LEADING ARTICLE

NECROTISING ENTEROCOLITIS IN THE NEWBORN INFANT

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SING MED J. 1989; NO 30: 431 – 432

The aetiology of neonatal necrotising enterocolitis (NEC) is unclear and the sequence of events in the pathogenesis of NEC has not been fully established. Many studies support the contention that immature intestinal barrier may be the determining factor for the development of NEC (1-4). The increase in incidence of NEC in the newborn in recent years is seen in many neonatal units. Following advancement in neonatal intensive care, more low birth weight babies, especially the very low birth weight (VLBW) infants (birth weight< 1500gm) are surviving long enough to develop NEC (5,6). Epidemiological studies have not been able to identify all the risk factors for NEC. However prematurity has been shown to be a significant predisposing factor (7).

Though the aetiology of NEC has not been fully established, a few possible precipitating factors are said to be responsible for the development of the disorder. These include (1) gut ischaemia or mucosal injury following hypotension or disturbance of haemodynamics of the vascular supply of the gut, and (2) bacterial proliferation in the gut and (3) effects of enteral feeding (8).

The management of NEC is therefore directed mainly at prevention by modifying the possible precipitating factors. Surgery for NEC is not always satisfactory as the mortality rate of surgical treatment of NEC is high (9) and morbidities are many including colonic strictures, fistulae and the short gut syndrome together with malabsorption and post-operative diarrhoea (10).

Gut ischaemia or mucosal injury may be avoided if hypotension and hypoxaemia are promptly attended to and resuscitation of birth asphyxia is vigorously performed. Exchange transfusion when strongly indicated should be performed cautiously and umbilical arterial catheter removed as soon as possible.

Invasion of the immature gut wall by bacteria may be the starting point for the pathological process of NEC. Modifying the bacterial flora or reducing the bacterial population in the gut should theoretically reduce the incidence of NEC (11). The question whether NEC can be prevented by antibacterial agents deserves more attention. In recent years, attention has been focused on prevention of bacterial proliferation in the gut. The use of prophylactic antibiotics has been advocated. Reports on the prophylactic use of oral vancomycin, kanamycin and gentamicin have been published and the results are inconclusive (11-15).

The neonates has very few plasma cells in the intestinal wall (16). These plasma cells produce secretory IgA (sIgA) thereby conferring the newborn gut the resistance to pathogens that contaminate their gastrointestinal tract. Experiments with germ-free animals indicate that colonisation of the intestine is the main stimulus for initiating IgA production by plasma cells in the lamina propria of the intestinal wall (17). We have not been able to find any report on the use of non-pathogenic organisms such as *Lactobacillus* to colonise the newborn gut in preventing NEC. Theoretically *Lactobacillus* also prevent colonisation and invasion of the gut by other pathogenic organisms and its effects should be as good as bacterial elimination by oral antibiotics. Also, one must bear in mind that widespread use of antibiotics can induce antibiotic-resistant bacteria. At present we are conducting a trial in our Unit on the efficacy of *Lactobacillus* in reducing the incidence of NEC.

Though there were few reports of NEC occurring in infants who have never been fed, NEC indeed often manifests after feeds have been introduced (18). It is hypothesized that gut bacteria require food substrate in order to multiply sufficiently to invade the susceptible bowel wall (11). Also there are very few epidemiological studies to see the relationship of NEC and the age at which feeds were introduced. Since the immature gut is undergoing a process of maturation after birth, delaying feeds would mean allowing more time for maturation of the newborn gut. Therefore feeding a baby at a later age of life would also mean that introducing feeds to an older baby with a more mature intestinal tract, thereby reducing the risk of developing NEC. In one study of neonatal NEC, it was shown that the larger the infant, the earlier was the onset of the disease (19) and this may reflect feeding the bigger babies too early. In another study however, the group of babies with delayed enteral feeds has lower incidence of NEC (11). Other predisposing factors include hyperosmolarity of the infant formula and oral drugs (20), the rate of administration of milk feeds or the volume load within the gut lumen (the rate of or percentage of volume increase of milk feeds) may also lead to gut mucosa damage. A cautious approach to feeding by adopting a slowly progressively feeding regimen has been advocated and virtual disappearance of NEC was reported (21).

Enchancing the immature intestinal barrier by feeding the infant with breast milk which contains many factors such as the immunoglobulins particularly the sIgA, the lymphocytes and macrophages, etc., that potentially mature the barrier (22,23) may prevent the occurrence of NEC.

A large multicentered and collaborative study utilising antenatal corticosteroids showed a significant decreased incidence of NEC in infants treated with steroids (2). There may be some evidence that corticosteroids may reduce the incidence of NEC since they are one of the growth factors implicated in the physiological maturation of the intestinal barrier. It was documented that intestinal cell proliferation occurs after glucocorticoid injection and that mucosal atrophy was observed after adrenalectomy (24). However, such form of treatment requires further investigation.

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