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MILTEFOSINE: THE ADVANTAGES OF ORAL TREATMENT IN TEGUMENTARY LEISHMANIASIS – CASE REPORT

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Abstract: Introduction: Cutaneous leishmaniasis (TL) is an infection by the protozoan of the genus Leishmania, which mainly affects the population in socioeconomic vulnerability, with a high incidence. However, there is a lack of search for new effective treatments with more convenient dosages and route of administration than Meglumine, a drug with high toxicity for parenteral use. Recently, Miltefosine was incorporated into the Unified Health System, as a treatment for LT, opening a new chapter in combating the infection, as it was the first medication for this purpose to be used orally. Objective: To demonstrate the effectiveness of treating a case of TL with the use of Miltefosine in relation to the classic treatment with Meglumine. Material and Method: The present study reports a case of a 55-year-old male patient, from Rondonópolis/MT presenting a pustular lesion, with evolution to an ulcerated lesion, associated with local phlogistic signs and palpable lymph nodes in the cervical region. In addition to using articles from the database: Scielo, Ministry of Health and ScienceDirect, based on the keywords: "cutaneous leishmaniasis", "miltefosine", "meglumine. Results: Miltefosine, as it is administered orally, guarantees a large advantage over Meglumine, ensuring greater adherence and accessibility to treatment, not requiring hospitalization or frequent visits to health services, and has few side effects. In addition to presenting a cure rate similar to Meglumine. Conclusion: The incorporation of Miltefosine in the treatment of TL represents a breakthrough. As it is an orally administered drug, it ensures greater comfort, less need for monitoring and low-severity adverse events, with similar efficacy and greater safety compared to Meglumine, until then the first-line treatment for TL. The greatest precaution in the use of Miltefosine is its teratogenic effect, recommending the mandatory use of contraceptives during

treatment and 4 to 6 months after its end. This way, Miltefosine guarantees greater adherence and accessibility to the treatment of tegumentary Leishmaniasis, already made available by the Unified Health System. recommending the mandatory use of contraceptives during treatment and 4 to 6 months after its end. This way, Miltefosine guarantees greater adherence and accessibility to the treatment of tegumentary Leishmaniasis, already made available by the Unified Health System. recommending the mandatory use of contraceptives during treatment and 4 to 6 months after its end. This way, Miltefosine guarantees greater adherence and accessibility to the treatment of tegumentary Leishmaniasis, already made available by the Unified Health System.
Keywords: "Cutaneous leishmaniasis", "miltefosine", "meglumine".

INTRODUCTION

Tegumentary leishmaniasis (LT) is a parasitosis caused by the protozoan of the genus Leishmania, characterized by ulcerative lesions on the skin. An important public health problem in the Americas due to its high prevalence. In addition, it mostly affects the socioeconomically vulnerable population, making control more difficult (PAHO, 2018).

Only in the year 2020 in Brazil we had 16,432 cases of tegumentary leishmaniasis (TL), with a predominance in the North and Midwest regions with incidence rates respectively about 5 and 2 times the national average of 7.8/100,000 inhabitants (BRAZIL, 2022). Even though there is a high incidence, as it is a neglected disease, there are few pharmacological novelties for the treatment of TL.

The drugs recommended by the Ministry of Health until 2018 for the treatment of TL were all for parenteral use (BRAZIL, 2020). Meglumine antimoniate was the first choice treatment, which could be administered either intramuscularly (IM) or intravenously (IV). The dose can vary between 10 mg and 20 mg Sb+5/kg/day, suggesting 15 mg Sb+5/kg/day for 20 consecutive days; in case of therapeutic failure, the scheme could be repeated for another 30 days (BRAZIL, 2017).

Therapy with meglubin antimoniate requires strict monitoring with electrocardiography, blood count, creatinine, urea, transaminases, bilirubin, gamma glutamyl transferase, alkaline phosphatase, amylase and lipase. In addition to requiring hospitalization or frequent trips to health services, and an uncomfortable route of administration. These factors are unfavorable to adherence to therapy.

Recently, Ordinance No. 56, of 2018, incorporated Miltefosine as the first option in the treatment of TL, a drug administered orally (VO) and similar in effectiveness to meglubine antimoniate. The current therapeutic scheme recommends 2 or 3 capsules/day divided into 2 to 3 doses per day, preferably administered after meals in order to mitigate its main adverse effects, nausea and vomiting, which are, however, mild and transient. and well tolerated. The treatment is carried out in two stages of 14 days each; between each stage monitor levels of urea, creatinine and liver enzymes (BRAZIL, 2020). The greatest precaution in the use of Miltefosine is its teratogenic effect, recommending the mandatory use of contraceptives during treatment and 4-6 months after its end.

VO administration is more convenient, which is an advantage of using Miltefosine in relation to previous treatments with IM or IV routes. Furthermore, it ensures greater adherence and accessibility to the treatment since it does not require hospitalization or even frequent visits to health services. These factors are sensitive for the population most affected by TL who live in socioeconomic

vulnerability and many live in areas of difficult access.

GOAL

Demonstrate the effectiveness of treating a case of LT with the use of Miltefosine, in relation to the classic treatment with Meglumine, comparing adherence to treatment, cure rate, route of administration and side effects.

CASE REPORT

VlN 55 years old, male, from Rondonópolis/MT, agricultural worker, without previous comorbidities, weight 99 kg, was admitted to the service on 08/26/2022 with a history of pustular lesion in the left chin region for approximately 30 days, which evolved into an ulcerated lesion measuring 5 cm in its largest diameter with drainage of purulent secretion, associated with phlogistic signs at the site and a palpable lymph node in the left anterior cervical region. At the origin, a scraping had been performed for leishmaniasis, with a negative result and a biopsy of a fragment of the lesion. He used azithromycin 500 mg a day, without improvement, and was later transitioned to amoxicillin with clavulanate 500/125 mg 3 times a day, still without satisfactory response.

Anatomopathological examination showed sections of ulcerated skin with pseudoepitheliomatous hyperplasia, containing a chronic granulomatous inflammatory infiltrate in the dermis, with giant cells of the Langhans and suppurative type. Globular structures are also identified in the dermis, also stained with giemsa. Pass negative. The histological aspect favors leishmaniasis, within an adequate clinical context.

Opted for treatment with Miltefosine, incorporated in 2018 as the first line in the treatment of tegumentary leishmaniasis in the SUS. Medication started on 09/09/2022 at a dose of 150 mg/day divided into 3 daily doses, in 2 stages of 14 days each. The patient was instructed on the importance of contraceptive methods due to the drug's teratogenicity.

In the reassessment at the end of the first stage, there was a significant improvement in the lesion, with scar tissue already present. Complaint of epigastric pain, associated with nausea, with improvement with antiemetic, without the need to discontinue treatment. Laboratory tests of the day: HB 15.3, HT 44.4, leukocytes 7,900, platelets 197,000, creatinine 1.08, TGO 16, TGP 19, blood glucose 87. Serology American tegumentary leishmaniasis IgG non-reactive. Cervical US with reactive-looking adenopathy in the left cervical region.

Return after completion of treatment on the 28th day with significant improvement, complete healing of the lesion, mild adverse effects and easy to control. Laboratory tests:

Clinical evolution:

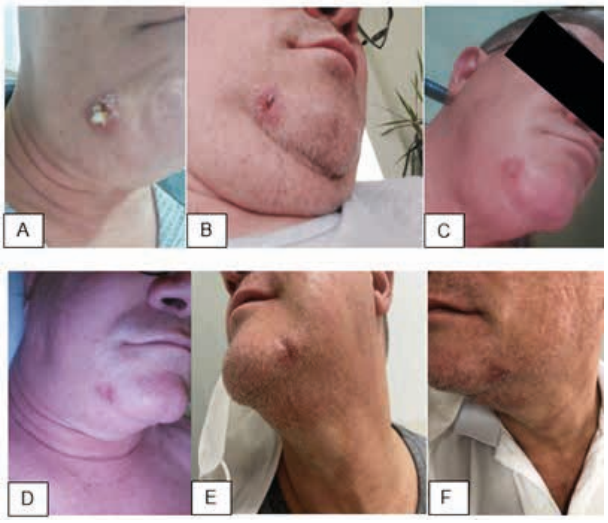

Figure 1. Image of the patient's clinical evolution. A) Image before treatment, on 07/25/2022. B) Image before treatment, on 08/08/2022. C) Image before treatment, on 08/27/2022. D) Beginning of the day 09/09/2022. E) Image during treatment, on 09/14/2022. D) Image after treatment, on 10/07/2020.

Source: Low quality photos, taken with the front camera of the cell phone, authorized by the patient

CONCLUSION

Cutaneous leishmaniasis being a neglected disease, affecting populations in socioeconomic vulnerability, the incorporation of Miltefosine represents a breakthrough. A drug administered orally, thus ensuring greater comfort to the patient; with less need for monitoring and low-severity adverse events, and similar efficacy and greater safety compared to Meglumine, the hitherto first-rate treatment for CL. The greatest precaution in the use of Miltefosine is its teratogenic effect, recommending the mandatory use of contraceptives during treatment and 4-6 months after its end. This way, Miltefosine guarantees greater adherence and accessibility to the treatment of Tegumentary Leishmaniasis, already made available by the Unified Health System.

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