International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Unmet Need of Measure of Antibiotic Concentration in Biological Fluids in Optimization of Dosage Regimen of Antibiotics: An Observational Study

Dr Kavita Topno[1], Dr Marshall Daud Kerketta[2], Dr. Shadab Alam[3], Dr. Nidhi Ekka[4], Dr. Aman Kumar Gupta[5], Dr. Ankit Kumar[6], Dr. Sidyant Singh[7]

[1]M.B.B.S. M.Sc. (Crra), Department of Pharmacology, Rajendra Institute of Medical Sciences (RIMS) Ranchi, Jharkhand, India
[2]M.B.B.S., M.S., Department of Surgery, RIMS, Ranchi.
[3]M.B.B.S., M.D., Department of Pharmacology, RIMS, Ranchi
[4]M.B.B.S., M.S.(Student), Department of Surgery, RIMS, Ranchi
[5]M.B.B.S., M.S.(Student), Department of Surgery, RIMS, Ranchi
[6]M.B.B.S., M.S.(Student), Department of Surgery, RIMS, Ranchi
[7]M.B.B.S., M.S.(Student), Department of Surgery, RIMS, Ranchi.

OPEN ACCESS

Corresponding Author:

Dr Marshall Daud Kerketta
M.B.B.S., M.S., Department of Surgery, Rims, Ranchi

Received: 30-04-2026
Accepted: 25-05-2026
Available online: 09-06-2026

Copyright© *International Journal of Medical and Pharmaceutical Research*

ABSTRACT

Introduction- Bioavailability (BA) for antibiotic at steady state concentration (Css) for bacteriostatic, bactericidal plasma concentration at non -protein bound state is a step forward to rational use of drugs, especially antimicrobials. Modified routes of administration to reduce total duration and amount of drug administered, hence less ADR, and drug resistance, and super infection.

Material And Method: This is an observational study done at medical record department, of tertiary care Centre at Jharkhand India. The focus of the study decided post study 240 Bed Head Tickets (BHT). On reviewing the 240 BHTs from our departments in view with two or more drugs prescribed in large quantity and prolonged period, are increased chances of resistance, adverse drug reaction, superinfection. Antimicrobial prescription variability is also due to patient's attitude, as some of patient's left against medical advice.

Result: Data shows - (1) Empirical choice was cephalosporins I.V. intermittently administered.

(2) Large total amount of individual drug and dosage regime probable longer duration of hospital stay, or probably nutritional and immunological status of patient causing interindividual variation pharmacokinetics pharmacodynamics (PK/PD).

(3) Polypharmacy.

Discussion- Concentration time curve bioanalytical study is important for both time dependent antibiotics and concentrated dependent antimicrobials. That could optimize, the antibiotics dosage regime and routes of administration. Hence reduction in probable longer duration of hospital stay. Confounding factors should be addressed which probably are nutritional and immunological status of patients causing interindividual variation in pharmacokinetics/pharmacodynamics (PK/PD). But since there were no records regarding measurement of body weight, waist size, arm circumference at deltoid region. Positively almost all patients were investigated for LFT and RFT. The limitation of this study are inclusion and exclusion criteria as there was incidence of LAMA (Left Against Medical Advice) causing lowest dosage regimen antibiotics administered.

Keywords: Antimicrobials, resistance, dosage regimen, bio-availability, PK/PD.

INTRODUCTION

Two or more antimicrobials prescribed in large doses for prolonged duration of treatment can lead to drug resistance, superinfection. HPLC serves as a validated method for measuring the PK/PD(Pharmacokinetic/Pharmacodynamic) ratio.

Cumulative measure of pharmacokinetic is done by comparing Peaks in Chromatography with baseline as zero or mean of 1st readings of plasma concentration of individuals.

Concentration- response or time-curve is PK-PD relation that starts with binding of ligand(drugs) with receptors- to response we measure. Antimicrobials are ligands (L) that binds with receptors [R] microbial proteins like penicillin binding protein (PBP) in cell wall of microbes such as bacteria clostridium tetani, anaerobes Bacteroides fragilis, fusobacterium etc. [1]. AMR (antimicrobial resistance) stewardship program endeavoring on rationale use of antimicrobials [2]. The prolong duration of treatment by antibiotics leads to administration of large dose antibiotics. Simultaneous quantitative measure of antibiotics concentration both at plasma and wound fluid can provide evidence for relation of appropriate dosage for clinical outcome. In patients with mixed infection, larger doses of two or more drugs are given simultaneously, resistant strain multiply to cause superinfection [3].

MATERIAL AND METHOD:

Source of information: -- BHTs of different wards at Medical Record Department, RIMS, Ranchi. Data collected from Medical Record Department to focus on rationale use of antimicrobials, difference in dosage regimen, multiple antimicrobial prescribing trends, use of various combinations of AWaRe group antimicrobials.

Step 1- Method development mentioned by using columns for – 1. Serial number, 2.I Indoor unique ID number.,3. Demography and personal details of patient. 4. Date of admission. Provisional diagnosis/final diagnosis with date .5. Treatment started with date and dosage regimen of antibiotics. 6.Date of stopping the antibiotics, 7. Total days spent in hospital,8. Investigations, 9. Address

Added drug prescribed on admission selected were N=240[Surgical ward BHT n=60; Gynaecology ward BHT n=60; Medicine ward BHT n=60; Orthopedics' ward BHT n=60.]

Step 2. Random collection of data by filling the tables mentioned.

Step 3. of BHTs with lowest and highest dosage regimens of most frequent antibiotics administered in treatment chart of different patients of different wards.

Step 4. Compilation of most frequent administered antibiotics as total amount antibiotic consumption in one episode of dosage regimen for longer duration hospital stay, Table-1. Cefoperazone and ceftriaxone are 3rd generation cephalosporins, being empirically prescribed are Watch group drugs, Table-2, polytherapy-Table-3.

Antimicrobial prescription variability also is due to patient's attitude as some patients leave against medical advice. Following are the headings covered to compiled table data-

1) Variations in dosage regimen antibiotics administered in post -operative patients.
2) Variation choice from AWaRe group, dosage regimen and trends in prescribing antimicrobials.
3) Trends in prescribing multiple antimicrobials with variable dosage regimen.

Antimicrobials characterized by 3 basic parameters:

(1) **Efficacy=Emax** [Full bactericidal response elicited at some concentration of drug]
(2) **Potency= EC50 or IC50**[Inhibitory concentration the plasma concentration of drug producing bacteriostatic effect]

Drug with greater efficacy is more therapeutically beneficial than one that is more potent.

(3) H or Hill factor or slope of curve.

Econ Control bacterial microbes log 10 CFU /ml in X axis of a sigmoid curve without treatment. **Minimum Inhibitory Concentration (MIC)** is the lowest concentration antibiotic after 24 hours Incubation Period with inoculation of 10^4 to 10^5 CFU/ml causing complete destruction or survival of less than 0.1% of inoculum.

The pharmacokinetic basis of antimicrobial therapy

In clinical trials, the following are the two most important factors in predicting successful clinical and microbiological outcomes in patients.

1.**C MAX at** C 1 central compartment maximum plasma concentration of drug in plasma,12Xmic (12 times the MIC, minimum inhibitory concentration).

2.**Site of infection** (drug penetration at the site of infection through anatomical compartment depends on the physical barriers such as epithelial layers ,membrane transporters, drug's chemical nature).Orally administered drug absorbed through GI Tract (g) absorption constant (ka) and passes through Multicompartmental Pharmacokinetic; drug concentration are different in central ,C 2 site oof infection, and C 3 compartment other tissues of the body change.[4]

Basic PK Parameters-Therapeutic Drug Monitoring

1.**Bioavailability** (*f*) is fraction of administered drug reaching the systemic circulation.

F=AUC oral route/AUC by IV route (*F* is 100% for IV drug,0-100% for non -IV drugs).

2. **Clearance [CL]** rate at which drug is removed per unit time from plasma.

CL=K_e (Rate of elimination / Volume of distribution mg per minute/mg per ml.

After reaching the plateau phase, five $t_{1/2}$ CL can be derived also from steady state Concentration.

C_{SS} = K_e *V d and K_e (elimination constant) = 0.693/$t_{1/2}$.

3.**Vd (L)**= D/C (total drug administered / plasma concentration), estimates total amount of drug in the body at any time and loading dose (Loading Dose=V d* desired concentration) [CL Renal =Rate of secretion -Rate of absorption /plasma concentration].

4.**Elimination half-life.** time duration in which plasma concentration of drug fall by 50% [$t_{1/2}$]=0.693xVd/CL [0.693 is log 2, representing exponential rate of Elimination.]

5.**AUC Total amount of drug concentration in plasma at any point of time.**

Important parameters derived from CL and Dose. AUC=D/CL.

Common AUC estimates are AUC $_{exact}$, AUCO, $AUCO_{24}$ area can also be calculated by adding area of discrete set of blocks set up by dose and interval on axis X concentration X concentration, axis Y called Trapezoid method.

C_{ss} (**Steady state concentration**) is attained when rate of,

Rate of administration=Rate of elimination, for fixed time interval regimen50% of C_{ss} achieved in $1*t^{1/2}$,

90% 0f C_{SS} achieved in $3.3*t_{1/2.}$,

95% of C_{ss} achieved in 4-5* $t_{1/2}$

Stronger relationship exists between the plasma concentration (C_{SS}) of drugs and effect, than between dose and effect. Timely communication of results to clinicians is important and the clinicians should interpret the C_{ss} in context of patient's status.{4}.

Table 1.- Variations in dosage antibiotics administered in post-operative patients.

Sl.no.	**UHID**	**Age years/ Sex**	**Diagnosis**	**Antibiotic**	**Dose/ regime**	**Date/admission**	**Date/discharge**	**Antibiotic consumed/Total days of hospital stay**
1	20220175950	83/M	cholecystectomy	Inj. Cefo-Sulbact	1.5gm iv BD	29-05-2022	07-06-2022	26gm / 10 days
2	20220127351	42/M	Int. haemorrhoid	Inj. Cefo-Sulbact	1.5gm iv BD	03-06-2022	8/6.22	14gm/ 6 days
3	20220173945	32/M	Fournier's gangrene	Inj. Cefo-Sulbact	1.5gm iv BD	27-05-2022	08-06-2022	21gm/42 days
4	20220098284	67/M	Scrotal abscess	Inj. Cefo-Sulbact + Inj. Metronidazole	1.5gm iv BD + 100ml iv TDS	22-05-2022	03-06-2022	36gm + 7.2gm / 12 days
5	20220156932	75/M	Ac. pancreatitis	Inj. Cefo-Sulbact + Inj. Metronidazole	1.5gm iv BD + 100ml iv TDS	16-05-2022	01-06-2022	30gm + 10gm / 16 days
6	20220094987	64/M	Ac. Cholecystitis	Inj. Cefo-Sulbact + Inj. Amikacin + Inj.Metronidazole	1.5gm iv BD + 1gm iv	25-03-2022	06-04-2022	36gm + 12gm+ 36gm /12days

					OD + 100ml iv TDS			
7	20220184639	40/M	Ac. pancreatitis	Inj. Cefo-Sulbact + Inj. Metronidazole	1.5gm iv BD + 100ml iv TDS	03-06-2022	09-06-2022	14gm +2.1gm / 7days
8	20220136787	70/M	Sigmoido-caecal swelling	Inj. Cefo-Sulbact	1.5gm iv BD	27-04-2022	09-06-2022	135gm/45days
9	20220140181	13/F	Ac. cholecystitis	Inj. Cefo-Sulbact	1.5gm iv BD	27-05-2022	07-06-2022	30gm/ 10days
10	20220161658	29/F	Cholelithiasis	Inj. Cefo-Sulbact + Inj. Metronidazole.	1.5gm iv BD + 100ml TDS	18-05-2022	06-06-2022	54gm + 5.4gm / 18days
11	20220146273	24/M	Ac. pancreatitis	Inj. Pip-Tazobactam	4.5gm iv BD	06-05-2022	07-06-2022	45gm /10days
12	20220184795	32/M	Ac. Necrotizing pancreatitis	Inj. Meropenem	1gm iv BD	03-06-2022	08-06-2022	12gm /6days

Inj. Cefo-Sulbact = Injection Cefoperazone -Sulbactam

Table- 2.: Variation dosage regimen and trends in prescribing antimicrobials.

S no.	**Name /combination ratio**	**AWaRe group**	**ATC code**	**Minim. Dosage regimen total gm / Days**	**Maxim. Dosage regimen total gm/ Days**	**Variation of dosage regimen**	**Prescription %**
1	Inj. Cefoperazone-sulbactam / (2:1)	Watch-Access	J01DD12	14gm/6D	135gm/45D	121gm/39D	80%
2	Inj. metronidazole	Access	J01XD01	1.4L/7D	3.6L/18D	2.2L/11D	50%
3	Tab. Amoxy-Clav (4:1)	Access	J01CR02	6.25gm/5D	10gm/8D	3.75gm/3D	25%
4	Inj. Meropenem	Reserve	J01DI03	12gm/6D	24gm/12D	10gm/9D	20%
5	Inj. Ceftriaxone	Watch	J01DD04	14gm/7D	20gm/10D	6gm/3D	20%
6	Tab Ofloxacin	Watch	J01MA01	1.4gm/7D	2.0gm/10D	1.2gm/3D	19%

7	Inj. Cefotaxime	Watch	J01DD01	14gm/7D	20gm/10D	6gm/3D	19%
8	Inj. Amikacin	Access	J01CA01	3gm/3D	16gm/16D	13gm/13D	15%
9	Inj. Levofloxacin	Watch	J01MA12	10.5gm/7D	15gm/10D	14.5gm/	10%
10	Inj. Ciprofloxacin	Watch	J01MA02	800ml/4D	2000ml/10D	1200ml/6D	10%
11	Inj.Piperacillin-tazobactam (8:1)	Watch-Access	J0CR05	31.5gm/7D	76.5gm/17D	45gm/10D	6%
12	Tab. Ampicillin	Access	J01CA01	7gm/7D	7gm/7D	NONE	5%
13	Tab. Clindamycin	Access	J01FF01	9gm/10D	9gm/10D	NONE	2%
14	Tab Cefalexin	Access	J01DB01	14gm/7D	14gm/7D	NONE	2%
15	Inj. Cefotaxime	Watch	J01DD01	14gm/7D	20gm/10D	6gm/3D	19%

DISCUSSION:

We should endeavor to improve antibiotic safety. Cefoperazone and ceftriaxone are 3rd generation cephalosporins. being empirically prescribed are Watch Group Drugs. Optimization of dosage-based 3rd Generation Cephalosporines based on evidence by TDM will save drug from large amount being administered, drug-resistance. Evidence differentiating between possible Adverse Drug Reaction (ADR) from toxicity, therapeutic from sub therapeutic dose. Pharmacokinetic data obtained by TDM of patient will contribute relevant data from for ICMR-AMR surveillance program of this region.

Acknowledgements:

I should be grateful for all MRD staff, nurses who made treatment practically administered, and doctors and patients who remain unsung.

Funding Statement

No funding.

Conflict Of Interest

None.

Author's contribution:

1. Conceptualizing, Writing. ---- Dr Kavita Topno.
2. Proof Reading, Data Analysis--Dr Marshall Daud Kerketta
3. Analysis---Dr Shadab Alam
4. Data Collection—Dr Nidhi Ekka, Dr Aman Kumar Gupta, Dr Sidyant Singh
5. Data Correction and Analysis- Dr Ankit Kumar.

REFERENCES: -

1. Wallenburg E, Ter Heine R, Schouten JA, et all: An integral pharmacokinetic analysis of piperacillin and tazobactam in plasma and urine in critically ill patients. Clin. Pharmacokinet.2022,61:907-18,10.1007/s40262-022-01113-6.

2. Access, watch, reserve classification of antibiotics; WHO-EMP-IAU-2019.11-eng.
3. Satoskar RS, Rege NN, Bhandarkar SD: Pharmacology and Pharmacotherapeutics,24th Edition.Elsevier,2015.
4. Phe K, Heil EL, Tam VH: Optimizing pharmacokinetics-pharmacodynamics of antimicrobial management in patients with sepsis: a review. J Infect Dis.2020, 222: S132-41.10.1093/ infdis/ jiaa118.