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NEW LIPID FORMULATIONS OF AMPHOTERICIN B

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Amphotericin B has been the standard treatment for invasive fungal infections for over 4 decades. Although no new antifungal agent has surpassed this drug for its broad spectrum of antifungal activity, clinicians have struggled with the impressive side effect profile that includes: infusion related symptoms and thrombophlebitis, fever, chills, malaise, hypotension, azotemia, renal tubular damage, hypokalemia and anemia. Three new lipid formulations of Amphotericin B (AmB) have been introduced recently and they provide significant advantages to the clinician and patient. AmB lipid complex (ABLC, Abelcet®), AmB-colloidal dispersion (ABCD, Amphocil®) and liposomal AmB (AmBisome®). These lipid formulations in general retain the antifungal activity of AmB; they concentrate in liver, spleen, lung and phagocytic cells and have little glomerular toxicity and no effect on hematocrit. This reduced toxicity may be attributed to the finding that AmB toxicity relates to the concentration of free drug and that lipid bound drug is less damaging to cells. However, all but AmBisome® are associated with infusion toxicity related to AmB. Major advantages of these preparations include a lower side effect profile and the ability to administer larger doses over a longer duration than has been possible with AmB. Relative to AmB, C_{max} and AUC are higher and V_d smaller with AmBisome®; C_{max} is lower with ABLC and ABCD; AUC is smaller with ABLC and equivalent with ABCD. In most studies, clinical results with the new lipid preparations have been similar to AmB alone. In the neutropenic patient with cancer, the ability to spare some toxicity may be a major cost-effective advantage, given the large number of medications usually administered. AmBisome®, ABLC and ABCD all have been studied in neutropenic patients and in those undergoing bone marrow transplantation and are well tolerated. In one relevant study, 338 neutropenic adults and children with FUOs were randomized to AmB, 1 mg/kg/d or AmBisome® at 1 or 3 mg/kg/d. Significantly less nephrotoxicity and severe hypokalemia were observed in AmBisome® treated patients with no significant difference in success. Several studies report the successful use of lipid preparations of AmB in patients who are intolerant to conventional AmB. Cost effectiveness analyses are needed to fully assess the cost-benefit of these preparations. Intralipid preparations were associated with increased acute respiratory events and probably should not be used.