P12 STANDARD OR INDIVIDUALISED GENTAMICIN DOSING FOR NEONATES?

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Aim NICE guidance for treatment of suspected early on-set sepsis (EOS) in neonates recommends 5 mg/kg of gentamicin every 36 hours for all, and measurement of a pre-dose trough concentration with dosing adjusted accordingly. At our hospital individualised pharmacokinetics are used to calculate dose and dosing frequency. The study aims to establish if 5 mg/kg of gentamicin every 36 hours is appropriate for all.

Method All babies receiving gentamicin for EOS from birth to 72 hours were included. Patient details including date of birth, gestational age, weight, dose given, administration time, two post-dose blood concentrations and sample time were collated and used to calculate individualised elimination rate constant, half-life and distribution volume. Peak concentrations, 1-hour post-dose and pre-dose troughs were predicted using these pharmacokinetic parameters for both the individualised dosing regime and the standard regime of 5 mg/kg every 36 hours. These were compared with the target concentration:

1 hour post dose peak 8 to 12 mg/L; pre-dose trough less than 1 mg/L.

All data were entered into Microsoft Excel.

Results Ninety-one neonates were studied. Gestational age ranged (mean±standard deviation) 23 to 42 weeks (33±4 weeks). Weight ranged 0.67 to 4.68 kg (2.44±1 kg).

5 mg/kg under-dosed 28 neonates (30%): 5.9–7.9 mg/L, 7.1 mg/L±0.6 mg/L. In such cases a dose of 6 mg/kg would be more appropriate.

Four babies (4.4%) were overdosed: 12.1–14.1 mg/L, 12.7 mg/L±0.9 mg/L. In such cases 4 mg/kg would be more appropriate.

A loading dose of 5 mg/kg was therefore not appropriate in a third of neonates. Monitoring a pre-dose trough concentration will not identify if babies are given too low or too high a dose. There is no established method to predict which patients require a dose of 4 or 6 mg/kg. An individualised approach allows dosing to be fine-tuned from the start of a treatment course, according to each neonate’s unique pharmacokinetic parameters.

In seven neonates (7.7%), dosing every 36 hours would give a trough concentration greater than 2 mg/L.

In 32 neonates (35%), dosing every 36 hours would give a trough concentration greater than 1 mg/L. In such cases an extended dosing interval would be required, unless the trough was high because the initial dose was too much.

Giving gentamicin every 36 hours will achieve a trough less than 2 mg/L as per NICE guidelines in most babies. However if treatment exceeds 3 doses, only 65% of patients would achieve a target gentamicin concentration under 1 mg/L. Longer dosing intervals, or perhaps smaller doses, would thus be needed.

Limitations of the study include the small volume of drug administered to neonates less than 1 kg, with possible administration error which influences reported concentration, and impacts on subsequent pharmacokinetic calculations. Other limitations relate to clinical acuity such as renal function and hydration levels, which were not recorded.

Conclusion Sixty-five percent of neonates treated with 5 mg/kg of gentamicin every 36 hours achieve a 1 hour post dose peak concentration of 8 to 12 mg/L and pre-dose trough of less than 1 mg/L. Thirty-five percent do not. Dosing individualisation is still necessary. The study reports results from an individualised dosing process based on two-timed gentamicin concentrations.