Research Article

Monitoring of Gentamicin Serum Concentrations Among Newborns in the Neonatal Ward at Hospital Sultan Ismail Petra, Malaysia

Adnin Abdullah[1], Nur Adilah A. Rahman[1], Rosnani Ab. Rahman[1], Hafizuddin Awang[2]

1. Department of Pharmacy, Hospital Sultan Ismail Petra, Malaysia; 2. Besut District Health Department, Malaysia

Introduction: Gentamicin is the empirical therapy of choice for sepsis in newborns, with dosing of 4mg/kg every 24 – 36 hours, depending on premenstrual age. The objective of this study was to investigate the therapeutic drug monitoring (TDM) outcomes (within therapeutic ranges or toxic) of the current IV Gentamicin regimen in treating infections among neonates.

Materials and Methods: This retrospective cohort study was conducted at Hospital Sultan Ismail Petra (HSIP). Data were abstracted and collected for neonates treated with gentamicin who were admitted to the neonatal ward from January 2020 to December 2022. Trough and peak levels were measured on the third dose, where the therapeutic ranges were <1.0 mg/L and >5.0 mg/L, respectively. Elevated serum creatinine was defined as a serum creatinine level (SCr) >71 μmol/L. Multivariable logistic regression was performed to identify the risk factors for acquiring toxic trough levels.

Results: A total of 227 patients were included. The total number of patients achieving the targeted peak level was 74.90%. More than half of the patients (52.0%) experienced toxic trough levels. The mean serum trough and peak levels (standard deviation) were 1.23 (1.11) mg/L and 7.31 (3.93) mg/L, respectively. The risk factor associated with toxic trough levels was elevated SCr (odds ratio 2.55, 95% confidence interval [1.19,5.46], p=0.016).

Conclusion: The current gentamicin regimen resulted in an alarming proportion of patients having toxic trough levels, particularly those with elevated SCr. The study findings underscore the need to refine the dosing regimen to optimise efficacy and minimise toxicity in neonates.

Corresponding author: Hafizuddin Awang, drhafizuddin@moh.gov.my

 doi.org/10.32388/Q7JA3H

Introduction

As widely known, Gentamicin is an aminoglycoside that binds to the 30S ribosomal subunit, resulting in the inhibition of the synthesis of bacterial cell walls. One of the main drawbacks of Gentamicin is its nephrotoxicity, as it is predominantly excreted in the urine due to its water solubility characteristic. This nephrotoxin will bind to the proximal tubular brush border membrane, and high concentrations of the drug may lead to proximal tubular damage and cause renal injury[1].

For decades, Gentamicin has been the mainstay empirical therapy for sepsis in newborns, frequently used in combination with beta-lactam antibiotics such as ampicillin or penicillin[2][3]. Sepsis in newborns can cause chronic illnesses, and the mortality rate can reach up to 50% without proper management[4]. Gentamicin is a narrow therapeutic drug that requires therapeutic drug monitoring (TDM) during the treatment period in order to ensure the efficacy of the drug while avoiding toxicity due to the use of Gentamicin.

International guidelines differ in dosing regimens for Gentamicin, ranging from 4-5 mg/kg every 24-36 hours. Current World Health Organization (WHO) guidelines recommend a once-daily dosing regimen, from 3-7.5 mg/kg/day according to age and birth weight[5]. According to currently available knowledge, term infants should receive IV Gentamicin 4.0-4.5 mg/kg every 24 hours[6]. Kidney function is reduced in preterm neonates owing to incomplete nephrogenesis; hence, a longer dosing interval of 36 to 48 hours is recommended for preterm neonates[6].

In Hospital Sultan Ismail Petra (HSIP), neonates who are at risk for neonatal sepsis, such as being premature, having very low birth weight, and maternal factors such as Group B Streptococcus status, presence of chorioamnionitis, or prolonged rupture of membranes, will be treated in the neonatal ward. Gentamicin will be prescribed as the empirical treatment at a dose of 4 mg/kg, either 24 or 36 hours depending on the postmenstrual age, in combination with beta-lactam antibiotics, commonly benzylpenicillin, at a dose of 100,000 u/kg 12 hours or 100,000 u/kg 6 hours based on indication. Peak and trough levels were measured on the third dose of therapy. The therapeutic ranges for trough and peak levels were <1.0 μg/mL and >5.0 μg/mL, respectively.

The standard Gentamicin dosing regimens may not be able to produce the intended therapeutic peak and trough serum concentrations in all patient populations. Hence, determining factors correlated with

undesirably high or low peak or trough values could be useful to neonatal practitioners in predicting which patients are most likely to have serum drug levels outside the therapeutic range[7].

Methodology

This study was conducted in the neonatal ward at Hospital Sultan Ismail Petra (HSIP), Kuala Krai, Kelantan, Malaysia. Newborns who received Gentamicin treatment for more than 3 days were monitored by taking trough and peak levels. Data collection was done from January 2020 until December 2022 using data collection forms extracted from the TDM request form and electronic lab systems.

Newborns who met the inclusion criteria were included in this study. The criteria include term and premature babies treated with IV gentamicin, for whom data on pre and post serum concentration of gentamicin were available. Patients were excluded if the sample was rejected due to sampling error (sample lysed, inadequate blood volume), or if the sampling was a gentamicin random level for toxicity monitoring only. Any invalid results were excluded together with patients with incomplete data that is required for this research (such as missing data for urea and serum creatinine level).

A data collection form was used to record patients' demographic data, total daily dose of gentamicin, serum creatinine level, diagnosis, urea level, dosing interval of gentamicin, and total dose per body weight of gentamicin.

Descriptive statistics were performed using the Statistical Package for the Social Sciences version 26.0. Mean and standard deviation were calculated to express the data. The chi-square test was used to analyse the statistically significant relationship between the categorical data and toxicity. $p<0.05$ indicates statistical significance. Multivariable logistic regression was also performed to identify the risk factors of acquiring toxic trough levels.

Results

A total of 286 samples were reviewed, and samples that met the inclusion criteria were analysed. Only 59 samples were not included in the analysis due to random sampling time (n=5), blood lysed (n=18), sampling error including wrong sampling time and inadequate blood volume (n=4), lack of SCr or urea baseline (n=20), and invalid result (n=12).

Premature, n (%)	60 (26.43%)
Term, n (%)	167 (73.57%)
Body weight, kg, mean ± SD	3.03 ± 0.57
Total daily dose, mg, mean ± SD	12.0 ± 2.32
Dosing interval 24 hourly, n (%)	205 (90.31%)
Dosing interval 36 hourly, n (%)	22 (9.69%)
Total dose/kg body weight, mg/kg, mean ± SD	3.92 ± 0.27
Serum creatinine (SCr), µmol/L, mean ± SD	57.64 ± 15.00
Serum urea, mmol/L, mean ± SD	3.99 ± 6.33
Trough level, mg/L, mean ± SD	1.23 ± 1.11
Peak level, mg/L, mean ± SD	7.31 ± 3.93

Table 1. Demographic and Clinical Characteristics (n= 227)

SD: Standard deviation

A summary of the neonates' demographic data is presented in Table 1. The majority of the neonates (73.57%) were categorized as term, where their gestational age was more than 37 weeks. The dosing interval of 24 hourly was vastly used in more than 90% of the neonates.

Table 2 shows common clinical diagnoses, where the most diagnoses reported in this facility were congenital pneumonia and presumed sepsis.

Clinical Sepsis, n (%)	5 (2.20)
Congenital pneumonia, n (%)	171 (75.33)
Congenital sepsis, n (%)	1 (0.44)
Presumed sepsis, n (%)	37 (16.30)
GBS sepsis, n (%)	1 (0.44)
Hypoxic Ischemic Encephalopathy (HIE), n (%)	2 (0.88)
Meconium Aspiration Syndrome (MAS), n (%)	5 (2.20)
Neonatal Jaundice secondary to Sepsis, n (%)	2 (0.88)
Prematurity with Respiratory Distress Syndrome (RDS), n (%)	1 (0.44)
Presumed Meningitis, n (%)	2 (0.88)

Table 2. Neonatal initial diagnoses before starting empirical treatment with gentamicin.

Gentamicin serum concentrations

Gentamicin was started in the majority of neonates on the first day of life. Table 3 shows the percentage of target peak and trough levels with dosing of 4mg/kg/dose. A trough level above 1mg/L is considered toxic, whereas a peak level of 5mg/L and above is considered effective. The majority of neonates treated with a dose of 4mg/kg/dose achieved effective peak levels of more than 5mg/L (74.9%), hence we can conclude that a dose of 4mg/kg is effective in achieving its desired effect. However, more than half of the neonates (52%) had toxic trough levels with the current dosing regimen.

Trough, n (%)	
Non-toxic <1mg/L	109 (48.00%)
Toxic ≥ 1mg/L	118 (52.00%)
Peak, n (%)	
Effective, ≥5mg/L	170 (74.90%)
Sub-therapeutic <5mg/L	57 (25.10%)

Table 3. Percentage of target peak and trough at 4mg/kg/dose (n = 227)

We also found that only a small percentage of neonates with effective peak levels had supra-therapeutic levels (8.8%), where the concentration was more than 12mg/L, as shown in Table 4.

Effective Peak Level	
Normal ≥ 5 – 12 mg/L, n (%)	150 (66.10%)
Supratherapeutic > 12mg/L, n (%)	20 (8.8%)

Table 4. Percentage of normal and supra-therapeutic effective peak levels at 4mg/kg/dose (n = 170)

The postmenstrual age, body weight, dosing interval, and diagnosis were further analysed against trough and peak levels, as shown in Table 5. Preterm neonates had a higher percentage of having toxic trough levels (58.33%) as compared to term neonates (49.70%). Nevertheless, dose and body weight played no significant role in having a toxic trough level or sub-therapeutic peak level, as shown in Tables 6 and 7. Furthermore, for the most common diagnoses in the neonatal ward, more than 50% of the newborns who were diagnosed with congenital pneumonia (n=171) and presumed sepsis (n=37) experienced toxic trough levels.

	Gentamicin Trough Concentration			Gentamicin Peak Concentration		
	Non-toxic	Toxic	p-value	Effective	Sub-therapeutic	p-value
All	109 (48.00%)	118 (52.00%)	0.251	170 (74.90%)	57 (25.10%)	0.711
PMA Age, n (%)						
Premature	25 (41.67%)	35 (58.33%)		46 (76.67%)	14 (23.33%)	
Term	84 (50.30%)	83 (49.70%)		124 (74.25%)	43 (25.75%)	
Mean body weight (SD), kg	3.03 (0.60)	3.09 (0.54)	0.47	3.06 (0.56)	3.04 (0.59)	0.78
Mean actual dose (SD), mg	11.88 (2.48)	12.19 (2.17)	0.308	12.10 (2.32)	11.94 (2.34)	0.718
Mean dose per body weight (SD), mg/kg	3.90 (0.33)	3.95 (0.2)	0.165	3.92 (0.254)	3.93 (0.328)	0.724

Table 5. Comparison of Neonatal Demographic Data with Trough and Peak Serum Gentamicin Concentrations.

doi.org/10.32388/Q7JA3H

	Gentamicin Trough Concentration			Gentamicin Peak Concentration		
	Non toxic	Toxic	p-value	Effective	Sub- therapeutic	p-value
Diagnosis						
Clinical sepsis	4 (80.00%)	1 (20.00%)	0.197	2 (40.00%)	3 (60.00%)	0.102
Congenital pneumonia	82 (48.00%)	89 (52.00%)	0.973	131 (76.61%)	40 (23.39%)	0.297
Congenital sepsis	0 (0%)	1 (100%)	1.000	1 (100.00%)	0 (0%)	1.000
Presumed sepsis	16 (43.20%)	21 (56.80%)	0.525	29 (78.38%)	8 (21.62%)	0.593
GBS sepsis	1 (100%)	0 (0%)	0.480	0 (0%)	1 (100.00%)	0.251
HIE	0 (0%)	2 (100%)	0.499	2 (100.00%)	0 (0%)	1.000
Meconium aspiration syndrome	2 (40.00%)	3(60.00%)	1.000	3 (60.00%)	2 (40.00%)	0.602
NNJ secondary to sepsis	2 (100%)	0 (0%)	0.229	0 (0%)	2 (100.00%)	0.062
Prematurity with RDS	1 (0%)	0 (0%)	0.480	0 (0%)	1 (100.00%)	0.251
Presumed meningitis	1 (50.00%)	1 (50.00%)	1.000	2 (100.00%)	0 (0.00%)	1.000

Table 6. Association between dose and body weight with gentamicin concentration

	All	Gentamicin Trough Concentration			Gentamicin Peak Concentration		
		Non toxic	Toxic	p-value	Effective	Sub-therapeutic	p-value
Mean trough level (SD), mg/L	1.23 (1.11)	0.59 (0.26)	1.83 (1.26)	<0.001			
Mean peak level (SD), mg/L	7.31 (3.93)				8.52 (3.81)	3.69 (0.89)	<0.001

Table 7. Mean Trough and Peak Level (SD), mg/L

doi.org/10.32388/Q7JA3H

	Gentamicin Trough Concentration			Gentamicin Peak Concentration		
	Non toxic	Toxic	p-value	Effective	Sub-therapeutic	p-value
Mean serum urea (SD), mmol/L	3.56 (4.12)	4.39 (7.83)	0.326	3.86 (4.6)	4.29 (9.81)	0.685
Mean SCr (SD), µmol/L	54.72 (15.19)	60.34 (14.35)	0.008	59.61 (14.29)	51.77 (15.62)	0.001

Table 8. Comparison of Mean Serum Urea and Mean SCr with Peak and Trough Serum Gentamicin Concentrations, Non Toxic, Toxic, Effective and Sub-Therapeutic.

The p-value is greater than 0.05, indicating that there is no statistically significant difference in mean serum urea levels between the non-toxic and toxic groups for gentamicin trough and peak concentration. On the other hand, the mean serum creatinine levels differ significantly between the non-toxic and toxic groups for gentamicin trough concentration (p = 0.008). There is also a significant difference in mean serum creatinine levels between the effective and sub-therapeutic groups for gentamicin peak concentration (p = 0.001) (Table 8). These results suggest that serum creatinine levels might be a more sensitive indicator of toxicity and effectiveness of gentamicin concentrations compared to serum urea levels in this context. We further analyzed the factor of serum creatinine by categorizing the data into normal and elevated serum creatinine levels. It was observed that toxic levels were significantly associated with elevated serum creatinine levels (SCr >71 µmol/L), as detailed in Table 9.

	Non-toxic	Toxic	Total	p-value
Normal SCr (<71 µmol/L) n (%)	98 (51.85)	91 (48.15)	189	0.010
Elevated SCr (>71 µmol/L) n (%)	11 (28.94%)	27 (71.05%)	38	

Table 9. Relationship between serum creatinine level and percentage of non-toxic and toxic trough levels. (n=227)

doi.org/10.32388/Q7JA3H

Neonatal variables	Odd Ratio (95% Cl)	p-Value
Serum Creatinine (umol/L)*	2.55 (1.19 - 5.64)	0.016
Urea (mmol/L)	1.028 (0.983 - 1.074)	0.231
Gestational Age	0.767 (0.416 - 1.413)	0.394

Table 10. Multivariate analysis of factors associated with elevated gentamicin trough concentration. (n = 227)

* *Normal SCr (<71 µmol/L), Elevated SCr (>71 µmol/L)*

Discussion

Among 286 TDM forms for IV Gentamicin received in 2020-2022, only 227 patients were included in this study. Another 59 patients were excluded as rejected samples due to sampling errors such as sample lysed (n=18), inadequate blood volume (n=4), gentamicin TDM form was requested for random level to monitor for toxicity only (n=5), invalid result such as pre-level was higher than post-level (n=12), and incomplete patient important data required for this study such as missing data for SCr (n=20).

In this study, we found that 74% (n=170) of those receiving IV Gentamicin 4mg/kg achieved effective peak levels of more than 5mg/L, as shown in Table 3 (mean peak level = 7.31 ± 3.93 mg/L, $p < 0.001$). This finding corresponds with a previous study where 82.3% of neonates receiving intravenous Gentamicin at the same dose of 4mg/kg achieved effective peak levels[8].

From the findings, we ascertained that from the 170 samples that achieved effective peak levels, only 8.8% (n=20) had supratherapeutic levels with peak levels of more than 12mg/L. On the other hand, there were at most 25.10% (n=57) that experienced subtherapeutic peak levels of less than 5mg/L. This outcome suggested that the 4mg/kg dose is considered effective in the neonatal population at our hospital.

Previous studies identified that only 30% of neonates treated with gentamicin exhibited potential toxicity as the trough levels exceeded 1.0 µg/mL[5]. Contrary to our findings, most neonates treated with IV Gentamicin had experienced toxic trough levels in at least 52% of them who had trough levels more above 1.0µg/mL (mean trough level = 1.23 ± 1.11 mg/L, $p < 0.001$). Similar to a study by Mulhall et al.[9],

who presented similar findings where 63% of the neonates treated with IV gentamicin were reported to have potential toxic levels of gentamicin, with most babies being premature with low gestational age, low birth weight, and in the first week of life[9].

Considering the regimen adjustment was based on neonates' birth weight (BW) and gestational age (GA), it was anticipated that there would be no significant statistical differences in the mean peak and trough concentrations among all neonates categorized by GA and BW in this study, as shown in Table 5.

In the neonatal ward, the predominant diagnoses included congenital pneumonia (n=171) and presumed sepsis (n=37), as reflected in our sample. Both diagnoses showed high efficacy rates (>70%) with the current treatment regimen of 4mg/kg: congenital pneumonia at 76.61% (n=131) and presumed sepsis at 78.38% (n=29). However, more than half of the cases exhibited toxic trough levels, with congenital pneumonia at 52% (n=89) and presumed sepsis at 56.8% (n=21).

Even though the standard dose of 4mg/kg demonstrates a high efficacy rate, aminoglycosides are commonly known to exhibit nephrotoxicity. Therefore, elevated SCr levels in newborns can be influenced by gentamicin trough levels. A study conducted in Iowa, USA, revealed that neonates with mildly elevated serum creatinine levels (71.6 - 87.5 μmol/L) and elevated serum creatinine levels (≥ 88.4 μmol/L) were significantly associated with a twofold and 4.5-fold increase in gentamicin trough levels, respectively, compared to neonates with normal baseline serum creatinine levels (SCr ≤ 70.7μmol/L)[10].

In our NICU, among babies with elevated SCr (≥71μmol/L, n=38), it is revealed that the majority of neonates from this group (71.05%, n=27) experienced toxic trough levels (p=0.01), as shown in Table 9. Thus, a multivariable logistic regression was performed to identify the risk factors of acquiring toxic trough levels (Urea level and SCr), and it was found that SCr significantly affects the toxic trough level of neonates (odd ratio 2.55, 95% confidence interval [1.19, 5.46], p=0.016). This finding was known to correspond with the study by Antolik et al.[10].

We used SCr ≥71μmol/L as the cutoff point for elevated SCr, as our ward avoids the use of Gentamicin for neonates with SCr levels ≥88.4μmol/L. Instead, the use of a 3rd generation cephalosporin, such as Cefotaxime, will be added as an alternative due to its lower nephrotoxicity effect while still offering spectrum coverage against gram-negative bacteria. However, caution is highly necessary to prevent the overuse of third-generation cephalosporins to mitigate the emergence of resistant gram-negative bacteria[11].

In our study, the trough level was toxic in more than half of the babies, probably due to sepsis and renal immaturity. As mentioned by a previous study, in full-term neonates, factors such as renal immaturity, dehydration, birth asphyxia, sepsis, and maternal conditions, for instance, preeclampsia and genetic factors, will impact babies' kidney development[12]. Medications such as gentamicin, especially, may increase the likelihood of high SCr. Fortunately, gentamicin-induced kidney injury is often reversible upon discontinuation of the medication[12].

Consequently, a study also revealed that 8.3% of the study participants with high baseline SCr experienced a 10-fold (83%) increase in SCr within 7 days of initiating gentamicin treatment[12]. Therefore, it is very crucial to take into account serum creatinine levels when determining the initial dose of IV gentamicin for neonates, aiming for an effective and safe treatment regimen.

By conducting this study, we finally discovered that the current gentamicin regimen of 4mg/kg 24 hourly in term neonates and 4mg/kg 36 hourly in preterm neonates, used in our neonatal ward, resulted in an alarming proportion of patients having toxic trough levels, particularly with elevated SCr. The study findings underscore the need to refine the dosing regimen to optimise efficacy and minimise toxicity in neonates. In patients with SCr $\geq$71μmol/L, the dosing interval of gentamicin may be prolonged by 12 hours to prevent toxic trough levels.

Additionally, as discussed by Murphy et al.[1], adequate hydration by clinicians may also reduce or prevent nephrotoxicity, and early signs of fluid overload must be closely monitored, for example, by doing daily weights and observing the intake/output of babies at risk[1]. Early monitoring of gentamicin in patients with elevated SCr (i.e., TDM on the second dose of IV Gentamicin) can be proposed, as 25% of all patients from a previous study that received gentamicin therapy for more than 48 hours without monitoring of gentamicin concentration and renal function will develop acute kidney injury (AKI) that may progress to chronic kidney disease (CKD)[12].

We acknowledge that there are several limitations to our study. Firstly, the sample size for preterm neonates was relatively small, which prevents us from determining whether post-menstrual age significantly impacts toxic trough levels. Additionally, we observed that some TDM request forms were incomplete. For instance, the length of the babies and details of concomitant drugs were not consistently provided in the forms, which are crucial data points needed to enhance the value of our research.

We also acknowledge other constraints. For instance, some samples had human error in sending them to the lab after more than 4 hours, resulting in deterioration and lysis of the sample. Furthermore, the TDM

forms are entirely handwritten, leading to potential errors such as incorrect ID and registration numbers, which can hinder the traceability of patients' medical profiles and lab values, which is known as human error in writing. However, with technological advancements, we now see that laboratory information systems are fully computerized, thereby preventing such errors in the future.

Conclusion and recommendations

In summary, elevated SCr levels in neonates indicate reduced kidney function, which can lead to prolonged half-life, altered clearance, and delayed attainment of steady-state concentrations of gentamicin, necessitating adjustments in dosing and careful monitoring to ensure effective and safe therapy. The current gentamicin regimen resulted in an alarming proportion of patients having toxic trough levels, particularly with elevated SCr. The study findings underscore the need to refine the dosing regimen to optimise efficacy and minimise toxicity in neonates.

Statements and Declarations

Conflicts of interest

The authors declare that they have no conflict of interest in terms of financial, institutional, and other possible relationships.

Funding

No funding was received for this study.

Ethical approval issue

This study received approval from the Medical Review and Ethical Committee (MREC) of the National Institute of Health (NIH), Ministry of Health Malaysia NMRR-17-3217-39258(IIR).

Author contribution

Conception: A.A., N.A.A.R, R.A.R.; Writers: A.A., N.A.A.R, R.A.R., H.A.; Data collection and/or processing: A.A., N.A.A.R.; Supervision: R.A.R.; Analysis and/or Interpretation: A.A., N.A.A.R, R.A.R., H.A.

References

1. ^a, ^b, ^cMurphy HJ, Thomas B, Van Wyk B, Tierney SB, Selewski DT, Jetton JG. Nephrotoxic medications and ac ute kidney injury risk factors in the neonatal intensive care unit: clinical challenges for neonatologists and nephrologists. Pediatric Nephrology. 2019 Oct 12.
2. ^Chattopadhyay B. Newborns and gentamicin--how much and how often? Journal of Antimicrobial Chem otherapy. 2002 Jan 1;49(1):13–6.
3. ^Rao SC, Srinivasjois R, Moon K. One dose per day compared to multiple doses per day of gentamicin for tre atment of suspected or proven sepsis in neonates. Cochrane Database of Systematic Reviews. 2016(12).
4. ^Nizet V, Klein J. Bacterial sepsis and meningitis. Infectious Diseases of the Fetus and Newborn Infant. 2014 Dec 24;8:217-71.
5. ^a, ^bMustafa S, Noor S.L.A.M, Razman R, Yusuf WNW. Monitoring of Gentamicin Blood Level in one-week-of-life Neonates Admitted to a Special Care Nursery Ward. Gulhane Medical Journal. 2022 Mar 7;64(1):27–31.
6. ^a, ^bMohamad N, Rusli RA, Chelliah OA, Azmi Y, Chian TS, Leong GC, et al. Clinical Pharmacokinetics Pharm acy Handbook. 2nd ed. Putrajaya: Pharmacy Practice & Development Division, Ministry of Health Malaysi a; 2019.
7. ^Stach LM, Pallotto E, Sandritter TL. Development of criteria for gentamicin monitoring in a neonatal inten sive care unit. American Journal of Health-System Pharmacy. 2012 Aug 1;69(15):1319-25.
8. ^Low YS, Tan SL, Wan AS. Extended-interval gentamicin dosing in achieving therapeutic concentrations in malaysian neonates. The Journal of Pediatric Pharmacology and Therapeutics. 2015 Apr 1;20(2):119-27.
9. ^a, ^bMulhall A, de Louvois J, Hurley R. Incidence of Potentially Toxic Concentrations of Gentamicin in the neo nate. Archives of Disease in Childhood. 1983 Nov 1;58(11):897–900.
10. ^a, ^bAntolik TL, Cunningham KJ, Alabsi S, Reimer RA. Empirical Gentamicin Dosing Based on Serum Creatini ne Levels in Premature and Term Neonates. American Journal of Health-System Pharmacy. 2017 Apr 1;74 (7):466–72.
11. ^Koda-Kimble MA. Koda-Kimble and Young's Applied Therapeutics: The Clinical Use of Drugs. Lippincott W illiams & Wilkins; 2012 Feb 1.
12. ^a, ^b, ^c, ^dJames ME, Naburi H, Mugusi S, Kunambi PP, Mwakyandile T, Mnkugwe RH, Khalfan MA, Moshi MJ, Minzi OM, Sasi P. Gentamicin concentration and acute kidney injury in term neonates treated for neonatal sepsis with gentamicin and ampicillin-cloxacillin combination. Antimicrobial Agents and Chemotherapy. 2 024 Jun 5;68(6):e01495-23.

Declarations

Funding: No specific funding was received for this work.

Potential competing interests: No potential competing interests to declare.