Acta Tropica 182 (2018) 246–250

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Liposomal amphotericin B treatment of Old World cutaneous and mucosal leishmaniasis: A literature review

Vincent Mosimann[a,b,*], Andreas Neumayr[a,b], Daniel H. Paris[a,b], Johannes Blum[a,b]

[a] Swiss Tropical and Public Health Institute, Socinstrasse 57, 4002 Basel, Switzerland
[b] University of Basel, Petersplatz 1, 4001 Basel, Switzerland

ARTICLE INFO

Keywords:
Cutaneous leishmaniasis
Mucosal leishmaniasis
Old World leishmaniasis
Systemic treatment
Liposomal amphotericin B

ABSTRACT

Old World cutaneous and mucosal leishmaniasis is a potentially serious disease. Systemic treatment approaches with pentavalent antimonials, liposomal amphotericin B, fluconazole and miltefosine are increasingly used despite the absence of supportive evidence – to date, no prospective clinical trials have been conducted for systemic treatment of these diseases.

We performed a literature search to delineate the contemporary evidence for the use of liposomal amphotericin B, and found that although cure rates of 17/20 (85%) were achieved in immune competent patients with Old World cutaneous leishmaniasis and cure rates of 10/13 (77%) for Old World mucosal leishmaniasis due to *L. infantum*, the available data is highly limited with high variation in total treatment dosages. The presented findings reflect a lack of consensus on the optimal treatment dosage and on the schedule of application.

1. Introduction

Old World cutaneous leishmaniasis (OWCL) varies widely in its cutaneous presentation, ranging from a single circumscribed skin lesion, that may heal spontaneously, to large and multiple locally destructive forms, as well as rare cases presenting with mucosal involvement (OWML). Appropriate treatment depends on the clinical features of the lesion and the infecting *leishmania* spp. (Blum et al., 2014). Uncomplicated cases of OWCL caused by *Leishmania major* may have a self-limiting course showing spontaneous healing without antiparasitic treatment. In most other cases local treatment such as intralesional pentavalent antimonials in combination with local cryotherapy, topical paromomycin or thermotherapy is indicated. Only in patients with OWML or with complicated cutaneous leishmaniasis (CL) – defined as (i) more than three lesions, (ii) lesions with diameters > 30 mm, (iii) lesions in anatomic locations unsuitable for local treatment, and/or (iv) lesions refractory to local therapy – systemic treatment is recommended (Blum et al., 2014; Blum et al., 2012).

Common drugs for systemic treatment of OWCL and OWML are pentavalent antimonials, liposomal amphotericin B (L-AmB), fluconazole and miltefosine. Up to date, no prospective clinical trials have been conducted, comparing the efficacy of any of these drugs and the choice of either regimen is currently entirely based on retrospective case descriptions and case series.

Amphotericin B targets the membrane of promastigotes and amastigotes and is mostly given intravenously. In contrast to miltefosine and pentavalent antimonials, L-AmB is registered and available in most countries and is approved for use during pregnancy (Morgan et al., 2007; Fontenele e Silva et al., 2013). L-AmB has a role in the treatment of visceral leishmaniasis (VL) as efficacy of 95–100% and has been reported in the Indian subcontinent (*L. donovani*) and in Southern Europe (*L. infantum*) (Sundar et al., 2008; Cascio et al., 2004). Surprisingly despite the good data on VL, there are nearly no data on Old World CL and ML. Also the role of L-AmB in New World CL and ML has yet to be defined since only case reports and small case series are reported. Due to its extensive use in fungal infections and in VL, the safety profile of L-AmB is well known. To date L-AmB treatment in OWCL and OWML is increasingly used without any underlying scientific evidence, and robust randomized clinical trials are clearly required. To shed light on the contemporary evidence we conducted a literature search focused on the treatment with L-AmB for treatment of OWCL and OWML.

2. Materials and methods

We performed a literature search (PubMed MEDLINE), using the keywords “cutaneous leishmaniasis”; “mucosal leishmaniasis”; and “liposomal amphotericin B”. We included case reports and case series in English; French; German; and Spanish published before 31th December 2016. By applying a two-step review; first the titles and abstracts were reviewed and all publications reporting the treatment outcome(s) of

* Corresponding author at: Swiss Tropical and Public Health Institute, Socinstrasse 57, 4002 Basel, Switzerland.
E-mail address: vincent.mosimann@unibas.ch (V. Mosimann).

https://doi.org/10.1016/j.actatropica.2018.03.016
Received 11 November 2017; Received in revised form 20 February 2018; Accepted 10 March 2018
Available online 14 March 2018
0001-706X/

Table 1
Epidemiologic, clinical and diacnostic data of cutaneous and mucosal leishmaniasis due to *L. infantum/donovani* treated with L-AmB.

	Ref.	Age/sex	Clinical presentation	Immunosuppression	Diagnosis/species (geographical)	Treatment before L-AmB	Treatment regime	Total dose	Outcome	Follow up
1	Hervas	7/m	Lesion on cheek	–	PCR/*L. infantum*	-Topical -Fluconazole	3 mg/kg/d for 13 d	39 mg/kg	Poor response	–
2	Crowe	76/m	Lesion on the face	–	PCR/*L. infantum*	–	3 mg/kg/d 1–5d + 10 + 3month	21 mg/kg	Cure	8 months
3	Paradisi	56/m	Three lesions on the leg	–	PCR/*L. infantum*	-Topical -Itraconazole	3 mg/kg/d for 1–5 d + 14 + 21	21 mg/kg	Cure	9 months
4	Rosal	0.3/m	Lesion on cheek	–	Culture/(*L. infantum*)	- Topical	5 mg/kg/d for 10 d	50 mg/kg	Cure	2 years
5	Richter	58/m	Buccal lesion	Chronic Hepatitis C	PCR/*L. infantum*	–	1 mg/kg/d for 20 days/3 mg/kg/d for 1–10 d + 21	53 mg/kg	Relapse/Cure	30 months
6	Richter	67/f	Buccal lesion	SLE with immunosuppressiv treatment	PCR/*L. infantum*	–	3 mg/kg/d for 1–6 d + 15 + 21	24 mg/kg	Relapse	–
7	Richter	44/m	Nasal lesion	–	PCR/*L. infantum*	–	3 mg/kg/d for 1–6 d + 15 + 21/1 mg/kg/d for 10 d	34 mg/kg	Relapse/Cure	30 months
8	Faucher	65/m	Nasal lesion	HIV (ND)	PCR/*L. infantum*	–	10 mg/kg/d for 2 days (IM)	20 mg/kg	Cure	–
9	Faucher	40/m	Vocal cord lesion	–	PCR/*L. infantum*	–	3 mg/kg/d for 1–5 d + 10	18 mg/kg	Cure	1 month
10	Leitner	49/m	Lesion on the tongue	–	PCR/*L. donovani complex*	–	3 mg/kg/d for 5d/3 mg/kg/d for 5d	30 mg/kg	Poor response/ Cure	–
11	Pittalis	79/m	Lesion on the tongue	G6PD-deficiency/Asthma with corticosteroid treatment	PCR/*L. infantum*	–	3 mg/kg/d for 1–5 d + 14 + 21	21 mg/kg	Cure	3 years
12	Casolari	53/m	Lesion on the larynx	–	PCR/*L. infantum*	–	3 mg/kg/d for 5 d	15 mg/kg	Cure	1 year
13	Ehlert	50/m	Buccal lesion	NIV (ND, CD4 296cells/uL)	PCR/L. Infantum	–	1 mg/kg/d for 21 d + all 3 weeks	26 mg/kg°	Relapse	–
14	Perez	49/m	Lesion on the larynx	Chronic steroidal treatment	Culture/(*L. donovani*)	–	5 mg/kg/d for 10 d	50 mg/kg	Relapse	–
15	Gökmen	81/m	Lesion on the larynx and CL	–	PCR/*L. infantum*	–	3 mg/kg/d for 1–5 d + 14 + 21	21 mg/kg	Cure	–
16	Madeddu	44/m	Buccal lesion	HIV (ND, CD4 343cells/uL)	IFA/(*L. infantum*)	–	4 mg/kg/d for 1–5 d +10 + 17 + 24 + 31 + 38	40 mg/kg	Cure	4 years
17	Guddo	59/m	Lesion on the larynx	–	*L. donovani complex*	–	0.5 mg/kg/d for 10 d	5 mg/kg	Cure	–

PCR = polymerase chain reaction; IFA = indirect fluorescent antibody; SLE = systemic lupus erythematosus; ND = newly diagnosed.