Strongyloidiasis and acquired immunodeficiency syndrome

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Resumen

La estrongiloidiosis es una infección parasitaria ampliamente difundida en muchos países del mundo, especialmente en regiones tropicales. El *Strongyloides stercoralis* parasita el tubo digestivo humano y puede causar una enfermedad intestinal grave, de evolución crónica, con diarrea y mal absorción, que puede perdurar por décadas, gracias a la capacidad que tiene este gusano de producir ciclos de autoinfección interna. En inmunosuprimidos puede ocasionar enfermedad multisistémica, con compromiso de diversos órganos internos. Estos cuadros son comúnmente observados en enfermos que utilizan dosis altas de corticoides, en portadores de neoplasias hematológicas, trasplantados de órganos sólidos y también, en personas infectadas por el virus de la inmunodeficiencia humana. A pesar de los primeros informes no demuestran una asociación entre la estrongiloidiosis y el síndrome de la inmunodeficiencia humana, hoy, no tenemos más dudas en relación al carácter oportunista de este gusano en enfermos con esta retrovirosis. Cuadros de hiperinfección, y menos comúnmente de enfermidad diseminada ya fueran documentados en estos pacientes, en general, asociados a bacteriemia y meningitis por microorganismos entéricos. El diagnóstico de esta parasitosis se puede basar en el encuentro de los parásitos en heces, esputo, líquido cefalorraquídeo y otros fluidos orgánicos, a través de técnicas adecuadas. Biopsias del tracto digestivo también pueden contribuir para el diagnóstico. Tiabendazol es la droga de elección para el tratamiento de los casos con enfermedad intestinal crónica y también, de las formas diseminadas. Recientemente, la ivermectina demostró buena eficacia en la terapéutica de esta parasitosis, incluso en enfermos con SIDA.

Palabras clave: Strongyloides stercoralis. Estrongiloidiosis. SIDA. Inmunosupresión.

Summary

Strongyloidiasis is a parasitic infection occurring worldwide, particularly in tropical regions. *Strongyloides stercoralis* parasitizes the digestive tract of humans and can cause severe intestinal disease of chronic evolution, accompanied by disabsorptive diarrhea, which can persist for decades due to the ability of the worm to produce cycles of internal autoinfection. In immunosuppressed individuals, *S. stercoralis* can cause multisystemic disease compromising different vital organs. These manifestations are commonly observed in patients receiving high doses of corticosteroids, patients with hematologic neoplasias, solid organ transplant recipients, and also in individuals infected with the human immunodeficiency virus. Although the first reports were unable to demonstrate a clear association between strongyloidiasis and acquired immunodeficiency syndrome (AIDS), today no doubts remain regarding the opportunistic character of this helminth in patients with AIDS. Signs and symptoms of hyperinfection and, less commonly, disseminated disease have been reported in these patients, generally associated with bacteremia and/or meningitis caused by enteric microorganisms. The diagnosis of strongyloidiasis is mainly based on the detection of parasites in feces, sputum, cerebrospinal fluid and other organic fluids using adequate techniques. Digestive tract biopsies also contribute to the diagnosis. Thiabendazole is the drug of choice for the treatment of cases with chronic intestinal disease as well as for disseminated forms of the disease. More recently, ivermectin has shown good efficacy in the treatment of this helminthiasis, including in patients with AIDS.

Key words: Strongyloides stercoralis. Strongyloidiasis. AIDS. Immnunodeficiency.

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Introduction

Strongyloidiasis is a human intestinal parasitosis caused by nematodes of the genus *Strongyloides*, with two species infecting humans. The most important is *S. stercoralis*, which affects 30 to 100 million individuals worldwide and is endemic throughout Latin America, the United States, Southeast Asia and sub-Saharan Africa[1]. A similar species, *S. fuelleborni*, also infects humans but its geographic distribution is restricted to a few regions on the African continent and Papua New Guinea. Strongyloidiasis caused by *S. stercoralis* represents today one of the most important human parasitic

diseases, primarily due to its potential of producing disseminated and lethal disease in immunosuppressed patients[1,2]. *S. stercoralis* was first identified in 1876 in feces from French soldiers returning from Indochina. This nematode possesses the peculiar ability to replicate in the human organism through cycles of internal autoinfection, leading to chronic disease which can persist, often silent, for many decades[3].

The parasite and its evolutive cycle

In humans, *S. stercoralis* normally inhabits the small intestine, with predominant installation in the duodenum and upper portion of the jejunum. In the severe forms of the parasitosis, larvae and adult worms can be found from the pyloric antrum to the end of the large intestine. The life cycle of this helminth is complex: in humans only female parasites are found which reproduce by parthenogenesis, i.e., in the absence of males. The females deposit embryonated eggs from which first-stage rhabditiform larvae emerge that are eliminated in the feces. These larvae evolve in the soil in two ways: a) in a direct manner with transformation into filarioid forms which infect humans, and b) in an indirect manner, when rhabditiform larvae transform into free living male and female adults; the union of these helminths again generates rhabditiform larvae which subsequently transform into the filarioid form that is able to infect the human host. Regardless of their origin, these filarioid larvae penetrate the human skin, enter the bloodstream, cross the lungs, reach the upper airways, are swallowed, and finally reach the small intestine where they mature into parthenogenetic female parasites[2-4]. *S. stercoralis* is able to reproduce within the human host using a mechanism of autoinfection. The rhabditiform larvae transform into the filarioid form in the gastrointestinal tract, penetrate the mucosa, migrate to the lungs, and subsequently return to the small intestine for maturation. Some authors have argued that the pulmonary cycle only represents one of the many paths followed by the larvae until they return to the duodenum. Nevertheless, its capacity of performing cycles of endogenous reinfection in the host results in a chronic infection that can persist for more than 60 years[1-3].

Epidemiological aspects

The prevalence of strongyloidiasis varies considerably according to the geographic area studied, with its endemicity being higher in tropical regions, although its occurrence has also been reported in developed countries[4,5]. In the United States, strongyloidiasis has been described in different states, with the prevalence of positive fecal specimens ranging from 0.4 to 4.0%, and is more commonly found in the rural areas of Kentucky and Tennessee[4,6]. In developing countries, the prevalence of this parasitic infection is quite high (Table 1)[4,6]. In Europe, strongyloidiasis is rare, although it can be found in restricted areas of Portugal, Italy, Romania (6.9%) and in Baltic countries. Two disseminated cases of the disease have been reported in Spain in the eighties[7-9].

In Brazil, the prevalence of infection with *S. stercoralis* is high, although it may also vary according to the geographic region studied. Parasitologic surveys carried out at the end of the sixties have shown a 2.4% positivity, with a predominance of the parasitosis in the states of Goiás, Amapá and Rondônia[3]. This positivity reached 85% among less privileged social classes. In Minas Gerais, situated in the center region of Brazil, a recent survey carried out on 900 school children from suburban and rural areas showed a 13% prevalence, a rate considered to be high[10]. Recent reports by our group which studies strongyloidiasis have shown a prevalence of this parasitic infection in HIV- positive patients ranging from 2.5 to 12%[11]. As shown in Table 2, variable prevalence rates have been observed for other regions of Brazil[3,4,12-14].

The disease in immunocompetent individuals

Primary infection with *S. stercoralis* starts with the penetration of the skin by the filarioid larvae from where they reach the lungs. This initial stage of the parasitosis is usually asymptomatic, although clinical signs and symptoms resembling Löffler's syndrome such as cough, dyspnea, lung infiltrates and blood eosinophilia are occasionally observed in some individuals. When the parthenogenetic females reach sexual maturity in the small intestine, digestive symptoms can be observed in about 50% of cases, including anorexia, nausea, vomiting, abdominal pain, and diarrhea accompanied by fat malabsorption and protein loss. Peripheral eosinophilia and a nonspecific increase in IgE levels are common laboratory findings. Cutaneous involvement, known as "larva currens", is characterized by an urticarial, migratory and creeping eruption which episodically appears on the buttocks, thighs and in the lower region of the trunk, probably resulting from filarioid larvae invading and migrating

Table 1. Recent data on the prevalence of Strongyloides stercoralis in parasitologic feces exams carried out in developing countries

Country	Number of fecal specimens examined	Positive specimens (%)
Argentina	207	2.0
Mexico	100	2.0
Peru	175	13.8
Honduras	266	2.6
Thailand	491	11.2
Ethiopia	1239	13.0
Kenya	230	4.0
Nigeria	2008	25.1
Sudan	275	3.3
Laos	669	19.0

Table 2. Prevalence of infection with Strongyloides stercoralis in parasitologic feces exams carried out in different Brazilian states

State	Year	Number of specimens examined	Positive specimens (%)
Goiás	1971	3036	30.76
São Paulo	1971	1341	6.3
Amazonas	1979	240	1.7
Pernambuco	1982	4312	3.1
Rio Grande do Norte	1987	4441	2.96
Federal District	1991	547	3.3
Goiás	1995	144	1.4
Pará	1996	91	8.8
Ceará	1996	100	2.0
Minas Gerais	1996	715	2.1

to the skin in the perianal region. The duration of this condition is ephemeral (a few days) but it usually recurs after different periods of time. Intestinal radiologic findings concerning the chronic form of strongyloidiasis have demonstrated duodenal edema with irregular and enlarged mucosal folds, duodenojejunal ulcerations and strictures. The disease can persist in immunocompetent individuals for years or decades in the absence of external reinfection due to the parasite's mechanism of autoinfection[1,3,5,6].

Strongyloidiasis in immunosuppressed individuals: definition of terms

Multiplication of *S. stercoralis* can become uncontrolled in immunosuppressed individuals, culminating in a very severe form of the disease. This clinical form is currently divided into two modalities[15]:

a. **Hyperinfection syndrome.** this form is characterized by acceleration of the normal life cycle of the parasite in the human host, leading to a marked increase in parasite burden and massive migration of filarioid larvae from the gastrointestinal tract to the lungs, with these larvae being easily detected in feces and sputum.

b. **Disseminated strongyloidiasis.** this form occurs when filarioid larvae released from the intestine into the circulation are found in organs other than those of their normal migration cycle, which normally only involves the liver and lungs. In this clinical form, young parasites can reach the heart, kidneys, central nervous system, pancreas, thyroid, adrenal glands, lymph nodes, etc.

Both conditions are severe and result in substantial morbidity and mortality of the human host[2,3].

Clinical manifestations in immunosuppressed individuals

Systemic strongyloidiasis can occur under a large number of immunosuppressive conditions, especially in cases of suppression of cellular immunity. Individuals subjected to high doses of corticosteroids for any reason are particularly predisposed to developing severe forms of the parasitosis[2,3,5]. Patients with certain disorders such as lymphomas and other hematologic neoplasias, renal, liver or heart transplant patients, individuals with advanced neoplasias undergoing chemotherapy, undernourished patients, and individuals with renal or chronic liver failure represent examples of individuals who are at high risk of developing systemic and potentially fatal forms of strongyloidiasis[1,3]. Corticosteroids suppress the immune mechanisms that control the multiplication of parasites in humans and accelerate the maturation of eggs and larvae in the intestine. These hormones block the action of mast cells and eosinophils and the IgE-mediated antibody response, as well as immune mechanisms at the intestinal level, events considered to be fundamental for the control of the multiplication of *S. stercoralis*[2,3,16]. Patients with collagen disease, nephrotic syndrome, inflammatory bowel disease, chronic autoimmune hepatitis and bronchial asthma should be treated prophylactically with thiabendazole or ivermectin to prevent the occurrence of severe forms of the parasitosis in endemic areas[3]. In Brazil, signs and symptoms of disseminated strongyloidiasis have been observed in patients with leprosy during the reactional phase because these individuals require the use of high doses of corticosteroids to control the symptoms of the reaction. Both diseases are endemic in Brazil and the attending physicians frequently forget the probable presence of this helminth when treating these patients[3].

The systemic form of strongyloidiasis clinically manifests with fever, discomfort, decline in general condition, and a combination of gastrointestinal and respiratory signs and symptoms[1,3,6,9]. Abdominal pain and distension, vomiting, intense diarrhea and anorexia are commonly observed in these patients, in addition to respiratory manifestations characterized by cough, dyspnea and hemoptysis. Respiratory insufficiency accompanied by the presence of a diffuse interstitial-micronodular infiltrate in both lungs represents the final event of this severe form of strongyloidiasis. Bacteremia and meningitis caused by enteric bacteria *(Escherichia coli, Klebsiella pneumoniae)* are found in more than half of the cases of disseminated disease and represent an important key to the diagnosis. The occurrence of these infections reflects the passage of enteric microorganisms carried by the helminth itself during its migration or massive bacterial invasion of intestinal ulcers produced by this agent. Blood eosinophilia is usually not present in these patients. The mortality rate in systemic cases of the parasitosis commonly exceeds 80%[1,3,6,15].

Strongyloidiasis and human T-cell lymphotropic retrovirus type I (HTLV-1) infection

Studies carried out in Japan and Caribbean countries have reported a positive correlation between the severe forms of strongyloidiasis and HTLV-1 infection[17]. Various authors have speculated about the possible role of immunosuppression induced by this retrovirus in the persistence and dissemination of the helminth. However, other studies in the literature have not confirmed this association. In a prospective study carried out in our service on 30 patients with HTLV-1, only one showed asymptomatic infection with *S. stercoralis*. Since the study area is hyperendemic, a higher positivity rate of this helminthiasis would have been expected in these patients[1,17].

Strongyloidiasis and human immunodeficiency virus (HIV-1) infection

Since the onset of acquired immunodeficiency syndrome (AIDS), the interest of researchers in this retroviral infection and the interaction between so-called tropical diseases and HIV infection has steadily increased[14]. Today, it is known that Chagas' disease and visceral leishmaniasis are opportunistic diseases in patients with AIDS. Strongyloidiasis was expected to show the same behavior in endemic regions in the Americas, Africa and Asia, since most of the systemic forms of the disease occur in patients presenting marked suppression of cellular immunity, as is the case for patients with AIDS[19]. At the beginning of the epidemic of this viral infection, the Centers for Disease Control and Prevention (CDC) in the United States included severe strongyloidiasis in the list of opportunistic diseases that define a suspected case of AIDS. However, after some years, since the number of cases of disseminated strongyloidiasis reported in the literature was small, the CDC removed this parasitosis from the list of AIDS-defining infections[19, 20].

The prevalence of *S. stercoralis* in HIV/AIDS patients has varied according to the geographic area studied. In 1981, a preliminary study from New York showed that 3.9% of homosexual men seen at a venereal disease clinic were infected with this helminth; most of them were probably HIV positive, but despite the potential of developing disseminated disease, no case was reported in that study[21]. Several other investigations have reported variable prevalence rates of this helminthiasis in patients with HIV/AIDS. In African countries, for example, infection with *S. stercoralis* has been found in 2 to 5% of patients infected with this retrovirus, but disseminated strongyloidiasis was apparently rare[22]. In a study carried out in the Caribbean (Martinique), 10 of 98 patients with AIDS were found to have strongyloidiasis, two of them also infected with HTLV-1, but no case of disseminated disease was observed[23]. Another study carried out in the same geographic region, in Puerto Rico, analyzing autopsy material obtained from 100 patients with AIDS, demonstrated the presence of *S. stercoralis* in 3% of cases, with the disease confined to the small intestine in all of them[24].

In Brazil, few studies have determined the presence of this nematode in patients with HIV/AIDS[11,25-28]. Table 3 shows the results of the analysis of some of these investigations.

Most patients with HIV/AIDS and intestinal strongyloidiasis are asymptomatic, including many individuals with advanced retroviral disease. The parasitosis is discovered occasionally upon routine parasitologic examination. Until 1994, only 14 cases had been described, but it is currently calculated that about 100 have been published in the literature or presented at specialty congresses or symposia[15].

Table 3. Prevalence of infection with S. stercoralis in Brazilian patients with HIV/AIDS: results of parasitologic feces exams and autopsy studies

State	Year	Number of HIV/AIDS patients	Number of infected patients (% positivity)
Rio de Janeiro	1989	99 (f.e.)	15 (15.2)
Minas Gerais	1996	50 (autopsy)	2 (4)
Pernambuco	1996	119 (f.e.)	4 (3.4)
Minas Gerais	1996	101 (f.e.)	6 (6)
Rio Grande do Sul	1996	87 (f.e.)	1 (1.1)
Minas Gerais	1996	228 (f.e.)	9 (3.8)
São Paulo	1999	564 (f.e.)	70 (15)
Minas Gerais	1999	650 (f.e.)	25 (3.8)
Brasília	2000	30 (f.e.)	1 (3.3)
Goiás	2002	58 (f.e.)	3 (5.2)
Minas Gerais	2002	100 (f.e.)	12 (12)

f.e.: parasitologic feces exam

Cases of *S. stercoralis* hyperinfection were diagnosed in Brazil, Argentina, the United States, France and Germany[29-37]; in the last country, a case of the severe form of the parasitosis was described in a Brazilian patient who certainly acquired the infection in his country of origin[37].In New York, most severe cases of strongyloidiasis have been documented in patients originating from Puerto Rico where the infection is endemic[15]. In Brazil, most of the severe clinical forms of this parasitosis in patients with AIDS have been observed in our region, Minas Gerais[32]. The reason for this finding is unclear, but the inclusion of strongyloidiasis in the differential diagnosis of many clinical syndromes observed in our patients has surely contributed to the frequent documentation of the infection.

Clinical evaluation of 25 cases of strongyloidiasis associated with advanced AIDS in our service showed the presence of fever in 18 (72%), profuse diarrhea in 15 (60%) and persistent cough in 13 (52%). Seven cases (28%) were diagnosed as having "hyperinfection" syndrome, in five cases the diagnosis was made post mortem, and in the other two cases filarioid larvae were detected in sputum. Autopsy did not show parasites outside the organs normally invaded by the helminth during its migration (intestine, liver, lungs), thus characterizing the previously defined "hyperinfection" syndrome. No expressive peripheral eosinophilia was observed in the severe cases of this parasitosis. All patients died due to the severity of their symptoms[32].

In another recent study from our group conducted on 100 patients with AIDS, most of them with TCD4 lymphocyte levels < 100 cells/ml, 12 individuals infected with *S. stercoralis* were identified; three of them were also infected with *Isospora belli*. Two of these patients had systemic disease: the first patient developed bacteremia and *E. coli* meningitis, as well as diarrhea resulting from strongyloidiasis; the second patient showed the presence of diffuse bilateral pulmonary infiltrates and larvae were found in his sputum; in addition, he developed *E. coli* meningitis. Both patients survived after adequate treatment[28].

Bacterial infections in the form of bacteremia and meningitis generally caused by enteric microorganisms are usually also present in the severe forms of strongyloidiasis in patients with HIV/AIDS. *E. coli, K. pneumoniae* and *Streptococcus bovis* are the most commonly found agents in patients with AIDS and strongyloidiasis. The presence of bacteria in the blood and/or meninges of these patients should remind the physician of strongyloidiasis as a trigger of these infectious processes[3,32,35].

Although most cases of co-infection documented in the literature developed *S. stercoralis* hyperinfection syndrome, disseminated forms with larvae only being present in the central nervous system have been reported[30,34]. The use of corticosteroids (e.g., for the treatment of severe pneumocystosis) and HIV infection associated with HTLV-1 seem to contribute to the dissemination of the parasite. Mortality is very high in these cases[23].

Severe systemic forms of strongyloidiasis frequently affect the lungs. Diffuse interstitial infiltrates observed upon chest X-ray and/or computed lung tomography have shown the simultaneous massive presence of larvae and bacteria in this organ. Thus, the inclusion of strongyloidiasis in the differential diagnosis of these pulmonary symptoms together with pneumocystosis, tuberculosis, histoplasmosis and cytomegalovirus infection is fundamental in the case of patients with AIDS originating from endemic areas[27,32,38].

Our experience and that of other investigators thus differs from previous studies which failed to demonstrate an increased prevalence of the severe

forms of strongyloidiasis in patients with AIDS. Most of our patients are symptomatic and many develop severe forms which lead or markedly contribute to the lethal course of the disease. There is no obvious explanation for these findings, except for the marked immunosuppression induced by HIV itself. Enteropathy caused by this virus, hypochlorhydria and achlorhydria, conditions frequently observed in these individuals, might also have a permissive effect on the reproduction of the parasite in the gastrointestinal tract, and contribute to the exacerbation of its normal cycle in the organism[15]. Systematic autopsy studies carried out on patients with AIDS deriving from endemic areas may contribute to increasing the number of diagnosed cases of this co-infection[27,32].

Diagnosis of strongyloidiasis

The diagnosis of strongyloidiasis is based on the detection of the parasitic forms of *S. stercoralis* using direct and indirect methods. Among the direct techniques, parasitologic methods have been most widely used in clinical practice; however, they are of low sensitivity since parasites are frequently absent or are present in small numbers. Thus, repeated feces exams are necessary to improve the sensitivity of these tests. Using appropriate techniques, three parasitologic exams lead to a diagnostic accuracy of 50%, while 100% is reached when seven exams are carried out. The specific methods most frequently used to diagnose strongyloidiasis are the Berman-Moraes and Rugai-Matos-Brisola tests. Both methods show high sensitivity that can be attributed to the hydro- and thermotropism of the larvae which leave the fecal material, migrate in the direction of hot water and are deposited at the bottom of the funnel due to gravity. When carried out correctly and on repeated samples, these tests can diagnose helminthiasis in about 90% of cases[1,3-5,10,17].

Other techniques have also been applied to the diagnosis of this parasitosis, including direct examination of feces stained with Lugol's solution, detection after concentration in formalin-ethyl acetate, culture on agar plates and filter paper, or the Harada-Mori technique[39]. Comparison of these techniques in terms of their efficacy in diagnosing strongyloidiasis showed a high sensitivity for the agar plate culture technique, which can reach 90%. This method consists of placing fecal samples on an agar plate and incubating them for 48 hours. Larvae actively move on the plate carrying bacteria and leaving behind visible trails. These mobile larvae can then be visualized under a microscope[39].

In immunosuppressed individuals, including patients with AIDS, the parasite burden is high in the organism, thus facilitating the detection of abundant filarioid larvae. These larvae can also be identified in other organic fluids such as sputum, cerebrospinal fluid and ascitic fluid[32,34]. Duodenal fluid has frequently been used for the diagnosis of strongyloidiasis, particularly in immunosuppressed children, with this fluid being nowadays easily collected by upper digestive tract endoscopy. Histopathologic examination of the duodenal mucosa or, sometimes, of the gastric mucosa and mucosa of the large intestine may unexpectedly reveal the presence of parasites, a fact observed in patients with AIDS. Unfortunately, in many patients with severe disease and marked immune suppression, strongyloidiasis is only diagnosed at autopsy[24,27].

Immunologic tests detecting IgG, IgM, IgA and IgE antibody classes have been used for the diagnosis of strongyloidiasis. Various techniques have been employed such as indirect hemagglutination, indirect immunofluorescence, immunoblot and ELISA[40]. The immunoenzymatic test (ELISA) has been indicated as the immunologic test of choice for the diagnosis of strongyloidiasis due to its high sensitivity[40]. The main limitation of these serologic tests is the need to obtain sufficient amounts of antigen that will permit its subsequent fractionation and analysis. Nowadays, soluble somatic extracts prepared from the filarioid larvae of *S. stercoralis* or *S. ratti*, or a metabolic excretion/secretion antigen collected from the fluids of preincubated mobile larvae are used to carry out these reactions, with excellent results. However, demonstration of antibodies, even when correct, does not distinguish between a past or present infection, since antibody levels remain detectable for years after antihelminthic treatment[40,41].

Treatment of *S. stercoralis* infection

Strongyloidiasis is a helminthiasis that is difficult to treat. Even when using drugs known to be active, probably not all parasites present in the organism are eradicated. Although most treated individuals show negative parasitologic exams, it is possible that many of them continue to harbor the helminth. Various drugs have been used for the treatment of this infection:

a. *Thiabendazole* is the drug of choice for the treatment of this disease. It is administered by the oral route at the dose of 50 mg/kg/day for 2 to 3 days, with the total daily dose not exceeding

3 g. The drug seems to act on both adult forms and larvae. In immunosuppressed patients, prolonged treatment for 7 to 10 days is recommended to prevent early relapse. The rate of cure in immunocompetent individuals is 90%. Approximately 30% develop side effects such as nausea, vomiting, abdominal pain, dizziness and liver diseases. Oral administration leads to good absorption of the drug which is predominantly eliminated through urine[1,3,5].

b. *Cambendazole* is a benzimidazole derivative which leads to cure in up to 90% of patients with the parasitosis. The drug is administered by the oral route as a single dose of 5 mg/kg, showing few side effects (abdominal pain, nausea, diarrhea, dizziness). Experience with the treatment of patients with AIDS, however, is not available[3].

c. *Albendazole*. The therapeutic efficacy of this drug, at the dose of 40 mg/day for 3 days, in the treatment of human strongyloidiasis is low, reaching rates of cure of only about 40%. Even at higher doses, this drug is not recommended for the treatment of this infection, especially in the case of immunosuppressed patients, and is counterindicated in pregnant women[42].

d. *Ivermectin* seems to be extremely efficient in the treatment of strongyloidiasis. It shows a rate of cure of about 85% in immunocompetent patients when administered orally as a single dose of 200 µg/kg. In disseminated or severe cases which are particularly observed in patients with AIDS, this drug has been employed in a multidose regimen, i.e., 200 µg/kg/day on days 1, 2, 15 and 16, with clinical and parasitologic cure having been observed in most cases treated with this regimen (a cure rate of about 90%). However, therapeutic failure has recently been reported in patients with hypogammaglobulinemia A. The World Health Organization currently considers ivermectin the drug of choice for the treatment of this helminthic infection[43-45].

e. *Mebendazole* has no action on *S. stercoralis* at the recommended doses. However, high doses of this anthelmintic (0.5 to 1.5 g/day for 2 to 3 weeks) might cure cases refractory to treatment with other drugs. Its use in patients with any type of immunosuppression, however, is not justified[8].

The control of cure adopted by most investigators is based on the execution of three parasitologic feces exams on days 7, 14 and 21 post-treatment. Monthly parasitologic exams are recommended in patients with AIDS in order to detect possible relapses[1,3,15].

In the case of the disseminated forms of strongyloidiasis, the use of broad-spectrum antimicrobial drugs (cephalosporin, quinolones) in combination with antihelminthic therapy is recommended in order to combat bacterial infections caused by enteric microorganisms which frequently accompany severe manifestations of the disease[15,18,32]. In patients concomitantly affected with AIDS and strongyloidiasis who develop systemic and/or recurring manifestation of the disease, the prophylactic secondary use of thiabendazole (monthly for 2 to 3 days) or periodic ivermectin is indicated to prevent new episodes of this illness[15,32].

References

1. Mahmoud AAF. Strongyloidiasis. *Clin Infect Dis* 1996; 23:949-53.
2. Neva FA. Biology and immunology of human strongyloidiasis. *J Infect Dis* 1986;153:397-496.
3. Ferreira MS. Estrongiloidíase. En: Veronesi R (ed) *Doenças Infecciosas e Parasitárias*. Rio de Janeiro: Guanabara Koogan, 1991:856-65.
4. Genta RM. Global prevalence of strongyloidiasis: critical review with epidemiologic insights into the prevention of disseminated disease. *Rev Infect Dis* 1989;11:755-67.
5. Hamer DH. Intestinal Nematodes. *Infect Dis Clin Pract* 1996;473-481.
6. Siddiqui AA, Berk SL. Diagnosis of *Strongyloides stercoralis* Infection. *Clin Infect Dis* 2001;33:1040-7.
7. Scalia M, Brustia R, Gattis S, *et al.* Autochthonous strongyloidiasis in Italy: an epidemiological and clinical review of 150 cases. *Bull Soc Pathol Exot Filiales* 1984; 77:328-32.
8. Ruiz-Macia JA, Pons Miñano JÁ, Bermejo-Lopez J, *et al.* Estrongiloidiasis diseminada: estudio clinico – patológico de um caso diagnosticado en autopsia. *Rev Clin Esp* 1987;180:381-4.
9. Cappel-Font S, Pujol-Farriols R, Garan Alemany J, Pallares Giner R, Campo-Guerri E. Hiperinfestación por Strongyloides stercoralis. *Med Clin* (Barcelona) 1982; 79:232-5.
10. Machado ER, Costa-Cruz JM. *Strongyloides stercoralis* and other enteroparasites in children at Uberlândia city, state of Minas Gerais, Brasil. *Mem Inst Oswaldo Cruz* 1998;93:161-4.
11. Costa-Cruz J, Ferreira MS, Rossin IR. Intestinal parasites in AIDS and + HIV patients in Uberlândia, Minas Gerais, Brazil. *Mem Inst Oswaldo Cruz* 1996; 91:685-6.

12. Melo AL. Strongyloides stercoralis. En: Neves DP (ed) *Parasitologia*. Rio de Janeiro: Atheneu, 1995:297-305.

13. Rey L. Estrongiloidíase. En: Rey L (ed) *Parasitologia*. Rio de Janeiro: Guanabara Koogan, 1992:217-20.

14. Ferreira MS. A síndrome da imunodeficiência adquirida e as doenças endêmicas no Brasil. *Rev Soc Bras Med Trop* 1996;29:531-5.

15. Celedon JC, Mathur-Wagh V, Fox J, García R, Wiest PM. Systemic strongyloidiasis in patients infected with human immunodeficiency virus. A report of 3 cases and review of the literature. *Medicine* 1994;73:256-63.

16. Genta RM. Dysregulation of strongyloidiasis: A new hypothesis. *Clin Microbiol Rev* 1992;5:345-55.

17. Grove DI. Human strongyloidiasis. *Adv Parasitol* 1996; 38:251-309.

18. Scowden EB, Schaffner W, Stone WJ. Overwelming strongyloidiasis: An unappreciated opportunistic infection. *Medicine* (Baltimore) 1978;57:527-44.

19. Centers for Disease Control. Update: Acquired immunodeficiency syndrome (AIDS) in the United States. *MMWR* 1982;31:508.

20. Centers for Disease Control. Revision of the CDC Surveillance case definition for acquired immunodeficiency syndrome. *MMWR* 1987;36(15): 3S-15S.

21. Philips SC, Mildvan D, William DC, Gelb AM, White MC. Sexual transmission of enteric protozoa and helminths in a venereal-disease clinic population. *N Engl J Med* 1981;305:603-6.

22. Kapita B, Calebunders R, Lusakumunu K, Henry MC. Parasitoses opportunistes en Afrique. Clinique et diagnostic. *Ann Parasitol Hum Comp* 1990;65 (Suppl 1):45-7.

23. Plumelle Y, Edouard A. *Strongyloides stercoralis* in T-cell leukemia / lymphoma in adults and acquired immunodeficiency syndrome. *Rev Med Interne* 1996; 17(2):125-9.

24. Hillyer GV, Climent C. Acquired immunodeficiency syndrome and parasitic diseases in Puerto Rico. *Bol Asoc Med PR* 1988;80:312-9.

25. Moura H, Fernandes O, Viola JPB, Silva SP, Passos RH, Lima DB. Enteric parasites and HIV infection: ocourrence in AIDS patients in Rio de Janeiro, Brazil. *Mem Inst Oswaldo Cruz* (Rio de Janeiro) 1989;84(4):527-33.

26. Feitosa G, Bandeira AC, Sampaio DP, Badaro R, Brites C. High prevalence of giardiasis and strongyloidiasis among HIV infected patients in Bahia, Brazil. Braz J Infect Dis 2001;5(6):339-44.

27. Borges AS, Ferreira MS, Nishioka S, Silvestre MTA, Silva AM, Rocha A. Agreement between premorten and posmorten diagnoses in patients with acquired imnunodeficiency syndrome observed at a Brazilian Teaching Hospital. *Rev Inst Med Trop São Paulo* 1997; 39:217-21.

28. Ferreira MS, Borges AS. Prevalência da infecção pelo *S. stercoralis* em pacientes com SIDA; resultados dos exames coproparasitológicos realizados em 100 casos consecutivos e revisão da literatura nacional. Observaciones no publicadas.

29. Trione N, Corti M, Castello T, Abuin JC, Bellegarde E. Infección diseminada por *Strongyloides stercoralis* en pacientes com SIDA. A proposito de 2 observaciones. *A Ge La* 2001;31:399-402.

30. Dutcher JP, Marcus SL, Tanowitz HB, *et al.* Disseminated strongyloidiasis with Central Nervous System Involvement Diagnosed Antemorten in a Patient with Acquired Immunodeficiency Syndrome and Burkitt's lymphoma. *Cancer* 1990;66:2417-20.

31. Maayan S, Whormser GP, Widerhorn J, Sy ER, Kim YH, Ernst JÁ. *Strongyloides stercoralis* Hiperinfection in a Patient with the Acquired Immunodeficiency Syndrome. *Am J Med* 1987;83:945-8.

32. Ferreira MS, Nishioka AS, Borges AS, *et al.* Strongyloidiasis and Infection Due to Human Immunodeficiency Virus: 25 cases at a Brazilian Teaching Hospital, Including Seven Cases of Hyperinfection Syndrome. *Clin Infect Dis* 1999; 28:154-5.

33. Morgello S, Soifer FM, Lin CS, Wolfe DE. Central nervous system *Strongyloides stercoralis* in acquired immunodeficiency syndrome: a report of two cases and review of the literature. *Acta Neuropathol* (Berl) 1993;86:285-8.

34. Takayanagui OM, Lofiano MM, Arango MB, Chimelli L. Detection of *Strongyloides stercoralis* in the cerebrospinal fluid of a patient with acquired immnodeficiency syndrome. *Neurology* 1995;45: 193-4.

35. Jain AK, Agarwal SK, el – Sadr W. Streptococcus bovis bacteremia and meningitis associated with *Strongyloides stercoralis* colitis in a patient infected with human immunodeficiency virus. *Clin Infect Dis* 1994;18:253-4.

36. Harcourt-Weebster JN, Scaravalli F, Darwish AH. *Strongyloides stercoralis* hyperinfection in an HIV positive patient. *J Clin Path* 1991;44:346-8.

37. Stey C, Jost J, Lüthy R. Extraintestinal strongyloidiasis in the acquired immunodeficiency syndrome. *Dtsch Med Wochenschr* 1990;115:1716-9.

38. Wehner JH, Kirsch CM. Pulmonary manifestations of strongyloidiasis. *Semin Respir Infect* 1997;12:122-9.

39. Arakaki T, Iwanaga M, Kinjo F, Saito A, Asato R, Ikeshero T. Efficacy of agar-plate culture in detection of *Strongyloides stercoralis* infection. *J Parasitol* 1990; 76:425-8.

40. Genta RM. Predictive value of an enzyme-linked immunosorbent assay (ELISA) for the serodiagnosis of strongyloidiasis. *Am J Clin Pathol* 1988;89:391-4.

41. Sato Y, Takara M, Otsuru M. Detection of antibodies in strongyloidiasis by enzime linked immunosorbent assay (ELISA). *Trans R Soc Trop Med Hyg* 1985: 79:51-5.

42. Amato Neto V. Demarcação da atividade antihelmíntica do albendazol: estudo referente à estrongiloidiase humana. *Rev Med Inst Trop São Paulo* 1985;27:95-8.

43. Salazar AS, Berk SH, Howe D, Berk SL. Ivermectin vs thiabendazole in the treatment of strongyloidiasis. *Infect Med* 1994;60:50-9.

44. Torres JR, Isturiz R, Murillo J, Guzman M, Conteras R. Efficacy of ivermectin in the treatment of strongyloidiasis complicating AIDS. *Clin Infect Dis* 1993;17:900-2.

45. Ashraf M, Gue CL, Baddour LM. Case Report: strongyloidiasis refractory to treatment with ivermectin. *Am J Med Sci* 1996;311:178-9.