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Liposomal amphotericin B for treatment of neonatal fungal sepsis-experience from a tertiary care centre.

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Abstract

Fungal sepsis is increasing in neonatal intensive care units. Traditionally used drugs like Amphotericin B is often associated with serious side effects. Liposomal Amphotericin B was proved to be a safe alternative in adults but there exists only limited data regarding its use in newborns. We analysed the data from our tertiary level neonatal intensive care unit during the period of November 2011 to October 2012. Only babies with clinical features of sepsis and positive fungal cultures were included in this study. Thirty five babies received liposomal Amphotericin B at a dose of 5 mg/kg once daily during this period. Serial blood cultures, blood counts, septic screening, renal and liver function tests were done before and after starting the treatment for all these babies. Candida albicans was the predominant organism isolated in these babies (55%).Candida glabrata and Candida parapsiliosis were the next. Treatment with liposomal Amphotericin B resulted in survival of 89% of septic babies affected with albicans and 83% of non-albicans. Mean duration of treatment was 18.6+/_1.2days for albicans and 19.1+/-1.2days for non albicans. Mean duration for culture negativity was 11.6+/_2.2 days for albicans and 12.0+/-2days for non albicans. No significant side effects were noted.

Keywords: Newborn, Fungal sepsis, Candida, Liposomal Amphotericin B

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Introduction

Fungal sepsis is increasing in neonatal intensive care units. This is attributed to increased survival of preterm babies, use of broad spectrum antibiotics, parenteral nutrition and invasive procedures [1-3]. Mortality rate in neonatal fungal sepsis varies from 30 to 50 percent [4, 5] .This may be increased if other co-morbidities exist. In recent years there has been an increased incidence of septicaemia due to non- albicans Candida species [5]. Conventional Amphotericin B was traditionally used to treat this condition but with significant side effects. Thrombophlebitis and significant metabolic abnormalities were often noted as side effects of this drug. Nephrotoxicity and hepatotoxicity were other significant side effects [6]. Moreover exposure to light often reduces the efficacy of this drug [6]. Strict storage conditions and difficulty in infusion also restricted the use of this drug in neonatal intensive care units for fungal sepsis. Liposomal Amphotericin B was proved to be a safe alternative but there exists only limited data regarding its use in newborns. We report our experience with newborns who received liposomal Amphotericin B for the treatment of proven fungal sepsis.

Material and Methods

We analysed the data from babies who got admitted to neonatal intensive care unit from Nov 2011 to October

2012. Only babies with clinical features of sepsis and positive fungal cultures were included in this study. Apnoea, shock, bradycardia, hypoglycaemia, respiratory distress, temperature instability, skin colour change and thrombocytopenia were considered as clinical signs suggestive of fungal sepsis. During this period 3100 inborn babies were admitted in this tertiary care neonatal intensive care unit. Thirty five babies whose blood culture grown fungus were included in this study. Out of these 5 were term babies. All babies were investigated with micro ESR, C reactive protein, blood counts, lumbar puncture, serial blood culture, renal function test, liver function test, chest X-ray and ultrasound cranium. Blood cultures were performed using BACTEC method. All these babies received liposomal Amphotericin B (LAMBIN) in a dose of 5mg/kg once daily as IV infusion over 30 minutes. Serial blood cultures, blood counts, septic screening, renal and liver function tests were done before and after starting the

treatment for all these babies. Cessation of symptoms with negative culture was considered as the end point of treatment. Any side effects related to drug administration were noted. Data was expressed in mean ±SD.

Results

Prematurity, perinatal asphyxia, use of broad spectrum antibiotics, parenteral nutrition were the risk factors noted. Skin colour change, thrombocytopenia and apnoea were the common clinical signs identified in these babies.

Table 1. *Risk factors and clinical signs of fungal sepsis*

Risk factors	Number(%)
Prematurity	30(85%)
Broad spectrum antibiotics	30(85%)
Asphyxia	10(28%)
Parenteral nutrition	10(28%)
Mechanical ventilation	10(28%)
Central line	8(23%)
Clinical sign	
Skin colour change	25(71%)
Thrombocytopenia	18(51%)
Apnea	17(48%)
Temperature change	15(42%)
Bradycardia	15(42%)
Respiratory distress	13(37%)
Hypoglycemia	13(37%)
Shock	10(28%)

Candida albicans was the predominant organism isolated in these babies (55%).Candida glabrata and Candida parapsiliosis were the next. Out of the 35 positive culture reports 19 were albicans and 14 were glabrata and 2 were paraspiliosis (Table 2). All the term babies with Candida sepsis had perinatal asphyxia. Maternal genital tract colonization was documented in only three babies. Cerebrospinal fluid cultures were positive for Candida in three babies. Urine culture was negative for all babies. No baby had evidence of joint infection. All these babies received liposomal Amphotericin B in a dose of 5 mg/kg once daily as intravenous infusion over 30 minutes. No infusion-related side effects were noted in these babies. Renal and liver functions did not show significant changes after the treatment. No significant metabolic abnormalities were noted. Transient hypokalaemia was noted in three babies and it subsided without any treatment.

Serial blood cultures revealed the efficacy of liposomal Amphotericin B (Table 2).Treatment with liposomal Amphotericin B resulted in survival of 89% of septic babies affected with albicans and 83% of non-albicans. Mean duration of treatment was 18.6±1.2days for albicans and 19.1+/-1.2days for non albicans. Mean duration for culture negativity was 11.6±2.2 days for albicans and 12.0±2days for non albicans. All three babies with fungal meningitis responded well to liposomal Amphotericin B. Out of the 31 babies who survived only two babies were readmitted in the six weeks follow up. Both these babies showed negative fungal culture during this period.

Table 2. *Type of fungus identified and outcome of treatment*

Species	Number (%)	Survival-number (%)	Duration of treatment (Days Mean+/-SD)	Duration for negative culture (Days Mean±/SD)
Albicans	19(55%)	17(89%)	18.6±1.2	11.6±2.2
Non albicans (glabrata+ parapsiliosis)	16(45%)	14(83%)	19.1±1.2	12.0±2.0

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Discussion

Present study of 35 neonates with severe and prolonged fungal sepsis is the largest series reported from this part of the country on treatment with liposomal Amphotericin B. This study confirms the effectiveness and safety of this drug. Among the cases 89% albicans and 83% of non albicans infected babies survived. All three patients with Candida meningitis also responded with this treatment.Seivers et al and Jarlov et al also demonstrated the high penetrance of liposomal Amphotericin B into central nervous system [7,8]. This is particularly important in newborns, where disseminated infection often affects the central nervous system also.

Initial experience with liposomal Amphotericin B in neonatal fungal infections was described by Lackner and associates [9]. He described two babies with Candida infection. Present study demonstrated high efficacy of liposomal Amphotericin B (89%). The study done by Sarcella and colleagues described a survival rate of 72%, but they started the treatment with 1 mg/kg and increased the dose

stepwise to 5 mg/kg [10]. Leibovitz also described high survival among 40 newborns with fungal sepsis with a dose of 5 mg/kg [11]. Juster-Reicher described survival rate of 92% among 24 babies with fungal sepsis over four years [12]. This study involved only low birth weight babies. In our infants the mean duration of treatment was 18.6 days. This is comparable to Sarcelles et al and Juster-Reicher (21days) but less than that of Lackner et al (26 days).

No major side effect was noted with this drug. This is comparable with other studies. Al Arishi and Weitkamp also described nil toxicity of this drug in their case series [13,14]. Sarcella et al described transient hypokalaemia with this drug. Three of our babies also had hypokaleamia but none of them were clinically significant.

It can be concluded that liposomal Amphotericin B is a safe and effective drug for neonatal fungal sepsis.

References

1. Johnson DE, Thompson TR, Green TP, Ferrieri P. Systemiccandidiasis in very low-birth-weight infants (<1500 grams).Pediatrics 1984; 73: 138-143.
2. Weese-Majer DE, Wheeler Fondriest D, Brouillette RT, Shulman ST. Risk factors associated with candidemia in the neonatal intensive care unit: a case-control study. Pediatr Infect Dis J 1987; 6: 190-196.
3. Ng PC. Systemic fungal infections in neonates. Arch DisChild 1994; 71:F130-5.
4. Butler KM, Baker CJ. Candida: an increasingly important pathogen in the nursery. Pediatr Clin North Am. 1988; 35: 543-563.
5. Leibovitz E, Iuster-Reicher A, Amitai M, Mogilner B. Systemic Candida infections associated use of peripheral venous catheters in neonates: a 9-year experience. Clin Infect Dis 1992; 14: 485-491.
6. Baley JM, Meyers C, Kliegman RM, Jacobs MR, Blumer JL.Pharmacokinetics, outcome of treatment, and toxic effects of Amphotericin-B and 5-flurocytosine in neonates. J Pediatr 1990; 116: 791-787.
7. Sievers R, Neubauer AP, Natzschka J. Liposomal amphotericinB for treatment of a disseminated Candida infection with encephalitis and osteoarthritis in a preterm neonate.Monatsschr Kinderheilkd 1994; 142: 266-268.
8. Jarlov JO, Born P, Bruun B. Candida albicans meningitis in a 27 weeks premature infant treated with liposomal amphotericinB (AmBisome). Scand J Infect Dis 1995; 27: 419-420.
9. Lackner H, Schwinger W, Urban C . Liposomal amphotericin B (AmBisome) for treatment of disseminated fungal infections in two infants of very low birth weight. Pediatrics. 1992; 89: 1259-1261.
10. Scarcella A, Pasquariello MB, Giugliano B. Liposomal amphotericin B treatment for neo natal fungal infections. Pediatr Infect Dis J 1998; 17: 146-148.
11. Leibovitz E, Iuster-Reicher A, Flidel-Rimon O. High-dose (5-7 mg/kg/day) liposomal amphotericin B (AmBisome) in the therapy of neonatal systemic candidiasis in very low birth weight infants: a 6-year experience (1995-2001). In: Program and abstracts of the 10th International Congress on Infectious Diseases; March 11-14, 2002; Singapore. Abstract 30.003.
12. Juster-Reicher A, Leibovitz E, Linder N. Liposomal amphotericin B (AmBisome) in the treatment of neonatal candidiasis in very low birth weight infants. Infection. 2000; 28: 223-226.
13. Al Arishi H, Frayha HH, Kalloghlian A, Al Alaiyan S. Liposomal amphotericin B in neonates with invasive candidiasis. Am J Perinatol 1998; 15: 643-548.
14. Weitkamp JH, Poets CF, Sievers R, Musswessels E, Groneck P, Thomas P .Candida infection in very low birth-weight infants: outcome and nephrotoxicity of treatment with liposomal amphotericin B (AmBisome). Infection 1998; 26: 11-15.

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