
SAFETY AND EFFECTIVENESS OF HIGH DOSE/LONG DURATION ABLC THERAPY

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Purpose

To determine the safety of high dose/long duration (HD/LD) Amphotericin B Lipid Complex (ABLC) treatment of fungal infections in comparison to low dose/short duration (LD/SD) ABLC therapy.

Methods

A large multi center patient registry, the Collaborative Exchange of Antifungal Research (CLEAR) was used to retrospectively review patients treated with HD/LD (>5mg/kg/d for >12d, median dose of 5.6 mg/kg/d, range of 5 – 10 mg/kg/d for a median duration of 21 days, range of 13 - 182 days) and LD/SD (≤5mg/kg/d for ≤12d, median dose of 4.2 mg/kg/d, range of 0.2 – 5 mg/kg/d for a median duration of 7 days, range of 1-12 days). To be eligible for the CLEAR registry, hospitalized patients must have received at least four doses of ABLC for treatment of a documented or suspected fungal infection. Data were collected for patients treated during January 1996 through November 2000 from 160 hospitals in the United States and Canada.

Results

HD/LD ABLC treatment was used in 309 patients (9% of the CLEAR registry) and 1417 patients were treated with LD/SD ABLC (40% of the registry). A greater preponderance of mould infections was found in the HD/LD patients compared to the LD/SD (28% and 12% respectively, $P<0.001$) and 16% and 9% respectively ($P<0.001$), were diagnosed with multiple fungal pathogens in the HD/LD and LD/SD groups. Infection sites were similar in both groups however in the HD/LD group infections in the CNS (8%), sinuses (12%), liver (4.9%) spleen (1.9%) and eye (1.9%) occurred more frequently compared to the LD/SD group (5% CNS, $P=0.03$; 3% sinuses, $P<0.001$; 2.2% liver, $P=0.008$; 0.6% spleen, $P=0.037$; and 0.3% eye, $P=0.003$).

Median change from baseline serum creatinine (S-Cr) was equal in both groups (0.1 mg/dL) and both populations showed a similar rate of doubling in S-Cr at end of therapy (15% in HD/LD and 13% in LD/SD patients, $P=0.766$).

Patients in the HD/LD group who concomitantly received other potentially nephrotoxic medication(s) did not show an increased risk for developing renal failure as measured by doubling of baseline S-Cr (15% doubling in both HD/LD patients treated and not treated with concomitant nephrotoxins). In the LD/SD dose group 16 % showed doubling of S-Cr from baseline if patients were concomitantly treated with other potentially nephrotoxic drugs compared to 9% in the LD/SD patient group who were not treated with concomitant nephrotoxins. Overall clinical response rate defined by clinician assessments of cured or improved, was 50% and 51% in the HD/LD and LD/SD groups respectively ($P=0.773$).

Conclusion:

ABLC doses of >5mg/kg/d for >12 days does not appear to compromise patient renal function even in patients who receive concomitant nephrotoxic medication(s).