Assessment and management of oral health in liver transplant candidates

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ABSTRACT

Liver transplantation has become a standard treatment for end-stage liver disease and the number of recipients has grown rapidly in the last few years. Dental care during pre-transplant workup is important to reduce potential sources of infection in the drug-induced immunosuppression phase of liver transplantation. Objectives: The objectives of this study were to document the prevalence of oral abnormalities in patients on a liver transplant waiting list presenting to an urban dental school clinic, discuss the appropriate dental treatment according their systemic conditions and compare their oral manifestations with those of healthy individuals. Material and Methods: A pilot study was conducted involving 16 end-stage liver disease individuals (study group- SG) attending the Special Care Dentistry Center of the University of São Paulo and 16 control individuals (control group- CG) with no liver diseases, receiving dental care at the Dental School of the University of São Paulo. These individuals were assessed for their dental status (presence of oral disease or abnormalities), coagulation status, and dental treatment indications. Results: The patients from SG exhibited a greater incidence of oral manifestations compared with CG (p=0.0327) and were diagnosed with at least one oral disease or condition that required treatment. Coagulation abnormalities reflecting an increased risk of bleeding were found in 93.75% of the patients. However, no bleeding complications occurred after dental treatment. Conclusions: The patients with chronic liver diseases evaluated in this study exhibited a higher incidence of oral manifestations compared with the control group and had at least one oral disease or abnormality which required dental treatment prior to liver transplantation. Careful oral examination and evaluation of the patient, including laboratory tests, will ensure correct oral preparation and control of oral disease prior to liver transplantation.

Key words: Oral health. Dental care. Liver transplantation.

INTRODUCTION

There several liver conditions that cause chronic or continuing liver inflammation, and the most common causes of end-stage liver disease are chronic viral hepatitis B and C, alcohol-related liver disease, autoimmune hepatitis, primary sclerosing cholangitis, primary biliary cirrhosis, steatohepatitis, liver disorders inherited or present at birth, and drug-induced liver damage.

In Brazil, since 2006, donor liver allocation has been based on the model for end-stage liver disease (MELD) scoring system. At present, the MELD has been validated on a broad series of patients with liver diseases of various etiologies and severity. The lab values used in the MELD calculation are serum bilirubin, International Normalization Ratio (INR) and serum creatinine (Figure 1).

The relationship between the introduction of the MELD allocation system in Brazil and a reduction of donor organ waiting list mortality is controversial. However, the number of recipients of liver transplants has grown dramatically in the last few years and is likely to continue to do so in the future.
The improved survival rates and transplant outcomes is predicated upon proper screening and evaluation, as well as breakthroughs in surgical techniques and immunosuppressive therapies. Despite these breakthroughs, infection continues to be a leading cause in graft loss or death of transplant recipients. Although evaluation for chronic systemic infections in transplant recipients is standard, this cannot be said of pre-transplantation dental evaluation.

A survey of United States organ transplant centers, conducted between 2003 and 2004, found that among the 294 respondents, 28 (9%) of organ transplant centers reported one or more incidents of sepsis of dental origin in transplant recipients. In this same survey, 34 (11%) transplant centers reported experiencing one or more episodes of a dental infection prior to transplantation that needed cancellation or postponement of the surgery.

A study performed by the Starzl Transplant Institute involving 300 candidates for liver transplantation conducted between January 2004 and March 2005, reported that oral health attributes (i.e., gingivitis, dental plaque, dental caries, periodontal disease, edentulism, and xerostomia) were similar to those seen in the general population. Candidates for liver transplantation who have not had a dental evaluation for more than 1 year were significantly more likely to present with neglected oral health, untreated dental conditions or habits (e.g., smoking) that were potential precursors and risk factors for dental disease.

Providing oral health care pre- and post-liver transplantation is essential for a better prognosis and quality of life of transplant recipients. The main concern before the transplantation is to eliminate oral foci of infection, such as those of periapical and periodontal origin. During the post-transplant period, the dental professional must be aware of the increased susceptibility to infection in the patient, and the risk for organ rejection, both of which emphasize the importance of vigilant oral health maintenance. Patients are severely immunocompromised and must be well-educated and treated for the rest of their post-transplant lives.

The objectives of this study were to document the prevalence of oral disease and abnormalities in patients on a liver transplant waiting list presenting to an urban dental school clinic, discuss the appropriated dental treatment, according their systemic conditions and compare the oral manifestations with those of healthy individuals.

**PATIENTS AND METHODS**

This study was approved by the Research Ethics Committee of the School of Dentistry of the University of São Paulo. All patients signed an informed consent form.

A pilot study was conducted involving 16 end-stage liver disease individuals (study group - SG) attending the Special Care Dentistry Center of the University of São Paulo and 16 control individuals (control group - CG) with no liver diseases, who were receiving dental care at the Dental School of the University of São Paulo. SG was formed by all patients with end-stage liver disease that had been referred to the Special Care Dentistry Center for routine dental treatment.

Medical history review and physical examination, with data recorded on a form specifically designed for this study, were compiled in a special form for all the patients.

All patients were questioned about variables such as demographics and history of liver disease. Coagulation studies [i.e., prothrombin time (PT)/International Normalization Ratio (INR), activated partial thromboplastin time (aPTT), and platelet count] were also performed on all patients.

The dental status of each patient was evaluated at the initial visit by two trained oral medicine dentists. The patient evaluation consisted of a clinical examination of the hard and soft oral tissues and a radiographic examination which consisted in panoramic and periapical radiography. All abnormalities detected in each patient were recorded using a special form designed for this study.

Based upon each patient’s dental treatment indications and needs, a dental treatment plan was formulated, and specific dental management recommendations for each patient were presented.

**RESULTS**

Among 16 individuals from SG, 13 were male and 3 were female, ranging in age from 37 to 68 (median age of 51 years). Of the 16 individuals from CG, 13 were male and 3 were female, ranging in age from 34 to 70 (median age to 50 years).

The patients with end-stage liver disease presented hepatitis C and alcohol related liver disease (5/16; 31.25%), hepatitis C (5/16; 31.25%), alcohol-related liver disease (3/16; 18.75%), hepatitis and alcohol related liver disease B (2/16;...
12.5%) and Wilson disease (1/16; 6.5%) (Figure 2).

Abnormal coagulation test results, reflecting an increased risk of bleeding, were found in 15 patients from SG (15/16; 93.75%). The most common finding was an abnormally low platelet count (56 to 96x10^9/L) found in 11 patients (11/16; 68.75%), followed by prolonged PT (10 to 52 s) in 13 patients (13/16; 81.25%), prolonged aPTT (52 to 46.9 s) in 5 patients (5/16; 31.25%), and increased INR (>1.3) in 7 patients (7/16; 43.75%).

Data collected from oral and radiographic examinations showed that all patients from SG (100%) were diagnosed with at least one oral disease or condition that would require dental treatment prior to liver transplantation. Caries was diagnosed in 13 patients (13/16; 81.25%); periodontal disease in 11 patients (11/16; 68.75%); petechiae in 3 patients (3/16; 18.75%); oral candidiasis in 2 patients (2/16; 12.5%); and gingival overgrowth, ulceration caused by cytomegalovirus (CMV), xerostomia and angular cheilitis were diagnosed 1 patient (1/16; 6.25%). The patients from CG presented caries (7/16; 43.75%), periodontal disease (10/16; 62.5%) and oral candidiasis (1/16; 6.25%).

The diagnosis of ulceration caused by CMV was detected with PCR real time. Gingival overgrowth was associated with severe periodontal disease and poor oral hygiene. The petechiae were associated in the three cases with thrombocytopenia.

The individuals from SG exhibited a higher incidence of oral diseases compared with those from CG (p=0.0327). Figure 3 summarizes the oral

| Patients | Age | Subject | Liver diseases diagnoses |
|----------|-----|---------|-------------------------|
| 1        | 44  | Male    | Hepatitis type B and alcohol-related liver disease |
| 2        | 52  | Male    | Hepatitis type C |
| 3        | 46  | Male    | Hepatitis type C and alcohol-related liver disease |
| 4        | 37  | Male    | Hepatitis type C and alcohol-related liver disease |
| 5        | 47  | Male    | Hepatitis type C |
| 6        | 43  | Male    | Hepatitis type C and alcohol-related liver disease |
| 7        | 54  | Male    | Alcohol-related liver disease |
| 8        | 57  | Male    | Hepatitis type C and alcohol-related liver disease |
| 9        | 43  | Male    | Wilson disease |
| 10       | 60  | Male    | Hepatitis type B and alcohol-related liver disease |
| 11       | 44  | Female  | Hepatitis type C |
| 12       | 60  | Male    | Hepatitis type C |
| 13       | 68  | Female  | Hepatitis type C |
| 14       | 43  | Male    | Alcohol-related liver disease |
| 15       | 55  | Male    | Alcohol-related liver disease |
| 16       | 61  | Female  | Hepatitis type C and alcohol-related liver disease |

Figure 2- Characteristics of the liver transplant candidates

Figure 3- Oral manifestations of study group and control group patients
CMV=cytomegalovirus
conditions found in all individuals enrolled in this study. Table 1 shows the oral manifestations from SG and abnormalities coagulation.

After the initial exam and diagnosis of oral diseases, indicated dental treatment procedures were performed on all patients (SG and CG) by the same dentists and included 20 restorations, 21 periodontal scaling and root planning procedures, 6 extractions, 1 incisional biopsy, 3 brush (exfoliative) cytology exams, 2 prosthetic rehabilitations (1 removable prosthesis and fixed prosthesis) and 2 endodontic treatments.

Although the majority of patients showed abnormal coagulation values, none of them exhibited critical values that would represent a contraindication for invasive dental treatment. For this reason, the dental treatments were conducted in our outpatient clinic. Procedures that involve bleeding, such as dental extraction, biopsy and periodontal treatment, were conducted using hemostatic local measurements, such as tranexamic acid paste and absorbable gelatin sponge, as recommended by Ramstrom, et al.8 (1993) and Rada7 (2006).

### Table 1- Oral manifestations and coagulation abnormalities

| Patients | Oral manifestations | Platelet (56 to 96x109/L) | aPTT (46.9 to 52 s) | PT (10 to 52 s) | INR (>1.3) |
|----------|---------------------|---------------------------|---------------------|-----------------|------------|
| 1 PD, GO, caries | 70                  | 49                        | 8                   | 1.1             |
| 2 PD, caries    | 62                  | 39.25                     | 15.15               | 1.26            |
| 3 PD           | 99                  | 42                        | 10                  | 0.72            |
| 4 PD, caries, OC | 56                  | 51                        | 7                   | 1.6             |
| 5 DP, caries    | 54                  | 47                        | 15                  | 1.15            |
| 6 caries       | 42.6                | 45.7                      | 14.5                | 1.82            |
| 7 DP, caries    | 50                  | 44.6                      | 24.3                | 1.66            |
| 8 PTC, OC, AC   | 96                  | 46.3                      | 25.7                | 1.54            |
| 9 PD, caries, PTC, CMV, xerostomia | 41 | 41.5 | 19.6 | 1.52 |
| 10 PD, caries, PTC | 64.5                | 46.9                      | 18                  | 2.67            |
| 11 caries      | 257                 | 37                        | 13                  | 1.14            |
| 12 PD, caries   | 101                 | 36                        | 14                  | 1               |
| 13 PD, caries   | 336                 | 25.2                      | 14.9                | 0.9             |
| 14 caries      | 290                 | 29.5                      | 12.9                | 1.12            |
| 15 caries      | 38                  | 31.8                      | 17.3                | 1.31            |
| 16 PD, caries   | 18                  | 35.2                      | 16.7                | 1.29            |

Legend: PD=periodontal disease; GO=gingival overgrowth; OC=oral candidiasis; PTC=petechiae; AC=angular cheilitis; CMV=ulceration caused by cytomegalovirus; aPTT=activated partial thromboplastin time; PT=prothrombin time; INR=international normalization ratio

### DISCUSSION

Transplant centers are very specialized facilities that are usually located at university teaching hospitals or large medical centers. They require a large staff of surgeons and other professionals to evaluate and select patients, and perform surgery and follow-up care. However, even though patients are on waiting lists for matching donor livers for time enough to receive definitive dental treatment, this is not a major priority on the protocols of some transplant centers in our city.

The individuals from SG exhibited a higher incidence of oral manifestations compared with CG (p=0.0327) and all of them were diagnosed with at least one oral abnormality that required dental treatment prior liver transplantation in order to avoid potential complications due to infection after transplantation secondary to drug-induced, anti-organ rejection immunosuppression.

The major concern for dental management of patients with end-stage liver disease is the occurrence of bleeding disorders. Routine dental procedures such as dental prophylaxis, tooth extractions, minor periodontal surgeries, and even administration of local anesthetic for restorations can result in serious complications if the dentist is not
The difficulty lies in assessing bleeding risk for procedures with a moderate level of invasiveness such as subgingival scaling (especially in the presence of more severe periodontal disease) and extensive (e.g., subgingival) restorations. The patients with chronic liver diseases evaluated in this study exhibited a higher incidence of oral manifestations compared with the healthy control group and had at least one oral disease or abnormality that required dental treatment prior to liver transplantation. Patients with chronic liver diseases may present at any dental office for treatment and therefore general dentists should be aware of the unique concerns involving their assessment, education, treatment and maintenance of oral health.

CONCLUSION

The patients with chronic liver diseases evaluated in this study exhibited a higher incidence of oral manifestations compared with the healthy control group and had at least one oral disease or abnormality that required dental treatment prior to liver transplantation.

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