
INCIDENCE AND CONSEQUENCES OF NEPHROTOXICITY IN HSCT TREATED WITH EMPIRIC AMPHOTERICIN, MICA FUNGIN OR NO ANTI-FUNGAL AGENT

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When choosing prophylactic anti-fungal regimens in the setting of hematopoietic stem cell transplantation (HSCT) it is imperative that the risk of nephrotoxicity be a major consideration in which agents to use. It has been shown retrospectively that nephrotoxicity in this setting results in increased length of stay and higher costs. We report a prospective study in 21 HSCT patients (11 allogeneic and 10 autologous) in which actual creatinine clearance was measured by a 24 hour urine creatinine clearance (CrCl). A baseline was measured at the start of transplantation and then again at 2 weeks, 4 weeks, 3 months and 6 months after transplant. The incidence of nephrotoxicity (defined as a decline in CrCl by 50% or more from baseline) within the first month of transplantation was 55% in the allogeneic transplants with the incidence being 100% in those who received empiric therapy with conventional amphotericin, 20% with micafungin (FK463), and 50% in patients who did not require any anti-fungal agent. In the allogeneic patients with nephrotoxicity there was an average increased cost of \$54,280 and an average increased length of stay of 13.5 days longer than those without nephrotoxicity. In the autologous HSCT there was a 40% incidence of nephrotoxicity despite only two patients requiring empiric anti-fungal treatment. One of these patients received conventional amphotericin and had a rapid 75% decrease in CrCl and one received micafungin and had a slight increase in CrCl. In the autologous patients with nephrotoxicity there was an average increased cost of \$20,722 and an average increased length of stay of 6 days longer than those patients without nephrotoxicity. The majority of patients who developed nephrotoxicity within the first 30 days of transplant continued to have nephrotoxicity when measured at 3 months and 6 months suggesting that early toxicity also leads to long term toxicity sequelae in these patients.

Conclusions: Based on this prospective study in HSCT patients there is a high risk of nephrotoxicity in both allogeneic and autologous patients. Use of conventional amphotericin resulted in 100% nephrotoxicity whereas patients receiving micafungin only had 16.6% nephrotoxicity. Early nephrotoxicity resulted in increased length of stay and significantly increased costs and long term nephrotoxicity. Based on this data it is imperative that the risk of nephrotoxicity be evaluated when choosing an anti-fungal agent in this high risk setting.