

Impact of a Multimodal Approach in Prevention of Surgical Site Infection in Hepatic Transplant Recipients

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ABSTRACT

Introduction. In liver transplant (LT) recipients, surgical site infection (SSI) represents an important cause of morbidity and mortality.

Objective. This study measures the impact of a multimodal approach to the incidence of surgical site infection in LT recipients.

Materials and Methods. All of the LT recipients in our department were registered on the national database in solid organ transplant. A study was performed in two analytical-interventional phases. Phase 1 took place between July 14, 2009, and February 20, 2014. Phase 2 took place between February 21, 2014, and July 15, 2015. The multimodal change implemented during phase 1 was that 0.5% alcoholic chlorhexidine and ether were applied to the surgical field; surgical prophylaxis was primarily with ampicillin/sulbactam plus cefazolin. In phase 2, 2% alcoholic chlorhexidine alone was applied to the surgical field. The prior standard prophylaxis was changed to piperacillin tazobactam administered during surgery as a continuous infusion of 13.5 g over 8 hours with a pre-precision loading dose of 4.5 g. The loading dose of piperacillin tazobactam was combined with a single dose of gentamicin of 5 mg/kg.

Results. One hundred eight patients have received transplants since the start of the program: 82 patients during phase one and 26 patients during phase two. During phase 1, 13 cases of SSI were recorded, representing a rate of 15.85 per 100 transplants. Sixteen micro-organisms were isolated during phase 1, of which 12 corresponded to gram-negative bacilli. With regard to resistance profiles, 13 showed multidrug resistant and extensively drug resistant profiles. During phase 2, no cases of SSI were recorded (relative risk = 0.158 [95% confidence interval 0.0873–0.255], $P = .0352$).

Conclusion. A multimodal approach allowed for the reduction of the incidence of SSI in LTs and offered a protective strategy.

IN PATIENTS receiving liver transplants, bacterial infections lead to significant morbidity and mortality. Surgical site infections (SSI) and infections associated with biliary tree complications are the most common in this population of transplant recipients [1,2]. They are secondary to multiple causes, such as the complexity of the surgical technique, the fact that the surgery is performed in the potentially infected environment of the abdominal cavity,

and the state of the patient's immune system at the time of the transplantation [3]. There is a growing incidence of infections due to multiresistant micro-organisms with a

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subsequent increase in transplant-associated morbidity and mortality [4].

The incidence of SSI varies broadly depending on the center, with reported values between 4% and 48% reported [3–6]. There are scarce data published in Latin America suggesting that SSI rates are high. Among other things, the high degree of variability reported between different centers derives from the different risk factors that may be present at said centers. Unmodifiable risk factors include surgical technique, hyperbilirubinemia, ascites, the Model for End-stage Liver Disease (MELD) [3,6] value, the need for retransplantation, et cetera [7]. Modifiable risk factors include skin preparation and suitable antimicrobial prophylaxis before the surgical procedure.

A number of different interventions allow for the incidence of SSI to be reduced. These include testing for and decolonization of nasal *Staphylococcus aureus* carriage [8], antibiotic prophylaxis strategies directed towards the findings of rectal swabs, intestinal decontamination, et cetera. The impact of suitable surgical prophylaxis on SSI has been widely demonstrated and various protocols exist in line with the various transplantation centers [3,9].

The aim of this study was to measure the impact of a multimodal approach including revised skin preparation procedures and the application of an innovative antimicrobial prophylaxis adapted to the microbiological results and surveillance exudates obtained at our center on SSI incidence.

MATERIALS AND METHODS

We performed an analytical interventional study in two phases at the Unidad Bi Institucional de Enfermedades Hepáticas Complejas (Hospital Militar, Hospital de Clínicas), Programa de Trasplante Hepático, Uruguay.

Study Type

All of the liver transplant (LT) recipients in our program were registered on the national database in solid organ transplant. Study period for phase 1 was from July 14, 2009, to February 20, 2014; the period for phase 2 was from February 21, 2014, to July 15, 2015.

Inclusion Criteria

All of the LT and liver-kidney transplant recipients in the program were included.

Data Collection Protocol

A data collection proforma was designed, which was integrated into an SPSS 19 base codified for the analysis of same. IBM® SPSS® Statistics version 22.0 (SPSS Inc., Chicago, IL) software was used to execute statistical analysis. The pretransplantation data collected were age, sex, disease leading to organ failure, organ transplanted, MELD score, hospital stay, and survival on discharge. At the time of transplantation, skin preparation methods, antiseptic used, use of ether to stick down adhesive surgical field, type of organ transplanted, surgical prophylaxis used, whether SSI arose, SSI type, micro-organisms isolated, sensitivity profile, and length of surgery.

With regard to skin preparation processes in phase 1, the skin was disinfected with 0.5% alcoholic chlorhexidine and ether was used to improve the adherence of the adhesive surgical field (this

was not included in protocol, but came to our attention on assessment of the processes used); from patient 1 to patient 65, antimicrobial prophylaxis was administered with ampicillin/sulbactam 3 g intravenously, along with cefazolin 2 g intravenously, 30 minutes to 60 minutes pre-incision. From patient 66 to patient 82, piperacillin tazobactam (PTZ) 4.5 g was administered during induction, along with gentamicin 5 mg/kg intravenously as a single dose. In phase 2, skin was disinfected with 2% alcoholic chlorhexidine and the adhesive surgical field was applied without the use of ether. Surgical prophylaxis was based on a loading dose of PTZ 4.5 g intravenously associated with a single dose of gentamicin 5 mg/kg 30 minutes to 60 minutes pre-incision. This was followed up with a continuous infusion of PTZ 13.5 g intravenously over 8 hours (Table 1).

Definitions

SSI was defined according to recommendations of the Centers for Disease Control and Prevention [10].

Infectious complications associated with the biliary tract secondary to ischemia of the hepatic artery or venous thrombosis were not considered SSIs. Two patients in each phase fell into this category.

The proposal of Magiorakos et al [11] was used for the classification of multiresistance.

The MELD score calculates the probability of survival of a patient with end-stage liver disease based on the following objective variables: bilirubin, international normalized rate (INR), and creatinine levels. It is a prognostic tool which correlates very well with 3-month mortality rates.

Data was handled and results are presented without disclosing the identities of the patients.

Statistical Analysis

Numeric variables were presented with SD. Fischer exact and χ^2 tests were used when variables could be divided into categories or for nominal variables. $P < .05$ was considered significant. Relative risks (RRs) and 95% confidence intervals (CIs) were calculated using standard methods. For continuous variables, the Student t test was applied.

RESULTS

During the study period analyzed, 108 patients received transplants at our center. In phase 1, 53 (64%) were males, with an average age of 49 years. In phase 2, 16 (61.5%) were males, with an average age of 49 years. The predominant disease during both phases was alcoholic cirrhosis (25% and 19% for phases 1 and 2, respectively) (Table 2).

During phase 1, 13 cases of SSI were diagnosed, representing a rate of 15.85% per 100 LTs. The average presentation time was 17 days post-procedure (patient 25 [P25]:8 days–P75:23 days.). There were 7 cases of superficial incisional SSI, with 3 deep and 3 organ space infections. Sixteen micro-organisms were isolated, 12 gram-negative bacilli (GNB): *Klebsiella spp*, $n = 7$; *Acinetobacter baumannii*, $n = 2$; *Enterobacter cloacae*, $n = 1$; *Aeromonas spp*, $n = 1$; and *Pseudomonas aeruginosa*, $n = 1$. The sensitivity profile is shown in Table 3. Four gram-positive cocci were isolated: *Enterococcus spp*, $n = 4$; two of these were sensitive to ampicillin and two to vancomycin.

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