Contamination of the Preservation Solution in Solid Organ Transplantation

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ABSTRACT

Introduction. Preservation solutions (PS), in which grafts for patients undergoing liver transplantation are stored, represent a medium suitable for microorganism growth and a potential source for transmission of pathogenic germs to the transplant recipients. The aim of the present study was to review the relevant literature for the incidence and predictors of positive microbiological findings in the PS.

Patients and Methods. We performed a literature review of publications on bacterial and fungal contamination of PS during cold organ storage focusing on its impact on bacteremia and/or nosocomial infection of the recipient.

Results. Overall 19 studies were reviewed, published between the years 2000 and 2016, that encompassed a total of 5647 patients. Positive cultures were identified in 1428 patients (25%). The documentation of bacteremia showed a wide deviation with documented ranges between 0% and 69%. Data on the identification of same species or of related nosocomial infections were only sparsely available; same species were found in a rate of 0% to 8%, and nosocomial infections were attributed to them in an incidence of 0% to 19%.

Conclusions. Our study underlines both the limited published data and the contradictory available information on contamination of preservation solution in solid organ transplantation, not allowing for any recommendations. The necessity for prospective, multicentric studies on this topic is mandatory.

THE GREAT evolution in surgical techniques, anesthesia, perioperative management and immunosuppression during the past 4 decades returned solid organ transplantation from an "experimental" surgical procedure to a standard of care for patients with end-stage liver disease after careful selection [1–4]. However, short-term posttransplant results may be limited through infectious complications, which remain a significant cause of morbidity and mortality in this particular group of patients [5]. The frequent admissions of the patients to the hospital, the reduced general condition due to the organ failure, the hospitalization status per se prior to organ transplantation, and the provided immunosuppression contribute to an increased risk of posttransplant infection. Furthermore, the preservation solutions (PS), in which grafts are stored, represent a medium suitable for microorganism growth and a potential source for transmission of pathogenic germs to the transplant recipients. However, the prevalence and the clinical consequences of bacterial and fungal contamination of this fluid are not completely understood, and literature on this topic is controversial [6–24]. The aim of the present study was to review the relevant literature for the incidence and predictors of positive microbiological findings in the PS.

MATERIALS AND METHODS

For the purposes of the present study, we performed a literature review of publications on bacterial and fungal contamination of PS during cold organ storage, focusing on its impact on bacteremia and/or nosocomial infection of the recipient. The MEDLINE database was searched. The terms "transplantation," "preservation

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Table 1. Literature Review of Publications About Bacterial and Fungal Contamination of Preservation Fluid During Cold Organ Storage and the Impact of Such Contamination on Bacteraemia or Nosocomial Infection of the Recipient

Author; Year	Number of Grafts (N)	Organ	Positive Cultures, n (%)	Bacteremia (%)	Same Species, n (%)	Related NI, %	Suggestion
Zibari [6]; 2000	599	Heart	46 (7.5)	27	8	0	Contamination should not be a contraindication for transplant
		Liver		22	0	0	
		Kidney		0			
Wakelin [7]; 2005	269	Kidney	61 (23)			0	Routine culturing of PS and appropriate treatment
Cerutti [8]; 2006	610	Liver	293 (48)	21	11/610 (1.8)	4	Donors with prolonged ICU stay are at risk of infection Older donor age associated with pathogen transmission to the recipient
Mattner [9]; 2008	282	Heart-Lung	150 (53)	69	11/282 (3.9)	19	Despite high contamination rates, infection is rare after transplant with adequate preoperative antibiotics and aseptic surgery
		Heart		22			
		Lung		34			
		Liver		28		1.3	
Canaud [10]*; 2009	874	Kidney	8 (1)			0.2	Early antifungal therapy recommended
Ruiz [11]; 2009	60	Liver	89 (98)	4 (7)	0	0	No routine culturing of PS necessary
Botterel [12]*; 2010	659	Heart	0/62 (0)	(3.4)	3/659 (0.4)		Optimization of microbiological procedures
		Kidney	11/356 (3)				
		Liver	10/241 (4)				
Veroux [13]; 2010	62	Kidney	24/62 (39)	0	0	0	Prophylactic antibiotic therapy
Audet [14]; 2011	232	Liver	91/232 (39)			5.6	Periodic detection Antibiotics “on demand”
Chaim [15]; 2011	121	Liver	15/121 (12)	(0.8)	1/121 (0.8)	0.8	Optimization of microbiological procedures
Janny [16]; 2011	477	Liver	45/477 (9.5)			1.7 (8/45)	Appropriate antibiotics “on demand”
Mattana [17]; 2011	136	Kidney/ Pancreas	38/136 (28)				Contamination not associated with recipient’s infection
Sauget [18]; 2011	426	Liver Kidney	131/426 (31)		12/426 (2.8)		Only 1 case was cross-transmitted via the transplant
Grąt [19]; 2012	46	Liver	39/46 (85)			0	Contamination may lead to temporary impairment of graft function
Yansouni [20]; 2012	331	Kidney Liver Pancreas Heart	205/331 (62)				Contamination associated with clinical bacterial infections
Bertrand [21]; 2013	165	Kidney	62/165 (38)	2/62 (1.2)	2/62 (1.2)	0	No routine culturing of PS necessary May increase the rate of ESBL-PE emergence
Rodrigues [22]*; 2013	70	Kidney	6/70 (9)			2.9 (2/70)	Routine culturing is crucial
Garcia-Zamora [23]; 2015	178	Liver	79/178 (44)				A standardized protocol including fungal and bacterial cultures could be beneficial
Oriol [24]; 2016	50	Liver	46/50 (92)	14/50 (28)			Administration of targeted antimicrobial treatment for organisms isolated in the preservation fluid

Abbreviations: ESBL-PE, extended-spectrum β-lactamase–producing Enterobacteriaceae; ICU, intensive care unit; NI, nosocomial infection; PS, preservation solution.
*Fungal infections.

solution," and "contamination" were combined and yielded 86; articles that referred to nonsolid organ transplantation, case reports, and reviews were excluded.

RESULTS

Overall 19 studies were reviewed that were published between the years 2000 and 2016 and encompassed a total of 5419 patients. The characteristics of the included studies are summarized in Table 1. Positive cultures were identified in 1324 patients (24%). The documentation of bacteremia showed a wide deviation with documented ranges between 0% and 69%. Data on the identification of the same species or of related nosocomial infections were only sparsely available; the same species were found in a rate of 0% to 8%, and nosocomial infections were attributed to them in an incidence of 0% to 19% (Table 1).

DISCUSSION

According to the results of every study, a variety of suggestions could be composed, even though they were sometimes contradictory [6–24]. Contamination of PS should not be considered a contraindication to organ transplantation [6] since it is not associated with the recipient's infection [9,17] nor it is extremely rarely cross-transmitted via the solid-organ transplantation [8,15,18]. However, other authors concluded that contamination might lead to temporary impairment of graft function [19] or can be associated with clinical bacterial infections [20]. Though some investigators propose that nonroutine culturing of PS is needed [11,21] or putting the periodic detection forward and the application of antibiotics "on demand" [14,16], others underline the necessity for optimization of the microbiological procedures [12,15]. Routine culturing is critical [22], as well as appropriate treatment [7].

Concerning the use of antimicrobial therapy, a range of different suggestions can be found, including prophylactic antibiotics [9,13], antibiotics "on demand" [14,16], early antifungal therapy [10], and no antibiotics [21]. Bertrand et al described that the use of pre-emptive antibiotics for patients with positive PS cultures was an independent risk factor for extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-PE) acquisition in both univariate and multivariate analyses [21]. The application of more sensitive culture methods increased the incidence of identification of bacterial contamination of PS and led to a correspondingly higher prescription of antibiotics, ESBL-PE carriage, and related infections [21]. Therefore, according to the authors, the systematic use of PS blood bottle cultures in kidney transplantation may have no benefit and might increase the rate of ESBL-PE emergence [21]. Interestingly, the second study suggesting no routine culturing of PS [11], applied posttransplant infection prophylactic protocol consisting of ampicillin, and cefotaxime for 48 hours.

Cerutti et al analyzed the results of microbiologic cultures obtained before organ recovery in intensive care unit (ICU) and routinely at operation from 610 consecutive liver donors and demonstrated both high contamination rates of 48% and considerable bacteremia in 21% of the instances [8]. Nonetheless, although 1-year patient/graft survival rates were not influenced by donor culture positivity, pathogen transmission occurred in 11 cases with significant recipient 1-year mortality [45%]. This was the first study to highlight prognostic factors for donor infection, such as an ICU stay of 3 or more days, in multivariate analysis [8]. In conclusion, donors with a prolonged ICU stay were found to be at increased risk of infection, while older donor age was associated with pathogen transmission to the recipient [8].

Controversy remains regarding the need for routine culturing of PS [11,21,22] and the consequent management in cases of positive results [9,10,13,14,16,21]. Contamination of PS may have from no consequences to the recipient related to life-threatening complications [19,20]. However, due to the poor data available, no satisfactory level of evidence exists; as a result, no recommendation by the transplant registries can be made. The present study underlines both the limited published data and the equivocal available information on contamination of PS in solid organ transplantation, so no recommendation can be made. The necessity for prospective, multicentric studies on this topic is mandatory.

REFERENCES

[1] Scharschmidt BF. Human liver transplantation: analysis of data on 540 patients from four centers. Hepatology 1984;4:95S–101S.

[2] Pichlmayr R, Brölsch C, Wonigeit K, et al. Experiences with liver transplantation in Hannover. Hepatology 1984;4:56S–60S.

[3] Adam R, Karam V, Delvart V, et al. Evolution of indications and results of liver transplantation in Europe. A report from the European Liver Transplant Registry (ELTR). J Hepatol 2012;57:675–88.

[4] Davis MK, Hunt SA. State of the art: cardiac transplantation. Trends Cardiovasc Med 2014;24:341–9.

[5] Saner FH, Olde Damink SW, Pavlakovic G, et al. Pulmonary and blood stream infections in adult living donor and cadaveric liver transplant patients. Transplantation 2008;85:1564–8.

[6] Zibari GB, Lipka J, Zizzi H, Abreo KD, Jacobbi L, McDonald JC. The use of contaminated donor organs in transplantation. Clin Transplant 2000;14:397–400.

[7] Wakelin SJ, Casey J, Robertson A, et al. The incidence and importance of bacterial contaminants of cadaveric renal perfusion fluid. Transpl Int 2005;17:680–6.

[8] Cerutti E, Stratta C, Romagnoli R, et al. Bacterial- and fungal-positive cultures in organ donors: clinical impact in liver transplantation. Liver Transpl 2006;12:1253–9.

[9] Mattner F, Kola A, Fischer S, et al. Impact of bacterial and fungal donor organ contamination in lung, heart-lung, heart and liver transplantation. Infection 2008;36:207–12.

[10] Canaud G, Timsit MO, Zuber J, et al. Early conservative intervention for candida contamination of preservative fluid without allograft nephrectomy. Nephrol Dial Transplant 2009;24:1325–7.

[11] Ruiz P, Gastaca M, Gonzalez J, et al. Incidence and clinical relevance of bacterial contamination in preservation solution for liver transplantation. Transplant Proc 2009;41:2169–71.

[12] Botterel F, Foulet F, Legrand P, et al. Yeast contamination of kidney, liver and cardiac preservation solutions before graft: need for standardisation of microbial evaluation. J Hosp Infect 2010;76:52–5.

[13] Veroux M, Corona D, Giuffrida G, et al. Acute renal failure due to ureteral obstruction in a kidney transplant recipient with Candida albicans contamination of preservation fluid. Transpl Infect Dis 2009;11:266–8.

[14] Audet M, Piardi T, Panaro F, et al. Incidence and clinical significance of bacterial and fungal contamination of the preservation solution in liver transplantation. Transpl Infect Dis 2011;13:84–8.

[15] Chaim FH, Boin IF, Ataide EC, Stucchi RS. Perfusion fluid contamination in relation to recipient survival and acute cellular rejection in orthotopic liver transplantation: retrospective analysis. Transplant Proc 2011;43:1313–5.

[16] Janny S, Bert F, Dondero F, et al. Microbiological findings of culture-positive preservation fluid in liver transplantation. Transpl Infect Dis 2011;13:9–14.

[17] Mattana AM, Marra AR, Machado AM, Lopes Filho Gde J, Salzedas Netto AA, Gonzalez AM. Evaluation of the presence of microorganisms in solid-organ preservation solution. Braz J Infect Dis 2011;15:528–32.

[18] Sauget M, Verdy S, Slekovec C, Bertrand X, Talon D. Bacterial contamination of organ graft preservation solution and infection after transplantation. Transpl Infect Dis 2011;13:331–4.

[19] Grąt M, Ligocka J, Lewandowski Z, et al. Incidence, pattern and clinical relevance of microbial contamination of preservation fluid in liver transplantation. Ann Transplant 2012;17:20–8.

[20] Yansouni CP, Dendukuri N, Liu G, et al. Positive cultures of organ preservation fluid predict postoperative infections in solid organ transplantation recipients. Infect Control Hosp Epidemiol 2012;33:672–80.

[21] Bertrand D, Pallet N, Sartorius A, et al. Clinical and microbial impact of screening kidney allograft preservative solution for bacterial contamination with high-sensitivity methods. Transpl Int 2013;26:795–9.

[22] Rodrigues BF, Natário AS, Vizinho RS, et al. Candida species contamination of preservation fluid-outcome of renal transplantation in 6 patients. Transplant Proc 2013;45:2215–9.

[23] Garcia-Zamora C, Segura J, Lopez-Lopez V, et al. Clinical Significance of Contamination of the Preservation Solution in Liver Transplantation. Transplant Proc 2015;47:2322–3.

[24] Oriol I, Lladó L, Vila M, et al. The etiology, incidence, and impact of preservation fluid contamination during liver transplantation. PLoS One 2016;11:e0160701.