Characterizing Modifiable Risk Factors for Liposomal Amphotericin B Nephrotoxicity

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Background

- Amphotericin B is often used as an alternative agent to first-line therapy due to its adverse effects including potential for nephrotoxicity.
- Several studies have identified nephrotoxicity risk factors and mitigation strategies relating to liposomal amphotericin B therapy.
- At the University of Washington Medical Center (UWMC) Montlake Campus and Fred Hutchinson Cancer Care (FHCC), IV hydration is recommended to mitigate nephrotoxicity secondary to liposomal amphotericin B.

Objectives

To characterize incidence and risk factors for nephrotoxicity secondary to liposomal amphotericin B

Methods

Study Design
- Single center retrospective chart review
- October 1, 2020 through January 1, 2022

Inclusion Criteria
- ≥18 years-old
- Received ≥1 dose of L-AMB inpatient
- History of hematological malignancy or transplant

Exclusion Criteria
- Non-IV administration
- Insufficient data to determine renal function

Statistical Analyses
- Descriptive statistics to characterize baseline characteristics
- Univariate associations using Student t-test and Chi-squared for continuous and dichotomous data, respectively

Results

Baseline Characteristics:

Demographics	N (%)
Age, year, *mean ± SD*	52.6 ± 15.6
Female	27 (35.1%)
BMI, kg/m^2, *mean ± SD*	26.3 ± 6.6
≥1 Chronic Comorbidity	38 (49.4%)
Malignancy Type	
Hematological	41 (53.2%)
HCT	14 (18.2%)
Solid Organ Transplant	5 (6.5%)

Potential Risk Factors *n (%)*	N=77
L-AMB Dose, mg, *mean ± SD*	378 ± 119
L-AMB Dose, mg/kg, *mean ± SD*	4.9 ± 0.7
L-AMB Duration, days, *mean ± SD*	8.2 ± 7.5
≥1 Concomitant Nephrotoxin	67 (87%)
Concomitant Nephrotoxin, *mean ± SD*	2 ± 1.1
Pre-IV Hydration	68 (88.3%)
Post-IV Hydration	53 (68.8%)

Of 100 patients reviewed, 77 were included in the analysis
- 19 excluded for non-IV administration
- 4 for insufficient data)

Concomitant Nephrotoxins	Usage Frequency in all Patients	Frequency of Nephrotoxicity with Use
ACE inhibitors	1 (1.3%)	1 (100%)
Acyclovir (≥10 mg/kg)	19 (24.7%)	7 (36.8%)
Aminoglycosides	2 (2.6%)	0 (0%)
Calcineurin inhibitors	11 (14.3%)	4 (36.4%)
Chemotherapy	4 (5.2%)	1 (25%)
Foscarnet	1 (1.3%)	0 (0%)
Ganciclovir	4 (5.2%)	2 (50%)
Loop diuretics	33 (42.9%)	11 (33.3%)
NSAIDs	1 (1.3%)	1 (100%)
Piperacillin-tazobactam	9 (11.7%)	6 (66.7%)
Vancomycin	42 (54.5%)	14 (33.3%)

Primary Outcomes:

Nephrotoxicity* Outcomes	n (%)
Onset, days, *median (IQR)*	3 (3-6)
Incidence	26 (33.8%)
New renal replacement therapy	9 (11.7%)
ICU level of care required	32 (41.6%)
Mortality during treatment	11 (14.3%)

*based on KDIGO criteria

Secondary Outcomes:

Nephrotoxicity Risk Factors *mean ± SD*	No Nephrotoxicity (n=51)	Nephrotoxicity (n=26)	P-value
Age, year	55.4 ± 16.3	47.3 ± 12.7	**0.03**
BMI, kg/m^2	25.6 ± 5.8	27.8 ± 7.9	0.16
BMI ≥30 kg/m^2, *n (%)*	10 (19.6%)	6 (23.1%)	0.13
L-AMG Dose, mg	359.7 ± 93	414.6 ± 154	0.06
L-AMG Dose, mg/kg	4.86 ± 0.7	4.96 ± 0.8	0.59
L-AMB Duration, days	6.2 ± 6.4	10.2 ± 9.1	**0.03**
≥1 Concomitant Nephrotoxin, *n (%)*	44 (84.6%)	23 (88.5%)	0.79
IV Hydration, *n (%)*	46 (90.2%)	22 (84.6%)	0.47

2-tailed, p<0.05 statistically significant

Conclusions

- L-AMB nephrotoxicity occurred in 1/3 of patients despite high utilization of pre and post hydration
- Nephrotoxicity was associated with younger age and longer durations of therapy
- Despite an early onset of nephrotoxicity, therapy was often continued with ~12% of patients ultimately requiring renal replacement therapy