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Antimicrobial Susceptibility of Bacteria Isolated from Newborns with Suspected or Confirmed Necrotising Enterocolitis

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Abstract

Aim. This audit aimed to identify which bacteria were associated with necrotising enterocolitis (NEC) and determine their antibiotic sensitivities.

Methods. A retrospective audit of all infants with a diagnosis of suspected NEC or confirmed NEC and a positive culture (blood/faeces/operative specimen or vascular access device) between January 2000 and September 2007 was performed.

Results. Ninety nine infants had a diagnosis of suspected (45) or confirmed NEC (54). Seventeen patients had suspected (5) or confirmed (12) NEC and a positive culture result. 12 babies had positive blood cultures associated with their NEC. Only 4 of the 12 cases of NEC with a positive blood culture received adequate first line cover for their subsequently identified infecting organism.

Conclusions. Due to the limitations of this study we are unable to make general recommendations on the first line antibiotic choice for babies with suspected or confirmed NEC. Our current regime of Ampicillin, Gentamicin and Metronidazole failed to adequately treat 8 of the 12 organisms subsequently isolated in blood cultures. Only the combination of Vancomycin and Meropenem would have adequately treated all the bacteria identified. The concern with this approach is the possible emergence of multi drug resistant bacteria.

Introduction

Necrotising enterocolitis (NEC) is a common condition in neonatal intensive care units. NEC is potentially life threatening with overall survival after NEC ranging from 70-90% (1).

The initial clinical presentation is variable but may include general deterioration in the patients condition, lethargy, temperature instability, apnoea, shock, peritonitis, pallor, skin mottling, jaundice, bleeding and mild feed intolerance (1). The classic presentation of NEC is a triad of abdominal distension, bloody mucous stools and bile stained aspirates (1).

The exact aetiology of NEC is unknown however multiple risk factors have been identified including prematurity, hypoxia, exchange transfusion, intrauterine growth restriction, loss of mucosal integrity, patent ductus arteriosus, indomethacin, enteral feeds and microbial infection (1, 2). A number of organisms have been isolated from babies with NEC in both epidemics and sporadic cases (2-6). The largest of these (6) was published in 1994 and it is uncertain if the organisms isolated in sporadic NEC are still the same.

Based on local experience the current clinical practice for infants with suspected or confirmed necrotising enterocolitis is to: cease enteral feeds; commence intravenous fluids; aspirate the nasogastric tube regularly; collect a blood culture; commence

antibiotics (Ampicillin, Gentamicin and Metronidazole); perform an abdominal radiograph and arrange paediatric surgical review (7). Antibiotic regimes are adjusted according to organism culture sensitivities once available.

The main objective of this retrospective audit was to identify which bacteria were associated with NEC in our population and determine their antibiotic sensitivities.

Methods

A retrospective audit of all infants with a diagnosis of suspected NEC or confirmed NEC and a positive culture (blood or operative specimen or rectal swab or vascular access device) collected within 72 hours in the Grantley Stable Neonatal Unit, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia between January 2000 and September 2007 was performed. Suspected NEC is defined as symptoms of NEC as described above without abdominal radiograph changes (Includes all Bell (8) stage 1 and some stage 2). Confirmed NEC is defined as symptoms of NEC with abdominal radiograph changes including any of the following: bowel wall oedema; pneumatosis intestinalis; portal vein gas and pneumoperitoneum (includes all Bell (8) stage 3 and some stage 2).

Blood culture bottles were placed in the BacT/Alert® microbial detection system (bioMérieux Inc, Hazelwood, USA). Swabs and catheter tips are directly plated on enrichment broth and then incubated at 35 degrees. They are examined for growth at 24 hours, 38 hours and 7 days. Positive cultures are then inoculated onto Horse Blood agar, Chocolate agar, MacConkey agar and Brain Heart Yeast agar.

Antibiotic sensitivity testing was done using the Vitek®1 (bioMérieux Inc, Hazelwood, USA) method prior to 2005 and the Vitex®2 (bioMérieux Inc, Hazelwood, USA) method subsequently. Disc sensitivity or resistance was determined using CLSI (Clinical and Laboratory Standards Institute) standards.

Results

During this time period 9966 infants were admitted to our nursery. 99 infants had a diagnosis of suspected (45) or confirmed NEC (54). Seventeen patients (Table 1) had suspected (5) or confirmed (12) NEC and a positive culture (blood/faeces/operative specimen or vascular access device) result within 72 hours of onset of symptoms. All cases were sporadic. In total 21 different organisms were identified (see Table 1). Three of these patients had more than one organism identified. One patient had *Staphylococcus aureus* and *Enterococcus faecalis* in a peritoneal swab and *Escherichia coli* in a blood culture. Another patient had *Staphylococcus aureus* and *Alpha haemolytic Streptococcus* isolated from both the umbilical artery and umbilical vein catheter tips. The third patient had *Group B Streptococcus* isolated on a blood culture, *Escherichia coli* on a rectal swab and *Enterococcus faecalis* on operative peritoneal swab. 12 babies had positive blood cultures associated with their NEC.

Table 1: Infecting organism, site of culture and antibiotic sensitivities.

Patient Number	Birth Weight (grams)	Gestational age	Died	Bell staging	Laparotomy	Organism	Culture site
1	790	26+2	No	3	Yes	*Staphylococcus epidermidis*	Peritoneal swab
2	667	25+1	Yes	3	Yes	*Staphylococcus epidermidis*	Peritoneal swab
3	600	23+1	Yes	3	Yes	*Staphylococcus epidermidis*	Blood
4	600	27+3	Yes	3	Yes	*Staphylococcus epidermidis*	Blood
5	800	25+3	No	1	No	*Staphylococcus capitis*	Blood
6	754	25+1	Yes	3	Yes	*Staphylococcus haemolyticus*	Blood
7	2360	35+4	No	2	No	*Staphylococcus aureus*	Blood
8	1059	31+6	No	1	No	*Staphylococcus aureus*	Blood
9	862	26	Yes	3	Yes	*Staphylococcus aureus*	Peritoneal swab
10	3480	41+2	No	3	Yes	*Staphylococcus aureus*	UAC &UVC tips
10	3480	41+2	No	3	Yes	*Alpha haemolytic Streptococcus*	UAC &UVC tips
11	2300	36+5	No	3	Yes	*Group B Streptococcus*	Blood
11	2300	36+5	No	3	Yes	*Escherichia coli*	Rectal swab
9	862	26	Yes	3	Yes	*Escherichia coli*	Blood
12	2860	34+2	Yes	3	No	*Escherichia coli*	Blood
13	730	24+6	Yes	3	Yes	*Escherichia coli*	Bowel tissue
14	1982	31+1	No	2	No	*Escherichia coli*	Blood
15	1565	34+2	No	3	Yes	*Enterococcus faecalis*	Blood
9	862	26	Yes	3	Yes	*Enterococcus faecalis*	Peritoneal swab
16	1200	30+1	No	1	No	*Citrobacter koseri*	Blood
17	835	25+1	No	3	Yes	*Serratia marcescens*	Peritoneal swab

Due to the possibility that organisms identified on peritoneal swab, rectal swab and vascular access device may have only be colonising organisms only those babies with a positive blood culture have been listed with the organism and antibiotic sensitivity in table 2. 5/12 babies with NEC and a positive blood culture died giving a mortality of 42%.

Discussion

Our first line choice of antibiotics for babies with suspected NEC consisting of Ampicillin, Gentamicin and Metronidazole failed to adequately

Table 2: Organisms identified in blood cultures of babies with confirmed or suspected NEC.

Patient	Died	Organism	A	P	F	C	G	I	M	V
3	Yes	*Staphylococcus epidermidis*		R	R		R			S
4	Yes	*Staphylococcus epidermidis*		R	R		R			S
5	No	*Staphylococcus capitis*		R	R		R			S
6	Yes	*Staphylococcus haemolyticus*		R	R		R			S
7	No	*Staphylococcus aureus*		R	S	S				S
8	No	Staphylococcus aureus		R	S					S
11	No	Group B Streptococcus	S	S						S
9	Yes	*Escherichia coli*	S				S			
12	Yes	*Escherichia coli*	S				S		S	
14	No	*Enterobacter cloacae*	R						S	
15	No	Enterobacter faecalis	S							S
17	No	*Citrobacter koseri*	R						S	

A = Ampicillin, C = Cefotaxime, F = Flucloxacillin, G = Gentamicin, I = Imepenem, M = Meropenem, P = Penicillin, V = Vancomycin, R = Resistant, S = Sensitive.

cover the 4 coagulase negative *Staphylococci* and the 2 *Staphylococcus aureus*. Due to the laboratory reporting only limited sensitivities it is uncertain whether the *Enterobacter cloacae* or the *Citrobacter koseri* were sensitive to Gentamicin (they were both resistant to Ampicillin). Our current first line choice of broad spectrum antibiotics (Ampicillin, Gentamicin and Metronidazole) only adequately treated 4 of the 12 cases of NEC and a positive blood .

From our limited data it would appear that only the combination of Meropenem and Vancomycin would have adequately covered all the isolated organisms. While it is often presumed that the infectious agent associated with NEC is bacteria, a number of other organisms, particularly viral have been implicated (3-5). The retrospective nature of this study has limited the search for other possible infecting organisms as viral cultures and rectal swabs are not routinely collected. It is also possible that some of the cases have been incorrectly labelled as NEC when they may have been septic ileus (particularly the 5 cases where there was no abdominal radiograph changes). The small number of babies with a positive blood culture is also a concern however a long time period was examined to identify these cases. Another limitation is that the study is confined to one centre and the external validity of the results is therefore poor.

Importantly there were 77 infants who had no organism identified on blood culture. A large number of babies would therefore need to be treated with Vancomycin and Meropenem to adequately cover the few with positive blood culture. The use of such broad spectrum antibiotics may lead to the emergence of multi resistant bacteria and the initial choice of narrow spectrum antibiotics has been recommended (9, 10). However, we have previously shown that coagulase negative *Staphylococci* have a relatively long incubation time (median 28.9 hours) and thereby continuing with our current antibiotic choice for NEC may significantly delay the commencement of an appropriate antibiotic (11).

Due to the limitations of this study we are unable to make general recommendations on the first line antibiotic choice for babies with suspected or confirmed NEC. Our current regime of Ampicillin, Gentamicin and Metronidazole failed to adequately treat 8 of the 12 organisms subsequently isolated in blood cultures. The only combination of antibiotics that would have adequately treated all the bacteria identified was Vancomycin and Meropenem. The concern with this approach is the possible emergence of multi drug resistant bacteria. Further research is required to determine the best antibiotic regime for babies with suspected or confirmed NEC.

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