NECROTIZING ENTEROCOLITIS IN INFANTS WEIGHING < 2000 G.

Pages with reference to book, From 37 To 39

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ABSTRACT

Over a 4 year period, nine of 180 (5%) infants weighing less than 2000 G,admitted to the Aga Khan University Hospital (AKUH) developed necrotizing enterocolitis (NEC). An outbreak of NEC occurred in 1989, during which six infants developed the clinical illness. Overall incidence was 1.1%. Thirty-one birth weight and gestation matched controls were selected for comparison. Risk factors usually considered as predisposing factors, i.e., low 5 min Apgar score, rate of maternal complications, respiratory distress syndrome, mechanical ventilation, umbilical catheterisation, patent ductus arteriosus, use of antibiotics and feeding practices were found with equal frequency in both cases and controls. Six infants had positive blood and/or peritonealfluid cultures (66%) compared to onlyfive (16%) in the control group (P <0.01). Our data suggests that prematurity and sepsis are important predisposing factors for development of NEC (JPMA 42:37, 1992).

INTRODUCTION

NEC is an acquired disease of premature and term infants admitted to neonatal intensive care units. Two distinct forms i.e., endemic and epidemic have been recognized. In the epidemic form, clustering of cases is superimposed on endemic cases. The usual incidence is between 1-5%, can be as high as 12% in infants weighing_ 1500 G1-3. Most (75-80%) of the cases occur in premature infants4 with a mortality of upto 55%[1-3]. Many factors have been implicated in the pathogenesis of NEC including prematurity[4], birth asphyxia[5] umbilical catheterization[6], exchange transfusion[7,8], respiratory distress syndrome[9], premature rupture of membranes[10], patent ductus arteriosus and hypotension[10]. However, many earlier reports describing risk factors for NEC lacked appropriate controls and subsequent studies found no difference in prevalence of most of the aforementioned risk factors among cases and controll[1,3,11,12], except prematurity. The purpose of this study was to identify risk factors for development of NEC in the newborn population at AKUH.

PATIENTS AND METHODS

A retrospective chart review was conducted of infants who developed NEC after admission to neonatal intensive care unit from December, 1986] December, 1990. The newborn service at AKUH cares for approximately 2000 babies/year including nearly 300 newborn babies admitted to neonatal intensive care unit (NICU). Records of patients and controls were located from indexing coding unit and NICU admission logbook. NEC was diagnosed and staged using the classification of Bell[13]. Cases were included only if an infant experienced a first episode of stage II or stage III NEC. NEC stage I was only included if associated with recognized complications developed e.g., abdominal distension, bilious vomiting and hematochezia. Nine cases were identified according to these criteria. Seven infants had stage II or III NEC. Matched controls for birth weight and gestation were selected for comparison. Six cases (67%) occurred in 1989, majority (83%) occurring between June and July and therefore, all premature infants weighing 700- 1900 G born during the period January-December, 1989 were included in as controls for comparison. In addition for each case, clinical features, laboratory and

radiological findings, treatment and outcome were recorded. All cases with NEC had a full septic workup including lumbar puncture, cessation of oral feeds nasogastric drainage, appropriate I.V. fluids, blood and plasma transfusions were done and cefotaxime and amikacin were administered for 10-14 days, as per NICU policy[14]. Clindamycin was added if there was suspicion of bowel perforation. Laboratory tests were repeated as necessitated by patient's condition. Nutrition support was provided by total parenteral nutrition. All babies were seen by the paediatric surgeon and the usual indication for surgical intervention was radiological and clinical evidence of bowel perforation. The data was analyzed by Chi-square analysis and the two tailed students t test as necessary. Statistical significance was set at 95%.

RESULTS

Nine cases of NEC were diagnosed at AKUH from December, 1986 to December, 1990. All occurred in preterm babies between 30-35 weeks gestation. The overall prevalence of NEC among babies admitted to NICU was 1.1% and was significantly higher in very low birth weight infants 8.7% ($P < 0.0001$). The overall mortality was 44%. The age at the diagnosis ranged from 3-32 days. One infant weighing < 1000g developed NEC at 32 days of age. The rest of the infants had the onset of the illness between 3-25 days. Early and late presentation in relation to gestation or birth weight was not evident from this study.

TABLE I. Common clinical manifestations in patients with NEC.

Clinical manifestations	No. of cases	Percentage
Feeding intolerance	9	100
Abdominal distension	9	100
Bilious vomiting	5	55
Nonbilious aspirates	1	11
Hematemesis	2	22
Hematochezia	6	66
Occult blood	1	11
Pneumatosis intestinalis	2	22
Bowel perforation	5	55
Portal gas	1	11
Shock with DIC*	5	55

*Disseminated intravascular coagulation.

Table I shows the clinical features of NEC in affected infants. Only two patients had an uncomplicated course. Seven (78%) were critically ill. Three patients with bowel perforation underwent surgical exploration, but two died. Two patients, one weighing 720 G with bowel perforation and the other with only evidence of portal gas were managed conservatively and both survived. Two patients weighing 1.2 kg and 1.28 kg had a fulminating course and died at 17 and 50 days of age respectively. No surgical intervention was done in these two cases. There was a male preponderance. The number of infants with intrauterine growth retardation in both groups was equal. All infants had normal hematocrits.

Traditional factors implicated in pathogenesis of NEC were compared between two groups (Tables IT and III).

TABLE II. Comparison of risk factors.

Risk factors	Infants with NEC	Controls
Maternal complications		
Precipitate labour	-	1
Leaky membranes	2	6
PIH*	2	10
Abruptio placenta	2	4
UTI with untreated diabetic ketoacidosis	1	-
Hepatitis	1	-
UTI** (klebsiella pneumonia and resistant falciparum malaria	-	1
All differences are nonsignificant		

* = Pregnancy induced hypertension

** = Urinary tract infection

TABLE III. Comparison of risk factors.

	NEC n = 9	Controls n = 30	P value
Birth weight (gm)	1418 ± 328	1546 ± 350	NS
Gestation (weeks)	31 ± 2	31.6 ± 2.1	NS
Sex			
Male	9	18	< 0.05
Female	0	13	
Apgar score			
<6 at 5 min	3	8	NS
RDS	7	12	NS
TTN	0	3	
Mechanical ventilation	7	9	NS
Umbilical catheterization			
UA*	5	10	
UV**	2	3	
PDA***	5	7	NS
Exchange transfusions	3	3	NS
Prior antibiotic therapy	9	25	NS
Feeding history			
On enteral feeds	7	30	NS
Duration of NPO**** before institution of feeding (days)	3.3 ± 3	3.6 ± 4.4	NS
Daily formula increments (mls/kg/day)	43.0 ± 32.0	59.0 ± 40.6	NS
No. of days to full feeds	5.3 ± 2.2	4.6 ± 5.4	NS
Sepsis	6	5	0.01

Values are mean SD or n (%)
* = Umbilical artery
** = Umbilical vein
*** = Patent ductus arteriosus
**** = Nil per oral

Respiratory distress syndrome, a low 5 mm apgar score, mechanical ventilation, maternal complications, patent ductus arteriosus, use of umbilical catheters, antibiotic use prior to the onset of NEC, exchange transfusion and feeding practices occurred with equal frequency in both groups. All affected infants received a combination of breast milk, an infant formula (Morinage, a commercial brand of infant formula) or Enflac premature formula. Six infants had positive bacterial isolates (5 from blood and one from the peritoneal fluid only). One infant had simultaneous positive blood and peritoneal fluid cultures. The organisms isolated were kiebsiella pneumoniae, enterobacter cloacae, staphylococcus aureus, pseudomonas and enterococcus species. All 4 babies with fatal outcome had positive blood or peritoneal cultures. Two of these cases also developed terminal candidial septicemia.

DISCUSSION

Our patients with NEC are similar to patients described in the literature[1,3,10-12], except for a significant difference in sex distribution betwen the two groups. All infants with NEC were males. This observation could possibly be biased because of the small number of patients in this study. Although aetiology and pathophysiology of NEC remains unclear, many perinatal events have been implicated in its pathogenesis[5-10,14,15]. These factors are thought to be the cause of systemic hypoxia and local tissue hypoxemia[4,16]. However, many controlled studies have contradicted this hypothesis as these factors are not lust confined to NEC infants but are also common in other high risk infants who do not develop NEC[11,17-20]. Similarly we also did not find these factors to be predictive of NEC. Other factors e.g.,

enteral feeds, increments in volume/day and type of feedings were also examined. No differences were found between the groups. Two infants who developed NEC in our series were never fed. These observations do not support previous reports which suggest that aggressive feeding practices have an adverse effect[14,15,21]. All our infants received mixed feedings e.g., breast milk, regular infant formula and enfalac premature formula. Therefore protective effect of breast milk[22] could not be determined. Nonetheless NEC has been reported in infants who were never fed[23] or exclusively breast fed[19]. The role of bacteria in the pathogenesis of NEC remains controversial. There is sufficient evidence to support the hypothesis that an infectious agent contributes to the etiology of NEC e.g., clinical features resembling sepsis, epidemic clustering of cases and interruption of epidemics by infection control measures. Although no common bacterium or virus has been isolated as the cause of NEC, nonetheless, clustering of instances have occurred in the nurseries associated with agents such as escherichia coli, klebsiella, pseudomonas, enterobacter cloacae, salmonella and clostridial species[24-29]. Of these the bacteria most commonly linked with NEC are klebsiella[30], escherichia coli[24] and clostridia[31]. The mechanism by which these bacteria cause the disease is not clear. Lawrence et al[32] postulated that the immature intestine of human neonates may be vulnerable to damage by bacterial toxins following initial colonisation with bacteria. Others have postulated changes in the gut milieu causing suppression of competitive strains of bacteria and overgrowth of virulent bacteria[30]. Other studies have also suggested that clostridial exotoxm is capable of causing direct mucosal injury[31]. In this study infants with NEC had a significantly higher frequency of septicemia i.e., 6/9 (66%) vs 5/31 (16%) in control group ($P< 0.01$). The organisms isolated were pseudomonas (peritoneal fluid and blood in two different patients respectively), kiebsiella (from blood and peritoneal fluid in the same patient), enterobacter cloacae (blood), enterococcus (blood) and staph aureus (blood) in each of the last 3 patients respectively. The frequency of positive blood culture was higher than the 30-35% reported in the literature[33,34]. It is possible that bacterial proliferation may have been responsible for initial injury to the immature intestinal mucosa and predisposed to NEC in our patient population. Although NEC is amultifactorial disease, sepsis may bean important predisposing factor in premature infants in developing countries. With the advent of neonatal intensive care units, this disease will also become more prevalent in this part of the world. Newborn infants especially preterm infants, who present with signs of sepsis and gastrointestinal disturbances, should be thoroughly investigated for this problem.

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