Received: 17 October 2022 | Revised: 23 January 2023 | Accepted: 25 January 2023

DOI: 10.1002/phar.2784

PHARMACOTHERAPY accp

CASE REPORT

Dosing implications for liposomal amphotericin B in pregnancy

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Abstract

Liposomal amphotericin B (LAmB) is used in the treatment of opportunistic fungal and parasitic infections, including leishmaniasis. Given its lack of known teratogenicity in pregnancy, LAmB is a preferred agent for treatment for these patients. However, significant gaps remain in determining optimal dosing regimens for LAmB in pregnancy. We describe the use of LAmB for a pregnant patient with mucocutaneous leishmaniasis (MCL) using a dosing strategy of 5 mg/kg/day for days 1–7 using ideal body weight followed by 4 mg/kg weekly using adjusted body weight. We reviewed the literature for LAmB dosing strategies, particularly dosing weight, in pregnancy. Of the 143 cases identified in 17 studies, only one reported a dosing weight, in which ideal body weight was used. Five Infectious Diseases Society of America guidelines in total discussed the use of amphotericin B in pregnancy but no guidelines included recommendations for dosing weight. This review describes our experience in using ideal body weight for dosing LAmB in pregnancy for the treatment of MCL. Use of ideal body weight may minimize risk of adverse effects to the fetus compared to the use of total body weight while maintaining efficacy for treatment of MCL in pregnancy.

KEYWORDS
ideal body weight, leishmaniasis, liposomal amphotericin B, mucocutaneous, pregnancy

1 | INTRODUCTION

Leishmaniasis is a zoonotic disease caused by a flagellated protozoan parasite transmitted by the bite of a female sandfly.[1,2] Infections are divided into three primary forms: cutaneous leishmaniasis (CL), mucocutaneous or mucosal leishmaniasis (MCL), and visceral leishmaniasis (VL).[3] *Leishmania* parasites are traditionally divided into Old World (Eastern Hemisphere) and the New World (Western Hemisphere) species. More than 1 billion people live in areas endemic for leishmaniasis, with an estimated 30,000 new cases of VL and more than 1 million new cases of CL occurring annually.[4] The number of MCL cases that occur is likely often underestimated and misdiagnosed due the heterogeneity of presentation and underrecognition by clinicians in non-endemic regions.[5]

MCL is defined as concomitant presentation of cutaneous disease with distinct ulceration of the mucous membranes of the nose, mouth, pharynx, or larynx.[6] MCL lesions can cause disfigurement and secondary life-threatening infections.[7] MCL is mainly caused by species in the New World *Leishmania* subgenus and *Vianna* subgenus, to which the primary species of *L. braziliensis*, *L. guyanensis*, and *L. panamensis* belong.[8] According to the World Health Organization (WHO), MCL is endemic in Central and South America, with almost 90% of MCL cases occurring in Bolivia, Brazil, and Peru.[9]

Pregnancy is associated with an increased susceptibility to many infectious diseases, including parasitic infections.[10] This is thought to be due to a number of factors. To accommodate the genetic differences between the mother and the fetus and to prevent allogeneic rejection of the fetus, cell-mediated immunity is suppressed.[10]

[Correction added on April 10, 2023 after first online publication. The author order and Jeffrey's ORCID has been updated in this version.]

The Th2-stimulating cytokines dominate and suppress local type 1 T-helper cell responses.[11] Other factors, such as CD-4 function downregulation and decreased lymphocyte stimulation, also play a role in immune modulation in pregnancy.[12–14] Given endemic fungal and parasitic infections are primarily controlled by cell-mediated immunity, they may disseminate more commonly during pregnancy.

During pregnancy, larger CL lesions with a highly exophytic appearance are more typical.[3,15] Additionally, vertical transmission from mother to infant may occur either transplacentally in utero or during labor.[16,17] Animal models have demonstrated that vertical transmission can occur in both VL and CL/MCL.[18] Miscarriages, preterm births, small-for-gestational-age infants, and fetal loss/stillbirths have been described in both VL and CL/MCL.[15,19,20]

Although various treatment options exist for MCL, pregnancy significantly limits the number of safe agents available. Additionally, management of MCL remains more complex as there have been fewer trials evaluating MCL compared to CL and VL.[21,22] The oral agent miltefosine is the only agent approved by the United States Food and Drug Administration (FDA) for the treatment of CL, MCL, and VL. However, it is contraindicated in pregnancy due to risk for fetal death and teratogenicity observed in animal studies.[23] Traditional options for treatment, including pentavalent antimonial compounds, sodium stibogluconate and meglumine antimoniate, have been shown to increase the risk of miscarriages and preterm births.[24,25] Furthermore, caution is recommended in the first trimester of pregnancy with second-line therapies which include ketoconazole, itraconazole, fluconazole, and allopurinol. Additionally, these agents have also not been extensively studied for the treatment of MCL.[21] The other option for MCL treatment is amphotericin B deoxycholate, which is a polyene antimicrobial agent. Although this agent is considered the systemic treatment option for MCL during pregnancy, common adverse effects such as renal toxicity, electrolyte imbalances, and infusion-related reactions limit its use. Lipid-formulated amphotericin B (AmB) preparations have reduced renal toxicity and infusion-related reactions compared to conventional AmB while maintaining the same effectiveness.[22,26–29]

Significant gaps remain in knowledge of AmB pharmacokinetics and pharmacodynamics in special populations including neonates, children, pregnant, and obese patients.[30] The clinical dosing of medications is typically based on data from studies performed in men and nonpregnant women and does not account for the physiologic differences specific to pregnant women.[31] This remains true for liposomal amphotericin B (LAmB), where the FDA-recommended dosing for VL is based on studies from which pregnant women were excluded.[32] Although LAmB is typically dosed using total body weight, whether the same should be done in pregnancy remains unclear. Given AmB exhibits dose-dependent nephrotoxicity, alternative dosing weight strategies may be considered to reduce adverse effects while retaining efficacy.[33]

Due to the potential risks to mother and fetus associated with MCL, LAmB was initiated in the following patient case. We reviewed the literature to determine dosing strategies for LAmB during pregnancy. Our findings from the literature review and dosing weight strategy rationale are described.

2 | CASE REPORT

A 40-year-old female, estimated 34 weeks gestation, presented to the emergency department with skin lesions to the nose, forehead, and arm. On admission, the patient's body mass index was 30.5 kg/m^2 (weight: 75.6 kg, height: 157.5 cm). These lesions developed over the course of a 7-month journey from Brazil to the United States. A computed tomography of the facial bones revealed mucosal thickening and a large nasal soft tissue mass, extending into the subcutaneous tissue and anterior nasal cavity. Histopathologic evaluation of skin punch biopsies of the arm and forehead lesions were nondiagnostic of leishmaniasis. Based on this clinical presentation, including location of the skin lesions and negative workup for alternative differential diagnoses, the patient was presumptively diagnosed with MCL. Treatment was initiated with LAmB. A fresh-frozen sample of the skin biopsy sent to the University of Washington Medical Center later tested positive by *Leishmania* polymerase chain reaction for *L.* (*V.*) *guyanensis* species complex [*L.* (*V.*) *guyanensis*, *L.* (*V.*) *panamensis*, and *L.* (*V.*) *shawi*], confirming the diagnosis of MCL.[29]

The dosing regimen initiated, while the patient was in her third trimester of pregnancy, was 5 mg/kg daily dosed using ideal body weight for days 1–7. On day 8 of LAmB treatment and after spontaneous labor, the patient gave birth to a healthy male infant weighing 2620 g with an Apgar score of 9 and 9. Treatment continued postpartum with once weekly LAmB dosing using 4 mg/kg with adjusted body weight until resolution or stabilization of skin lesions was achieved. Ideal body weight (kg) was calculated as 45.5 + 2.3 (height [inches] − 60). Adjusted body weight (kg) was calculated as the ideal body weight + 0.4 (total body weight − ideal body weight). A total LAmB dose of 55 mg/kg was administered over the course of 8 weeks (Table 1). During the treatment course, no adverse events occurred. Potassium and magnesium were repleted per standard of care during the inpatient portion of the treatment course.[29]

TABLE 1 Liposomal amphotericin B dosing regimen for treatment of mucocutaneous leishmaniasis in pregnancy.

	LAmB-dosing regimen
Days 1–7	5 mg/kg/day based on IBW
Patient gave birth	
Day 14	4 mg/kg based on AdjBW
Day 21	4 mg/kg based on AdjBW
Day 28	4 mg/kg based on AdjBW
Day 35	4 mg/kg based on AdjBW
Day 42	4 mg/kg based on AdjBW

Abbreviations: AdjBW, adjusted body weight; IBW, ideal body weight; LAmB, liposomal amphotericin B.

In addition to LAmB therapy, the patient underwent three nasal debridements at the 1, 4, and 6 month marks. Following the second nasal debridement, the skin lesions continued to improve, and no new skin lesions were noted. Six months posttreatment, the patient remains in good health with ongoing follow-up with infectious disease and ears, nose, and throat providers. To the best of our knowledge, the infant has had no complications and continues to receive routine childhood care. Both mother and infant will remain under active surveillance for at least 1 year posttreatment due to risk of recurrence.

3 | AIM

We sought to systematically evaluate the literature for dosing strategies with LAmB in pregnancy. The review encompassed dosing strategies in pregnancy using LAmB for all indications with a particular interest in reviewing the dosing weight used for LAmB during pregnancy.

4 | METHOD

Using the PubMed database, we searched all case reports of LAmB use in pregnancy. The MeSH terms used for the search were as follows: "liposomal amphotericin B," "L-AmB," and "pregnancy." Inclusion criteria for the studies were as follows: (i) patient was pregnant at the time of treatment; (ii) LAmB dosing strategy during pregnancy was described; and (iii) study design included randomized controlled trials and prospective (prospective cohort) or retrospective (case–controlled studies, retrospective cohort) observational studies. Studies were also included regardless of indication for LAmB use. Studies were excluded if they were conducted in nonhuman subjects, or if they did not include LAmB dosing and duration of use.

Review articles that appeared in the search were analyzed for additional case reports and studies.

We also searched the Infectious Disease Society of America (IDSA) guidelines for any references that discussed use of AmB in pregnancy.

We analyzed the timing of LAmB use relative to the pregnancy (e.g., first, second, or third trimester) as well as dose strength, duration, and dosing body weight reported.

5 | RESULTS

Our search strategy identified 40 unique studies. Of these, 12 were excluded at the title and abstract screening stage, leaving 28 full text articles for review. Nine studies met inclusion criteria. An additional eight studies were included after searching the references of included studies. In total, 143 cases across 17 studies of LAmB use in pregnancy were included in this review (Figure 1).[17,34–49]

In the identified cases, 39 uses (27.3%) of LAmB occurred in the third trimester, 41 uses (28.7%) in the second trimester, 26 uses (18.2%) in the first trimester, and 30 cases (21.0%) did not specify the trimester. Seven cases (4.8%) were reported using total mean gestational age. Of the indications for LAmB use, 140 cases (97.9%) described LAmB use for VL, two cases (1.4%) for blastomycosis, and one case (0.7%) for pulmonary histoplasmosis. Doses ranged from 3 to 7 mg/kg given on consecutive days, alternating days, and on a weekly basis (Table 2).

At the time of our review, only one publication discussed the use of a dosing weight for LAmB which was used for treatment of pulmonary histoplasmosis in pregnancy.[29,43] No cases were found describing dosing weight of LAmB to treat MCL in pregnancy. The remaining studies included dosing strength and duration, but no description of dosing weight used. No studies identified patient-specific factors (e.g., trimester, weight, and organ function) that influenced choice in LAmB dose or frequency.

Of the 143 cases reviewed, one case reported electrolyte abnormalities of hypomagnesemia and hypokalemia related to LAmB therapy. There were nine (6.3%) premature births, seven (4.9%) miscarriages, and one (0.7%) stillbirth. One maternal death occurred following one dose of LAmB.

Maternal cure by the end of treatment or at follow-up was reported for 117 (81.8%) cases. Of these cases, 112 reported cure while five reported lack of cure or patient death during treatment.

Infant outcomes were reported for 33 (23.1%) of the cases. Six cases of VL across three studies reported vertical transmission from mother to fetus. Two of the cases of vertical transmission were also in cases of lack of maternal cure.

Five IDSA guidelines in total discussed the use of AmB in pregnancy.[21,50–53] VL guidelines provided recommendations for using LAmB specifically. Blastomycosis and histoplasmosis guidelines recommended lipid formulation AmB, and coccidioidomycosis and candidiasis guidelines recommended AmB (Table 3). No guidelines included recommendations for dosing weight in pregnancy.

6 | DISCUSSION

This case of a pregnant patient with MCL presented several challenges in selecting a treatment strategy. First was the limited information available for treating MCL during pregnancy. Guidelines are available for treatment of CL and VL during pregnancy, but not for MCL.[21] For treatment of VL during pregnancy, LAmB is recommended.[21] However, whether the same dosing strategies should be used for managing MCL in pregnancy remains undetermined.

Antimonials, AmB, pentamidine isethionate, and more recently, the oral drug miltefosine constitute the therapeutic armamentarium for systemic treatment of CL and MCL. The FDA-approved oral agent miltefosine for treatment of CL, MCL, and VL is contraindicated in pregnancy due to risk for fetal death and teratogenicity observed in animal studies.[23] There are also increasing levels of resistance against antimonials and potentially miltefosine which is an important

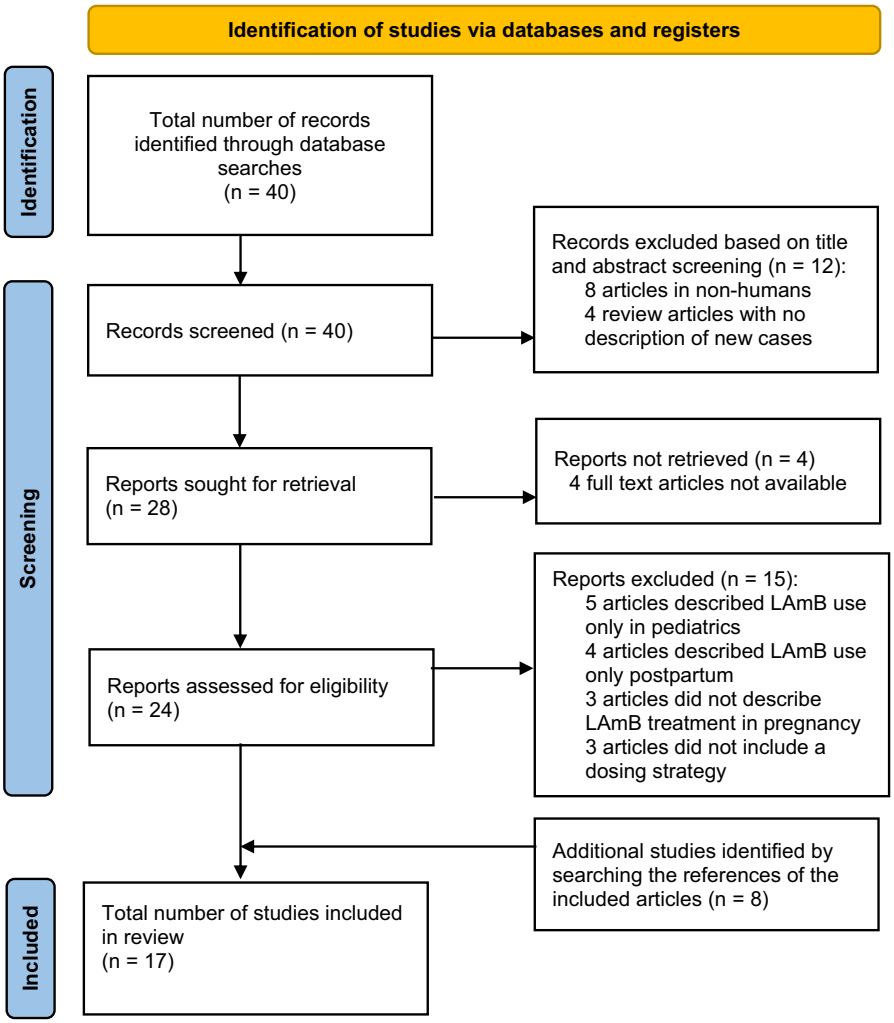

FIGURE 1 Preferred Reporting Items for Systematic Reviews (PRISMA) flow diagram of publications screened. LAmB, liposomal amphotericin B.

drawback in the treatment of leishmaniasis.[54] Amphotericin B deoxycholate has been used as rescue therapy for CL and MCL. However, newer lipid formulations are better tolerated. No randomized controlled clinical trials of AmB formulations have been completed for CL/MCL and standard dosage regimens have not been established.

AmB has demonstrated to be a safe systemic antifungal drug in pregnancy. Reproduction studies of LAmB conducted in rats and rabbits showed no fetal harm at doses up to 0.8 times the human dose.[55] Although no randomized controlled studies have been conducted in pregnant women using LAmB, case reports of patients using LAmB during various stages of pregnancy also point to the safety and efficacy of LAmB (Table 2). In one study comparing LAmB to sodium stibogluconate for VL treatment in pregnancy, no spontaneous births occurred in any trimester for the LAmB group with doses up to 7 mg/kg/day.[56]

LAmB has a unique composition, containing cholesterol and charged phospholipids, which stabilize the liposomes and prolongs time in plasma. As a result of sequestering the drug in long-circulating liposomes, LAmB increases total AmB concentrations while decreasing free AmB concentrations in the plasma. Additionally, the liposomal formulation enables targeting of the drug to tissues via the uptake of intact liposomes.[56] Thus, tolerance is greatly improved and adverse effects including electrolyte abnormalities and nephrotoxicity are reduced. Using liposomal formulations, it is possible to deliver larger doses of the drug over shorter periods of time.[57]

Only one article from our review described a specific dosing weight for the use of LAmB in pregnancy.[43] The authors describe using ideal body weight for treatment of pulmonary histoplasmosis for a patient in the second trimester of pregnancy. Although there is limited information on the dosing weight for LAmB in pregnancy, one study in obesity showed that there is an increased risk of side effects from LAmB, particularly nephrotoxicity, and early discontinuation of therapy when total body weight is used.[58] For dosing with LAmB 5 mg/kg in obese patients with invasive fungal infections, the use of adjusted body weight was associated with a lower incidence of nephrotoxicity development and no significant difference in efficacy compared to total body weight. For those dosed with LAmB 3 mg/kg, there were no differences in safety or efficacy outcomes for adjusted body weight versus total body weight.[58]

No case reports were found for the treatment of MCL during pregnancy with LAmB at the time of this systematic review. The publication of the case report described in this review represents the first case in the literature.[29] Because of this, a unique dosing strategy was designed for treatment of our patient. The proposed

TABLE 2 Summary of studies with dosing regimens for liposomal amphotericin B in pregnancy.

References	Study type	Number of patients	Trimester	Indication	LAmB dosing	Dosing weight used	Reported maternal outcomes	Reported fetal outcomes
Pekelharing et al.[34]	Retrospective cohort study	85	First: 26.8% Second: 35.1% Third: 38.1%[a]	VL	LAmB 5 mg/kg for 6–12 doses (30–60 mg/kg total)	No information provided	For patients with VL in pregnancy, initial cure was achieved for 61% treated with LAmB 30 mg/kg, while 35.6% required extension of treatment to achieve initial cure. Overall, initial cure rates were 96.5% and the mortality was 1.8% in the cohort of pregnant women with VL A total of 20% of patients experienced an adverse pregnancy outcome. Most involved miscarriages in the first trimester or premature deliveries in the third trimester	No information provided
Salih et al.[35]	Retrospective cohort study	23	Not included	VL	LAmB at a total dose of 30 mg/kg, divided into 10 doses of 3 mg/kg on consecutive days. Slow responders received up to a total dose up to 50 mg/kg	No information provided	Treatment responses at 6 month follow-up visits[b]: Final cure: 43% Lost to follow-up: 38% Relapse: 7% Death: 6% Unknown: 6%	No information provided
Mueller et al.[36]	Retrospective cohort study	12	First; 17% Second; 50% Third; 33%	VL	LAmB 3–7 mg/kg on days 1, 2, 3, 4, 10, and 15	No information provided	100% discharged as cured 75% remained pregnant at discharge	No spontaneous abortions occurred during treatment Two healthy infants born during the study One premature infant died after treatment was complete

TABLE 2 (Continued)

References	Study type	Number of patients	Trimester	Indication	LAmB dosing	Dosing weight used	Reported maternal outcomes	Reported fetal outcomes
Figueiró-Filho et al.[37]	Case report	2	Mean gestational age was 28.7 ± 7.8 weeks[b]	VL	LAmB 3 mg/kg/day for 20 days	No information provided	Followed up for at least 1 year and considered to be healthy, free of disease, and in adequate nutritional status on the basis of clinical, serological tests, and bone marrow aspirate[a]	Followed up for at least 1 year and considered to be healthy, free of disease, and in adequate nutritional status on the basis of clinical, serological tests, and bone marrow aspirate
Pagliano et al.[38]	Case series	5	Mean gestational age was 11.8 ± 2 weeks	VL	LAmB 3 mg/kg/day on days 1–5 and 10	No information provided	No case had a rise in blood urea and creatinine levels during treatment. Anti-*Leishmania* antibodies declined until they became undetectable by month 6. No relapse was observed	Five healthy newborns were delivered; Apgar score ranged between 7 and 9, and weight ranged between 3200 and 3700 g At delivery, four newborns had detectable levels of anti-Leishmania antibodies; all became negative within 6 months
Sinha et al.[39]	Observational cohort study	3	Not included	VL	LAmB at a total dose of 20 mg/kg divided into 5 mg/kg on days 0, 1, 4, and 9	No information provided	Successfully treated. LAmB was considered safe and effective	Successfully treated. LAmB was considered safe and effective
Pagliano et al.[40]	Case series	2	Not included	VL	LAmB 3 mg/kg/day on days 1–5 and 10	No information provided	Both patients showed a complete and long-term response	No abnormality was observed in newborns, who were disease-free after 2 years of follow-up
Argy et al.[41]	Case report	1	Second	VL	LAmB 4 mg/kg/day for a total dose of 40 mg/kg, followed by LAmB 5 mg/kg every 15 days until delivery	No information provided	After birth, few intracellular *Leishmania* amastigotes were found during the microscopic evaluation of the placenta, confirmed by positive PCR results of Leishmania parasites	Spontaneous vaginal delivery at 36 weeks. The newborn infant was diagnosed with congenital VL and received an additional course of LAmB
Cunha et al.[17]	Case report	1	Second	VL	LAmB 3 mg/kg/day for 7 days	No information provided	Treatment with LAmB showed significant clinical and laboratorial improvement	The newborn was born healthy at term, with delivery performed without complications

(Continues)

TABLE 2 (Continued)

References	Study type	Number of patients	Trimester	Indication	LAmB dosing	Dosing weight used	Reported maternal outcomes	Reported fetal outcomes
DeWitt et al.[42]	Case report	1	Second	Disseminated blastomycosis	LAmB 3–5 mg/kg/day for 60 days	No information provided.	Complete resolution of symptoms at 9 month follow-up	Delivered at 35 weeks. Healthy without complications at the time of publication
Lewis et al.[43]	Case report	1	Second	Pulmonary histoplasmosis	LAmB 4 mg/kg daily. After 2 weeks, received 4 mg/kg three times weekly for 6 weeks total	Ideal body weight	After 6 weeks of outpatient treatment, a chest X-ray demonstrated no remaining disease	Delivered at 37 weeks without evidence of histoplasmosis
Baker et al.[44]	Case report	1	Third	Disseminated blastomycosis	LAmB 5 mg/kg for 2 weeks	No information provided	At 6 months of therapy, a CT of the chest showed no residual disease	Born full term by normal spontaneous vaginal delivery and was well appearing on exam. Remained healthy at 1 year
Panagopoulos et al.[45]	Case report	1	Third	VL	LAmB 3 mg/kg/day for 5 days followed by two more doses on days 14 and 21	No information provided	One month after treatment, laboratory findings were within normal range and liver and spleen sizes were almost normal. The patient remained healthy at 14 months after integration of treatment with no signs of relapse	Delivered 2 months after treatment, weighing 3480 g, with an Apgar score of 9 and 10. The infant became serologically negative within 6 months of being born. Remained healthy at 12 months after birth
Silva et al.[46]	Case report	1	First	VL	LAmB 4.8 mg/kg/day for 7 days and additional dose on day 10	No information provided	Patient showed clinical improvement, however, without eradication of the parasite	Transplacental transmission not documented
Ritmeijer et al.[47]	Retrospective cohort study	2	Not included	VL	LAmB six infusions of 5 mg/kg on alternate days	No information provided	Discharged without a test of cure but with good response to treatment	No information provided
Zinchuk et al.[48]	Case report	1	Third	VL	LAmB 3 mg/kg on days 1–5 and on day 10	No information provided	Periodic rise in temperature without apparent cause during LAmB treatment	Amastigotes of *Leishmania infantum* identified from bone marrow examination, and patient received further treatment

TABLE 2 (Continued)

References	Study type	Number of patients	Trimester	Indication	LAmB dosing	Dosing weight used	Reported maternal outcomes	Reported fetal outcomes
Dereure et al.[49]	Case report	1	Second	VL	LAmB 3 mg/kg/day for 5 days followed by sixth dose 10 days later	No information provided	Some small cutaneous lesions and two enlarged lymph nodes remained present. Amastigote forms of *Leishmania* were present on histological sections of one lymph node. The patient was in good health 1 month after treatment	Delivered at term. Normal systemic examination at 6 month checkup

Abbreviations: LAmB, liposomal amphotericin B; PCR, polymerase chain reaction; VL, visceral leishmaniasis.

[a]Outcomes reported for all primary VL patients regardless of pregnancy status.

[b]Includes all study groups.

treatment regimen as shown in Table 1 consists of 5 mg/kg/day using ideal body weight for days 1–7 followed by postpartum dosing of 4 mg/kg weekly using adjusted body weight.

The decision to use ideal body weight to treat MCL in the pregnant patient was made based on both disease state and patient-specific factors. A higher dose of 5 mg/kg was opted given that disseminated MCL in pregnancy is considered more refractory to treatment with standard dosing.[59] *L. (V.) guyanensis* can also have increased disease severity and resistance to anti-Leishmanial drugs.[54,60,61]

As the patient was pregnant at the time of therapy initiation, we also wanted to avoid administering a supratherapeutic dose and increasing risk of toxicity. Physiologic changes that occur in pregnancy and affect medication pharmacokinetics are complex. Several factors were taken into account for consideration of dosing weight to minimize toxicity. Circulating plasma volume increases by 30–40% above nonpregnant volumes beginning as early as 6–8 weeks of gestation and peaking at 28–34 weeks.[62] Serum albumin concentration also drops during pregnancy by 20%–40%, increasing the concentration of free drug in the plasma.[63] LAmB produces higher drug levels in the plasma and higher levels of AmB in the tissue compared to other formulations.[38] The nonliposomal pool of AmB present in the plasma after LAmB administration is 95%–99% protein bound and confined to the plasma, as evidenced by a volume of distribution of 0.22 L/kg.[56,64] Given AmB is largely protein bound, we anticipated an increase in the proportion of free AmB per LAmB dose while administered during pregnancy. The use of total body weight to dose LAmB in pregnancy may increase the overall pools of liposomal and nonliposomal AmB in the plasma and in turn increase the risk of nephrotoxicity. Like other tissue, AmB also crosses the placenta and achieves therapeutic concentrations in the fetal circulation, with cord blood: maternal serum ratios ranging from 0.38 to 1.[65,66] Use of ideal body weight further minimizes risk of adverse effects to the fetus compared to the use of total body weight.

Although glomerular filtration rate and renal blood flow increase by 50%, as early as 14 weeks in pregnancy, leading to decreased half-lives of medications, the terminal half-life of LAmB is longer than 5 days.[67] The use of ideal body weight over total body weight would not likely cause underdosing via elimination given the drug is dosed every 24 h. Therefore, ideal body weight was chosen as it more closely approximates a prepregnancy weight and excludes accumulated fluid weight experienced during pregnancy. Additionally, the patient was uncertain of her prepregnancy weight. Another option to consider is using a patient's prepregnancy weight, particularly if the prepregnancy weight closely approximates the patient's ideal body weight.

LAmB dosing was switched to 4 mg/kg weekly using adjusted body weight postpartum. Using the patient's postpartum adjusted body weight with 4 mg/kg achieved the same dose as using ideal body weight with 5 mg/kg. In total, the patient received 55 mg/kg of LAmB over 8 weeks.

Although lipid formulations of AmB including LAmB are recommended across guidelines for the treatment of fungal and parasitic infections in pregnancy, there is no standardization across LAmB-dosing regimens.[21] This is compounded by a lack of consistency in reporting parameters for LAmB dosing in pregnancy. In particular, there is a lack of reporting on the dosing weight used to dose LAmB

TABLE 3 IDSA practice guidelines with amphotericin B recommendations in pregnancy.

Pathogens	Practice guidelines	Amphotericin B recommendations in pregnancy
Blastomycosis	IDSA[50]	Lipid formulation AmB 3–5 mg/kg/day
Candidiasis	IDSA[51]	AmB is the treatment of choice
Coccidioidomycosis	IDSA[52]	First trimester nonmeningeal coccidioidal infection: IV AmB First trimester coccidioidomycosis: intrathecal AmB
Histoplasmosis	IDSA[53]	Lipid formulation AmB 3–5 mg/kg/day for 4–6 weeks
Visceral leishmaniasis	IDSA/ASTMH[21]	The benefits of antileishmanial therapy during pregnancy typically outweigh the potential risks to the fetus—particularly if persons are treated with LAmB

Abbreviations: AmB, amphotericin B; ASTMH, American Society of Tropical Medicine and Hygiene; IDSA, Infectious Diseases Society of America; IV, intravenous; LAmB: liposomal amphotericin B.

in pregnancy. As the safety of LAmB in pregnancy has been established, randomized controlled trials to determine optimal dosing regimens of LAmB across indications in pregnancy are warranted. In addition, pharmacokinetic and pharmacodynamic studies of LAmB in pregnancy warrant investigation including physiologically based pharmacokinetic modeling.

7 | CONCLUSION

The literature describing dosing weight for LAmB in pregnancy is limited and pregnancy-specific dosing guidelines are lacking. Based on LAmB pharmacokinetics and pharmacodynamics in pregnancy, use of ideal body weight to dose LAmB in pregnancy represents a valid option for reducing risk of adverse effects while retaining drug efficacy. Given all other available systemic drugs except AmB are contraindicated or restricted for treatment of leishmaniasis in pregnancy, including MCL, further studies are needed to determine optimal dosing for AmB in pregnancy.

ACKNOWLEDGMENTS

The authors acknowledge Catherine Tom-Revzon.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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How to cite this article: O'Grady N, McManus D, Briggs N. Azar MM, Topal J, Davis M, Dosing implications for liposomal amphotericin B in pregnancy. *Pharmacotherapy*. 2023;43:452-462. doi:10.1002/phar.2784