Infection by Cryptosporidium parvum in renal patients submitted to renal transplant or hemodialysis

Abstract The frequency of infection by Cryptosporidium parvum was determined in two groups of renal patients submitted to immunosuppression. One group consisted of 23 renal transplanted individuals, and the other consisted of 32 patients with chronic renal insufficiency, periodically submitted to hemodialysis. A third group of 27 patients with systemic arterial hypertension, not immunosuppressed, was used as control. During a period of 18 months all the patients were submitted to faecal examination to detect C. parvum oocysts, for a total of 1 to 6 tests per patient. The results showed frequencies of C. parvum infection of 34.8%, 25% and 17.4%, respectively, for the renal transplanted group, the patients submitted to hemodialysis and the control group. Statistical analysis showed no significant differences among the three groups even though the frequency of C. parvum infection was higher in the transplanted group. However, when the number of fecal samples containing C. parvum oocysts was taken in account, a significantly higher frequency was found in the renal transplanted group.

Key-words: Cryptosporidiosis. Cryptosporidium parvum. Renal transplantation.

Resumo Determinou-se a freqüência de infecção por Cryptosporidium parvum em dois grupos de pacientes com doença renal, submetidos a imunossupressão. O primeiro grupo era constituído por 23 pacientes submetidos a transplante renal e o segundo por 32 indivíduos portadores de insuficiência renal crônica, periodicamente submetidos a hemodiálise. Um terceiro grupo de 27 pacientes com hipertensão arterial sistêmica, não imunossuprimidos, foi utilizado como controle. Os pacientes, acompanhados durante 18 meses, foram submetidos a exames parasitológicos para detecção de oocistos de C. parvum nas fezes, em quantidade que variou de 1 a 6 exames por paciente. Os resultados revelaram frequências de infecção por C. parvum iguais a 34.8%, 25,0% e 17,4%, respectivamente, para os pacientes submetidos a transplante renal, hemodiálise e os pertencentes ao grupo controle. Não se observaram diferenças significativas entre os três grupos embora note-se tendência a maior frequência de infecção entre os pacientes submetidos a transplante renal. Todavia, quando se considerou o número de amostras fecais com presença de oocistos de C. parvum encontrou-se frequência significativamente maior entre os pacientes transplantados.

From the beginning of the eighties on, infection by *Cryptosporidium parvum* has been recognized as a frequent cause of enteric alterations, and less commonly extraintestinal disease in immunosuppressed patients, mainly those who have AIDS, with several grades of severity, depending on the level of involvement of their immune system. Cryptosporidiosis has been observed even in non-immunosuppressed individuals, but without the same severity because of a self-limited clinical course.

The consumption of food as well as the utilization of, and contact with, water contaminated by the oocysts of *C. parvum*, as well as contact with either animals or human beings infected by this coccidian are considered to be sources of *Cryptosporidium* infection. The occurrence of intrahospital transmission of *Cryptosporidium* has been reported.

Cryptosporidiosis shows a worldwide distribution and has been diagnosed at higher prevalence rates in developing countries. In Brazil it has frequently been found in AIDS patients and in non-immunosuppressed diarrhoeal children, but *C. parvum* oocysts have been found even in patients with non-diarrhoeal faeces.

In the present study we investigated the occurrence of *C. parvum* infection in renal immunosuppressed patients submitted either to renal transplantation or hemodialysis. Elsewhere we had analyzed the presence of other intestinal parasites in the same patients.

Three groups of adult patients of both sexes seen at the Nefrology Clinic of the Department of Medicine, Medical School of Santa Casa de São Paulo (Brazil) from September 93 to April 95, were examined for the presence of *C. parvum* oocysts in the stool by staining with carbol-fuchsin after concentration by the formol-ether technique. The first group consisted of 23 renal transplanted patients kept in immunosuppression in order to avoid rejection; the second of 32 patients with chronic renal insufficiency immunosuppressed as a consequence of their disease and kept on hemodialysis, and the third one, considered as a control group, consisted of 27 patients with systemic arterial hypertension without any immunosuppression.

Each patient was submitted to different numbers of faecal examinations for the detection of *C. parvum* oocysts during a period of

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of samples</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 2-3 4-6</td>
<td>patients</td>
</tr>
<tr>
<td>Transplanted</td>
<td>11 5 7</td>
<td>58 23</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>10 16 6</td>
<td>78 32</td>
</tr>
<tr>
<td>Control</td>
<td>9 8 10</td>
<td>82 27</td>
</tr>
</tbody>
</table>

No significative difference in the frequency of infection by *C. parvum* was found among groups, as shown in Table 2 (Chi square = 2.70; DF = 2; p = 0.259), although the difference between the transplanted group and the control group almost achieved significance (p = 0.09).

However, when the number of faecal samples that were positive for *C. parvum* oocysts was considered (Table 3) a significant difference was found between the transplanted group and the control group (Chi square = 5.77; DF = 1; p = 0.016).
Infection by *C. parvum* has been considered as one of the most important causes of diarrhoea in immunocompetent children and as an important morbid agent, hardly controlled and, sometimes, uncontrollable, in immunosuppressed patients\(^2\)\(^{23}\).

Many times, especially when CD4+ cells counts are below 180 per mm\(^3\), cryptosporidiosis had been found to impair the clinical outlook of patients presenting congenital hypogammaglobulinemia, neoplasms, and mainly AIDS, or submitted to bone-marrow and solid organ transplantations\(^3\)\(^{6}\)\(^{7}\)\(^{10}\)\(^{16}\)\(^{19}\)\(^{22}\)\(^{26}\).

On the other hand, frequently *C. parvum* oocysts have been found in both asymptomatic and oligosymptomatic patients, especially children\(^{17}\)\(^{24}\)\(^{25}\), who, in addition to some synanthropic animal species, are the major natural sources of cryptosporidiosis infection\(^1\)^\(^{11}\).

Experiments carried out on animals have shown either activation of latent *Cryptosporidium* infections or aggravation of mild infections by the prolonged use of immunosuppressive drugs\(^{20}\)\(^{21}\). Thus, organ transplantation patients submitted to immunosuppression to avoid rejection could be considered as a group of risk for cryptosporidiosis\(^5\), as they are for other opportunistic infections. Indeed, there are some reports of the occurrence of severe diarrhoea caused by *C. parvum* infection in transplanted patients\(^7\)\(^{16}\)\(^{22}\)\(^{26}\). At the same time, asymptomatic or oligosymptomatic infections caused by this coccidian in transplanted patients or even in individuals immunosuppressed due to other causes, may often become exacerbated because of the impaired immune system of the host\(^8\).

Roncoroni et al\(^{22}\) detected 11 patients infected by *Cryptosporidium* among 14 who had presented diarrhoea after renal transplant. In another group of patients examined for *Cryptosporidium* oocysts before and after the renal transplant, they frequently found *Cryptosporidium* asymptomatic infections. In the present study, among 23 patients submitted to renal transplant 8 (34.8%) were shedding *C. parvum* oocysts at least one of the stool samples examined during a period of 18 months (Tables 1 and 2). Most of these patients had no diarrhoea when they were eliminating *C. parvum* oocysts and they did not differ significantly from the control groups in terms of frequency of *Cryptosporidium* infection (p = 0.09). However, the number of stool samples that were positive for *C. parvum* oocysts was significantly higher in the transplanted patients when compared to the control group (p = 0.01), probably as a consequence of a larger number of infectious episodes or to the prolonged course of *C. parvum* infection in these patients.

Among the patients with chronic renal insufficiency submitted to hemodialysis, 25% showed at least one faecal sample containing *C. parvum* oocysts and 10.3% of all the samples examined were positives (Tables 2 and 3). No significant differences were found between this group and the control group, suggesting that the level of immunosuppression in these patients was not sufficient to increase their risk of being infected by *Cryptosporidium*.

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**Table 2 - Frequency of infection by *C. parvum* in all the studied groups.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Positive</th>
<th></th>
<th>Negative</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nr</td>
<td>%</td>
<td>nr</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Transplanted</td>
<td>8</td>
<td>34.8</td>
<td>15</td>
<td>65.2</td>
<td>23</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>8</td>
<td>25.0</td>
<td>24</td>
<td>75.0</td>
<td>32</td>
</tr>
<tr>
<td>Control</td>
<td>4</td>
<td>17.4</td>
<td>23</td>
<td>82.6</td>
<td>27</td>
</tr>
</tbody>
</table>

**Table 3 - Number of positive faecal samples for *C. parvum* oocysts in all the patient groups.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Positive</th>
<th></th>
<th>Negative</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nr</td>
<td>%</td>
<td>nr</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Transplanted</td>
<td>10</td>
<td>17.2</td>
<td>48</td>
<td>82.8</td>
<td>58</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>8</td>
<td>10.3</td>
<td>70</td>
<td>89.7</td>
<td>78</td>
</tr>
<tr>
<td>Control</td>
<td>4</td>
<td>4.9</td>
<td>78</td>
<td>95.1</td>
<td>82</td>
</tr>
</tbody>
</table>

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**DISCUSSION**

Infection by *C. parvum* has been considered as one of the most important causes of diarrhoea in immunocompetent children and as an important morbid agent, hardly controlled and, sometimes, uncontrollable, in immunosuppressed patients\(^2\)\(^{23}\).

Roncoroni et al\(^{22}\) detected 11 patients infected by *Cryptosporidium* among 14 who had presented diarrhoea after renal transplant. In another group of patients examined for *Cryptosporidium* oocysts before and after the renal transplant, they frequently found *Cryptosporidium* asymptomatic infections. In the present study, among 23 patients submitted to renal transplant 8 (34.8%) were shedding *C. parvum* oocysts at least one of the stool samples examined during a period of 18 months (Tables 1 and 2). Most of these patients had no diarrhoea when they were eliminating *C. parvum* oocysts and they did not differ significantly from the control groups in terms of frequency of *Cryptosporidium* infection (p = 0.09). However, the number of stool samples that were positive for *C. parvum* oocysts was significantly higher in the transplanted patients when compared to the control group (p = 0.01), probably as a consequence of a larger number of infectious episodes or to the prolonged course of *C. parvum* infection in these patients.
In summary, the results of the present paper suggest that patients submitted to renal transplant should be considered as a group at risk for Cryptosporidium infection and that it would be worthwhile to periodically submit these patients and the medical staff to coprological tests for C. parvum oocysts in order to avoid intrahospital transmission. Special care should be taken as well to prevent person-to-person transmission when there is someone infected in the transplantation section, since the available treatment of Cryptosporidium infection for immunosuppressed patients is not so efficient.

REFERENCES


