Analysis of the benefits of developing vaccines against leishmaniasis compared to the classic treatment

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ABSTRACT

Introduction: The treatment of leishmaniasis in humans faces challenges such as drug resistance and treatment abandonment. In this context, the search for an effective vaccine is crucial as a prophylactic measure. This study compares drug treatment and vaccination.
Methodology: An integrative review was carried out with the descriptors "leishmaniasis", "treatment", "vaccine" and "prevention" in databases such as PUBMED, Scielo, Medscape and DATASUS Tabnet.Results: Drug treatment includes three lines of medications, each with distinct challenges. On the other hand, vaccination is seen as a primary measure of immunoprophylaxis, with different generations of vaccines, including those based on the parasite's DNA. Discussion: In developing countries, such as Brazil, the need for effective and accessible treatment is pressing. Vaccination has advantages in cost and effectiveness, but more studies are needed to consolidate this form of prevention. Final Considerations: Investing in vaccines against leishmaniasis offers advantages in cost and effectiveness compared to drug treatment. Given the failures of conventional treatment, vaccination emerges as a promising prevention strategy.

Keywords: Leishmaniasis, Drug Treatment, Vaccine, Prophylaxis.

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INTRODUCTION

Leishmaniasis is an infectious and inflammatory disease that, depending on the condition, can affect from the skin and mucous membranes to visceral organs - liver, spleen and bone marrow, has as its etiological agent, the protozoan of the genus *Leishmania*, and is transmitted between mammalian hosts through the bite of the infected sandfly insect, belonging to the genus *Lutzomyia* (SANTOS et al., 2022). There is a variety of mammals that are natural reservoirs for *Leishmania,* among them are: domestic and wild dogs, jackals, raccoons and rodents. Classified in 2011 as a neglected tropical disease by the World Health Organization (WHO), the clinical manifestation of Leishmaniasis in humans occurs in three types of conditions: cutaneous or cutaneous leishmaniasis (CL), mucosal leishmaniasis, and visceral leishmaniasis (VL) or kala-azar (GRIENSVEN et al., 2019).

Cutaneous leishmaniasis is characterized by the presence of lesions exclusively on the skin that appear after an incubation period ranging from ten days to three months with the presence of an erythematous papule that progresses slowly to a nodule, accompanied by regional adenopathy, with the presence of ulcers with raised borders being common. In addition, the condition is usually asymptomatic (GONTIJO et al., 2003).

Regarding mucosal leishmaniasis, it is the result of the progression of tegumentary leishmaniasis, a consequence of hematogenous and/or lymphatic invasion of the parasite. In almost all cases, it is possible to observe the involvement of the nasal and oral mucosa. On the other hand, in human visceral leishmaniasis, the main signs and symptoms are splenomegaly, hepatomegaly, pallor, weakness, intermittent fever, and can lead to death in up to 90% of untreated cases (CAVALCANTE et al., 2022).

As for its geographical distribution, it is "a health problem in tropical and subtropical countries, distributed on four continents (Americas, Europe, Africa, and Asia), with an annual record of 0.7 to 1.3 million new cases, however, it is more frequent in South American countries" (OLIVEIRA, 2022).

According to data from the World Health Organization, approximately 90% of cases of visceral leishmaniasis are reported in Bangladesh, Brazil, Nepal, India, and Sudan. Mucocutaneous leishmaniasis predominantly affects Brazil, Bolivia and Peru, accounting for about 90% of cases. Meanwhile, approximately 90% of cutaneous leishmaniasis cases are recorded in Afghanistan, Brazil, Iran, Peru, Saudi Arabia, and Syria (RATH et al., 2003).

Thus, in view of the excerpt exposed above, it is possible to highlight Brazil as a hotbed of leishmaniasis, which is confirmed by DATASUS records (2024) that measure a number of 50,438 cases of VL and 296,353 cases of ATL, in the period between 2008 and 2022, of which 9,218 cases of

visceral leishmaniasis and 129,426 cases of American tegumentary leishmaniasis, occurred only in the North Region of the country, the place with the highest endemicity of Leishmaniasis in Brazil.

During the spatial analysis of the occurrence of leishmaniasis, DATASUS (2024) highlights that 65.1% of VL cases are male patients and, in relation to ATL, the proportion increases to an expressive 75.5%. This is probably associated with the type of work they do.

With regard to age, the most affected age group is adults between 20 and 59 years old, since they correspond to a share of 48% of all ACL infections in the state. This scenario is not reflected in VL, in which 39.2% of all cases are in the infant and adolescent age group, from 0 to 19 years old.

Furthermore, as far as the treatment of leishmaniasis is concerned, it is aimed at the drug route. However, recent experiments have enabled advances in relation to vaccination about the disease in question. In this sense, studies focused on vaccine immunization are crucial due to the growing resistance, toxicity, and high costs of the drugs currently used in the treatment of this disease (GHORBANI & FARHOUDI, 2018).

In the face of this disease, drug treatment has numerous drugs with various properties that have their respective advantages and restrictions. Therefore, first-line drugs include pentavalent antimonials (Sb5+), which are used in consolidated use and are the basis of anti-leishmania chemotherapy. In addition, pentamidine and amphotericin B are second-line medications, which are used as options of choice after antimonials (CROFT et al., 2003; SUNDAR, 2001).

Furthermore, miltefosine, a third-line treatment option, is a registered anticancer agent for the treatment of the cutaneous and visceral form of the disease, and its oral efficacy and short treatment period are notorious as the main advantages of this drug (AGUIAR & RODRIGUES, 2017).

In this context, studies related to the treatment of leishmaniasis have been developed, and it is important to highlight the relevance of drug treatment. However, in a parallel path, there is the applicability of vaccines, as well as the importance of developing new studies on the subject, in order to increase their effectiveness in the long term.

The present study aims to promote an analysis of the benefits of the development of anti-leishmania vaccination in comparison with the classic drug treatment for leishmaniasis.

METHODOLOGY

This is an integrative literature review that used as a database articles from the Pubmed, Scielo, MedScape and DynaMed platforms with the descriptors "leishmaniasis", "treatment" and "vaccine". Searches were carried out in the Outpatient Information System - SIA/SUS and in the DATASUS Tabnet data platform, and data related to age and gender were considered in the elucidation of the information.

In addition, systematic review and meta-analysis articles in Portuguese and English were considered as inclusion criteria. As exclusion criteria, narrative review articles, epidemiological profile, integrative reviews and case reports during the search on the platforms.

RESULTS

Leishmaniasis, an inflammatory infectious and parasitic disease that affects from the most superficial tissues (integumentary and mucosa) to the bloodstream and visceral organs, has a pharmacotherapeutic treatment divided into 1st, 2nd and 3rd line, with pentavalent antimony (Sb5+), the main drug of choice in the anti-leishmania treatment, produced.

However, among the main factors that call into question the viability of this means of treatment: the exacerbated use of oral medications, the high cost of certain drugs, the risk of toxicity, and side effects (AMARAL & CHAVES, 2021).

Antimonials have two preparations available, sodium stibogluconate (Pentostam®) and meglumine antimoniate (Glucantime®) with similar efficacy for the treatment of cutaneous and mucocutaneous forms of leishmaniasis (BERBERT et al., 2018).

Sodium stibogluconate has been used in the treatment of cutaneous and mucocutaneous leishmaniasis in the United States and in the treatment of visceral leishmaniasis, except in Europe and regions of India where there is resistance to it. Eventually, treated patients may be hospitalized when pentavalent antimony is administered, since there must be a periodic assessment of cardiac conductance with electroencephalographic (EEG) monitoring and laboratory tests - blood count, renal function test, amylase levels, lipase, and serum transaminases (STARK, 2023).

In addition to systemic use, antimonials can be administered by intralesional infiltration in order to increase the concentration of antimony in the lesion - this process can be performed with a solution of 1-3 ml of antimony in a cycle every five to seven days and can be repeated two to five times (VRIES, 2015).

However, studies confirm that the risk of liver and kidney toxicity can lead to chronic health problems for patients using antimonials. In addition, over six decades of antimonial use, the parasite has had enough time to develop resistance mechanisms. These include, preventing drug activation, decreasing parasite absorption, increasing drug efflux, and high thiol loading on macrophages (TASLIMI et al., 2016).

In the second line of drugs of choice for anti-leishmania treatment are amphotericin B and pentamidine. The first is effective against pentavalent antimony-resistant mucocutaneous disease and visceral leishmaniasis, but its use is limited in reflection of the risk of toxicity (PAHO, 2023).

The second presents a conditional recommendation in systemic treatment for patients with the cutaneous form of the disease, which consists of the use of intramuscular pentamidine isethionate with 4 -7mg/kg/day in three doses applied every 72 hours (PAHO, 2023).

In view of this, more recent lipid preparations have emerged: amphotericin B lipid complex, colloidal amphotericin B dispersion and liposomal amphotericin B (MARTINEZ, 2006). The latter is strongly recommended for the treatment of VL in pediatric and immunocompromised patients in the Region of the Americas (PAHO, 2023).

In continuity, liposomal amphotericin B has been chosen as the drug of choice for VL due to its rapid metabolism and lower toxicity. This is perceived by the ability of the drug to circulate in the body for a longer period of time and penetration into tissues more effectively because it is a small particle (GHORBANI & FARHOUDI, 2018).

Regarding the levels of hepatotoxicity and, above all, nephrotoxicity, this drug is superior to conventional amphotericin B because it has lower renal clearance, since it is able to retain it in its liposomal architecture for longer compared to the classic form (ADLER-MOORE & PRO, 2009).

Intramuscular pentamidine, effective against VL, is the drug of choice to treat *L. (Viannia) guyanensis* in French Guiana, where antimonial resistance is prevalent (STARK, 2023).

In a study by Amato (1997), seventeen patients diagnosed with cutaneous mucosal leishmaniasis were submitted to pentamidine therapy (4 mg/kg) every other day, resulting in healing of the lesions in sixteen individuals (94.1%). This result demonstrates the efficacy of this treatment for cases of leishmaniasis resistant to antimonials and amphotericin B.

However, an important disadvantage for pentamidine is the need to be applied by deep IM, in an outpatient setting, due to the possibility of immediate side effects, such as hypoglycemia and the appearance of reactions (plastrons) at the application sites, if administration is superficial. In addition, resistance and toxicity mechanisms resulted in the loss of space for amphotericin B (NEVES et al., 2011; GHORBANI & FARHOUDI, 2018).

In the third line of anti-leishmania medications is miltefosine (hexadecyl 2-ethyl phosphate), an anticancer agent and affordable therapy, administered orally and well tolerated for VL. Miltefosine is the only oral agent that has been shown to be effective against leishmaniasis and is approved for pediatric patients over 12 years of age, weighing more than 30kg, and adults (DUTHIE & REED, 2014).

From an analytical standpoint, phase 2 and 3 drug studies in India showed that miltefosine administered orally was 95-97% effective in curing patients with Indian visceral leishmaniasis. Oral treatment of 2.5 mg/kg/day lasting 4-6 weeks was generally well tolerated. Adverse effects included gastrointestinal distress and elevated creatinine levels, resolved with discontinuation of therapy (STARK, 2023).

Another 2011 phase IV trial in Bangladesh concluded that monotherapy with oral miltefosine (2.5 mg/kg/day) for 28 days is effective in treating VL in children and adults. However, due to its long half-life, it is a teratogenic drug with resistance potential (STARK, 2023; KEYNAN et al., 2008).

In this sense, it is noteworthy that most anti-leishmania drugs are highly toxic, have resistance problems or require hospitalization, and are therefore inadequate (FREITAS-JÚNIOR et al., 2012). Conversely, vaccination has the potential to provide not only long-term protection against disease, but can also impact infectious reservoirs to reduce transmission (DUTHIE et al., 2016).

This fact is true because vaccines are effective means of inducing an immune response to produce immunoglobulins and memory lymphocytes to control the infection. In addition, these vaccines stimulate humoral and cellular immunity, especially a strong Th1 response and cytotoxicity cells (DUTHIE et al., 2016).

In addition, vaccination is an economic strategy for the prevention of infectious diseases and, therefore, emerges as a relevant tool in the fight against leishmaniasis. Currently, there are different forms of vaccines: killed vaccines - attenuated, recombinant, subunits, VLP (virus-like particles) and DNA vaccines (NOAZIN et al, 2008).

According to FIOCRUZ (1997), the attempt at immunoprophylaxis against leishmaniasis has been going on for more than 100 years, and the first experiences date back to 1912, when Charles Morley Wenyon inoculated himself with residues from a lesion of Oriental Button, obtaining typical lesions in a certain period after such an event. The event is called "leishmanization".

Starting from the aforementioned conception, we can identify the strong immunological "root" of this event. What happened to botanist Charles can be explained by the important role of dendritic cells in this immune reaction, since they are potent professional antigen-presenting cells (APCs) that effectively link innate and adaptive responses because, when activated, they mature and initiate immune responses by presenting antigens to T cells, through major histocompatibility complex (MHC) (NUNES et al., 2023).

Thus, vaccines emerge as effective and economical means as the aforementioned immunization model to prevent infectious diseases. The three generations of anti-leishmania vaccines emerged with the common goal of making leishmaniasis, regardless of its classification, a preventable and preventable disease (SILVA et al., 2013).

Ghorbani & Farhoudi (2018) classify leishmaniasis vaccines into three generations – the first generation comprised of vaccines with the killed form of the parasite, the second generation composed of modified vaccines in which specific genes were removed, and a third generation, in which vaccines were produced based on the parasite's DNA.

Thus, in the first generation of vaccines against leishmaniasis (*L. major, L. amazonensis and L. mexicana*) there are autoclaved formulations and those composed of inactivated whole parasites. These vaccines can be produced in an economically viable manner in developing countries, presenting an attractive advantage that motivates the exploration of the pentavalent preparation proposed in Brazil by Armijos et al. (2003). The inactivation of the parasite was performed using merthiolate, resulting in the vaccine known as Leishvaccine®, which did not include adjuvants (ARMIJOS et al., 1998).

Another approach consisted of an autoclaved vaccine formulation, which demonstrated similar immunogenicity results. In Venezuela, a vaccine containing

L. mexicana mixed with the adjuvant *Bacillus Calmette-Guérin* (BCG) has been developed and applied as an immunotherapy strategy in CL patients, but prophylactic investigations of these vaccines remain inconclusive due to the lack of acceptable results (GHOURBANI & FARHOUDI, 2018).

The second generation uses vaccines with modified parasites, in which essential genes, how Timiddilato synthase, Dihydrofolate reductase cysteine proteinase and/or biopterin transporter, were eliminated. When used, they are capable of inducing adequate adaptive immune responses, resulting in an inactivated infection and, consequently, absence of disease in vaccinated individuals (KEDZIERSKI et al., 2006). The genetic modifications include the introduction of "suicide tapes" into the genome of the *Leishmania* and, although there are ethical considerations about living challenges in therapeutic approaches, studies suggest that immune responses against live pathogens can provide long-lasting immunity (KEDZIERSKI et al., 2006).

Another class of second-generation vaccines are vaccines extracted from Leishmania, such as Leishmune®, designed for canine visceral leishmaniasis, using purified *L. donovani*. Despite promising effects, obstacles, such as difficulties in clinical trials, prevented progress to phases II and III. These bacterial and viral vaccines have shown promising results, indicating specific immune responses (AFRIN et al, 2002).

Continuing, among the second-generation vaccines is the non-pathogenic Leishmania, such as *L. tarentolae*, which was studied as a vehicle for the delivery of antigens for vaccine formulation through a new recombinant antigen. However, it will require further studies in rodent models, with also the need to understand whether the parasite can actually replicate within the mammalian host, ensuring adequate stimulation of the immune response, without causing any pathological change (BANDI et al., 2023).

The third generation of vaccines considers the use of purified *Leishmania* antigens, because in addition to studies indicating that DNA vaccines are more stable, they also have a lower production cost compared to recombinant protein vaccines (SUSCHAK et al., 2017).

The distribution of these vaccines does not require a cold chain, providing flexibility in combining different genes into a single product. The mechanism of action of DNA vaccines involves the activation of innate immunity through unmethylated CpG sequences, leading to prolonged expression of recombinant proteins (PALATNIK-DE-SOUSA, 2008).

Finally, previously mentioned antigens were tested as individual vaccines or in combinations, demonstrating promising results in preclinical studies. However, Phase III clinical trials are not yet available to fully validate the efficacy of these vaccines. The second generation of vaccines, incorporating native antigens, could significantly increase the average efficacy of vaccines, highlighting the need for additional studies and clinical trials in Phase III in the near future (GHOURBONI & FARHOUDI, 2018).

DISCUSSION

There are several therapeutic approaches for the treatment of leishmaniasis, however, the options currently available are not sufficient to achieve complete eradication of this infection. It is possible that drug therapy may be able to suppress infections immediately (DUTHIE et al., 2016; SILVA et al., 2013). However, it has been restricted due to adverse side effects and bioavailability (DUTHIE et al., 2016).

In this context, the pharmaceutical industry has invested little in the development of new drugs to treat this disease. In Brazil, the drug of choice is still methylgluchamine antimoniate, whose advantage is that it can be administered on an outpatient basis, thus reducing the risks associated with hospitalization (TEIXEIRA et al., 2023). It is worth noting that antimony derivatives, used as very effective leishmanicides, have been commercialized since 1945 (STECK, 1978). Over time since its market launch, it is clear that low dosages and discontinuous treatments contribute significantly to the increase in resistant forms of the parasite (RATH, 2003).

Although its mechanism of action, chemical structure and composition are not completely understood, there is evidence that pentavalent antimony is reduced *in vivo* to its trivalent form, which justifies the toxicity of the drug, in which a high incidence of adverse events is observed that tend to increase during the course of treatment, such as myalgia, arthralgia, nausea, vomiting and abdominal pain (RATH, 2003). There is still a lack of simple and accessible methods that allow antimony speciation to determine the content of Sb and its potential toxic contaminants (DAGERT et al., 2006).

Amphotericin B, the drug of second choice, is the most potent leishmanicidal drug available on the market, but it can cause acute toxicity, hospitalization and high costs as main disadvantages. As advantages, it is the only option in the treatment of pregnant women and patients who have contraindications or who manifest toxicity or refractoriness to the use of antimonials (MINISTRY OF HEALTH, 2017; MINISTRY OF HEALTH, 2020). Amphotericin B has a lower level of toxicity

compared to antimoniates, but amphotericin deoxycholate can cause adverse reactions such as allergic reactions, fever, chills, and phlebitis (LOUÇÃO et al., 2018). The emergence of lipid presentations has brought more safety with a reduction in adverse effects, however, it has a high cost as a barrier to its wide use, being indicated only in severe forms and intolerance to antimoniates (AGUIAR & RODRIGUES, 2017).

According to Stark (2023) and Teixeira et al. (2023), with regard to the alternative option to second-line treatment, Miltefosine, initially developed as an antineoplastic drug, has the main advantage of oral administration compared to parenteral drugs widely used in endemic countries for the disease. In addition, for Costa Filho et al. (2008), Miltefosine demonstrates efficacy in severe or refractory cases and, compared to N-methyl glucamine, it is less toxic and more easily administered due to its oral form. This characteristic is extremely important in the poorest regions of Brazil, where leishmaniasis is more prevalent, such as in the North, Northeast and Midwest.

Thus, adherence to treatment tends to be higher with the use of Miltefosine. However, it is crucial to highlight a disadvantage of this drug: the potential teratogenic effect. Therefore, their prescription for women of childbearing age should be done with caution, and it is essential to provide guidance on the use of contraceptive methods in these cases (COSTA FILHO et al., 2008; MACHADO & PENNA, 2012).

For Ghorbani & Farhoudi (2018), considering that drug therapy is limited due to its high cost, toxicity, and potential side effects, patients with visceral leishmaniasis die without any treatment. In this context, the long duration of treatment and availability are the main factors that increase the chance of drug resistance in underdeveloped countries (FREITAS et al., 2012; RAJASEKARAN & CHEN, 2015).

Vaccination against visceral leishmaniasis has the potential to offer additional benefits compared with medication. While medication tends to be directed at treating the disease after infection, the vaccine seeks to prevent infection in the first place by offering a preventive and proactive approach (SILVA et al., 2013).

In view of the immunization processes associated with the previously mentioned forms of disease control, numerous studies have shown that IFN-ɣ and TNF-α-secreting Th1 cells play a fundamental role in immunity against leishmaniasis infections, in addition to the ability of neutrophils to influence adaptive immune responses through the production of chemokines during leishmaniasis infections, resulting in the recruitment of other immune cells (BACELLAR et al., 2002; CONCEIÇÃO et al., 2016; MOLL and BERBERICH, 2001; PETERS et al., 2008).

Vaccination is shown to be a more effective control in the long term, although current results do not demonstrate sufficient efficacy for this therapy to be implemented in practice in the short term, requiring further studies to allow the advent of new vaccines that act in a preventive manner,

avoiding an overload on the health system due to the increase in the number of cases of the disease (JAIN, 2015).

The leishmaniasis vaccines developed so far have advantages and disadvantages in their practical applicability, including low production costs, making it attractive for further development, but there are still obstacles to the standardization and regularization of this type of vaccine (NOAZIN et al., 2008). In addition, vaccines with live pathogens containing special antigens or with the live parasite genetically modified to produce a long-lasting immune response are controversial due to ethical issues. In this context, the use of this therapeutic approach for humans has not yet been approved, making it difficult to consolidate it (GHOLAMI, ZAHEDIFARD, RAFATI, 2016; GHORBANI & FARHOUDI, 2018; REQUENA et al., 2004).

In this sense, another possibility would be the vaccine extracted from leishmania, also called Leishmune®, which has as its main advantages its efficiency in combating visceral leishmaniasis, but still faces problems related to their standardization and production (GHORBANI & FARHOUDI, 2018).

Additionally, in the study conducted by GONZALO et al. (2002), certain vaccines were created based on viruses. Some of these included viruses that expressed the LACK of L antigen. *infantum*, which provided strong protection against *L. major* in mice, and viruses that expressed the surface of the G46/M-2/PSA-2 promastigote protein, conferring effective protection against *L. amazonensis*. The encouraging results of these strategies attested to the ability to strengthen the specific immune responses of CD4 and CD8 cells during the immunization process, resulting in a significant increase in IL-2, IFN-ɣ and TNF-α in the groups that received the vaccines (GONZALO et al., 2002; RAMÍREZ et al., 2001).

Such data corroborate the study by Petitdidier et al. (2016), which highlight the importance of recruiting new approaches in recombinant technology to improve vaccine formulation, resulting in more purified, stable, reproducible, and safe products, with a potential reduction in adverse reactions. The administration of key immunogenic proteins offers a conducive means to induce integrated immune responses, especially against specific protective antigens.

Third-generation vaccines, such as DNA vaccines, have been shown in studies to be more stable than recombinant protein vaccines. In addition, they have a lower production cost, indicating a promising advance in the development and improvement of this type of vaccine compared to other more conventional vaccines and treatments (GHORBANI & FARHOUDI, 2018).

In this context, in light of the socioeconomic aspects relevant to the epidemiological distribution of Leishmaniasis in Brazil, the presence of a clear social vulnerability becomes evident, which hinders adherence to the available therapeutic options, which often require high cost and precise administration. Thus, it is essential to establish health measures that are in line with the

panorama of this zoonosis, with particular emphasis on the specific approach to the socioeconomic conditions of Brazil (MINISTRY OF HEALTH, 2020). Therefore, the implementation of a comprehensive prophylactic intervention aimed at reducing the incidence of the disease and preventing new cases emerges as an advantageous strategy.

Considering these factors, Duthie et al. (2016) state that drug therapy has proven to be ineffective in eradicating this disease. However, vaccination emerges as a means of providing lasting protection and mitigating the transmission of infection. Therefore, the implementation of extensive vaccination programs becomes imperative to reduce the incidence of leishmaniasis (LUNA & CAMPOS, 2020). Therefore, the importance of investments in research for the development of more effective vaccines is noted, as well as funding and collaboration between institutions and researchers to accelerate progress in this area (GHORBANI & FARHOUDI, 2018). Unlike medication, which requires intervention after exposure to the parasite, vaccination can provide continuous protection, reducing the likelihood of infection and contributing to the reduction of parasite transmission in the community (MINISTRY OF HEALTH, 2020).

Finally, the vaccine can enhance the formation of immunological memory, resulting in the sustained ability of the immune system to identify and fight the pathogen in the future, thus conferring long-lasting protection (JAIN, 2015). In addition, it is essential to initiate educational practices in affected communities, which can include awareness campaigns on the pathology, modes of transmission, symptoms and, when available, the importance of immunization (MINISTRY OF HEALTH, 2020). In addition, it is crucial to highlight the relevance of training health professionals for the effective diagnosis and treatment of leishmaniasis (MINISTRY OF HEALTH, 2017).

FINAL CONSIDERATIONS

The analysis of the aspects of drug treatment and vaccination for Leishmaniasis revealed potential advantages in the development of vaccines compared to drug treatments. This is particularly relevant in terms of cost, an essential factor for the implementation of immunization programs in developing countries such as Brazil. In addition, the importance of studies and the development of more viable therapeutic approaches in terms of efficacy, safety and cost has become evident. Consequently, research indicates that high cost, prolonged duration of treatment, and availability are the main factors that increase the likelihood of drug resistance in underdeveloped countries.

Brazil is recognized as an endemic region for Leishmaniasis, presenting one of the highest rates of the disease compared to the surrounding regions. This reality justifies the development of more effective treatment methods, which are currently based primarily on drug therapy, in addition to prophylactic measures aimed at combating the vector through environmental hygiene practices. Considering these factors, drug therapy has shown limited efficacy in eradicating the disease.

However, vaccination has the potential to confer long-term protection and reduce transmission of infection, culminating in the urgent need for comprehensive vaccination programs to reduce the incidence of leishmaniasis. It is observed, however, that the ideal vaccine has not yet been developed, highlighting the urgency of in-depth studies in this field.

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