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Chapter 1

Introductory Chapter: Giardiasis - Still a Globally Relevant Protozoan and Zoonotic Disease

Alfonso J. Rodríguez-Morales, Adriana M. Trujillo, Jorge A. Sánchez-Duque and Ángel A. Escobedo

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1. Introduction

Giardiasis continues to be a significant parasitic disease in the world caused by the species of *Giardia* genus, particularly *Giardia intestinalis*, which affects humans and animals in a wide clinical spectrum, with zoonotic potential due to shared genotypes that can affect the same hosts. This protozoan disease occurs in developing as well as in industrialized countries, also affecting travelers. In recent years, multiple aspects in its epidemiology, but also and particularly in the long-term clinical consequences, have been highlighted. In this introductory chapter, a review on general aspects, based on recent experiences, is described.

2. Overview and general aspects of giardiasis

Giardia was described and was associated with the symptoms in 1681 for the first time when the Dutchman, Van Leeuwenhoek, found the trophozoites in his own feces; nevertheless, just until 1859, the first report was credited to the Czech Vilém Lambl [1–3]. *Giardia intestinal* is a flagellated protozoon (also known as *G. lamblia* or *G. duodenalis*) and is a tiny and ubiquitous intestinal and/or biliary parasite, which affects mammals, such as humans, pets, and livestock by inhabiting the upper part of the small intestine [4–6]. Frequently, this parasite contaminates water sources worldwide especially in temperate and tropical locations where sanitary conditions are suboptimal; for this reason, giardiasis is the commonest parasitic infection of the gastrointestinal tract, the most important responsible for outbreaks of diarrhea and sporadic endemic disease [7, 8].

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3. Epidemiology

Distributed worldwide, *Giardia* is probably the most frequent pathogenic intestinal protozoon in children and adults, and one of the most common nonviral causes of diarrhea, afflicting annually an approximate 280 million individuals. Due to its intensifying global burden and its developmental and socioeconomic impact on infected individuals, this parasitosis was incorporated in the Neglected Disease Initiative of the World Health Organization in 2004 [4, 7, 9, 10].

In developed countries, giardiasis is associated with social and climatic factors and is referred as a re-emerging infectious agent. Some epidemiological studies have shown that its prevalence varies between the population studied and the location, from 2 to 5% on industrialized countries to 20–30% in developing countries [1, 5, 11], and these changes in prevalence are associated, among others, with the hygiene infrastructure and the impact of the weather conditions, reason why environmental control efforts are necessary, which requires an integrated and systematic approach to decrease and mitigate the influence on the disease epidemiology; for this reason, it is linked to educational programs and other interventional measures [2, 6, 12].

Although in Latin America, a restricted quantity of population-based studies has been performed, in Cuba, according to the last national intestinal parasites survey (n = 5850), the prevalence of *Giardia lamblia* infection was determined to be at 6.02% (95%CI 5.40–6.63) [13].

This parasitosis is highly infectious where *Giardia* cysts are habitually excreted in considerable population, especially in young children after ingestion of contaminated water or food and through person-to-person contact. Cysts can survive for months in cold water, and they are relatively resistant to chlorination, reason why between 10 and 100 cysts are sufficient to establish infection 100% of the time. Consequently, ingestion of water or food that contains small levels of contamination can result in the disease, which is more recurrent in summer and fall. Other usual ways to transmit them could be among day care center attendees and people who live in residential institutions, and it could also spread by means of sexual activity, by oral-anal contact [1, 5, 11, 12].

4. Life cycle

Giardia intestinalis is a noninvasive protozoan parasite with a simple life cycle and a simplified metabolism that depends on the host for nutrients such as purines, pyrimidines, cysteine, and cholesterol. The genus *Giardia* and its life cycle are relatively well recognized and clearly defined; members of the genus are flagellated protozoans belonging to the class Zoomastigophorea and order Diplomonadida, which lives and multiplies by asexual multiplication frequently on the luminal surface of the small intestine of its vertebrate host [14–16].

The trophozoite, which is 9–21 μm long, 5–15 μm wide, and 2–4 μm thick, lives in the small intestine and is responsible for many manifestations of the disease. The cytoskeleton composed

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of unique families of structural proteins and carbohydrates involves two nuclei, a ventral sucking adhesive disk by which it may adhere to intestinal epithelial cells, a median body, and four pairs of flagella that behave differently during motility. The dorsal surface is pear shaped and bilaterally symmetrical, with the two highly characteristic nuclei best visualized after staining. The newly emerged trophozoites infect the duodenum and jejunum where there is a favorable alkaline pH; they attach intimately to the intestinal epithelium by their ventral disk and begin to multiply by binary fission. Detection of soluble cyst wall proteins in the feces forms the basis of many stool antigen assays [1, 8, 16, 17].

Giardia takes advantage of host conditions at each step of its descent through the human gastrointestinal tract. After ingestion, *Giardia* infection is initiated by the acidic milieu in the stomach and the presence of bile and trypsin in the duodenum, and then, it reproduces in the small intestine, yielding two trophozoites from each cyst, which quickly divide again. Exposure of cysts to gastric acid triggers excystation, although the "excyzoites" do not emerge from the cyst until it passes into the small intestine. In vitro trophozoites double in number every 6 hours in the fastest growing isolates. The emerging parasites (excyzoites) quickly transform into trophozoites that attach to the intestinal epithelial cells using the adhesive disk, which is a major virulence factor; in this way, any excreted cysts are mature, highly infectious, and quite resistant to disinfectants routinely used for water treatment such as chlorine [8, 16, 18].

When the trophozoite senses a change in the environment as the cell is transported further down in the small intestine, it starts the encystation; in the earliest moment of this process, some specific vesicles are designed that allow its development and maturation, probably as a result of cholesterol starvation. At the same time with several proteins implicated in metabolic pathways, after that, several proteins also change their expression by important gene expression changes. *Giardia* has a considerable metabolic capacity as another parasite that lacks pathways for de novo biosynthesis of pyrimidines and purines for nucleotide salvage, but this process is conditioned by oxygen concentration, despite anaerobic metabolism and generating reactive oxygen species (ROS) by the host [1, 14–17].

Giardiasis as a multifactorial disease involves in its pathobiology complex interactions between host and parasite, differences in nutritional status, immune status, co-infections, and intestinal normal flora that could contribute to the differences in disease outcome observed among individuals from developing against developed countries. The roles of the host's intestinal normal flora and co-infections during *Giardia* infections are still largely unascertained [3, 12, 15, 19].

Some morphologically identical but genetically distinct *Giardia* infect humans and animals that now are divided into eight assemblages (A–H) what could bring a clarification about infection outcome. Thus, assemblages A and B are found in human and other animals, being considered zoonotic, whereas the other assemblages display host specificity and do not infect humans (C and B in dog, F in cat, E in hoofed animal, G in rodents, and H in sea mammals). Interestingly, this proportion is not altered when comparing data from developing and developed countries, but the prevalence of mixed infections is higher in the developing countries [8, 15–18].

The two assemblages (A and B) are composed of genetically distinguishable isolates, which may vary in infectivity, antigenicity, and virulence. In addition, human hosts vary in susceptibility to infection and disease and in the response to tolerance to infection. In this way, *Giardia* is an intraluminal parasite that adheres to the epithelium by way of an adhesive or sucking disk, although invasion of the epithelium either does not occur or is rare. Meanwhile, the number of trophozoites in the intestine can be so large that adherent organisms cover much of the epithelial surface. This could disrupt the epithelial brush border and contribute to lack of disaccharidase as could be seen in some patients [8, 14, 15].

5. Clinical aspects

The clinical manifestations, course, and duration of *Giardia* infections are variable. In that way, infections may be self-limited or persistent, asymptomatic, or symptomatic. Usually, most patients remain asymptomatic, but when signs and symptoms occur and acute disease is established, manifestations happen normally in travelers and in outbreaks, and they are characterized by diarrhea, nausea, anorexia, dehydration, flatulence, eructation, distention, abdominal cramping, and weight loss. Contradictorily, fever and vomiting are uncommon [7, 13, 20].

The first signs of infection appear after 6–15 days. Most symptomatic infections resolve spontaneously; however, sometimes, hospitalization is required when infections have long-term consequences and do not respond to the normal treatment. Chronic *Giardia* infections are reported frequently in nonendemic areas and also could result in irritable bowel syndrome, food allergies, arthritis, aphthous ulcers, or chronic fatigue syndrome after resolution [3, 10–12].

In some cases, if acute symptoms are not treated on time, they can develop into a chronic stage, which can affect all age groups but children are at higher risk, in whom *Giardia* infections have been associated with lower serum level of zinc, iron, and vitamins (A, B12, and folate); despite similar anthropometric indicators among infected and uninfected individuals in early childhood, the failure to thrive and poor cognitive function are characteristics in them. Furthermore, the loss of lactose is common and can persist for some weeks after treatment, which is why it is necessary to be distinguished in symptomatic patients from relapse or reinfection. In extreme cases, malabsorption and weight loss are severe and mimic sprue [1, 2, 8].

A typical scenario is a mildly to moderately ill person who grumbles of a raised number of urgent loose stools, with flatus, cramping, anorexia, and weight loss. There may even be periods when the person feels better only to relapse and then become noticeably worse. Finally, after some days to several weeks, the person will seek medical help. Similar to other causes of infectious diarrheas, symptoms can carry on after successful treatment and evolve into irritable bowel syndrome and chronic fatigue, even 6 years after the infection. Infrequently, *Giardia* is also found in biliary and pancreatic ducts and can cause cholecystitis and pancreatitis, and other localizations reported are the urinary tract, gastric mucosa, and colonic and ileal

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mucosa. Extraintestinal manifestations and long-term consequences are unusual, but a series of sporadic cases documented them in a third of the patients. The signs can include rash, reactive arthritis, eye complaints, and cognitive deficiencies [1, 2, 9, 10, 20].

6. Diagnostics

The diagnosis of giardiasis is based on the detection of cysts, trophozoites, or parasite-specific antigens in fecal microscopic examination, complemented with microscopic examination of duodenal fluids or in other biological samples. Polymerase chain reaction has been largely experimental, but it is being increasingly used in field and laboratory settings; considering that excretion of cysts may be variable or in low concentrations (50–80% sensitive), two or three checkups may be necessary, leading to a late diagnosis (>2 weeks) [3]. Stool antigen tests are standard in most laboratories and are highly sensitive (>90%), specific (~100%), and relatively inexpensive and do not require a trained microscopist [2, 9, 13, 18].

The observation of small intestine biopsy specimens or intestinal contents for trophozoites was the previous "gold standard" for diagnosis, but now, it is uncommonly needed to establish or to confirm the diagnosis. A number of morphological characteristics of the trophozoite can be used for the initial diagnostic, but it is not possible to identify which specific species by light microscopy, the reason why another type of test could be used in the medical approach. Electron microscopy might be useful for the identification of some *Giardia* species, but it is not applicable for screening or routine use [15, 18].

The use of immunological methods offers an important alternative for the diagnosis. The use of fluorescence microscopy and the direct fluorescence antibody test, which recognizes surface epitopes on cysts, has been reported to achieve relatively high specificity (99.8–100%) and sensitivity (93–100%) for the detection. The detection of *Giardia* antigens in fecal samples is another approach. Various enzyme-linked immunoassays have been used and report specificities of 87–100% and sensitivities of 63–100%. Flow cytometry is another technique to identify the *Giardia* cysts when immunofluorescent staining and microscopic examination and/or enumeration report unsatisfactory results [15, 18].

In some cases, the laboratory findings are nonspecific, and in low-intensity infections, testing methods can be false negative for which it is required to repeat the test. On the other hand, the white blood cell count and liver function test results used to be normal. The electrolyte disturbances could be present if diarrhea and vomiting are severe. White blood cells, lactoferrin, blood, and mucus are not found in stools. Immunoglobulin levels are usually normal but usually low or absent in susceptible hypogammaglobulinemic individuals [2, 3].

7. Treatment

During the last 60 years of the past century, the arsenal of antigiardial drugs has been increasing, and they still are in use. Before the introduction of quinacrine, these infections were

treated with mercury, carbon tetrachloride, arsenicals, and bismuth; at present, an important number of agents have shown to be efficacious against *Giardia* in vitro and clinically. Nevertheless, current investigations try to establish an appropriate treatment regimen in giardiasis, but none of them appear to fulfill most of the criteria for an ideal drug. In fact, giardiasis is regularly considered an easily treated infection, but at times, due to treatment failure, re-infection or postinfection syndromes can have a huge impact on quality of life of the patient, which is why it is important to know at least six different classes of drugs, with different mechanisms, indication, and contraindications [1, 2, 21].

The 5-nitroimidazole (5-NI) derivatives remain the most frequently prescribed drugs, as well as metronidazole, tinidazole, and secnidazole. In spite of their efficacy, the treatment with these drugs is associated with several adverse effects, which are not always tolerable such as headache, metallic or bitter taste in mouth, nausea, vomiting, diarrhea, dizziness, general body discomfort, loss of appetite, etc. Whereas medical opposition may limit the use of some of them in singular cases, as in pediatrics, where their dose requirements make difficult the administration of tablet formulations to children. Finally, in the follow-up of some patients after treatment to evaluate the response to antigiardial drugs, a therapeutic failure is identified [4, 7, 21, 22].

Nitazoxanide is a new very broad spectrum 5-nitrothiazolyl derivative with a potentially useful activity against a range of biological agents. The effect of nitazoxanide in *Giardia* trophozoite includes ultrastructural changes in the cell morphology, swelling, and the formation of large empty areas in the cytoplasm and the disruption of the plasma membrane. An overall response rate of 75–94%, usually well tolerated, and a few adverse effects are the reason to choose this medicament [1, 22].

Some patients, who are being treated with the standard treatment that cures other patients, can continue with symptoms. In these cases, there are possibilities of different situations, including drug resistance, cure followed by reinfection, and also noncompliance and post-*Giardia* lactose intolerance, because when a drug-resistant giardiasis is identified, the stage changes and it is necessary to use another antigiardial compound with a different mechanism of action or a drug combination [1, 2, 4].

When there is a resistant *Giardia*, some therapeutic strategies could be used, since increasing the alternative dose and/or duration of the same one, changing another antigiardial, or using a drug combination might exert the synergistic effects. For this reason, the combination of the therapy should be reserved when single primary agents have failed to clear the infection. However, it also should be considered that administration of two or three drugs may have more profound physiological consequences, alter the intestinal microbiota, and increase the drug-related adverse events and health care costs [8, 9, 22].

8. Control and prevention

The interest in *Giardia* infection studies have been raising since its inclusion in the World Health Organization (WHO) in the Neglected Diseases Initiative in 2004 [9, 19]. In the same

way, a bibliometric study of scientific production on giardiasis reports 6964 papers between 1971 and 2010 available in PubMed, written in 27 different languages corresponding to original articles (78.5%), reviews (8.6%), case reports (6.8%), and letters to the editors (3.6%) that evidenced a steady growth of literature dedicated to *Giardia* and its infection throughout the 40-year analyzed period [7].

This pathogen has been highlighted for the importance in terms of patient well-being and its effects on quality of life for being a continuing cause of the patient's discomfort and pain. Unfortunately, due to a lack of political will, funding, interest from the scientific community, or the combination of all of these factors, giardiasis is not a health priority; that is why, it is important to take in mind that this infection is prevented by a scrupulous personal hygiene, proper disposal of sewage, removal or killing of cysts from water supplies, and preventing contamination of food and water [2, 20].

Actually, the global burden of chronic giardiasis is not known, and the difficulties in diagnostic tools, the lack of definition, and difficulties to quantify the impact of an infection that causes an acute or chronic one, principally symptomatic illness, contribute to the necessity to realize studies that estimate the problems in terms of cost, day lost for disability, and quality of life [9, 18].

Despite that, important contributions have been made regarding the spectrum of illness attributable to giardiasis. It is illustrated in the protective effect of *Giardia* against other types of diarrhea what could be due to the anti-inflammatory activity of *Giardia*. Nevertheless, further investigations on the pathogenic mechanisms are needed that could lead to potential interventions preventing the severe illness [2, 11].

Author details

Alfonso J. Rodríguez-Morales[1,2,3,4]*, Adriana M. Trujillo[1], Jorge A. Sánchez-Duque[1] and Ángel A. Escobedo[3,4,5]

*Address all correspondence to: arodriguezm@utp.edu.co

1 Public Health and Infection Research Group, School of Medicine and School of Veterinary Medicine and Zootechnics, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia

2 Committee on Zoonoses and Haemorrhagic Fevers, Asociación Colombiana de Infectología, Bogotá, DC, Colombia

3 Working Group on Zoonoses, International Society for Chemotherapy, Aberdeen, United Kingdom

4 Committee on Clinical Parasitology, Pan-American Association of Infectious Diseases, Panama City, Panama

5 Department of Parasitology, Academic Paediatric Hospital "Pedro Borrás," La Habana, Cuba

References

[1] Escobedo AA, Cimerman S. Giardiasis: A pharmacotherapy review. Expert Opinion on Pharmacotherapy. 2007;**8**(12):1885-1902

[2] Robertson LJ, Hanevik K, Escobedo AA, Morch K, Langeland N. Giardiasis—Why do the symptoms sometimes never stop? Trends in Parasitology. 2010;**26**(2):75-82

[3] Almirall P, Alfonso M, Ávila I, Salazar Y, Escobedo AA, Núñez FA, et al. Variaciones en las manifestaciones clínicas de la giardiosis en pacientes pediátricos hospitalizados, según grupos de edades. Revista Chilena de Infectología. 2013;**30**(5):502-506

[4] Pasupuleti V, Escobedo AA, Deshpande A, Thota P, Roman Y, Hernandez AV. Efficacy of 5-nitroimidazoles for the treatment of giardiasis: A systematic review of randomized controlled trials. PLoS Neglected Tropical Diseases. 2014;**8**(3):e2733

[5] Escobedo AA, Almirall P, Alfonso M, Cimerman S, Chacin-Bonilla L. Sexual transmission of giardiasis: A neglected route of spread? Acta Tropica. 2014;**132**:106-111

[6] Ryan U, Caccio SM. Zoonotic potential of *Giardia*. International Journal for Parasitology. 2013;**43**(12-13):943-956

[7] Escobedo AA, Arencibia R, Vega RL, Rodriguez-Morales AJ, Almirall P, Alfonso M. A bibliometric study of international scientific productivity in giardiasis covering the period 1971-2010. Journal of Infection in Developing Countries. 2015;**9**(1):76-86

[8] Escobedo AA, Lalle M, Hrastnik NI, Rodriguez-Morales AJ, Castro-Sanchez E, Cimerman S, et al. Combination therapy in the management of giardiasis: What laboratory and clinical studies tell us, so far. Acta Tropica. 2016;**162**:196-205

[9] Escobedo AA, Hanevik K, Almirall P, Cimerman S, Alfonso M. Management of chronic *Giardia* infection. Expert Review of Anti-infective Therapy. 2014;**12**(9):1143-1157

[10] Halliez MC, Buret AG. Extra-intestinal and long term consequences of *Giardia* duodenalis infections. World Journal of Gastroenterology. 2013;**19**(47):8974-8985

[11] Rodriguez-Morales AJ, Granados-Alvarez S, Escudero-Quintero H, Vera-Polania F, Mondragon-Cardona A, Diaz-Quijano FA, et al. Estimating and mapping the incidence of giardiasis in Colombia, 2009-2013. International Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases. 2016;**49**:204-209

[12] Escobedo AA, Almirall P, Rumbaut R, Rodriguez-Morales AJ. Potential impact of macroclimatic variability on the epidemiology of giardiasis in three provinces of Cuba, 2010-2012. Journal of Infection and Public Health. 2015;**8**(1):80-89

[13] Almanza C, Escobedo AA, Rodriguez-Morales AJ. *Giardia* infection in foreign visitors to Cuba. Travel Medicine and Infectious Disease. 2015;**13**(6):505-506

[14] Thompson RC, Monis PT. Variation in *Giardia*: Implications for taxonomy and epidemiology. Advances in Parasitology. 2004;**58**:69-137

[15] Einarsson E, Ma'ayeh S, Svard SG. An up-date on *Giardia* and giardiasis. Current Opinion in Microbiology. 2016;**34**:47-52

[16] Birkeland SR, Preheim SP, Davids BJ, Cipriano MJ, Palm D, Reiner DS, et al. Transcriptome analyses of the *Giardia lamblia* life cycle. Molecular and Biochemical Parasitology. 2010;**174**(1):62-65

[17] Carranza PG, Lujan HD. New insights regarding the biology of *Giardia* lamblia. Microbes and Infection. 2010;**12**(1):71-80

[18] Koehler AV, Jex AR, Haydon SR, Stevens MA, Gasser RB. *Giardia*/giardiasis—A perspective on diagnostic and analytical tools. Biotechnology Advances. 2014;**32**(2):280-289

[19] Duran C, Hidalgo G, Aguilera W, Rodriguez-Morales AJ, Albano C, Cortez J, et al. *Giardia* lamblia infection is associated with lower body mass index values. Journal of infection in developing countries. 2010;**4**(6):417-418

[20] Escobedo AA, Almirall P, Cimerman S, Rodriguez-Morales AJ. Sequelae of giardiasis: An emerging public health concern. International Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases. 2016;**49**:202-203

[21] Escobedo AA, Ballesteros J, Gonzalez-Fraile E, Almirall P. A meta-analysis of the efficacy of albendazole compared with tinidazole as treatments for *Giardia* infections in children. Acta Tropica. 2016;**153**:120-127

[22] Rodriguez-Morales AJ, Martinez-Pulgarin DF, Munoz-Urbano M, Gomez-Suta D, Sanchez-Duque JA, Machado-Alba JE. Bibliometric assessment of the global scientific production of nitazoxanide. Cureus. 2017;**9**(5):e1204

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