

Dental Management of Patients with Liver Transplant

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Special Precautions Before and After Transmission

In recent years, the number of people in need of liver transplantation has risen steadily as the percentage of people with severe liver disease is high. For this reason, dentists should be able to safely manage these patients and take any precautions necessary to ensure that dental treatment is safely conducted. At the same time, the life expectancy of patients who have undergone liver transplantation also increases. Finally, dentists should be particularly careful with these patients both post-transplantation and post-transplantation, since patients in the final stage waiting for the right donor are in critical condition.

Medical Details

The most common diseases for adults ending in need of liver transplantation are primary cirrhosis of the bile system, chronic hepatitis, hardening cholangitis, metabolic disorders and acute hepatic insufficiency. In children, usually a transplant is required due to metabolic disorders or atherosclerosis of the biliary system.

Indications for liver transplantation

- Cirrhosis (Viral B and C, Alcoholic, Primary Biliary, Autoimmune, Cryptogenic).
- Primary sclerosing cholangitis
- Hepatocellular cancer
- Hemochromatosis
- Alpha-1-antitrypsin deficiency
- Pharmaceutical hepatitis
- Budd-Chiari syndrome
- Wilson's disease
- Acute liver failure
- Absolute contraindications for liver transplantation
- Active substance abuse
- Psychosis or other psychosocial pathology
- Unstable, active cardiopulmonary disease
- Symptomatic myocardial ischemia
- Severe pulmonary hypertension
- Active, non-treatable extrahepatic malignant disease
- Active sepsis
- Active HIV infection
- Anatomical anomaly or extensive vascular thrombosis.

Patient selection

Critical questions in selecting patients for liver transplantation include: whether the patient can survive surgery and the immediate postoperative period and suffer from other disease states. The candidate for a transplant patient must meet certain criteria, which can be assessed based on clinical and laboratory findings.

The basic principle is that transplantation should be done at a sufficiently late stage of the disease so that the patient has every opportunity of automatic stabilization and recovery, but also at such a stage that there are sufficient chances of successful transplantation. This creates the need to select the patient suitable for transplantation at the right time.

Choosing the right reference time for a patient with chronic liver disease is facilitated by the assessment of parameters that determine the severity of liver damage and its life expectancy without transplantation.

Today, according to the new rules, the greatest emphasis is given not on the time a patient is on the waiting list of a suitable donor, but on the medical need for a transplant. On this basis, since 2002, a new MELD (Model for End Stage Liver Disease) rating system has been developed in the US as a priority patient priority in transplantation waiting. MELD is now adopted in Europe. The score is calculated based on three objective laboratory parameters, serum creatinine, bilirubin and INR. MELD score = $0.957 \times \log_e(\text{creatinine, mg / dL}) + 0.378 \times \log_e(\text{bilirubin, mg / dL}) + 1,120 \times \log_e(\text{INR}) + 0.643$.

In alcoholic cirrhosis, almost all transplant centers require complete abstinence from alcohol for at least 6 months prior to listing. It should be noted that this abstinence is able in some patients to lead to such improvement that no more transplantation is required.

In hepatocellular cancer, the mean five-year survival for patients transplanted for small tumors is greater than 80%. Characteristics associated with such survival include a diameter of < 5 cm for single volume, or up to 3 outbreaks, no more than 3 cm in diameter and lack of radiographic evidence of vascular infiltration.

Patients with acute hepatic insufficiency have a high priority for urgent liver transplantation, since mortality in these patients when coma is about 76%, without transplantation, and post-transplantation survival in some centers is 90%.

The large imbalance in the supply of implants from dead donors, in relation to needs, has led to the search for living donors, a more controversial development.

Donor safety is of prime importance. For this reason, the assessment of the condition of the donor should be very careful to exclude people at increased risk of morbidity or mortality. This estimate leads to a donor acceptance rate of about 40%.

The big advantage of live donor transplantation is the much shorter waiting time, and the best histocompatibility, since virtually donor and recipient are relatives. This explains the best 1-year survival in this group (90%), relative to 1 year survival in the implant group (80%).

Patients who are in the final stage of liver disease and are waiting for the graft, usually receive systemic medication, yet they can not survive without transplantation. Their condition is critical and they are often hospitalized for a long time.

When the right donor is found, hepatic patients are subjected to various laboratory and blood tests in order to accept the graft so that doctors can achieve a successful surgical approach.

Of course, a general blood test (red blood cells, hematocrit, white blood cells, platelets, etc.), as well as biochemical tests (blood sugar, urea, creatinine, etc) are essential. However, control of the coagulation mechanism (flow and coagulation time, prothrombin time, partial thromboplastin time) and urine testing, as well as the tests for liver enzymes and serum electrolytes, are required.

Especially for the liver, the increase in aminotransaminases, alkaline phosphatase, prothrombin time and serum bilirubin are indicative of an advanced stage of liver disease.

Immunosuppression

Administration of appropriate immunosuppressive therapy is a fundamental prerequisite for the successful outcome of a transplant, especially of the liver. Initially, immunosuppression was based on the combination of corticosteroids and azathioprine, but the administration of cyclosporin was accompanied by great advances in patient and graft survival. In addition, it is important to contribute to successful immunosuppression and Mycophenolate, which appears to replace azathioprine, while corticosteroids can safely be discontinued after 3 months.

Immunosuppressant combinations are changing and varying in the different transplant centers, and the idea of dose reduction and individualization is becoming increasingly acceptable.

In the context of all these medical data, dentists are required to deal with end-stage liver patients as well as transplanted patients. Medical history, immunosuppression and systemic medication are elements that dentists need to know. They must cure and relieve these patients, who have multiple oral manifestations, with safety and attention to their overall health condition that is already burdened.

Dental management

Patients with chronic end-stage liver disease

These patients have oral manifestations that require dental treatment. Usually, poor oral hygiene is observed due to their general condition. Therefore, advanced periodontal disease, chronic gingivitis, multiple carious lesions and endodontic problems with frequent extension to the abdominal tissues are observed.

Dentists should be aware of all dental treatment, and specifically initially with respect to:

- Analgesics in the class of non-steroidal anti-inflammatory drugs should be avoided.
- Antibiotics are administered with extreme caution because of their liver metabolism and metronidazole and vancomycin are avoided.
- Extensive bleeding may occur in chronic liver patients due to decreased coagulation factors and thrombocytopenia. So there is often a risk of bleeding after a surgical dental treatment for this and sometimes it is given vitamin K or platelets and perhaps the coagulation factor appears to be much reduced.
- Beware of blood pressure as these patients often have hypertension.
- Collaboration with the treating physician. If the patient is under surveillance and good control of liver disease, dental treatment does not change from the usual. However, it is recommended to contact the treating physician to inform dentists about the exact condition of the patient, the haematological condition and the medication he or she receives or will need to be given by the dentist.
- Medicines: Because many drugs are metabolised in the liver, apart from NSAIDs, administration of codeine, meperidine, diazepam, barbiturates and antibiotics should be avoided by metronidazole and vancomycin. Adrenaline in anesthetics should be restricted due to the frequent hypertension experienced by these patients.
- Urgent dental incidents of such patients should be treated in hospitals or clinics and of course after consultation with their physician.
- Follow-up of patients is necessary especially after intra-ocular surgery.

Patients just prior to liver transplantation

Patients in pre-liver transplantation should be treated by the dentist according to specific protocols. These include the full range of serious medical complications that may occur from end stage liver disease.

Most hospitals and medical centers, moreover, require dental examination of patients to be transplanted in order to avoid any contamination from the oral cavity and to avoid the need for some intraoral surgery in the post-transplant period, in which the patient is under immunosuppression.

The treatment protocols for these patients are not the same in the different medical centers, but it is always important to communicate with the patient's treating physician so that the dentist knows exactly the patient's condition and all the details of his health course.

The ideal in these situations is to restore the patient's oral health before transplantation, a process which often must be immediate and rapid as the transplant can be done in less than a week. The previous dental history and prognosis should be taken seriously by the dentist. Other factors that affect dental treatment of these patients are the financial possibility for treatment if they can tolerate dental treatment due to their condition, if they can access dental care and the stability of their medical condition. In addition, priority should be given to the general medical situation and the success of transplantation.

Always after contacting the responsible physician, careful dental examination and assessment of this dental condition should be undertaken. It is the doctor who must inform the dentist and make decisions about:

- The degree of liver dysfunction.
- The patient's ability to undergo dental treatment.
- The need for chemoprophylaxis for dental treatment. There is no evidence that chemoprevention is necessary in patients prior to liver transplantation, unless the patient is at risk of endocarditis or have decreased white blood cells. Again, if it is decided that the patient needs chemoprevention, there is no clear directive on the appropriate antibiotic. The dosage or duration of the dose. However, hepatic metabolizers should not be administered to patients with terminal liver disease or should be given at a reduced dose to avoid any undesirable effects.
- The need to take precautions to avoid serious bleeding.
- The patient's blood test results including the number of white blood cells (WBC), blood flow time, platelet count and gastrointestinal control (PT, TT, aPTT), and decide whether to use Hemostatic agents, fresh plasma, vitamin K or platelet delivery.

Poor Oral Status: In patients with advanced periodontal disease or many carious lesions, who are unable or indifferent to maintain their oral hygiene, it is usually chosen to extract all teeth and dentures.

Good oral condition (preservation of natural teething):

1. Export all non-recoverable teeth.
2. Extraction of all teeth with severe periodontal damage (pocket depth over 5 mm and mobility).
3. Extraction or endodontic treatment on dead teeth.
4. Repeat dentures if required.
5. Provide selective dental care as long as the patient's time and condition permits.
6. Implementing Preventive Programs.
7. Apply a full and effective oral hygiene program.
 - Brushing and using dental floss
 - Local fluorination
 - Configure your daily diet
 - Checking the plate and removing the tartar
 - Use of chlorhexidine daily.

Patients with moderate oral condition should be decided on dental treatment individually and with the decision of the therapist. However, the risk of some infection, the process required to avoid complications and the cost of dental treatment, should be discussed with both the patient and the transplant surgeon.

The dentist should carefully examine the patients and in any case stress that their oral condition affects their overall health status. But the doctor is the one who will make the final decision on the dentist's intervention or not.

Patients after liver transplant

Dental treatment of transplanted patients is demanding and requires specialized knowledge and good communication with the individual physician, so that it can be safely carried out for the patient.

The medical elements of patients with liver transplantation that are of major clinical importance for dental care can be divided into three stages:

1. Period immediately after transplantation (3 - 6 months).
2. Constant post-transplant period.
3. Chronic rejection period.

1st Stage: Period Immediately after Transmission

In this period, usually within the first 3 months after transplantation, patients receive immunosuppressants so that the organ does not reject the graft. At this stage, patients are at risk of complications, infections and immediate rejection of the graft. So the guidelines for dealing with these patients have been shaped both by taking into account their general health status and the specifics arising from taking immunosuppressants.

- Avoid any routine dental treatment.
- Follow all oral hygiene instructions.
- Only urgent dental care is provided, in the most conservative manner and after communication with the therapist.
- Particular attention should be paid to the immunosuppressive treatment of the patient. Their use has greatly increased the survival of the grafts but also the avoidance of rejection. However, ciclosporin and other immunosuppressants make serious interactions with many drugs used in dentistry (erythromycin, ketoconazole, carbamazepine and so on). Immunosuppressants also have several undesirable reactions that also affect the dentist:
 - These side effects may increase the risk of infection by viruses or bacteria.
 - Sometimes lymphoma, Kaposi's sarcoma, scaly leucopoeias or lip cancer.
 - Increases the risk of bleeding and auto-haemorrhage intraorally.
 - It can automatically cause bone fractures and rapid bone loss of the alveolar ridge.
 - Large mouth ulcers in the oral cavity.
 - There may be a collapse of the circulatory system after emotional or surgical stress.
 - Increased odds of hypertension.
 - Increased chance of developing diabetes mellitus and anemia.
- The dentist should know the drugs used in dentistry and are first metabolized to the liver.

- The dentist is informed by the patient's doctor about: the general state of the patient's health, the degree of immunosuppression, to identify potential interactions with medications and to make sure that the patient has overcome the critical stage.
- Possible medical complications at this stage:
 - Acute respiratory failure syndrome
 - Bacterial or viral infections,
 - Blood dyscrasias
 - Hypertension
 - Immediate renal or hepatic insufficiency and direct pancreatitis.
- Chemoprevention is required before any dental practice.
 - Amoxicillin 2gr + metronidazole 500mgr 1 hour before surgery.
 - Penicillin allergy: vancomycin or imipenem 1 gram IV by slow infusion, 1 hour before surgery.
 - EF: ampicillin 2gr + metronidazole 500mgr 1 hour before surgery.
 - Caution: clindamycin is hepatotoxic and should not be used in patients with liver transplantation.
- At this stage, the level of immunosuppression of the patient is very critical, as if the patient is very at risk of many infections, if lower, the patient is at risk of rejection of the graft.

Stage 2: Standing Period after Transmission

At this stage, the patient is no longer at risk of direct rejection of the graft and is considered to be in a steady state. So the dental treatment, always after contacting the treating physician, is shaped as follows:

- Maintain good oral hygiene.
- Constant programs to review the patient's oral condition every 3 to 6 months.
- Treatment and rehabilitation of all new dental lesions that arise.
- Use all precautionary measures to prevent infection of the patient.
- Inoculation of dental staff for hepatitis B.
- Avoiding contamination
 - Contact with the doctor for chemoprevention.
 - X-rays, blood tests for white blood cell levels and CD4 +, CD8 +
- Avoid bleeding
 - Exams for INR, PT, aPTT and platelet count
 - Special precautions and use of hemostatic agents if necessary
- Change in medication or dose reduction due to their metabolism in the liver, but also because they may be toxic for this.
- Decide whether steroids are needed and if so, whether an adrenal crisis may occur but whether it will be manageable.
- Examination of the oral cavity for signs of large immunosuppression or rejection of the graft. Bleeding, bruising, candidiasis, yellow mucous membranes, stomatitis, autoimmune haemorrhage, congestion and may be such signs and the dentist should inform the treating physician.
- Record blood pressure and monitor it in patients receiving ciclosporin or prednisone.

While these are the general guidelines for dental treatment of transplanted patients, there are some problems unique to those patients the dentist needs to know.

Risk of contamination: The risk of infection in immunocompromised patients intensifies chemoprevention. Many medical centers suggest chemoprophylaxis for any dental practice may cause bacteremia. However, there is no protocol that the dentist can follow. However, it is clear that the oral flora of these patients has been altered by taking immunosuppressants, so it is not easy to use a particular antibiotic and usually the choice is individualized. Because there is no scientific evidence on the subject, the dentist always communicates with the patient's therapist for the administration of antibiotics to invasive dental procedures. In general, however, it follows:

- a. Patients with good oral hygiene, stable health and without the need for extensive dental treatment do not take antibiotics.
- b. Patients who receive high doses of immunosuppressants and have active oral infections, such as periodontitis, should take antibiotics.

Virus infections: Post-transplant patients are particularly susceptible to viruses, particularly EBV, HSV, CMV, HBV, HCV, HIV, with more frequent CMV infection. So the dentist must know that:

- a. Patients with liver transplantation due to complications of chronic hepatitis may be carriers of hepatitis B or C virus.
- b. Also, a blood transfusion is used during surgery, which further increases the risk of hepatitis B or C infection.
- c. Precautions such as proper aseptic surgery and vaccination of staff do not differ from any other patient.

Excessive bleeding: Liver transplant patients usually take anticoagulants to prevent hepatic artery thrombosis. The dosage of anticoagulants may need to be modified prior to surgical intraoral surgery.

- a. If the INR is greater than 3.5, the surgery should be postponed and the treating physician decide whether it should and may reduce the dose 3 - 4 days of dental surgery.
- b. After surgery, the dentist should be ready to deal with a bleeding using thrombin, haemostatic or antithrombolytic agents.
- c. For patients who do not take anticoagulants, an extensive bleeding is indicative of graft rejection.

Adrenal stress due to stress: Many patients with liver transplant take steroids and because of the suppression of the adrenal glands, they are unable to control stress from various surgical dental surgeries. These patients need additional steroid doses to avoid possible adrenal crisis.

- a. If additional administration of steroids is required, the dosage and timing are decided by the therapist.
- b. When post-operative pain or complications are expected, the need for additional steroids is increased.
- c. Patients who take high doses of prednisone usually do not need additional steroids.
- d. Re-checks, preventative programs, non-invasive dental work and orthodontics usually do not require steroids.
- e. Adrenal crisis: hypotension, weakness, nausea, vomiting, headache. If it occurs, 100mgr of hydrocortisone is administered as an IV or EM and we call an ambulance immediately.

Hypertension: Generally, patients with liver transplantation often have increased blood pressure, which is enhanced by taking cyclosporine or prednisone.

3rd Stage: Year Disguision of the MESH

In this period only urgent dental treatments are allowed.

In the three stages analyzed, various complications may occur, with manifestations in the oral cavity, mainly from

- The transplant rejection.
- The high degree of immunosuppression.
- The side effects of immunosuppressive drugs.

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