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-incision 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 Hepatico, 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 vancomicyn.

Table 1. Measures Implemented for the Prevention of Surgical Site Infection in a Population Having Received a Liver Transplant. Unidad Bi-Institutional Unit for Complex Liver Diseases (Military Hospital, Hospital de Clinicas), Uruguay

Phase	Phase One Julio 14, 2009 to February 21, 2014 (Transplant 1–82)	Phase Two February 22, 2014 to July 15, 2015 (Transplant 83–108)
Search of nasal colonization by *Staphylococcus aureus*	Yes	Yes
Preoperative bathing with soapy 4% chlorhexidine	Yes	Yes
Standard surgical prophylaxis*	Ampicillin/sulbactam + cefazolin up to transplant no. 65 Piperacillin/tazobactam + gentamicin from transplant no. 66–82	Continuous infusion of piperacillin/tazobactam + gentamicin.
Skin asepsis by chlorhexidine	SI 0.5% chlorhexidine	SI 2% chlorhexidine
Surgical site cleaning and sealing sequence		
	1. Cleaning with clorhexidine. 2. Washing with ether without waiting for site to be dry. 3. Site sealing.	1. Washing with clorhexidine. 2. Waiting time for site to be dry/without the use of ether. 3. Site sealing.
Search of multiresistant organisms in rectal secretions	Yes	Yes
Adaptation of surgical prophylaxis according to pre-established parameters†	Yes	Yes

*In phase 1 the standard prophylaxis based on ampicillin/sulbactam + cefazolin was performed given the high incidence in our country of infections by *Acinetobacter baumanii*.

†Parameters considered for surgical prophylaxis adaptation: prior antibiotic exposure, infection of the donor, colonization by multiresistant micro-organisms in pretransplantation secretions, allergy to antibiotics, retransplantation.

In phase 2, no cases of SSI were recorded (RR = 0.158, [95%CI 0.0873–0.255], $P = .0352$).

Overall during phase 1, the standard surgical prophylaxis strategy was changed in 32 patients (39%), whereas it was changed in 6 patients in phase 2 (24%). The main reasons for changing in phase 1 were prior use of antibiotic (13 patients) followed by rectal colonization (7 patients); in phase 2, prior use of antibiotic (2 patients) was the primary cause.

Table 2. Overview of the Population Having Received a Liver Transplant. Bi-institutional Unit for Complex Liver Diseases (Military Hospital, Hospital de Clinicas), Uruguay

Variables	Phase One July 14, 2009 to February 21, 2014 (n = 82)	Phase Two February 22, 2014 to July 15, 2015 (n = 26)	*P* Value
Median age (P25–P75) years	49 (34.5–57.5)	49 (36.25–59.25)	.643
Male n, (%)	53 (64.6)	16 (61.5)	.775
MELD pretransplantation, median (P25–P75)	20 (16–22)	15 (14–22)	.027
Illness that determined organ failure n, (%)			
Alcoholic cirrhosis	21 (25.6)	5 (19.2)	
Autoimmune	13 (15.9)	4 (15.4)	
Chronic hepatitis C	8 (9.8)	4 (15.4)	
Primary biliary	5 (6.1)	3 (11.5)	
Cirrhosis			
Fulminant	4 (4.9)	0 (0)	
Others	31 (37.8)*	10 (38.5)†	
Transplanted Organ n, (%)			
Liver	79 (96.3)	24 (92.3)	
Liver-kidney	3 (3.7)	2 (7.7)	
Hospital stay	11.5 (9–18.5)	15 (10.25–29)	.268
Surgical information:			
Total surgery time (min; median (P25–P75)	465 (378–520)	420 (347–480)	.024
Surgery site infection	13 (15.85)	0 (0)	.035
Live at discharge n, (%)	73 (89)	24 (96)	.294

Abbreviations: MELD, Model for End-Stage Liver Disease; NASH, nonalcoholic steatohepatitis.

*Other illnesses from phase 1: Cryptogenic (4 patients), polycystic (3 patients), primary sclerosing cholangitis (3 patients), hepatitis B (3 patients), biliary atresia (2 patients), hemangioendothelioma (2 patients), and hemochromatosis, Wilson disease, deficit of alpha 1 antitrypsin, acute on chronic failure, portal cavernoma, and NASH (1 patient each). Seven patients had more than one causal factor.

†Other illnesses from phase 2: Primary biliary cirrhosis (3 patients), NASH (3 patients), cryptogenic (2 patients), and Wilson disease, primary sclerosing cholangitis, Budd-Chiari syndrome, and hepatitis B (1 patient each). One patient had more than one causal factor.

Table 3. Gram-negative Bacilli Isolated From Infection in the Surgical Site and its Susceptibility Profile. Liver Transplant. Bi-Institutional Unit for Complex Liver Diseases (Military Hospital, Hospital de Clinicas), Uruguay, July 14, 2009 to July15, 2015

MO	AMK	GEN	SAM	CXM	CRO	CAZ	CFZ	CIP	PTZ	SXT	FEP	Erta	MEM	IMP	COL
Klebsiella spp	S<2	R>16	R>32	R>64	R>64	R 16	R>64	R>4		R>320	I 2	S<0,5	S 0,25	S 0,25	
Klebsiella spp		R>16	R>32	R>64	R>64	R 16	R>64	R>2		R>320	R 8	S<0,5	S 0,25	S 0,25	
Klebsiella spp	I 8	S<1	R>32	R>64	R>64	I 4	R>64	R>2	S<4	R>320	I 2	S<0,5	S 0,25	S 0,25	
Pseudomonas aeruginosa	R 8	R>16			R 16	R 64			R>128	R>320	R 16		R>16	R>16	S<0,5
A. baumannii	R	R>16	R 16		R>64			R>4	R>128		R>64		R>16	R>16	S<0,5
Klebsiella spp	S<2	S<1	R>32	R>64	R>64	R 8	R>64	R>2	S 16	R>320	R 2	S<0,5	S 0,25	S 0,25	
Aeromonas	S				S	S			S		S		R	R	
Enterobacter sp	R>64	R>16		R>64	R>64	R 16	R>64	R>4	R>128	S<20	S 2	R 2	S 0,25	S 0,25	
Klebsiella spp	S 4	R>16	R>32	R>64	R>64	R 64	R>64	R>2		R>320	R>64	S<0,5	S 0,25	S 0,25	
Klebsiella spp	S<2	S<1	S 4	S<1	S<1	S 1		S<1	S<4	S<20	S<1	S<0,5	S 0,25	S 0,25	
A. baumannii	R 16	R 16			R>64	R 64			R>128	R>320	R>64		R>16	R>16	S<0,5
Klebsiella spp	R	S	R	R	R	R	R			R		S	S	S	

Abbreviations: MO, microorganisms; AMK, amikacin; GEN, gentamicin; SAM, ampicillin/sulbactam; R, resistant; I, intermediate; S, susceptible; CXM, cefuroxime; CRO, ceftriaxone; CAZ, ceftazidime; CFZ, cefazolin; CIP, ciprofloxacin; PTZ, piperacillin/tazobactam; SXT, trimethoprim-sulfamethoxazole; FEP, cefepime; Erta, ertapenem; MEM, meropenem; IMP, imipenem; COL, colistin.

In both phases, pretransplantation surveillance rectal and nasal swabs were collected.

Rectal swabs were positive for GNB in 14 patients (13%), with a total of 20 isolates (5 patients had more than isolate). In phase 1, 11 were positive (13%); in phase 2, 3 were positive (11.5%).

With regard to rectal swabs, during the first phase there were 15 isolates: *Klebsiella spp* (n = 6), *E. coli* (n = 5), *Stenotrophomona spp* (n = 1), *Acinetobacter baumannii* (n = 1), *Enterobacter spp* (n = 1), and *Pseudomonas aeruginosa* (n = 1). During the second phase, there were five isolates: *Klebsiella spp* (n = 2), *E. coli* (n = 1), *Acinetobacter baumannii* (n = 1), and *Enterobacter cloacae* (n = 1). The sensitivity profile is shown in Table 4.

DISCUSSION

This study represents the continuation of a study published by our group in 2013, in which we analyzed the incidence of SSI at our center [12].

In this study, performed over two phases, we identified a rate of 15.85 per 100 LTs in the first phase, whereas no cases of SSI were identified in the second phase post-procedure. This corresponded to a significant reduction in the incidence of SSI (CI 95% 0.0873–0.255) with regard to phase 1. We were able to demonstrate that, through the application of simple measures, it is possible to significantly reduce SSI in this patient population.

The data from the first phase are similar to those reported by other centers in Latin America [13], but higher than those from Spanish centers, such as the data reported by Asensio et al with an incidence of 8.8% SSI in LT recipients [5].

With regard to the general characteristics of the population on comparison of the two phases, we can observe (Table 2) that the patients' ages, types of organ transplanted, diseases responsible for organ failure, and survival rates all have similar characteristics.

When we analyze the MELD scores; they are significantly higher in the first phase compared with the second (average of 20 and 15, respectively), resulting in a statistically significant difference ($P = .027$). A likely explanation for this fact is that, in the first phase, four patients presented with a diagnosis of fulminant liver failure, whereas there were no patients with this diagnosis in the second phase. These patients presented with an average MELD score greater than the average for our population.

The other variable showing significant differences between the two phases was the time spent in the operating theater. One interpretation for this may be that the expertise gained over the course of performing 100 transplantations led to a reduction in operating times.

In phase 2, the concentration of alcoholic chlorhexidine used to disinfect skin was increased from 0.5% to 2%. This measure was justified by the fact that the 2% chlorhexidine preparation has been shown to be superior in terms of infection control. This has been widely demonstrated by

Table 4. Isolation of Gram-negative Bacilli and its Susceptibility Profile Found in Pre-transplantation Rectal Swabs in the Population Having Received a Liver Transplantation. Bi-Institutional Unit for Complex Liver Diseases (Military Hospital, Hospital de Clinicas), Uruguay, July 14, 2009, to July 24, 2015*

N° Trasplant	MO	AMK	GEN	SAM	AMP	CRO	CAZ	CFX	CIP	PTZ	SXT	FEP	MEM	IMP	COL
Phase one															
7	*K. pneumoniae*	S	S	S	R	S	S	S	S	S			S	S	
14	*K. pneumoniae*	R	R	R	R	R	R	R	R	R	S		S	S	
17	*P. aeruginosa*	S	R			R	S	R	S				S	S	
17	*K. pneumoniae*	S	S	R		R	R	R	R		R		S	S	
20	*E. coli*			R	R	R	R	R	R				S	S	
27	*E. coli*	S	S	S		S	S	S	S	S	S		S	S	
30	*K. pneumoniae*	S	S	R	R	S	S	S	R		R		S	S	
33	*A. baumanii*	R	R	R		R	R	R	S			S	S	S	S
33	*E. coli*	S	S	R	R	S	S	S	S						
37	*E. coli*			R	R	R	R	R					S	S	
40	*E. coli*	S	S	S	R	S	S	S	S				S	S	
42†	*K. pneumoniae*	R	R	R	R	R	R	R	R	R	R	R	R	R	S
42	*Stenotrophomonas sp*										S				
42	*Enterobacter sp*	S	R	R	R	R	R	R	R				S	S	
44†	*K. pneumoniae*	R	R	R	R	R	R	R	R	R	R	R	R	R	S
Phase two															
84	*K. pneumoniae*			R	R	R	R	R					S	S	
84	*E. cloacae*	R	R	R		R	R	R	R			S	S	S	
89	*E. coli*			R	R	R	R	R					S	S	
89	*K. pneumoniae*	S	S	S	S	S	S	S	S			S	S	S	
90	*A. baumanii*	R	R	R					R				R	R	S

Abbreviations: MO, microorganism; AMK, amikacin; GEN, gentamicin; SAM, ampicilin/sulbactam; AMP, ampicillin; CRO, ceftriaxone; CAZ, ceftazidime; CFX, cefuroxime; CIP, ciprofloxacin; PTZ, piperacillin/tazobactam; SXT, trimethoprim-sulfamethoxazole; FEP, cefepime; MEM, meropenem; IMP, imipenem; COL, colistin; R, resistant; S, susceptible; KPC, *Klebsiella Pneumoniae* carbapenemase – producing bacteria.

*There were no findings of vancomycin-resistant *Enterococcus* in rectal swabs.

†N° 42, 44: *K. pneumoniae KPC*.

various investigators. One noteworthy example is Casey et al, who recently reported that 2% alcoholic chlorhexidine was superior at reducing the number of micro-organisms on the skin compared with 0.5% chlorhexidine, as well as at reducing the incidence of SSI in coronary bypass surgery [14,15].

In addition to increasing the concentration of chlorhexidine to 2%, we stopped using ether to help stick down the surgical field, thus avoiding all measures with the potential to interact with the residual effect of the chlorhexidine.

With regard to the antimicrobial strategy used, in the end, this was administered progressively in phase 2 as shown in Table 1. There was an initial transitional phase in which the change was made from standard prophylaxis to PTZ 4.5 g intravenously 30 minutes to 60 minutes pre-incision, associated with gentamicin 5 mg/kg as a single dose (P63 to P82, inclusive). In the second stage, corresponding to phase 2, from patient 83 onwards, a loading dose of PTZ 4.5 g intravenously was administered alongside a single dose of gentamicin 5 mg/kg intravenously 30 minutes to 60 minutes pre-incision, in addition to a continuous infusion of PTZ 13.5 g intravenously administered over 8 hours during surgery to ensure stable levels during same. The antimicrobial strategies for the second phase were justified by the microbiological isolates obtained during phase 1 of our study.

On analyzing the microbiological findings from phase 1, these show a clear predominance of GNB − 12 of 16 isolates (75%) − a point of data which coincides with other series such as that of García Prado et al [9]. Of those GNB isolated, *Klebsiella spp* was the predominant micro-organism with 7 isolates (58%), 2 *Acinetobacter baumannii* (16.6%), 1 *Enterobacter cloacae* (8.3%), 1 *Aeromonas spp* (8.3%), and 1 *Pseudomonas aeruginosa* (8.3%). Gram-positive cocci made up 25% of isolates (4 of 16), all of which were *Enterococcus spp*.

Of those GNB isolated, 80% were multidrug resistant (MDR) and extensively drug resistant (XDR). The GNB with a greater percentage of MDR and XDR strains were *Klebsiella spp* (6 of 7 isolates, 86%) and *Acinetobacter baumannii* (2 of 2 isolates, 100%). These data are in line with those reported previously by our group at Uruguay's renal-pancreatic transplantation center [16] in which we identified an increase in MDR and XDR micro-organisms as an emerging problem at the national level. At the international level, in 2013, Freire et al [2] reported a predominance of GNB, with *Acinetobacter* and *Klebsiella* representing the predominant micro-organisms.

PTZ is one of the two agents recommended for LT recipients by the American Society of Health Systems Pharmacists 2013 [3]. Work groups such as Kim et al in 2007 [17] or Shi et al [18] have presented favorable results with its administration. With this antimicrobial agent, we achieve adequate coverage of MDR GNB and gram-positive cocci, with a more controlled impact on the ecology of the patient and unit. Because of its pharmacokinetic and

pharmacodynamic characteristics, for its correct administration in the intraoperative period, it requires top-ups every 2 hours. For this reason, and to avoid missed doses in terms of these top-ups, we opted for a continuous infusion during surgery. As far as we know, this is the first time this drug has been administered as a continuous infusion for the purpose of antimicrobial prophylaxis in the context of liver transplantation. This administration method is nothing new, given that it has been a frequent practice in intensive care units for several years now, with excellent results [19–22].

The association of a beta-lactam with an aminoglycoside is intended to produce, firstly, a synergistic effect and, secondly, to broaden the range of antimicrobial coverage with regard to enterobacteria producing extended spectrum beta-lactamases (ESBL) [23,24]. According to the data reported by Zelentsky et al [25], gentamicin dosed at 5 mg/kg allows stable aminoglycoside levels to be achieved without the need for intraoperative top-ups, thus reportedly avoiding harmful effects on the kidney. The use of aminoglycosides in the context of surgical prophylaxis is not new in the context of transplant recipients: Freire et al [26] report excellent results in renal transplant recipients with the administration of a single dose of amikacin.

Furthermore, the importance of adjusting antimicrobial strategy in line with surveillance cultures has been demonstrated by several investigators [27]. In this observational study on 710 patients, it was shown that rectal carriage of ESBL producing enterobacteria in the pretransplantation period was an independent risk factor for infection by these micro-organisms in the post-transplantation period. At our center, during phase 1 rectal swabs were positive for GNB in 11 patients (13% of cases), whereas during phase 2, 3 were positive (11.5%). This shows that during both phases rectal swabs provided a low yield for the purposes of identifying colonization by GNB (1 in 10 patients had a rectal exudate positive for GNB). Specifically with regard to the percentage of ESBL producing enterobacteria, these were observed in 6 patients of 108, corresponding to just 5.5% of the transplanted population. On the one hand, this supports the strategy of using broad-spectrum surgical prophylaxis with PTZ plus gentamicin; however, on the other, it questions the need to carry on taking surveillance cultures before liver transplantation. Lastly, it is important to note that, since 2012, we have not produced any isolates of *Klebsiella pneumoniae* carbapenemase producing enterobacteria at our center, which would require specific antimicrobial prophylaxis.

CONCLUSION

A multimodal approach allowed us to reduce the incidence of SSI in LT recipients, emerging as a protective strategy. The use of PTZ as an antimicrobial prophylaxis for surgery administered in the form of a continuous infusion associated with an aminoglycoside is a promising strategy.

REFERENCES

[1] Garcia-Prado ME, Cordero E, Alamo JM, Gomez MA, Pascasio JM, Sanchez M, et al. Descriptive study of infectious complications in 109 consecutive liver transplant recipients. Enferm Infecc Microbiol Clin 2009;27(4):199–205.

[2] Freire MP, SoaresOshiro IC, Bonazzi PR, Guimaraes T, Ramos Fiqueira ER, Bacchella T, et al. Surgical site infections in liver transplant recipients in the model for end-stage liver disease era: an analysis of the epidemiology, risk factors, and outcomes. Liver Transpl 2013;19(9):1011–9.

[3] Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013;70(3):195–283.

[4] Cervera C, Linares L, Bou G, Moreno A. Multidrug-resistant bacterial infection in solid organ transplant recipients. Enferm Infecc Microbiol Clin 2012;30(Suppl 2):40–8.

[5] Asensio A, Ramos A, Cuervas-Mons V, Cordero E, Sánchez-Turrión V, Blanes M, et al. Effect of antibiotic prophylaxis on the risk of surgical site infection in orthotopic liver transplant. Liver Transpl 2008;14(6):799–805.

[6] de Castro RRM, Trindade CW, Soares LSS, Martinho GH, Rodrigues FS, de Oliveira MTC, et al. Notificação de infecções hospitalares de pacientes submetidos a transplante hepático: casuística de cinco anos do Hospital das Clínicas da UFMG. Rev Méd Minas Gerais 2008;18(4):243–51.

[7] Shah H, Hellinger WC, Heckman MG, Diehl N, Shaley JA, et al. Surgical site infections after liver retransplantation: incidence and risk factors. Liver Transpl 2014;20(8):930–6.

[8] Weiser MC, Moucha CS. The current state of screening and decolonization for the prevention of *Staphylococcus aureus* surgical site infection after total hip and knee arthroplasty. J Bone Joint Surg Am 2015;97(17):1449–58.

[9] Garcia Prado ME, Matia EC, Ciuro FP, Diez-Cnedo JS, Sousa Martín JM, Porras López FM, et al. Surgical site infection in liver transplant recipients: impact of the type of perioperative prophylaxis. Transplantation 2008;85:1849–54.

[10] CDC. Surgical Site Infection (SSI) Event. 2014. Available at: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf. Accessed: January 2016.

[11] Magiorakos A, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 2012;18:268–81.

[12] Prieto J, Medina JC, Lopez M, Scalone P, Harguindeguy M, Leites, et al. Infección de sitio quirúrgico en el Programa de Trasplante Hepático en Uruguay: alta incidencia de bacilos gramnegativos multirresistentes y extremadamente resistentes. Rev Med Urug 2014;30(2):112–22.

[13] De Oliveira AC, Braz NJ, Ribeiro MM. Incidênciada in - fecção do si tio ci rúr gi co em um hos pi tal uni ver si ta rio. Cienc Cuid Sau de 2007;6(4):486–93.

[14] Casey A, Itrakiy A, Birkett C, Clethro A, Bonser R, Graham T, et al. A comparison of the efficacy of 70% v/v isopropyl alcohol with either 0.5% w/v or 2% w/v chlorhexidine gluconate for skin preparation before harvest of the long saphenous vein used in coronary artery bypass grafting. Am J Infect Control 2015;43(8):816–20.

[15] Hannan MM, O Sullivam KE, Murphy AM, McCarthy J, Ryan E, Hurley JP. The combined impact of surgical team education and chlorhexidine 2% alcohol on the reduction of surgical site infection following cardiac surgery. Surg Infect 2015 [Epub ahead of print].

[16] Medina JC, Antelo V, Nin M, Arteta Z, González F, Bazet B, et al. Infecciones bacterianas en pacientes receptores de trasplante renal y reno-páncreas: alta incidencia de micro-organismos multirresistentes. Rev Méd Urug 2012;28(3):190–8.

[17] Kim YJ, Yoon JH, Kim SI, Hong KW, Kim JI, Choi JY, et al. High mortality associated with Acine to bacter species infection in liver transplant patients. Transplant Proc 2011;43(6): 2397–9.

[18] Shi SH, Kong HS, Xu J, Zhang WJ, Jia CK, Wang WL, et al. Multidrug resistant gram-negative bacilli as predominant bacteremic pathogens in liver transplant recipients. Transpl Infect Dis 2009;11(5):405–12.

[19] Wiesmayr S, Stelzmueller I, Mark W, Tabarelli W, Tabarelli D, Laesser L, et al. Experience with the use of piperacillin-tazobactam in pediatric non-renal solid organ transplantation. Pediatr Transplant 2007;11:38–48.

[20] Tanaka K, Arakawa S, Miura T, Shigemura K, Nakano Y, Takahashi S, et al. Analysis of isolated bacteria and short-term antimicrobial prophylaxis with tazobactam-piperacillin (1:4 ratio) for prevention of postoperative infections after radical cystectomy. J Infect Chemother 2012;18:175–9.

[21] Roberts JA, Roberts MS, Robertson TA, Dalley AJ, Lipman J. Piperacillin penetration into tissue of critically ill patients with sepsis – bolus versus continuous administration. Crit Care Med 2009;37(3):926–33.

[22] Duhunty JM, Roberts JA, Davis JS, Webb SA, Bellomo R, Gomersall C, et al. Continuous infusion of beta-lactam antibiotics in severe sepsis: a multicenter double-blind, randomized controlled trial. Clinic Infect Dis 2013;56(2):236–44.

[23] Acosta Garcia H, Victoria GIL-Navarro M, CotrinaLuque J, Cisneros Herreros JM, LepeJimémez JA, Bautista Ploma J. Piperacillin-tazobactam in continuous or expanded perfusion vs intermittent perfusion. Farm Hosp 2012;36(5):424–9.

[24] Yang H, Zhang C, Zhou Q, Wang Y, Chen L. Clinical outcomes with alternative dosing strategies for piperacillin/tazobactam: a systematic review and meta-analysis. PLoS One 2015;10(1):e0116769.

[25] Fleischhack G, Schmidt-Niemann M, Wulff M, Wulff B, Havers W, Marklein G, et al. Piperacillin, beta-lactam inhibitor plus gentamicin as empirical therapy of a sequential regimen in febrile neutropenia of pediatric cancer patients. Support Care Cancer 2001;9:372–9.

[26] Zelenitsky SA, Silverman RE, Duckworth H, Harding GK. A prospective, randomized, double-blind study of single high dose versus multiple standard dose gentamicin both in combination with metronidazole for colorectal surgical prophylaxis. J Hosp Infect 2000;46:135–40.

[27] Bert F, Larroque B, Dondero F, Durand F, Paugam-Burtz C, Belghiti J, et al. Risk factors associated with preoperative fecal carriage of extended-spectrum β-lactamase-producing Enterobacteriaceae in liver transplant recipients. Transpl Infec Dis 2014;16(1):84–9.