

Literature review

Contamination of preservation fluid in kidney transplant. Report and literature review

Contaminación de líquido de preservación en trasplante renal. Reporte y revisión de la literatura

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Abstract

Chronic kidney disease is a public health problem with high morbidity and mortality, kidney transplantation being one of the current therapeutic alternatives. 12 published works concerning the contamination of the preservation fluid in kidney transplant, four case reports, and eight prevalence studies are included in this article. The prevalence of preservation liquid contamination for any microorganism ranged from 17.43% to 59.72%, while for those limited to the *Candida* sp report, the frequency varied from 1.69% to 8.57%. In the case reports, all were associated with *Candida* infection, with renal artery arteritis and graft loss as the most frequent complications. In our institution, of a total of 59 transplant patients, at least one microorganism was isolated in 20 cases (28.17%). Preservation fluid contamination is a frequent phenomenon in kidney transplantation. However, since no publications are describing the complications associated with infection by other microorganisms, we could say that contamination by *Candida* sp, despite not having a high prevalence, it is clinically the most relevant.

Keyword: organ preservation, kidney transplant, chronic kidney disease.

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Resumen

La enfermedad renal crónica es un problema de salud pública con una alta morbilidad y mortalidad. El trasplante renal es una de las actuales alternativas terapéuticas. Se incluyen en este artículo 12 trabajos publicados referentes a la contaminación del líquido de preservación en trasplante renal, 4 reportes de caso, y 8 estudios de prevalencia. En este estudio la prevalencia de contaminación de líquido de preservación para cualquier microorganismo varió entre 17,43 % a 59,72 %, mientras que para los limitados al reporte de *Candida* sp, la frecuencia varió de 1,69 % a 8,57 %. En los reportes de caso, todos fueron asociados a la infección por *Candida* sp, con arteritis de la arteria renal y pérdida del injerto como las complicaciones más frecuentes. En nuestra institución, Hospital de Especialidades de las Fuerzas Armadas N°1, de un total de 59 pacientes trasplantados se aisló al menos un microorganismo en 20 casos (28,17 %). Con estos resultados sugerimos que la contaminación del líquido de preservación es un fenómeno frecuente en trasplante renal, sin embargo al no poseer publicaciones en las que se describan las complicaciones asociadas a la infección por otros microorganismos, creemos que la contaminación por *Candida* sp, a pesar de no tener una gran frecuencia, es clínicamente la más relevante.

Palabras clave: preservación de órganos, trasplante renal, enfermedad renal crónica

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Introduction

Chronic kidney disease is currently a relevant public health problem, whose prevalence has been estimated to vary between 8% and 10% of the population worldwide. It is estimated that around 850 million people worldwide suffer from some degree of chronic kidney disease and also that its progression has led to a representative group of patients who require renal replacement therapies such as hemodialysis, peritoneal dialysis, or renal transplantation, which entails high expenses for the healthcare systems, representing 2.3 to 7.1 million premature deaths due to lack of access to dialysis, hemodialysis and kidney transplantation.¹

According to the Latin American Dialysis and transplant registry, in our region there is a prevalence rate of 509 patients on hemodialysis or peritoneal dialysis per million inhabitants, and a rate of 19 kidney transplants per million inhabitants.²

Kidney transplantation has been a therapeutic alternative in constant evolution within medicine and is associated with a better life expectancy in patients with end-stage chronic kidney disease when compared to other renal replacement therapies such as hemodialysis.³ Despite this, kidney transplantation has a high morbidity and mortality, with infectious diseases being complications that can even compromise the life of the patient.⁴ In this context, cases of infection associated with the graft, as well as with the various stages involving the transplant have been reported, which could compromise, as risk factors, antecedents of the donor, organ preservation media, surgical processes, previous conditions of the recipient, or even the factors of the responsible institution could influence, therefore, knowledge to prevent these complications is very relevant and necessary to achieve the best possible benefits. Then, the objective of this review is to present the available information on contamination of preservation fluid and its associated complications.

Materials and methods

Search strategy

A review of the published literature on contamination of the preservation fluid in kidney transplantation was carried out. No particular inclusion criteria were established during the search, however, we excluded all those works that did not refer exclusively to kidney transplantation, or those cases that presented complications associated with contamination of the preservation fluid but were presented in other series of cases.

We conducted the search through PubMed, using the combination of words «*Contamination of preservation fluid in kidney transplant*» [All fields] 12 publications were identified. After analyzing the title and abstract of all manuscripts found in the search, 5 papers were excluded. In addition, we conducted the search for articles through academic Google, where we identified 5 manuscripts that could be included, which yielded a total of 12 papers to be analyzed.

Report of our institution

A cross-sectional, descriptive, observational study was conducted during the month of February 2019 at the Hospital of Specialties of the Armed Forces No. 1 (*Hospital de Especialidades de las Fuerzas Armadas N.º 1*) in Quito, Ecuador, which included 69 kidney transplants of cadaveric donors performed between the year 2014 and January 2019, of which the microbiological culture of the preservation fluid was carried out in 59 cases. To obtain information regarding the microbiology results, we investigated the clinical history of each patient.

Results

12 published papers were included, all written in English, which were classified into two groups: case reports and prevalence studies.

Table 1. Prevalence studies of contamination of preservation fluid in kidney transplantation.

Rodríguez, et al., (2013) ⁵	Candida	6 of 70 cultures were positive for fungi, 4 <i>Candida albicans</i> and 2 <i>Candida glabrata</i>	8.57 %	Delayed graft function in 3 patients (50 %), and rupture of the anastomosis in 2 patients (33.33 %)
Bertrand, et al., (2013) ⁶	Any isolate	62 of 165 cultures were positive, 43 monomicrobial and 19 polymicrobial. Of these, 16 GNB (<i>Escherichia coli</i> in 8), 58 GPC (coagulase negative <i>Staphylococcus</i> in 43), GPB in 6 and <i>Candida albicans</i> in 3 isolates.	37.57 % (GNB 9.70 %; GPC 35.15 %; GPB 3.64 %; <i>Candida albicans</i> 1.81 %)	Not reported
Veroux, et al., (2010) ⁷	Any isolate	24 of 62 cultures were positive for at least one microorganism, the most frequent was <i>Staphylococcus epidermidis</i> in 8, <i>Candida albicans</i> in 5.	38.71 % (<i>Staphylococcus epidermidis</i> 12.90%, <i>Candida albicans</i> 8.06 %)	One patient infected with <i>Candida</i> had ureteral obstruction, hydronephrosis and acute kidney injury, without graft loss
Canaud, et al., (2009) ⁸	Candida	8 of 474 cultures were positive for <i>Candida</i> , 5 <i>albicans</i> , 3 <i>glabrata</i> , 1 <i>tropicalis</i>	1.69 %	Not reported
Maignon, et al., (2008) ⁹	Candida sp	8 of 214 cultures were positive for <i>Candida</i>	3.74 %	Delayed graft function in 4 patients (50 %) without graft loss
Wakelin, et al., (2005) ¹⁰	Any isolate	38 of 218 cultures were positive for at least one microorganism.	17.43 % (Coagulase negative <i>Staphylococcus</i> 12.39 %, Fungi 2.75 %, <i>Escherichia coli</i> 1.38 %, <i>Pseudomonas aeruginosa</i> 1.38 %, others 0.92 %).	Not reported
Ranghino, et al., (2016) ¹¹	Any isolate	101 of 290 cultures were positive for at least one microorganism.	34.83 % (17.59 % <i>Staphylococcus</i> sp, 3.45 % <i>Candida albicans</i>)	Not reported
Schiavelli, et al., (2018) ¹²	Any isolate	43 of 72 cultures were positive for at least one microorganism.	59.72 %	Not reported
Our institution	Any isolate	20 of 59 cultures were positive for at least one microorganism.	28.17 %	Not reported

* Regarding the total of both positive and negative cultures;

** Regarding the total of positive isolates; GNB, Gram-negative bacilli; GPC, Gram-positive cocci; GPB, Gram-positive bacilli; sp, species.

Table 1 summarizes the most significant findings in the works classified as prevalence studies.⁵⁻¹² In this group, the papers were published between 2005 and 2018. Those written by Bertrand et al,⁶ Veroux et al,⁷ Wakelin et al,¹⁰ Ranghino et al,¹¹ and Schiavelli et al,¹² presented the total microbiological isolations that evidenced contamination of the preservation fluid, while the rest presented only the contamination by *Candida* sp. In addition, in this group only 3 studies, Rodríguez et al,⁵ Veroux et al,⁷ and Matignon et al,⁹ presented the complications associated with contamination.

Among the total isolates referenced in each study, it was established that the prevalence of contamination of preservation fluid varied between 17.43% and 59.72% (mean 37.64%), when all positive cultures for any microorganism were considered, while for those limited to the report of *Candida* sp, the frequency varied between 1.69% and 8.57% (mean 4.67%). Among the species of *Candida* sp, the most frequent was *Candida albicans*. Regarding the associated complications, they were only reported in studies limited to contamination with *Candida*, of which the delayed graft function was the most frequent. However, in the studies that reported contamination by any microorganism, the most frequent was coagulase negative *Staphylococcus*, the main agent isolated in the contamination of preservation fluid.

Among the clinical case reports (**Table 2**),¹³⁻¹⁶ all presented contamination with *Candida*, with a total of

9 patients, among whom the associated complications were renal artery arteritis (6/9), rupture of the anastomosis (1/9), death (4/9), hypogastric artery aneurysm (1/9), rupture of the anastomosis (1/9), rupture of the renal artery (1/9) and graft loss (6/9).

Results of the institution

Between 2014 and January 2019, at least one microorganism was isolated in 20 cases out of a total of 59 transplanted patients (28.17%), according to the following detail; coagulase negative *Staphylococcus* (9/20), *Klebsiella* sp (3/20), *Pseudomona* sp (3/20), *Streptococcus* sp (2/20), *Staphylococcus aureus* (2/20), *Enterococcus faecalis* (1/20), *Aeromona* sp (1/20) and *Candida albicans* (1/20). No clinical complications associated with this contamination were identified in any of the cases.

Discussion

After the organ has been removed it must be stored until it is transplanted, an event that can take several hours considering that generally both the donor and the recipient are in different hospitals, for this reason it has been necessary to develop safe and effective ways to preserve the ex vivo organ, one of them being the use of preservation fluids whose usefulness is based on preventing cell edema in the organ to be transplanted, delaying cell lysis

Table 2. Reports of clinical cases associated with contamination of the preservation fluid in kidney transplant.

	Reported contamination	Number of patients	Complications
Dębska-Ślizień, et al., (2015) ¹³	<i>Candida</i>	2	Renal artery arteritis, delayed graft function, and death in both patients.
Mai, et al., (2006) ¹⁴	<i>Candida</i>	4	Fungal arteritis in the 4 patients, 2 died, and 2 had graft loss.
Gari-Toussaint, et al., (2004) ¹⁵	<i>Candida</i>	1	Rupture of the renal artery, with graft loss.
Spees, et al., (1982) ¹⁶	<i>Candida</i>	2	One patient presented hypogastric artery aneurysm, and other suffered a rupture of the anastomosis. One suffered graft loss.

and optimizing the functionality of the graft after restoration of perfusion.¹⁷

Although measures to prevent possible contamination of the preservation fluid are always considered, this is a present risk. In this context, we analyzed that the frequency of contamination of the perfusion fluid with any microorganism is high. However, the greatest complications have been reported when the contamination is given by *Candida* sp, whose frequency is relatively low. It is important to highlight that the most frequent microorganisms in the isolates have been reported in the human microbiome, so we consider that the main source of contamination could be a reduced control in the measures of asepsis and antisepsis at each stage of the kidney transplant, however, we need studies that can test this hypothesis to generate better control strategies.

As for the complications associated with *Candida* sp, fungal arteritis was especially frequent, with the consequent loss of renal graft. Regarding the pathophysiology behind this phenomenon, the association between fungal infection and endothelial damage has been demonstrated in murine models in which after inoculation of *Candida albicans* cell wall extracts (CAWE), protuberant lesions in the coronary, carotid, celiac, iliac arteries and abdominal aorta were evidenced, together with the expression of c-Jun N-terminal kinase (JNK), complications that had a reduced incidence by inhibiting JNK.¹⁷ In addition, the activity of JNK reduces the expression of genes involved in the synthesis of collagen such as COL3A1, a gene whose mutations have been associated with the development of aneurysms.^{18,19} The sum of all these phenomena could give a possible explanation for the importance of the complications associated with the contamination of the preservation fluid by *Candida* sp, however, it is important to investigate the expression of these molecular phenomena in the transplanted patient in order to explain the findings presented in this study.

Conclusions

The contamination of the preservation fluid is a frequent phenomenon in kidney transplantation;

however, not having publications describing the complications associated with infection by other microorganisms, we could say that the contamination with *Candida* sp, despite not having a great frequency, is the clinically most relevant.

Improving the procedures and developing better strategies of asepsis and antisepsis during organ ablation and implantation will optimize the processes during the transplantological activity, and it will be a challenge for the transplant teams.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethical responsibilities

Protection of people and animals

The authors declare that no experiments were performed on human beings or animals for this research.

Data confidentiality

The authors declare that they have followed the protocols of their workplace on the publication of patient data.

Right to privacy and informed consent

The authors declare that patient data do not appear in this article.

Contribution of the authors

David Garrido and Lorena Arias, data collection of cases in our hospital.

The five authors: review of the selected articles. They gave their ideas to modify the text when it was required as well as the approval of the final version.

Washington Osorio: review of the included prevalence studies.

Jorge Huertas: review of all the included publications as well as expert judgment in kidney transplant.

Sandra Valarezo: review of the clinical case studies included.

David Garrido and Washington Osorio: writing and editing of the main manuscript. Design of the tables presented.

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