Perfusion Fluid Contamination in Relation to Recipient Survival and Acute Cellular Rejection in Orthotopic Liver Transplantation: Retrospective Analysis

F.H.M. Chaim, I.F.S.F. Boin, E.C. Ataide, and R.S.B. Stucchi

ABSTRACT

Introduction. A perfusion fluid used in the preservation of a grafted liver represents a medium suitable for microorganism growth. This study investigated the prevalence of perfusion fluid contamination, acute cellular rejection (ACR) episodes, and patient survival rate.

Method. This is a retrospective study, based on an electronic database allocating cases of orthotopic liver transplantation. The exclusion criteria were as follows: having been submitted to multiple organ transplantation, liver retransplantation only, and those whose samples had not been collected or sent on the back table procedure or were unobtainable (usually the samples were sent when there was donor infection suspicion/positivity). Our posttransplantation infection prophylactic protocol consisted of ampicillin/sulbactam for 72 hours. The variables in the study were as follows: fluid contamination, presence of acute cellular rejection (ACR, Banff classification), and recipient survival at the first year. Statistical analysis was performed using descriptive statistics and chi-square with Fisher exact test considering significant $P < .05$.

Results. We observed perfusion fluid contamination in 15/121 (12.39%). The agents were as follows: Klebsiella pneumoniae in 6 (4.96%), Staphylococcus epidermidis in 5 (4.13%), and Acinetobacter baumanii in 3 (2.48%) and negative cultures in 106 (87.60%). Only 1 patient had matching for donor infection and positivity hemoculture after the transplantation ($K$ pneumoniae) and he was the only patient associated with fluid infection and death. The recipients who had their fluid preservation with positive cultures had more ACR and the survival rate was similar among those with or without infection.

Conclusion. Optimization of microbiological procedures can be performed including fungal and bacterial cultures.

There have been great advances in orthotopic liver transplantation (OLT) over the last few decades leading to the current treatment of choice for end-stage liver disease. The success of this procedure, however, is still linked to different factors among which an efficient conservation of the liver graft is included, keeping the organ in appropriate conditions—morphologically and biochemically—during the interruption in blood flow, from the organ removal until its implantation.

Thus, the development and improvement of techniques and means to preserve the organ to be transplanted, increasing the chance of success of the procedure, have become an unexplored and attractive field of scientific research, given that even in countries where such techniques are used effectively there is a shortage of organs, making it necessary to develop new methods to increase the number of transplants and reduce the number of deaths on the waiting list.1,2

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Although many studies have compared the preservation solutions using as variables acute rejection, graft dysfunction, and complications of the biliary tract, there are few studies that have looked into the incidence of perfusate contamination on OLT and its consequences on early surgical complications for the recipient.3–5

This study investigated the prevalence of contamination of the perfusion solution used for graft liver preservation and its implications regarding acute cellular rejection (ACR) episodes and patient survival at the first year after transplantation.

METHODS

This is a retrospective cohort cross-sectional study, based on an electronic database allocating cases of OLT performed from January 2000 to December 2008, at our institution. The cases in this study had these inclusion criteria: age older than 18 years and OLT from January 2000 to December 2008 in our service. The exclusion criteria were as follows: having been submitted to multiple organ transplantation, liver retransplantation only, and those whose samples had not been collected or sent on the back table procedure or were unobtainable (usually the samples were sent when there was donor infection suspicion/positivity). Our posttransplantation infection prophylactic protocol consisted of ampicillin and sulfactam for 72 hours.

The variables of interest in the study were as follows: perfusate contamination, presence of ACR in the first 3 months (Banff classification), and recipient survival at the first year. The cases have been divided according to the result of the diagnostic microbiology analysis into 2 groups: without contamination of the perfusion fluid and with contamination, regardless of the microbiological agent.

Statistical analyses were performed using descriptive statistics and chi-square with Fisher exact test considering significant P < .05.

RESULTS

We carried out 381 OLT and obtained total data access in 121 cases where the perfusion fluids were sent for microbiological analysis and the results were subsequently included in the medical records.

The predominant etiology was hepatitis C and alcohol in 51% of the cases and alcohol in another 14%.

We observed prevalence of 15 (12.39%) cases of perfusion fluid contamination. The agents were as follows: Klebsiella pneumoniae in 6 (4.96%), Staphylococcus epidermidis in 5 (4.13%), and Acinetobacter baumanii in 3 (2.48%) and negative cultures were observed in 106 (87.60%). Only 1 patient had matching for donor infection and positivity hemoculture after the transplantation (K pneumoniae) and he was the only patient associated with fluid infection and death. Regarding recipient survival, the distributions of the prevalence of rejection, retransplantation, and death at the first year after transplantation according to the contamination of perfusion fluid are shown in the Table 1.

DISCUSSION

Although many studies have compared the preservation solutions, using as variables acute rejection, graft dysfunction, and complications of the biliary tract, there are few studies that have looked into the incidence of perfusate contamination on OLT and its consequences on early surgical complications for the recipient.1–5

A perfusion fluid used in the preservation of the grafted liver represents a medium suitable for micro-organism growth.

In an observational study by Audet et al,3 a sample of 232 transplanted livers was collected. Perfusion fluid samples were stored for microbiological analysis from harvested donors. Bacteria were isolated in 91 of 232 samples and postoperative infections related to contaminated perfusion solution occurred in 13/91 (14.3%) cases. The contamination rate of the preservation medium appears to be high, but postoperative infections occur rarely according to these authors.

In our study we demonstrated contamination in perfusion fluid samples in 12.39% and only 1 recipient had suspicion of matching infection due to fluid or donor contamination (K pneumoniae).

The matching among positive cultures of the preservation fluids was reduced in our study but Ruiz et al4 have reported positive cultures of preservation fluids in 98% of patients, although most of them (75%) were superficial saprophytic flora, and they also related that microorganisms isolated from posttransplantation cultures did not match the ones obtained from the preservation solution. Their results did not support routine culturing of the preservation solution provided that an adequate posttransplantation antibiotic prophylactic regimen had been used.

The microorganisms isolated (Klebsiella, Staphylococcus, and Acinetobacter) in our study were similar to those reported by Ruiz et al.4 They had 15 (25.1%) cases from which high virulence pathogens (S aureus, Klebsiella, Escherichia coli, Enterobacter, and Pseudomonas aeruginosa) were isolated.

<table>
<thead>
<tr>
<th>Group</th>
<th>ACR‡</th>
<th>Retransplantation</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Without perfusion fluid contamination</td>
<td>7</td>
<td>6.60</td>
<td>6</td>
</tr>
<tr>
<td>With perfusion fluid contamination</td>
<td>4</td>
<td>26.67</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>9.10</td>
<td>6</td>
</tr>
</tbody>
</table>

*P < .05; Fisher exact test.
In fact, the prevalence of fluid contamination needs to be established and maybe seeding fungal cultures. Botterel et al recently reported that fungal fluid contamination occurred in 3.4% of all kidney and liver preservation fluids tested. Its clinical consequences and therapeutic management remain to be defined, which suggests that optimization/standardization of microbiological procedures is warranted, including analysis of large preservation fluids volume, seeding of fungal-specific with medium, and prolonged incubation.

We did not find any report on the correlation between ACR and fluid infection. However, we found more ACR correlated to positive fluid preservation because we reduced the immunosuppression with the aim of minimizing the problems with opportunistic infection or same transmission from the preservation fluid or the donor.

In conclusion, the recipients who had their fluid preservation with positive cultures had more ACR and similar survival rates compared with those with preservation fluid with negative cultures. However, optimization/standardization of microbiological procedures can be performed including fungal and bacterial cultures.

REFERENCES