Testing Hearing after Daily Gentamicin is not Efficacious

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Introduction

Penicillin and gentamicin are commonly used in combination as intravenous antibiotics in newborn babies where there is any concern about infection. Recommendations on gentamicin dosage and audiological follow up vary. We noticed an apparent high number of toxic levels in our population associated with few audiological side effects. We noticed the anxiety generated in some of the families waiting for hearing tests.

The British National Formulary for Children[1] gives a once daily dose of gentamicin of four to five mg/kg. The Neonatal Formulary used by neonatal units in the Northern Neonatal Network (NNN) suggests five mg daily[2] with the dose interval increased for babies less than 32 weeks gestation. In our units, which are level 1 units within the NNN, we use 5 mg/kg but there was felt to be a high number of trough gentamicin levels greater than 2 mg/l. Trough levels are taken one hour before the third dose is due. Concern about this issue was raised when implementing the National Patient Safety Agency care bundle for gentamicin (NPSA/2010/PSA001).

As an initial check of our practice a telephone survey was performed of the four Neonatal Units within NNN who were asked what dose of gentamicin they used. All used 5 mg/kg. They were also asked if they measured trough gentamicin levels on all babies before their third dose and if the level was high (>2 mg/l) were hearing tests requested. All four units did.

All the trough gentamicin levels on babies treated with gentamicin in County Durham and Darlington NHS Foundation Trust (CDDFT) from May 2010 to May 2011 were reviewed. Doses and timing of levels were checked. Local audiology policy was to do an immediate hearing test and follow up at nine months of age for all babies with toxic (greater than 2 micromol/l) gentamicin levels. Hearing tests were requested for babies according to this protocol and babies followed up to see the results.

Results

One hundred and ninety two babies had received gentamicin and had a trough level performed. Eighty four (43%) levels were higher than 2 mg/l, 62 (74%) of these 84 were in babies less than 37 weeks gestation and 22 (26%) were in term babies. Most were below 3 microg/l but a couple were over 4 microg/l. All cases had a correct dose and timing of gentamicin level.

None had hearing impairment at an initial test. Thirty one (37%) did not attend audiology follow up. None of those who did attend had neurosensory impairment but seven (8%) did have conductive impairment and are awaiting treatment of this before sensorineural loss can be excluded. Forty two (49%) were normal. (full results see table 1).

Table1: *Results of Hearing Tests after 8 Months*

Sensorineural loss	0 (0%)
Conductive loss	7 (8%)
Did not attend follow up	31 (37%)
Normal	42 (49%)
No referral found or unable to test	5 (6%)

Discussion and Recommendation

The Cochrane collaboration has published a review of once daily versus multiple doses daily of gentamicin for treatment in suspected sepsis[3]. The conclusion is that neither regime is superior although once daily dosage causes less toxicity – but they do not suggest a dose. A recently published pharmacokinetic study for once daily gentamicin supported extending the dosage interval in all neonates to 36-48 hours[4]. Four mg/kg may be an alternative lower dose. The National Institute for Clinical Excellence (NICE) is currently consulting on a guideline for neonatal infection that suggests 4.5 mg/kg at 36 hour intervals. Serious ototoxicity is normally only seen in babies who receive two aminoglycosides, a loop diuretic and aminoglycoside or seven to ten days of aminoglycoside[2]. The NHS National Newborn Hearing Screening Program (NHSP) recommends, "Immediate referral to Audiology by Paediatrician (whatever the levels) if child is suspected or known to have the A1555G mitochondrial mutation; otherwise and if high levels, referral to Audiology for behavioural assessment at 8 months, or sooner if Paediatrician feels desirable." [5]

There is not a departmental consensus on optimum dosing but we feel 4.5 mg/kg at 36 hour intervals is safest and adequate for our population. It also has the advantage that if stopped at 48 hours no gentamicin level is necessary.

Given the low incidence of neurotoxicity it would be necessary to test many more babies over many years to pick up one child with hearing impairment due to gentamicin toxicity. This has a financial burden and against a DNA rate of 37% we do not feel it to be justified. We would prefer to target the higher risk babies who receive gentamicin with a diuretic or at least seven days gentamicin. Therefore the department has changed policy to send babies for follow up hearing tests only if they received gentamicin with a diuretic or for seven days. We have therefore reduced the number of trough levels sent as these are only done if it is anticipated more than 48 hours will be needed. The result is used to alter the dosage and frequency but not to determine whether audiology follow up is necessary.

We would be interested to know of others' practice in this area and whether these data would influence them to change practice?

Conclusions

The authors feel that a different dosing schedule for gentamicin is worth considering in this population. 4.5 mg/kg every 36 hours for those aged over 32 weeks seems consistent with the latest guidance. Given the high rate of failure to attend clinic subsequently, follow up hearing testing for this population is not felt to be efficacious and our guideline for local targeted testing is suggested as an alternative.

References

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