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Abstract (poster session)

Frequency and impact of nephrotoxicity using different amphotericin B formulations

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Objective: To evaluate the incidence and impact of nephrotoxicity in patients receiving therapy with amphotericin B (AmB) deoxycholate (d-AmB), liposomal AmB (L-AmB), and AmB lipid complex (ABLC), in a clinical practice scenario. Methods: This was a historical cohort study conducted in a 1,200-bed university hospital. Patients admitted between 2003 and 2011, treated with a lipid formulation of AmB were evaluated for inclusion; patients who received d-AmB in the same period were randomly selected for inclusion, in a 3:1 ratio. Data was obtained regarding nephrotoxic drugs use, baseline underlying conditions, AmB exposure,and renal function. Nephrotoxicity was determined according to modified RIFLE criteria. Outcomes included dialysis, hospital mortality, and time to discharge or death. A stepwise logistic regression model was elaborated to evaluate predictors of mortality and nephrotoxicity. Results: A total of 490 patients were studied (d-AmB, n=281; L-AmB, n=111; ABLC, n=98). Mean age was 42 years - d-AmB patients were younger, in comparison to other groups (38 vs 46 years, $p<0.0001$). Median duration of treatment was 8 days. Mean dosing (mg/kg/day) was 0.91, 3.37, and 4.31 (for d-AmB, L-AmB, ABLC, respectively). Patients on L-AmB remained in the hospital for shorter periods after therapy (mean 34 days), in comparison to d-AmB (49 days) and ABLC (55 days) ($p=0.03$). A higher proportion of patients in the d-AmB group were included in the ‘risk’ (53.1% vs 31.7%; $p<0.0001$) and ‘injury’ (25.7% vs 9.9%; $p<0.0001$) RIFLE categories, in comparison to AmB lipid formulations. Rate of ‘failure’ was similar for all drugs (11.7% d-AmB vs 6.2% lipid formulations; $p=0.07$). No difference in dialysis was observed. In a logistic regression model, mortality was associated with need for dialysis (OR 4.9; CI 95% 2.66-9.37; $p<0.0001$) and ICU stay (OR 6.92; CI 95% 4.18-11.75; $p<0.0001$). Other variables that increased mortality were age (OR 1.02 per year), neoplasia (OR 3.36), previous nephropathy (OR 2.06), and shock (OR 3.35). L-AmB use was found to be a protective factor for mortality (OR 0.47; CI 95% 0.26-0.83; $p=0.0095$). Conclusion: results of this large study reinforce the importance of nephrotoxicity associated with d-AmB use, in comparison to the lipid formulations of AmB. L-AmB was associated with better outcomes (lower mortality and shorter hospital stay) when compared to ABLC. Differences in terms of drug composition, distribution, and clearance may explain these findings.