EVIDENCE-BASED CARE SHEET

Gentamicin Use in Neonates

What We Know

› Gentamicin is commonly prescribed for neonates with suspected serious bacterial infection (SBI) (e.g. septicemia, meningitis, severe urinary tract infections) or sepsis. It is used empirically for very low birth weight infants with risk of perinatal sepsis in the first week of life, and infants with proven neonatal sepsis with bacteria known to be gentamicin sensitive[1,5]

- Gentamicin is a bactericidal aminoglycoside antibiotic which inhibits bacterial protein synthesis. It is prescribed to treat infection caused by gram-negative bacteria (e.g., *Escherichia coli*, *Pseudomonas*, *Klebsiella*, *Serratia*) and gram-positive staphylococcus[2,5,7]
- Gentamicin and a β-lactam antibiotic (e.g., ampicillin, penicillin) are routinely prescribed empirically as first-line treatment for suspected SBI in infants who are < 60 days of age[2]

› Gentamicin can be administered IV, I.M., P.O., I.T, and topically[2,5]

- IV and IM routes are given the same dosage per weight. IVinfusionis given over 20-30 minutes.
- Intrathecal route- Gentamicin penetrates the cerebral spinal fluid poorly. Intrathecal route is reserved for infections such as meningitis, ventriculitis or infections which are unresponsive the to IV therapy.
- Gentamicin is poorly absorbed when given orally but can be given orally to prevent necrotizing enterococcus
- Topical gentamicin ophthalmic ointment can be administered to newborns for ocular infection but should not be used as routine prophylaxis for ophthalmia neonatorium.

› Gentamicin has a narrow therapeutic index, and its bactericidal activity is directly related to serum concentration[2,5]

- Peak concentration of 8–10 times the minimum inhibitory concentration (MIC) is recommended (e.g., 5–12μg/mL)[2]

› Peak concentration is achieved 30 minutes after a 30 minute IV infusion and 30–90 minutes after IM injection[2]

› Optimal gentamicin therapy is ensured through individualizing the dose based on the measurements of infant serum drug concentrations[3]

› One dose of gentamicin per day lessens the adverse effects of taking multiple doses a day while showing equal reduction in sepsis; one dose of gentamicin results in fewer failures to attain peak levels of 5 μg/mL[6]

› Gentamicin dose required to reach a therapeutic peak concentration is affected by the volume of distribution (V_D)[1]

› Neonates, particularly those born prematurely or those with sepsis or fluid retention, have an increased V_D because of their higher percentage of extracellular water[1]

› Gentamicin toxicity and the development of adverse effects (e.g., ototoxicity, nephrotoxicity) are directly related to prolonged exposure to sustained low concentrations as indicated by elevatedtrough concentration (i.e., trough concentration is the point at

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which the lowest blood level of the medication is present, which typically occurs just before the next dose is administered)[5]

› Trough should be maintained at < 1–2 μg/mL to prevent toxicity[1,2]

• Trough blood gentamicin concentration levels should be measured before administering a subsequent dose[2,4,5]

› Adjust trough concentration by increasing or decreasing dose interval (e.g., if the trough is too high, increase the period of time between doses to allow more of the drug to clear prior to the next dose)[1]

› Gentamicin is excreted by the kidneys, and a reduction in glomerular filtration rate (GFR) will reduce gentamicin clearance, raise trough concentration, and increase risk for toxicity[1]

› Elevated serum creatinine level, reduced urine output, shock, and inappropriate dosage strategies are risk factors for supratherapeutic trough levels in neonates who are receiving weight-based gentamicin doses[1,2]

› The dose and dose interval are manipulated to maximize the peak concentration while minimizing the trough concentration and preventing nephrotoxicity and ototoxicity[2]

• In neonates extended interval dose (EID)is preferred because it produces higher peak concentrations and nontoxic trough concentrations while reducing risk for adaptive antibiotic resistance[2]

– Guidelines vary, but in general the dose and interval are determined by the gestational age and weight of the neonate (i.e., the lower the gestational age, the higher the dose [related to the higher V_D] but longerdose interval due to low GFR from immature kidneys) [1,2]

- Premature infants dosage recommendation is 4–5 mg/kg IV every 24–48 hours[2,5]

- Term infants dose recommendation is 4–7 mg/kg IV every 24 hours[5]

– Dose and interval must be adjusted for patients receiving indomethacin[2]

– Ototoxicity can occur even at therapeutic serum trough levels; all infants treated Gentamicin for > 48 hours should have their hearing checked[5]

– EID has been associated with a pyrogenic endotoxin-likereaction involving fever, chills, tachycardia, and hypotension[2]

What We Can Do

› Learn about gentamicin use in neonates so you can accurately assess your patients' individualized characteristics and safely administer gentamicin to premature and term neonates; share this information with your colleagues

› Follow facility/unit protocols regarding IV access and neonatal IV administration

› Consult with the pharmacist to evaluate possible drug interactions during gentamicin use; alert the treating clinician of possible drug interactions and of indications (e.g., renal impairment) for altering the dose and/or interval

› Monitor peak and trough concentrations as ordered; inform the treating clinician of values that are outside the recommended range (e.g., peak > 12 μg/mL or < 5 μg/mL, and trough > 2 μg/mL)

› Educate the parents of the neonate regarding the need for antibiotic therapy; assess parental coping ability and provide emotional support and additional information as needed

Coding Matrix

References are rated using the following codes, listed in order of strength:

M	Published meta-analysis	**RV**	Published review of the literature	**PP**	Policies, procedures, protocols
SR	Published systematic or integrative literature review	**RU**	Published research utilization report	**X**	Practice exemplars, stories, opinions
RCT	Published research (randomized controlled trial)	**QI**	Published quality improvement report	**GI**	General or background information/texts/reports
R	Published research (not randomized controlled trial)	**L**	Legislation	**U**	Unpublished research, reviews, poster presentations or other such materials
C	Case histories, case studies	**PGR**	Published government report	**CP**	Conference proceedings, abstracts, presentation
G	Published guidelines	**PFR**	Published funded report		

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