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Factors influencing colonisation with gentamicin resistant Gram negative organisms in the neonatal unit

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SUMMARY The proportion of babies colonised with gentamicin resistant Gram negative organisms in a nursery over a 30 month period did not correlate with the quantity or duration of aminoglycosides used, but it did correlate with two indicators of workload: the number of baby days and a score based on the level of nursing care required. Spread of resistant organisms may be more likely as workload increases.

Aminoglycosides are widely used in the treatment of suspected neonatal sepsis so that colonisation and infection with aminoglycoside resistant Gram negative organisms is of major importance. Babies treated with antibiotics for more than three days are more likely to become colonised with Gram negative organisms,[1] and aminoglycoside resistant organisms are more likely to be selected by longer courses of aminoglycosides.[2] Factors other than antibiotic use could be envisaged as being important in determining colonisation with aminoglycoside resistant organisms. It is known that colonisation by organisms with varying sensitivity patterns may fluctuate with time for no clear reason.[3 4] The number of babies in our nursery colonised with gentamicin resistant Gram negative organisms, particularly a gentamicin resistant *Klebsiella oxytoca,* has recently increased. When two babies developed life threatening systemic infections with gentamicin resistant *Klebsiella oxytoca,* we changed from gentamicin to netilmicin as the aminoglycoside used for treating suspected sepsis. We have analysed factors which might be responsible for the emergence of gentamicin resistant Gram negative organisms using surveillance data that were prospectively collected.

Patients and methods

From 1 May 1984 data relating to infection were prospectively collected on all babies admitted to the neonatal unit. The only routine surveillance cultures performed were bacterial cultures of endotracheal secretions taken three times a week from babies receiving artificial ventilation. Bacterial cultures from nose, throat, umbilicus, and rectum and cultures of blood, urine, and cerebrospinal fluid were obtained from all babies with suspected sepsis before starting antibiotics. Specimens were inoculated onto blood agar plates aerobically and anaerobically, MacConkey plates, chocolate agar plates in 5% CO_2, and into cooked meat broth. Organisms were identified according to standard laboratory techniques.[5] Antibiotic susceptibility was determined by the method of Stokes and Ridgway.[6]

The results of bacterial cultures, including the reported antibiotic sensitivities, and the quantity and duration of antibiotics prescribed were prospectively recorded. The number of new aminoglycoside resistant and aminoglycoside sensitive Gram negative organisms cultured in each four week period was recorded. If a baby was colonised with more than one Gram negative organism, each organism was counted. Recolonisation was included if regular cultures showed a baby not to have been colonised for at least two weeks. Identification of organisms was by antibiotic resistance patterns.

The number of babies in the unit each day and the total number of baby days over each four week period was recorded. In addition babies were classified each day as receiving either intensive care, special care, or normal care according to the British Paediatric Association nomenclature.[7] Briefly, *intensive care* signifies continuous skilled supervision by nursing and medical staff, *special care* signifies observation and treatment falling short of intensive care but exceeding normal routine care, while

normal care is that usually given by the mother in hospital under supervision but requiring minimal medical or nursing involvement.

We have analysed variables that might correlate with colonisation by aminoglycoside resistant organisms. Netilmicin resistance was rare; only four babies in 30 months were colonised with such organisms, so the analysis was performed for gentamicin resistant Gram negative organisms, including organisms resistant to both gentamicin and netilmicin. The proportion of babies colonised with gentamicin resistant Gram negative organisms to babies colonised with any Gram negative organism was compared with the number of baby days of aminoglycosides given, the number of baby days of all antibiotics, the weight of aminoglycosides used, the weight of all antibiotics used, and the number of baby days in each four week period from 1 May 1984 until 31 October 1986. The last was used as an index of workload as medical and nursing levels remained virtually constant throughout the 30 month period. In order to get a more realistic measure of workload, based on the estimated relative amount of nursing time required, a workload score was calculated related to the level of care required. Each baby day of intensive care was scored as 5 points, a baby day of special care was scored as 3 points and a baby day of normal care as 1 point.[8] The total score in each four week period was then compared with the proportion of gentamicin resistant organisms. Statistical analysis was by Pearson correlation coefficient.

Results

In May 1984, at the start of surveillance, suspected sepsis was treated with benzylpenicillin (in the first 48 hours) or flucloxacillin (after 48 hours) together with netilmicin. In April 1985 (week 56) we changed from netilmicin to gentamicin. The incidence of colonisation with gentamicin resistant Gram negative organisms, mainly coliforms and Pseudomonas, fluctuated over the next two years (see figure) but there were no cases of systemic sepsis due to these organisms. In November 1986 (week 117), however, not only was there an increase in colonisation with gentamicin resistant Gram negative organisms but two babies developed systemic sepsis.

We suspected that the incidence of gentamicin resistant organisms might correlate with the quantity of antibiotics used. The mean duration of antibiotic courses was analysed for six month periods over the 2½ years. The mean (SD) duration in days of antibiotic courses in each consecutive six month period from 1 May 1984 was 5·45 (4·04), 5·59 (3·66), 4·74 (4·36), 3·61 (4·62), and 4·15 (3·47). It is evident that the increasing incidence of gentamicin resistance was not due to an overall increase in the

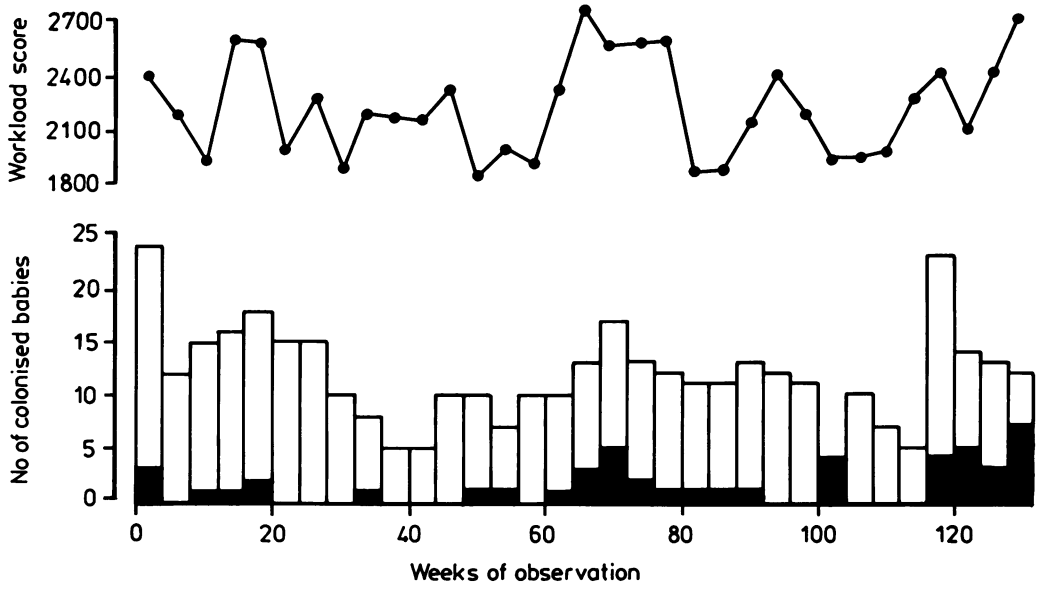

Figure *Relation between workload score in each four week period and number of babies colonised with gentamicin resistant (shaded blocks) and gentamicin sensitive (unshaded blocks) Gram negative organisms.*

duration of antibiotic courses. Furthermore no significant correlation was found between the proportion of gentamicin resistant organisms and the number of baby days of aminoglycosides ($r=0{\cdot}25$, $p>0{\cdot}1$), the number of baby days of all antibiotics ($r=0{\cdot}24$, $p>0{\cdot}1$), the weight in grams of aminoglycoside used ($r=0{\cdot}01$, $p>0{\cdot}1$), nor the weight of all antibiotics used ($r=0{\cdot}01$, $p=0{\cdot}1$).

A correlation was found between the number of baby days in each four week period and the proportion of gentamicin resistant organisms ($r=0{\cdot}42$, $p<0{\cdot}02$). Furthermore the correlation was even stronger between the score based on the level of intensity of neonatal care and the proportion of resistant organisms ($r=0{\cdot}50$, $p<0{\cdot}005$) as shown in the figure.

Discussion

Long courses of aminoglycosides may select for aminoglycoside resistant organisms in an individual baby.[2] The incidence of aminoglycoside resistant organisms in the neonatal unit may depend on other factors such as spread between babies. The importance of handwashing in preventing nosocomial spread of organisms has repeatedly been emphasised.[9] It may be as a corollary of this that understaffing and overcrowding of neonatal units have been shown to correlate with the incidence of infections.[10 11]

We deliberately did not collect colonisation data on all babies as this would have engendered considerable expense. This, however, inevitably made the surveillance incomplete. When more babies were being treated it would be expected that more cultures would be sent. For this reason, although there was also a significant correlation between the absolute number of babies colonised with resistant organisms and workload, this might have been an artefact produced by culturing more babies when the unit was busier. Therefore the best measure of incidence of gentamicin resistant Gram negative colonisation was the proportion of babies cultured who were colonised with gentamicin resistant organisms.

We thought initially that the incidence of colonisation with aminoglycoside resistant organisms would correlate with antibiotic use. Because no such correlation was found we examined other variables relating to workload. We found significant correlations between measures of workload and colonisation with resistant Gram negative organisms. Resistant organisms may be selected in an individual baby by a long course of antibiotics or introduced by a colonised baby transferred from another hospital. We were able to identify one baby in each of these categories as apparently initiating an 'outbreak' of colonisation with a particular resistant organism, although no formal identification was performed other than antibiotic resistance patterns. On other occasions the source of the resistant organism was not found. Spread of resistant organisms between babies may be more likely when the workload is high and normal aseptic precautions become compromised.

Aminoglycoside resistant organisms may colonise babies without causing systemic sepsis.[3 4] We do not change our antibiotic policy on the basis of colonisation data alone, although as colonisation precedes late onset systemic sepsis, widespread colonisation with resistant organisms is worrying. We consider the occurrence of cases of systemic sepsis due to organisms that are not covered by our antibiotic policy to be an indication to change the aminoglycoside in use.

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