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Feasibility and acceptability of single-dose liposomal amphotericin B for HIV-associated cryptococcal meningitis in low-resource settings: the AmbiOne mixed-methods study

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Introduction

In 2022, the World Health Organization (WHO) recommended a single high-dose liposomal amphotericin B (L-AmB) regimen with fluconazole and flucytosine as induction therapy for cryptococcal meningitis. Data from implementation of this regimen in routine care in low-resource settings remain limited. We aimed to describe mortality outcomes and implementation barriers for the single-dose regimen in low-resource settings.

Methods

We conducted a convergent mixed-methods study comprising a prospective cohort and a qualitative exploration of feasibility, acceptability through semi-structured interviews, and fidelity to the WHO package of care (L-AmB regimen with fluconazole and flucytosine). This package was embedded within routine care across three Médecins Sans Frontières-supported HIV inpatient sites: two specialist HIV units in the Democratic Republic of Congo and Guinea, and one Ministry of Health–led tertiary hospital in Mozambique. Adults (≥18 years) with HIV-associated cryptococcal meningitis received a single 10 mg/kg L-AmB infusion plus 14 days of fluconazole and flucytosine with standardised intracranial pressure (ICP) management and laboratory monitoring, per WHO guidelines. Primary outcomes were 2-week and 10-week mortality.

Ethics

This study was approved by the MSF Ethics Review Board under the AmbiOne protocol.

Results

Of 198 patients screened, 177 were enrolled between December 2023 and January 2026. Median age was 40 years (IQR 32–47); 49% (86/177) were female; median CD4 count was 50 cells/µL (IQR 35–121); 41% (73/177) had Glasgow Coma Score <15; and 39% (67/174) were newly diagnosed with HIV. 2-week and 10-week mortality were 22% (39/177, 95% CI 17–29) and 42% (75/177, CI 36–50), respectively; one (1%) person was lost to follow-up. Median time to death was 14 days (IQR 4–32). Median hospitalisation was 8 days (IQR 5–14). 37% (50/136) were discharged before day 7. Post-discharge mortality to 10 weeks was 25% (34/136). Fidelity to the WHO package of care was variable: 86% (150/177) received L-AmB within 4 hours of diagnosis, and 83% (147/177) received adequate ICP management, but only 34% (61/177) underwent minimum laboratory monitoring. Severe toxicity was uncommon: six (3%) participants had grade III/IV renal impairment, five (3%) had hypokalaemia, and the mean haemoglobin decline was 1.6 g/dL by day 7. Qualitative data demonstrated strong acceptability due to reduced intravenous burden, simplified monitoring requirements, and feasibility of earlier discharge. Hesitancy regarding the high single dose diminished with programme experience.

Conclusions

Implementation of this regimen in low-resource hospital settings was feasible and highly acceptable to healthcare workers. Limited capacity for laboratory monitoring underscored the operational advantage of low-toxicity regimens. While early mortality was comparable to trial settings, substantial post-discharge mortality shifted the main implementation challenge from inpatient management to post-discharge care. Support in the post-discharge period is critical to sustaining survival gains achieved during hospitalisation.

Conflicts of interest

All authors declare no competing interests.