

Treatment of mucosal leishmaniasis with amphotericin B lipid complex (ABLC)

Dear Editor

Mucosal leishmaniasis (ML) is a disease that can destroy cartilages, the pharynx and larynx, as well as bone structures of the face¹. The treatment of ML is essentially based on the use of antimonial pentavalent. However, this drug has several adverse effects (AEs) and contraindications. Amphotericin B has been an alternative to antimonial pentavalent, mainly the liposomal formulation (L-AMB)². However, the cost of the drug can be prohibitive to developing countries, and the ideal dose has not yet been established. Amphotericin B lipid complex (ABLC) is another lipid formulation of amphotericin B, with less nephrotoxicity than the deoxycholate formulation and is less expensive than L-AMB. As far as we know, this is the first report on a series of cases on the treatment of ML with ABLC. We report 13 cases of patients with ML treated with ABLC from a Brazilian cohort from January 2000 to July 2015.

Patients with confirmed ML older than 18 years and followed-up for at least 6 months were included in the cohort. Patients without confirmation of ML and refusal of treatment were excluded. The diagnosis of ML included the amplification of *Leishmania* spp. DNA in tissue samples by molecular techniques, isolation of parasites in cultures, or the finding of typical structures during the histological examination or in immunohistochemistry tests. Otorhinolaryngological evaluations were performed in all patients. Pentavalent antimonial was the first option of treatment. Lipid formulations were indicated after pentavalent antimonial failure, appearance of side effects or the presence of a contraindication for the pentavalent antimonial use. The choice of the lipid formulation of amphotericin B was a medical decision and in 13 cases ABLC (1–4 mg/kg/day to achieve a cumulative dose of 1,500 to 2,500 mg) was administered.

Cure, failure and recurrence episodes were previously defined³. AEs associated with the treatment of ML were analyzed during the hospitalization period. Acute kidney injury (AKI) was defined according to the AKIN criteria⁴.

The median age of the patients was 58 [IQR 55–65] years old and 53.8% of patients were men. Most patients presented symptoms for more than 5 years (65.4%). All species identified were *L. braziliensis*. Treatment of all patients with ML was performed in the hospital with a median hospitalization time of 25 [IQR 19–28] days. ABLC was associated with several infusion-related AEs (Table 1). The cure rate of the group that used ABLC was 46.1%, and 1 case considered previously cured has recurred. The dosage of ABLC varied from 1 to 4.5 mg/kg (average 2.6 mg/kg). The mean cumulative dose was 1,253 mg (planned cumulative dose of 1,500 to 2,500 mg).

Data on ABLC in the treatment of ML have not been published in the literature, although this drug has been used since the 1990s for the treatment of visceral leishmaniasis⁵. The results showed a success rate limited to 46.1% (6/13) and a relapse rate of 7.7%. Other drugs have shown clinical cure rates between 71.0% and 77.0% of the cases¹. Recurrence with the use of antimonial pentavalent is around 22%¹. However, the daily recommended dose was low, not achieving the adequate cumulative dose. The treatment of ML is still far from the ideal because the best performing drugs for this condition have numerous AEs, and drugs that

¹Pontifícia Universidade Católica do Paraná, Escola de Medicina, Curitiba, Paraná, Brazil

²Universidade de São Paulo, Faculdade de Medicina, Departamento de Moléstias Infeciosas e Parasitárias, São Paulo, São Paulo, Brazil

³Universidade de São Paulo, Instituto de Medicina Tropical de São Paulo, Laboratório de Parasitologia (LIM-46), São Paulo, São Paulo, Brazil

⁴Universidade de São Paulo, Faculdade de Medicina, Departamento de Otorrinolaringologia, São Paulo, São Paulo, Brazil

Correspondence to: Felipe Francisco Tuon Pontifícia Universidade Católica do Paraná, Escola de Medicina, Rua Imaculada Conceição, 1155, CEP 80215-901, Curitiba, PR, Brazil
Tel: +55 41 3271-1555

E-mail: felipe.tuon@pucpr.br

Received: 22 October 2018

Accepted: 23 October 2018

Table 1 - Clinical and laboratorial findings of 13 patients with mucosal leishmaniasis.

N	Sex	Age	Weight	Site	Previous treatment	Interruption due to side effects	Phebitis	Infusion side effects	AKI	CrCl* (mL/min)	Electrolyte disturbance	Myelo-toxicity	Dosage (mg/kg/d)	Cure
1	M	52	93	Palate and pharynx	No	Yes	Yes	Sweat, nausea, chest pain	No	77.2	No	Yes	3.0	No
2	F	72	63	Nasal septum	No	Yes	Yes	Chest pain	No	35	Yes	No	1.7	No
3	M	58	95	Nasal septum	Yes	No	Yes	Fever, sweat, nausea	No	108.2	Yes	No	1.1	Yes
4	F	55	64	Nasal septum	Yes	Yes	No	Chills	No	42.8	No	No	3.1	No
5	M	64	72	Nasal septum	Yes	Yes	No	Nausea and vomits	No	71.8	No	No	2.8	No
6	M	71	44	Palate, pharynx and larynx	No	No	Yes		No	60.2	Yes	No	4.5	Yes
7	F	53	45	Nasal septum	No	Yes	No	Nausea and vomits	No	54.4	Yes	No	2.0	No
8	F	53	45	Nasal septum	No	No	Yes	Nausea and vomits, chest pain	Yes	79.5	Yes	No	2.1	Yes
9	M	57	74	Nasal septum	Yes	No	No		No	62.7	No	No	2.0	Yes
10	F	61	58	Palate and pharynx	Yes	Yes	No	Fever	No	23.8	No	No	4.0	No
11	F	65	49	Palate, pharynx and larynx	Yes	No	No		No	51.6	No	No	3.1	Yes
12	M	57	74	Nasal septum	Yes	No	No		No	43.3	Yes	No	2.0	Yes
13	Male	76	62	Nasal septum and pharynx	Yes	No	Yes		No	52.3	No	No	2.4	No

*creatinine clearance

are safer to use have lower efficacy. ABLC presented a low rate of cure and several side effects, suggesting that the use of this drug is questionable.

Felipe Francisco Tuon¹
 Carolina Rocio Santos²
 Juliette Cieslinski¹
 Regina Maia de Souza³
 Rui Imamura⁴
 Valdir Sabbaga Amato²

AUTHORS' CONTRIBUTIONS

Felipe Francisco Tuon: wrote the manuscript; Carolina Rocio Santos: evaluated the cases; Juliette Cieslinski: reviewed the manuscript; Regina Maia de Souza: microbiological and others tests; Rui Imamura: follow up of patients and manuscript review; Valdir Sabbaga Amato: manuscript review.

REFERENCES

- Amato VS, Tuon FF, Bacha HA, Neto VA, Nicodemo AC. Mucosal leishmaniasis. Current scenario and prospects for treatment. *Acta Trop.* 2008;105:1-9.
- Amato VS, Tuon FF, Camargo RA, Souza RM, Santos CR, Nicodemo AC. Can we use a lower dose of liposomal amphotericin B for the treatment of mucosal American leishmaniasis? *Am J Trop Med Hyg.* 2011;85:818-9.
- Amato VS, Tuon FF, Imamura R, Abegão de Camargo R, Duarte MI, Neto VA. Mucosal leishmaniasis: description of case management approaches and analysis of risk factors for treatment failure in a cohort of 140 patients in Brazil. *J Eur Acad Dermatol Venereol.* 2009;23:1026-34.
- Bagshaw SM, George C, Bellomo R. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. *Nephrol Dial Transplant.* 2008;23:1569-74.
- Sundar S, Murray HW. Cure of antimony-unresponsive Indian visceral leishmaniasis with amphotericin B lipid complex. *J Infect Dis.* 1996;173:762-5.