necrosis. Results of liver tests became normal during the subsequent 2 months.

A 58-year-old man (patient 3) started therapy with trovafloxacín (200 mg/d for 21 days) for lobar pneumonia. He was also given codeine for cough, prednisone (30 mg/d), and ranitidine (150 mg/d) for 10 days. Fourteen days after starting therapy, he complained of asthenia and anorexia. Four days after treatment ended he presented because of fever and dark urine. He reported intake of alcohol (30 g/d). Physical examination showed no jaundice or signs of chronic liver disease. Serum chemistry indicated acute liver injury (table 1). Serology ruled out viral causes, and a screening for autoantibodies was negative. Laboratory findings were normal at 45 days.

We believe that these are the first published reports of acute hepatitis due to trovafloxacín. In each case, other causes of liver injury were ruled out. Withdrawal of the drug was followed by abatement of liver dysfunction. The histologic picture was similar in biopsy specimens for both patients (patients 1 and 2) from whom a specimen was obtained, and it was consistent with drug-induced hepatic injury. It is noteworthy that there was a delay of 4–10 days between the end of treatment and the onset of hepatitis; such a delay may hinder the diagnosis of iatrogenic liver injury. The association of hepatitis with hypersensitivity manifestations and the presence of eosinophils in the liver biopsy specimen suggest an immunoallergic mechanism.

Trovafloxicin, another fluoroquinolone with the same core structure as trovafloxicin, was withdrawn worldwide in 1992 after the detection of severe hemolysis, associated in more than one-half of the cases with renal failure and hepatic dysfunction [4]. Both drugs share a unique difluorinated side chain that is not found in the other quinolones and that renders these drugs highly lipophilic. It is surprising that, in light of these structural similarities, no special attention has been given to the approval and postmarketing surveillance of trovafloxicin.

M. Isabel Lucena,1 Raúl J. Andrade,2 Luis Rodrigo,3 Javier Salmerón,4 Arancha Alvarez,4 M. J. Lopez-Garrido,4 Raquel Camargo,2 and Ramiro Alcántara2
From 1Servicio de Farmacología Clínica y 2Unidad de Hepatología, Hospital Universitario, Facultad de Medicina, Málaga; 3Servicio de Gastroenterología, Hospital Central de Asturias, Oviedo; and 4Servicio de Gastroenterología, Hospital Clínico S. Cecilio, Granada, Spain

Cost Implications of Reporting Nonpathogenic Protozoa

Historically, clinical laboratories worldwide have reported intestinal protozoa, both pathogenic protozoa (PP) and non-pathogenic protozoa (NPP), to attending physicians. The majority of these organisms are nonpathogenic; they neither cause harm nor require medical therapy [1, 2]. Nevertheless, we have observed that many patients with NPP are treated and/or referred to infectious diseases specialists or gastroenterologists. At a time when health care programs, including laboratory testing, are targets for cost-cutting, it is worthwhile to re-evaluate this current policy of routinely reporting intestinal NPP. Reducing such reporting would reduce the costs of inappropriate medication, repeated stool sampling, and physician consultations that have little or no impact on health status. The present study, a survey of family physicians, was carried out to determine the number of patients infected with NPP annually in Ontario (1997 population, 11.4 million) and the costs associated with the healthcare management of these patients.

The Ontario Physician Human Resource Data Centre (OPHRDC) database (1996) lists 9869 family physicians. Because only collective attributes and no individual names were available from OPHRDC, we purchased a similar database (9140 names) of Ontario family physicians from a commercial supplier. Similar surveys have yielded response rates of 50%–62.6% [3, 4]; therefore, we chose to mail 880 surveys, to yield 370 usable responses for 95% CI, ± 5% error.

Costs of medication for treatment of NPP (adult dosage [5] for 1 course of therapy) were obtained from 7 pharmacies across Ontario. The mean costs in Canadian dollars for the 3 medications are as follows: metronidazole, $11.77; iodoquinol, $34.88; and paramomycin, $149.33.

The survey instrument (a confidential, numbered questionnaire) was sent in February 1998, along with a cover letter and a self-addressed, stamped envelope. The questionnaire design

References

Financial support: Faculty of Community Services, SRC Committee, at Ryerson Polytechnic University.

Reprints or correspondence: Prof. Marilyn B. Lee, School of Occupational and Public Health, Ryerson Polytechnic University, 350 Victoria Street, Toronto, Ontario, Canada M5B 2K3 (mblee@acs.ryerson.ca).

Clinical Infectious Diseases 2000;30:401–2
© 2000 by the Infectious Diseases Society of America. All rights reserved.
1058-4838/2000/3002-0034$03.00
was based on Dillman’s Total Design Method [6]. Twenty family physicians agreed to pretest the survey instrument. Postcard reminders were sent to all nonrespondents 2 weeks after the initial mailing. Two weeks later, a replacement questionnaire was sent to each of those who had not yet responded.

The adjusted response rate, which accounted for those nonrespondents who would not be eligible to participate, was 62% (494 of 797). The respondents’ attributes closely matched those in the OPHRDC database (sex ratio, years in practice, and size of town of practice).

From our survey results we estimated the number of patients with at least 1 NPP. The survey asked family physicians “to recall how many patients you have seen in the past two weeks who were positive for any of the following [NPP], Entamoeba coli, Iodamoeba butschlii, Endolimax nana, or Entamoeba hartmanni.” We calculated that 1533 patients with NPP were seen in Ontario within a 2-week period. However, this number had to be corrected to account for patients who have both NPP and PP. They occur together 28% of the time, according to our evaluation of 1997 laboratory reports of 372 patients with NPP from both the Centre for Travel and Tropical Medicine (CTTM) and the Toronto Public Health Laboratory (PHL). Thus, we estimated that 28,698 patients annually in Ontario will have at least 1 NPP, without PP.

Annual costs associated with medication were calculated with the knowledge that 68.5% (SE ± 4.3% [95% CI]) of respondents would treat their symptomatic patients who had NPP. From our clinical observations, we estimated that 70% of patients with NPP alone would be treated with metronidazole, 25% with iodoquinol, and 5% with paramomycin.

Costs associated with referrals were calculated with the knowledge that 21% (SE ± 3.7% [95% CI]) of family physicians would refer their symptomatic patients with NPP for evaluation by specialists who bill $105.00 per patient [7].

Costs associated with repeated stool samples were calculated with the assumption that those physicians who would medicate would also have their patients resubmit stool samples. The cost per sample for processing each parasitology stool sample, as estimated by the PHL is $27; for the private laboratories, which process 78% [8] of parasitology samples in Ontario, the cost is $25.85 [9]. Collectively, we estimated costs for medication, referrals, and repeated stool samples associated with management of NPP in Ontario to be $1,629,974 annually.

The calculated cost may be an underestimate, since additional stool samples or endoscopic procedures were not considered. Furthermore, indirect costs may be even more significant: delay in diagnosis of a treatable disease such as inflammatory bowel disease or Clostridium difficile–associated diarrhea, drug toxicity from unnecessary medication, and lost time from school or work. Alternatively, the calculated cost could be an overestimate if family physicians overestimated the number of patients seen with NPP in a 2-week period.

Considerable cost savings would result if a policy were adopted in Ontario of not reporting NPP, or, in cases where NPP are identified, of reporting with a written notation to the attending physician that the organisms are “not medically significant.”

Based on the numerous comments written on the survey instrument, we conclude that physicians would appreciate guidance on the management of intestinal protozoa; we present table 1 as a guideline.

Acknowledgments

We thank Cecilia Alterman for maintaining the database and Dr. T. Scholten for reviewing the manuscript.

Marilyn B. Lee,1 Jay S. Keystone,2 and Kevin C. Kain1
1School of Occupation and Public Health, Ryerson Polytechnic University, and 2Centre for Travel and Tropical Medicine, Toronto General Hospital, Toronto, Ontario, Canada

References


Table 1. Management of patients with intestinal protozoa.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Type of protozoa</th>
<th>Symptomatic patient</th>
<th>Asymptomatic patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giardia lamblia</td>
<td>PP</td>
<td>Treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>PP</td>
<td>Treat</td>
<td>Treat</td>
</tr>
<tr>
<td>Dientamoeba fragilis</td>
<td>PP</td>
<td>Treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Cryptosporidium parvum</td>
<td>PP</td>
<td>Treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Cyclospora</td>
<td>PP</td>
<td>Treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Entamoeba coli</td>
<td>NPP</td>
<td>Do not treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Entamoeba hartmanni</td>
<td>NPP</td>
<td>Do not treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Endolimax nana</td>
<td>NPP</td>
<td>Do not treat</td>
<td>Do not treat</td>
</tr>
<tr>
<td>Iodamoeba butschlii</td>
<td>NPP</td>
<td>Do not treat</td>
<td>Do not treat</td>
</tr>
</tbody>
</table>

NOTE. NPP, nonpathogenic protozoa; PP, pathogenic protozoa. For treatment data see [5].

a Except food handlers, immunocompromised hosts, or to control an outbreak.

b Infections due to E. histolytica should always be treated; Entamoeba dispar is nonpathogenic and patients with this organism need not be treated.