AMPHOTERICIN B AND NEONATAL SYSTEMIC CANDIDIASIS

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ABSTRACT - Systemic candidiasis is a major problem in high risk neonates. Mortality is high but may be reduced by prompt antifungal therapy.

We administered amphotericin B to 22 infants (18 preterm with mean birth weight < 1500g; mean gestational age 32 ± 2 weeks) and 4 full term newborn (mean birth weith, 3100 ± 200g, mean gestational age, 38 ± 3 weeks) infants with systemic candidiasis. During the 10-year period, 22 infants with systemic candidal infection were identified, 10 males and 12 females. Within 5 days of starting therapy, 3 infants died from overwhelming and severe multisystem involvement, including central nervous system candida infection.

Although amphotericin B may have contributed to the death of 4 infants, overwhelming disseminated candida infection was the more likely cause. Our experience supports the opinion that infants tolerate amphotericin B well.

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Key Words: Low birth weight, amphotericin B, neonatal candidiasis

INTRODUCTION

Systemic candidiasis is a major problem in neonates and infants, because of the increased survial of very low birth weight infants and the widespread use of invasive therapeutic and diagnostic techniques.

Prolonged antibiotic therapy has been associated with an increased risk of these hospital - acquired infections, which are a major cause of morbidity and mortality in newborn infants(2-4). Prompt antifungal therapy has reduced mortality especially if therapy is initiated early (3).

PATIENTS AND METHODS

We conducted a retrospective review of premature, full term and low birth weight (LBW) infants with systemic candidiasis at the Children's Medical Center Hospital of Tehran University from January 1, 1989 until December 3, 1997. Systemic candidiasis was diagnosed when candida was isolated from blood, cerebrospinal fluid, suprapubic urine aspirate, aspirates of otherwise sterile body cavities (e.g. pleural fluid, peritoneal fluid) or at autopsy.

The treatment regimens and cumulatative dose of amphotericin B was recorded. The use of other antibiotic agents was also noted.

RESULTS

Twenty-two infants with systemic candidiasis were identified, 10 males and 12 females, the mean gestational age was 28 weeks (range, 30-36 weeks), and mean birth weight was 1000 g (850-1500 g). All were infected by Candida albicans. During the 10 year period the 22 infants with systemic candidiasis represented 0.7% of the total neonatal intensive care admission and 1.5% of all very low birth weight (VLBW) infants. There was no apparent seasonal predilection. Candida was most frequently isolated from blood (18 cases).

Amphotericin B was given once daily as a 4-6 intravenous infusions, diluted in 5 or 10% dextrose water. The initial dose was 0.25 mg/kg and the dose was increased by daily increments of 25% to a maximum dose of 1 mg/kg. The mean cumulative dose of amphotericin B was 22 mg/kg. A test dose was given to 15 infants.

Within 5 days of starting therapy, 4 infants died from severe candidemia and CNS involvement. During therapy with amphotericin B, two infants developed a low urine output and elevated blood urea nitrogen (BUN).

Hypokalemia was observed in both of the two infants (serum potassium was 2.8 and 2.9 meq/l) which resolved without treatment. Evidence of hepatic toxicity during amphotericin B therapy was not observed. Before the commencement of amphotericin B therapy, all infants had received broad spectrum antibiotics (ampicillin and gentamicin or cefotaxime and vancomycin)

DISCUSSION

The antifungal activity of amphotericin B is related to its binding with ergosterol and other sterols of the fungal cell membrane, disrupting its integrity and transport characteristics, resulting in the loss of

intracellular potassium (4-6).

The major side effects of amphotericin B are transient nephrotoxicity, hepatotoxicity, and bone marrow suppression. Baley and coworkers reported 7 out of 10 VLBW infants with systemic candidiasis after treatment (1,3,6).

In contrast, all 5 VLBW infants treated by Johnson and coworkers tolerated therapy well and all survived despite abnormalities of renal, hepatic or hematopoietic function in some of the infants after amphotericin B(2-8).

In our patients, little evidence of toxicity was observed. The transient renal and hepatic abnormalities are more likely related to the systemic infection or other preexisting problems rather than amphotericin B toxicity. Amphotericin B and other antifungal agents, such as flucytosine, are the treatments of choice for severe disseminated fungal infections, but clinical studies have shown that amphotericin B incorporated in unilamellar liposomes (Am Bisome) is effective in the treatment of severe systemic fungal infections in children and adults. Our experience supports the opinion of others who have reported that unlike adults and older children who experience fever,(2-3) chills, nausea, and vomiting, infants and neonates tolerate amphotericin B well(4-7-8).

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