RISK FACTORS IN NEONATAL ANAEROBIC INFECTIONS

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Abstract- Anaerobic bacteria are well known causes of sepsis in adults but there are few studies regarding their role in neonatal sepsis. In an attempt to define the incidence of neonatal anaerobic infections a prospective study was performed during one year period. A total number of 400 neonates under sepsis study were entered this investigation. Anaerobic as well as aerobic cultures were sent. The patients were subjected to comparison in two groups: anaerobic culture positive and anaerobic culture negative and this comparison were analyzed statistically. There were 7 neonates with positive anaerobic culture and 35 neonates with positive aerobic culture. A significant statistical relationship was found between anaerobic infections and abdominal distention and pneumonia. It is recommended for those neonates with abdominal distention and pneumonia refractory to antibiotic treatment to be started on antibiotics with anaerobic coverage.

Acta Medica Iranica, 45(3): 245-248; 2008

Key words: Neonate, sepsis, anaerobe

INTRODUCTION

Anaerobic bacteria are well known causes of sepsis in adults but there are few studies regarding their role in neonatal sepsis. Incidence of 1.8-12.5 per 1000 live birth has been cited and 13-26 percent of neonatal bacteremia has been ascribed to anaerobes with a reported mortality rate of 4-25 percent (1-5).

In a study performed in 1974 by Chow *et al.*, 23 neonates with anaerobic bacteremia were studied during 3.5 year period corresponding to an incidence of 1.8 cases per 1000 live births and 26% of all neonatal bacteremia during the same period (1). Clinical picture in anaerobic bacteremia was indistinguishable from other causes of neonatal sepsis. Prolonged rupture of membranes, maternal amnionitis, prematurity, fetal distress, foul smelling of amniotic fluid and respiratory distress were the most prevalent accompanied risk factors. In spite of the bad general condition of these neonates at birth there was only one case of neonatal death. They concluded that although anaerobic infections were self limited and of good prognosis it can be the potential cause of significant neonatal mortality and anaerobic culture was regarded necessary in all cases of neonatal sepsis especially if aerobic culture was negative (1). In another investigation Tyler and Albers studied 319 neonates with ruptured membranes (5). Anaerobes were found in 4 cases corresponding to an incidence of 12.5 per 1000 live births and 13% of all cases of neonatal bacteremia. Incidence of anaerobic infections was reported to be 1.8% to 12.5% in Maryland Bethesda Hospital study (3).

Another study was performed by Mitra *et al.* in India by graduating society of medical education and research in which incidence of anaerobic infections and vertical transmission during early onset sepsis in pregnant women with perinatal risk factors were studied (2). 100 neonates were reviewed in this investigation. Anaerobic clostridium was found in

Received: 13 Sept. 2006, Revised: 5 Nov. 2006, Accepted: 17 Feb. 2007

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5% all with clinical symptoms. A total of 15 neonates had aerobic infections. There was no difference between anaerobic and aerobic infections with respect to sex, birth weight, gestational age, and no clinical symptom was regarded specific for anaerobic infections. Anaerobic bacteria were found from vaginal culture in 52% of mothers but without vertical transmission. All neonates with anaerobic infection were improved within 24-72 hours of antibiotic therapy.

This study was conducted to determine the prevalence and related risk factors of anaerobic infection in early onset neonatal sepsis in our hospital.

MATERIALS AND METHODS

This investigation was performed on all the 400 neonates who were under sepsis study during the study period from March 2005 to March 2006. We obtained informed consent from parents off all participants.

Blood samples were taken from antecubital or peripheral veins and were added to BD BACTEC plus anaerobic/F Becton Dickenson and company sparks (MD211 52) after preparation with betadin-alcohol solution. The samples would remain in room temperature before transfer to microbiology department and would be preserved for 14 days in incubator in Bactec 9120 system under 37° C temperature after transfer. Subcultures were done in the case of positive results in chocolate agar for aerobic bacteria and anaerobic blood agar for anaerobic bacteria. Group of neonates with positive anaerobic culture was compared with group of neonates randomly selected from negative anaerobic culture results for perinatal risk factors and clinical manifestations. SPSS software was used for analysis of data, with P value < 0.05 regarded as significant. Chi-squared test and Fisher exact test was used.

RESULTS

Seven neonates among 400 studied cases were positive for anaerobes, which comprised 1.6% of all cases under sepsis study. A total of 35 neonates were positive for aerobes, so there was 42 positive cultures altogether, anaerobic bacteria comprising 16% of total positive cultures. Prevalence of anaerobic infections was 4/1000 live births during the study period. Two patients among 7 anaerobic infections died, corresponding to death rate of 28%. Their death can not be attributed to their anaerobic infection, however. One neonate was the first twin of a 25 week twin pregnancy with birth weight of 470 g who expired in the context of pneumothorax. The other one was a 29 week small for gestational age neonate whose demise was due to pneumothorax and pulmonary hemorrhage.

Anaerobic and aerobic bacteria from 42 neonates and their corresponding death rates are summarized in table 1. There was more than one organism in 3 patients (marked with asterisks in the table). Antibiogram was available for only 5 neonates with anaerobic infection as indicated in table 2. Prevalence of perinatal factors associated with anaerobic infections in neonates with positive culture are shown in table 3. Prevalence of perinatal factors associated with aerobic infections in 35 neonates with positive culture are shown in table 4. Prevalence of clinical manifestations in anaerobic and aerobic infections are as follows in tables 5 and 6.

Table 1. Anaerobic bacteria isolated from 7 neonates and their associated mortality

	Patients	Death
Anaerobic organism		
Propionibacterium	4	1
Eubacterium	1	0
Peptostreptococcus	1(1)*	0
Bacteroides	1	1
Total	7	2(28%)
Aerobic organism		
Staph epidermidis	20(3)*	3
Staph hemolyticus	5(1)*	0
Staph saprophyticus	2	0
Staph aureus	1	0
Klebsiella	4(1)*	1
Acintobacter baumanni	2	1
Acintobacter lowffii	1	0
Alcaligenes	1	0
Enterobacter aerogenes	1	0
E coli	1	1
Total	35	6(17%)

Table 2. Antibiogram for 5 neonates with anaerobic infection (4):

	Organism	Penicillin	Imipenem	Metronidazole	Clindamycin
1	Propionibacterium	R	R	R	R
2	Propionibacterium	R	I	R	S
3	Propionibacterium	S	R	R	S
4	Bacteroides fragilis	R	I	R	R
5	Peptostreptococcus	R	I	I	R

Table 3. Perinatal factors associated with anaerobic infection

Risk factor	No. case	No. control	P	Odds	95% CI
Male	4	68	0.835	1.176	0.253-5.470
C/S	5	90	0.925	0.923	0.172-4.964
Prematurity	6	56	0.023	7.821	0.915-66.841
CPR	4	21	0.018	0.146	0.030– 0.700
UTI	1	4	0.230	0.192	0.019-1.992
PROM	2	20	0.397	0.459	0.083-2.530

Table 4. Perinatal factors associated with aerobic infections

Risk factor	No. case	No. control	P	Odds	95%CI
Male	22	197	0.735	0.890	0.452 – 1.751
C/S	25	243	0.879		
Prematurity	21	200	0.976	0.989	0.500 -1.960
CPR	13	84	0.168	1.671	0.819 – 3.412
UTI	2	19	0.985	0.985	0.221 – 4.403
PROM	5	56	0.696	0.825	0.309 -2.205

Table 5. Clinical manifestations in 7 neonates with anaerobic infection

Manifestation	No. case	No. control	P value	Odds	95%CI
Apgar <7	3	29	0.256	2.534	0.536-11.980
Fetal distress	2	8	0.079	0.165	0.028-0.989
Resp distress	7	2	0.000	64.500	16.306-255.133
Hypothermia	1	0	0.014	0.857	0.633-1.160
Pneumonia	3	0	0.000	0.571	0.301-1.085
Abd distention	1	0	0.014	0.857	0.633-1.160

Abd distention=abdominal distention resp distress=respiratory distress

Table 6. Clinical manifestations in 35 neonates with aerobic infection

Manifestation	No. case	No. control	*P* value	Odds	95%CI
Apgar <7	16	120	0.313	0.700	0.352-1.392
Fetal distress	6	59	0.884	0.934	0.374-2.334
Resp distress	13	148	0.437	0.758	0.374-1.537
Pneumonia	6	31	0.174	2.010	0.779-5.192
Abd distention	2	34	0.372	0.539	0.124-2.342
Fever	4	16	0.149	2.507	0.793-7.926
Meningitis	2	1	0.015	20.114	1.779-227.441
DIC	2	8	0.307	2.464	0.504-12.060
MSAF	3	17	0.431	1.719	0.480-6.157

Abd distention= abdominal distention resp distress=respiratory distress.

DISCUSSION

Anaerobic bacteremia existed in 7 out of 400 neonates corresponding to 16% of all positive blood cultures during the study period. This figure is between those of Chow (1) and Tyler-Albers (5) (26% and 13%, respectively). Prevalence of anaerobic infection was 4 per 1000 live births in this study. It was 1.8 and 12.5 per 1000 live births in Chow and Tyler-Albers studies, respectively.

Mortality for anaerobic infections was 28% in this study which is almost equal to the 26% reported in Tyler-Albers study. Considering their underlying factors the cause of death in two mentioned cases can not be attributed to anaerobic infection with certainty (25 and 29 weeks gestational ages and both in the context of pulmonary complications of pneumothorax and pulmonary hemorrhage). The rest of neonates with anaerobic infection responded to antibiotic therapy and had a self limited course. High mortality rate in Tyler-Albers study can be considered to be bias because most reported cases were single case report and only severe cases have been selected. There was only one death in Chow study corresponding to death rate of 4%. This patient had not been treated with antibiotic and had bronchopneumonia associated with multiple anomalies due to 13-15 translocation. Eight cases with anaerobic infection were improved without antibiotic therapy. The most prevalent risk factors in this study were prematurity and cardiopulmonary resuscitation at birth. Prolonged rupture of membrane and maternal amnionitis were the most prevalent associated risk factors in Chow study. More than half of the neonates with positive anaerobic culture had fetal distress, 74% had Apgar of less than 7 at first minute and 57% had respiratory distress. There was a significant relationship between foul smelling amniotic fluid and bacteremia in Tyler-Albers study.

The most prevalent clinical manifestations in anaerobic infections were pneumonia, abdominal distention and respiratory distress in this study. Overall clinical manifestations of anaerobic infections were indistinguishable from aerobic infections both in this and previous studies. With respect to significant relationship between these infections and pneumonia and abdominal distention in this study, it is recommended to investigate anaerobic infection in such clinical conditions that are resistant to empiric aerobic antibiotic therapy.

Conflict of interests

The authors declare that they have no competing interests.

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