

Dental management of liver transplant patients

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Dentists are responsible for understanding treatment regimens concerning a myriad of health issues. Increasingly, patients who have significant liver disease or have undergone liver transplant therapy will seek either preoperative or postoperative care. This article reviews current protocols for managing these patients.

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Since the first liver transplant was performed in 1963, liver transplants have become a life-saving surgical procedure for combating end-stage liver disease.¹ The immunosuppressive drug cyclosporine was introduced in 1980, followed by the development of a triple immunosuppressive anti-rejection regimen that utilized cyclosporine, azathioprine, and prednisone.^{2,3} The combination of these immunosuppressive drugs has helped to increase the survival rate among liver transplant patients. Current survival estimates within the U.S. for orthotopic liver transplant patients indicate one- and five-year survival rates of 87.5% and 73.9%, respectively.⁴

The first known report of a recommended dental protocol for patients undergoing a liver transplant was published by Svirsky in 1989.⁵ This article reviews current recommendations for safely providing dental treatment to liver transplant patients.

Pretransplant dental treatment

As the number of patients undergoing liver transplant procedures increases, many transplant centers now recommend or require prospective liver transplant patients to undergo a dental examination. Ideally, any existing dental disease should be treated prior to liver transplant surgery; as a result, dental professionals have become important members of the transplant team. The goal of dental treatment prior to transplant is the elimination of oral infection sites that can result in rejection of the newly transplanted liver due to a systemic infection. Pre- and post-transplant dental care is critical to the success of the transplant procedure and patient survival. To maintain health and to prevent rejection of the transplanted liver, continued dental care

must become an integral part of the patient's treatment plan for the remainder of his or her life.⁶

The protocol for dental management prior to transplantation consists of a comprehensive dental examination (including full-mouth radiographs) and a thorough medical history (see Table 1). The dental evaluation should focus on identifying and removing potential sources of oral infection. Patients with poor oral hygiene, severe dental disease, or a lack of motivation to improve their oral health can be difficult to manage. Dentists must stress the importance of eliminating any sources of infection that could jeopardize the success of the patient's liver transplant procedure.

Patients with severe dental disease should be encouraged to have their remaining teeth extracted and complete dentures fabricated. For those patients who desire to retain as many teeth as possible, teeth that are nonrestorable or have advanced periodontal disease should be extracted before transplantation. Teeth with nonvital pulps should be treated endodontically or extracted and all carious lesions should be restored.^{7,8}

Without a commitment to an excellent preventive dentistry program, dental disease is likely to recur. Dentists must instruct patients in oral hygiene, including effective brushing and flossing; in addition, diet counseling is essential to change poor eating habits that can lead to recurrence of dental disease. Topical fluoride should be initiated and the use of antimicrobial rinses such as chlorohexidine or Listerine (Pfizer Inc., New York, NY; 800.223.0182) must be emphasized. Patients who choose to retain their teeth must be made aware of the importance of maintaining good oral hygiene practices.^{7,8}

Before transplantation, the dentist must consult with the patient's physician to discuss several factors.^{7,8} The dentist should be informed about the patient's overall health status, the extent of organ dysfunction, and whether the patient is capable of undergoing necessary dental treatment. The risk of hemorrhage during invasive procedures is a possibility for patients prior to receiving a liver transplant. Preoperative evaluation is mandatory to ensure that the patient's coagulation system is intact. Preoperative evaluation should include a complete blood count and platelet count, prothrombin time or international normalized ratio (INR), and partial thromboplastin time. Patients undergoing invasive procedures with elevated prothrombin time and/or partial thromboplastin times may require a transfusion with fresh-frozen plasma.⁶

Post-transplant dental treatment

After transplantation, dental management of the patient can be divided into three periods: the immediate post-transplant period, the stable graft period, and the chronic rejection period.^{6,9} The type of dental care provided differs from one period to another (see Table 2). Infections from dental sources among liver transplant patients are rare; when they do occur, they either are not documented or the source of the infection is not diagnosed.⁹ At present, there are no data from clinical trials to support the need for prophylactic antibiotics whenever dental treatment is rendered to liver transplant patients.^{6,9}

Though supportive data are absent, it is common practice to prescribe prophylactic antibiotics during invasive procedures that have the potential of producing a bacteremia as well as during the first three months after surgery, when liver transplant patients undergo an intense immunosuppression regimen.^{6,8} Conversely, routine use of prophylactic antibiotics for dental procedures induces antibiotic resistance and increases the risk of infections by opportunistic organisms such as fungi.^{9,11} Another concern is

the potential for adverse interactions with some antibiotics; that is, macrolides that can increase the serum levels of drugs used for immunosuppression. Consulting with the patient's physician before prescribing antibiotics is advised.

No specific antibiotic, dosage, or duration of administration has been agreed upon concerning the use of prophylactic antibiotics.^{7,12} Some authors have recommended the current American Heart Association (AHA) standard regimen for prevention of endocarditis as adequate for this need.^{5,8,11,13} Little et al wrote that the "type of agents and regimen for this antibiotic prophylaxis is special for transplant patients" partly because of the post-transplant patient's susceptibility to subacute bacterial peritonitis (see Table 3).^{6,7} Compared to the current standard regimen recommended by the AHA, this "special" regimen is a "combination of antibiotics that provides for good gram-positive, gram-negative, and anaerobic bacterial coverage with bactericidal properties."⁶ When a single-drug therapy is desired or the patient is allergic to penicillin, imipenem (1.0 g) can be given intravenously one hour before the procedure. Vancomycin (1.0 g) administered intravenously over one hour is an alternative for penicillin-allergic patients with a documented anaphylactic reaction.^{6,7}

Immediate post-transplant period

The transplanted liver is most susceptible to rejection during the first three months of the immediate post-transplant period.¹⁴ Routine dental care must be avoided during the entire immediate post-transplant period, which encompasses the first three to six months following transplant. The patient undergoes an intense regimen of immunosuppressive drugs during this period and should be monitored closely for the development of infection.

Patients taking cyclosporine should be monitored for increased plaque retention and gingival hyperplasia. Dentists should emphasize oral hygiene instructions, including proper brushing, flossing, the use of antimicrobial rinses, and diet counseling. Emergency dental care should be provided only after close consultation with the patient's physician. If dental care must be provided, it should be as noninvasive as possible and prophylactic

Table 1. Pretransplant dental care guidelines.^{1,2,6,9,11}

- Consult with the patient's physician
- Evaluate the patient's coagulation status
- Consider antibiotic prophylaxis
- Perform a dental examination, including full-mouth radiographs
- Perform a dental prophylaxis
- Eliminate all dental disease, including partially erupted third molars
- If severe dental/periodontal disease, poor oral hygiene, or poor motivation exists, consider full-mouth extraction
- Postpone elective treatment
- Reinforce oral hygiene and home care instructions
- Initiate daily antibacterial mouth rinses

Table 2. Post-transplant dental care guidelines.^{1,2,10,11}

Immediate postoperative period (first three to six months)

- Avoid routine dental treatment
- Continue with oral hygiene procedures
- Provide necessary emergency dental care following physician consultation
- Try to keep procedures as noninvasive as possible
- Prophylactic antibiotics should be considered

Stable allograft period

- Active dental recall program, every three to six months post-transplant
- Treat all new dental disease
- Maintain effective oral hygiene procedures
- Consider prophylactic antibiotics for invasive procedures
- Physician consultation is mandatory
- Evaluate closely for altered oral flora

Chronic rejection of graft

- Render emergency dental treatment only

Table 3. Suggested prophylactic regimen for dental-oral procedures in the post-transplant patient.⁷

Medication	Regimen
Amoxicillin	2.0 g orally one hour before procedure
plus metronidazole	500 mg orally one hour before procedure
<i>Amoxicillin-penicillin allergy (for the prevention of spontaneous peritonitis)</i>	
Vancomycin 1.0 g IV	Infused slowly over one hour preoperatively
Imipenem 1.0 g IV	Infused slowly over one hour preoperatively
<i>Unable to take oral medication</i>	
Ampicillin	2.0 g intravenously one hour before procedure
plus metronidazole	500 mg intravenously one hour before procedure

Note: Clindamycin should not be used in most organ transplant patients because of the risk of acute liver toxicity.

antibiotics should be considered. When the patient's physician determines that the transplanted liver has healed adequately and is functioning properly, the patient will enter the stable graft period.

Stable graft period

Dental treatment can be less restrictive during the stable graft period. Routine dentistry can be rendered, including emergency dental care. The activation of a dental recall program of three to six months is critical for the continued re-assessment of the patient's oral hygiene status and treatment of new dental disease. Oral prophylaxis should be accomplished at each recall visit through the removal of plaque and calculus and a review of oral hygiene instructions. The patient should continue using antibacterial mouth rinses daily to control plaque formation. Other treatment requirements (that is, restorative dentistry or endodontics) may be planned and completed after consulting with the patient's physician. Prophylactic antibiotics should be considered whenever an invasive procedure is accomplished and/or a bacteremia is anticipated. Again, consultation with the patient's physician is mandatory.

Acute or chronic rejection periods

Acute rejection usually occurs within the first 5–15 days after transplantation; it is associated with malaise, fever, and abdominal pain.⁶ Routine dental procedures should be postponed during acute rejection; however, emergency dental treatment may be performed, with prophylactic antibiotics considered for procedures that produce bacteremia. The chronic rejection period is more insidious and may or may not be preceded by acute episodes.¹⁴ The first signs associated with liver failure may include ascites, spider angiomas, ankle edema, and jaundice.^{6,8} Emergency dental treatment should be rendered but only after consulting with the patient's physician.

Post-transplantation medical complications

Liver transplant patients may experience a myriad of complications that can lead to graft rejection. Infection is the most frequent cause of mortality and morbidity in liver transplant patients; however,

while 59–70% of recipients develop some type of infection, it appears that an infection of dental origin is uncommon.^{1,10,12-14} Infections are especially a source of concern during the immediate post-transplant period, when patients are taking strong immunosuppressive drugs. Besides infection, the patient may suffer from severe gingival hyperplasia due to cyclosporine; the excess growth of gingival tissue prevents patients from cleaning their teeth properly.¹⁴

Hyperplastic gingival tissue should be removed when the liver transplant patient has been declared stable. If nonsurgical therapy (that is, oral prophylaxis, effective oral hygiene instruction, removal of defective restorations or appliances, and antimicrobial rinses) are not effective, the tissue should be removed surgically. Surgery will eliminate false periodontal pockets and return the gingival tissues to their normal physiologic contours; at that point, patients will be able to clean their teeth properly. Tacrolimus is a recent immunosuppressor that has been successful at preventing gingival hyperplasia from occurring and at decreasing existing gingival hyperplasia caused by cyclosporine.¹⁵⁻¹⁹

Consultation with the patient's physician is necessary prior to any dental surgery. Liver transplant patients may be taking anticoagulants (that is, warfarin) to prevent hepatic vein thrombosis.⁸ The dosage may need to be reduced if the INR is above 3.5. Three to four days are needed to lower the prothrombin time effectively. The INR level should be evaluated on the day of surgery; most routine surgery can be performed if the INR is 3.5 or below. After surgery, the dentist should be prepared to deal with excessive bleeding by using splints, thrombin, and antifibrinolytic agents.^{7,8}

The advent of the triple combination of immunosuppressive drugs means there is an excellent chance that liver transplant patients will be taking steroids. Due to adrenal suppression, patients on steroid therapy may respond inadequately to stress resulting from surgical procedures. Depending on the dosage as well as the scope and type of surgery, patients may require additional steroids (administered pre- and postsurgery) to prevent acute adrenal crisis. Patients taking the equivalent of the normal daily output (5.0–6.0 mg) of prednisone do

not require supplementation for routine dental treatment, including minor surgical procedures; supplementation may be necessary for major surgical procedures.²⁰ A patient's normal maintenance dose may be doubled or tripled during the morning of the dental procedure and one hour before the procedure.⁸ If pain is anticipated the following day, the dosage should be doubled.⁸ Patients who already are taking supraphysiologic doses of steroids (to prevent rejection of their new liver) may not require supplements; consultation with the patient's physician is essential for determining if steroid supplementation is needed.

Although cyclosporine is essential for preventing rejection of the new graft, it has important side effects. Not only does cyclosporine cause gingival hyperplasia for approximately 30% of patients, it also can damage the kidney, leading to hypertension.^{7,8,21} When the liver transplant patient has been declared stable by his or her physician and a baseline blood pressure has been established, blood pressure should be monitored at each subsequent dental visit. The patient's physician should be notified if the patient's blood pressure is above the established baseline level.^{7,8}

Drug side effects

Antibiotics that are used routinely for oral and maxillofacial infections can be used safely by patients with chronic liver disease. There is little concern of producing toxicity from antibiotic usage since antibiotic metabolism in humans is predominately via renal filtration and tubular excretion.⁶ Codeine and the semi-synthetic opioids (such as oxycodone and hydrocodone) are conjugated in the liver; although they generally can be used safely, the dosage intervals need to be increased and the doses themselves need to be decreased.

The use of NSAIDs is somewhat controversial. NSAIDs are metabolized extensively by the liver and there is a risk of increased bleeding due to their antiplatelet tendency and ulcerogenicity. Acetaminophen, which is metabolized primarily by conjugation within the liver, is known to cause hepatotoxicity in association with acute overdoses. If acetaminophen or aspirin is used, the interval between doses should be increased; however, ibuprofen can be prescribed without

changing the normal dosing. Lidocaine generally is safe to use; while approximately 90% of lidocaine is metabolized in the liver, normal doses of lidocaine can be used during dental procedures.^{6,9}

Summary

It is likely that the dentist in a contemporary general practice will be required to provide dental treatment to a patient who has end-stage liver disease or has received a liver transplant. Many transplant centers require their patients to have a thorough dental examination and have all dental disease eliminated before transplant surgery. Establishing an effective preventive program, eliminating all dental disease, and performing frequent recall evaluations after surgery all are critical for success. Early medical consultation with the patient's physician is a must and will give the dentist a thorough knowledge of the patient's disease while allowing the dentist to coordinate any necessary dental treatment for the patient before and after transplant surgery.

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