be undertake, because these patients are showing signs of drug rejection and therefore, these patients have loss of hepatic function again.

Now, we can summarize that oral hygiene maintenance and oral care is one of the critical components of overall care of these patients. So, it is not that the patient should be dealt with when the patient walks in. This is a standard component of dealing with liver transplant patients.

In addition to that, whenever we see these patients, we have to remember that they have a high risk of infection, high risk of bleeding and any drug we give must be evaluated for the total dose and for the total time. Thank you.