

**Antibiotic and Analgesic utilization review in an orthopedics in-patient department of a tertiary care teaching hospital in Hyderabad**

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**ABSTRACT**

Drug utilization review is 'an authorized, structured, ongoing review of prescription, dispensing and medicine use' facilitating rational drug use. Antibiotics and analgesics are common and frequently prescribed in orthopedic department. We aimed to evaluate the usage of antibiotics & analgesics in orthopedics department. Six month prospective case observational study was conducted in Orthopedics Department, Gandhi hospital, Secunderabad with approval from Institutional Ethical committee, CMR College of Pharmacy. Final outcome obtained by statistical analysis using ANOVA. In this study, male gender of 20-40 yrs was pre-dominant with common diagnosis; fractures and trauma. Common antibiotic prescribed were; Ceftriaxone, Cephalexin & Amikacin and analgesics; Paracetamol & Diclofenac. A total of 311 times antibiotic and 222 times Analgesic were prescribed in collected cases respectively. 3 antibiotics and 2 analgesics per case were predominant. Antibiotic & analgesic drug switch were also seen in study. Drug utilization review indicates 83% and 88% rationality of antibiotics and analgesics respectively. Slight irrationality was observed, those mainly due to insufficient lab data. Overall utilization of both antibiotic and analgesic was approximately in rational manner in Orthopedics department. Inclusion of regular lab test will make the prescription more appropriate, ultimately leading to better patient care.

**Key words:** Drug utilization review, Antibiotic, Analgesic, Rational, Orthopedics department.

**List of abbreviation:** **DUR:** drug utilization review; **ANOVA:** Analysis of variance; **DUE:** drug utilization evaluation; **MUE:** Medication utilization evaluation; **GI:** Gastro intestinal; **HIV:** Human immunodeficiency virus; **ADR:** Adverse drug reaction; **ORS:** Oral rehydration therapy; **IVF:** Intravenous fluid; **IV:** Intravenous; **IM:** Intramuscular; **Govt:** Government

**INTRODUCTION**

Drug Utilization Review (DUR) or Drug Utilization Evaluation (DUE) or Medication Utilization Evaluation (MUE) defined as 'an authorized, structured, enduring review of prescription, dispensing and use of medicine'. DURs involve a comprehensive review of patients' prescription &

medication data; before, during, and after dispensing to ensure appropriate medication decision and positive patient outcomes. DURs classified as; **prospective-** evaluation of a patient's therapy **before** medication is dispensed, **concurrent-** ongoing monitoring of drug therapy **during** course of treatment, **retrospective-** review of therapy **after** patient has received the medication <sup>[1]</sup>. Primary aim

of DUR research is to facilitate rational use of drugs. DUR research itself does not necessarily provide answers, but contributes to rational drug use in important ways and amplify the understanding of how doctors decide to prescribe a drugs and being used. DUR research helps to estimate; the number of patient exposed to specified drug within a given time period, to what extent drugs are properly used, overused or underused, to determine the pattern or profile of drug used & extent to which alternative drugs are being used to treat particular clinical conditions, compare the observed patterns of drug used for treatment of a certain disease with current recommendations or guidelines and also used in the application of quality indicators to patterns of drug utilization.

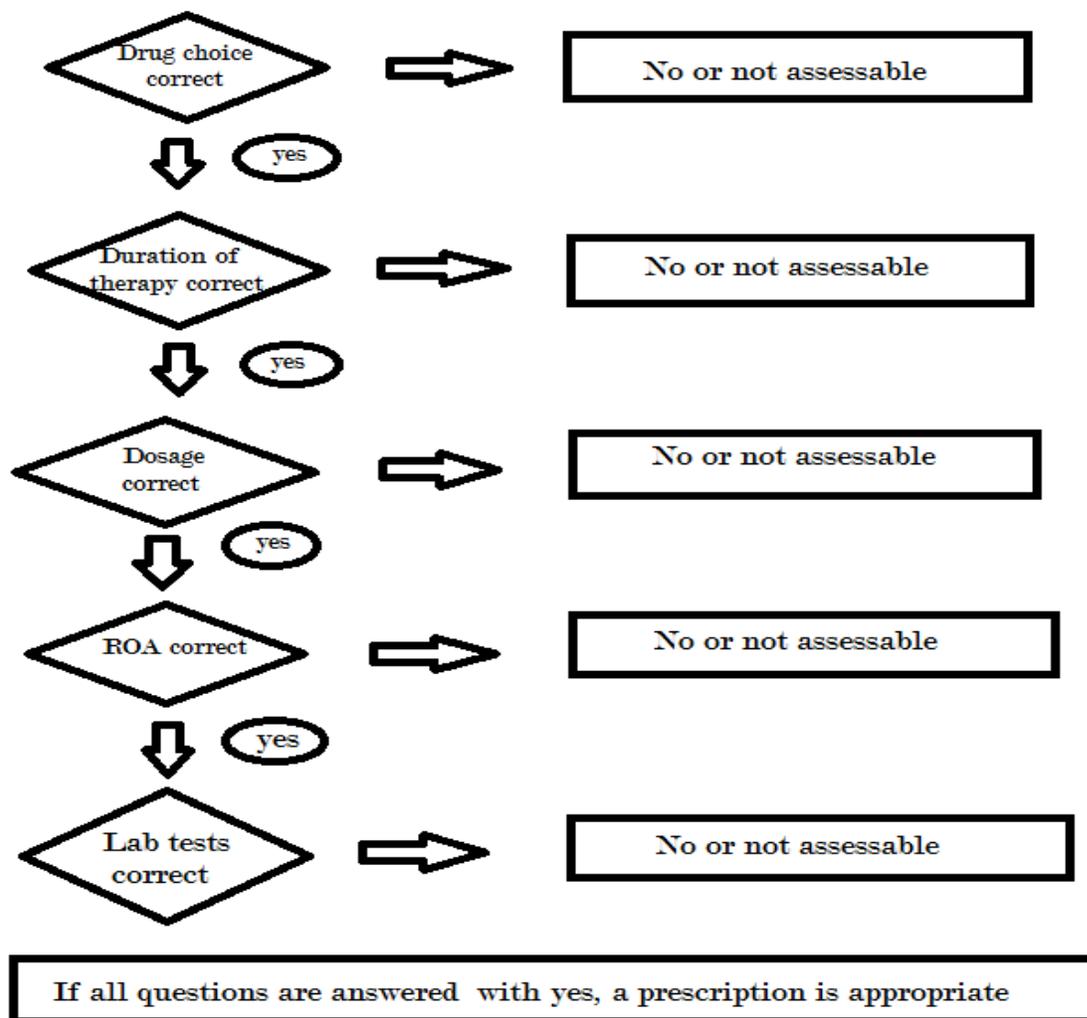
Periodic evaluation of drug utilization patterns need to be made to enable suitable modifications in prescription to increase therapeutic benefit & decrease the possible adverse effects. Study of prescribing patterns seeks to; monitor, evaluate and if necessary suggest modifications in the prescribing behavior of medical practitioners to make medical care rational and cost-effective. Drug prescribing studies aim to provide feedback to the prescriber and to create awareness among them about rational use of medicines<sup>[2]</sup>.

Antibiotics and Analgesics are most common and frequently prescribed drugs for long periods in department of orthopedics. It is well documented that injudicious use of these drugs increases mortality and morbidity due to adverse effects. Antibiotics are prescribed both as prophylactically (before orthopedics surgery) or to treat current infection<sup>[3-6]</sup>. Generally in any orthopedics case pair of antibiotics covering both the Gram-negative and Gram-positive infections is employed<sup>[7]</sup>. Whenever there is suspicion of an anaerobic infection, another antibiotic for anaerobes is added<sup>[8]</sup>. Analgesics are drugs, which possess significant pain relieving properties by acting in the central nervous system or peripheral pain receptors without significantly affecting consciousness<sup>[9]</sup>. Unfortunately, no single agent is an ideal choice for all types of patients or no single agent is suitable for all types of pain; hence physician has to choose the best suitable agent from available options based on different factors including; patient dynamics, medicine related factors and disease related aspects. Patient satisfaction also plays an important role in ensuring compliance with the

treatment, especially during long term treatment. Understanding physician's perspective while selecting an analgesic and significant barriers in effective pain management through a systematic approach and addressing them with appropriate measures could help for better outcomes<sup>[10]</sup>. Prolong use of antibiotics & analgesics leads to diverse clinical complications like; resistance, tolerability, various gastro intestinal (GI) complications and even treatment failure leading to mortality. Focusing on the above mention fact, it is extremely important to conduct periodic utilization pattern study with antibiotics and analgesics to measure their continuous efficacy in various hospitals/clinics. Taking into consideration about these facts we have decided to analyze various data related to antibiotic and analgesic prescription from orthopedics department to understand their utilization pattern and also to obtain the rationality of various antibiotic & analgesic prescriptions.

## METHODS

A prospective case observational study was conducted between August 2015 & January 2016 in department of Orthopedics, Gandhi hospital, Secunderabad. Permission for the study was obtained from Institutional Ethical Committee, CMR College of Pharmacy and also from the Hospital. Cases were collected and documented in a structured documentation form from in-patient department of orthopedics in a regular manner according to inclusion criteria, which includes; cases of on-specific diagnosis but with antibiotic and analgesic prescription and cases with antibiotic and analgesic prescription but with or without gastro protective agents. Study exclusion criteria includes; cases without antibiotic and analgesic prescription, cases with antibiotic but without analgesic prescription & vice-versa, HIV positive cases, cases of absconded patients and if patient expired. A total of 104 cases were collected during the study period. Case by case various drug utilization analysis parameters were discussed thoroughly with orthopedic surgeons in a regular manner to interpret the case information to obtain interpreted data and further analyzed statistically to get the final result. Study procedure is demonstrated in the following schematic representation (**Fig 1**).



**Fig 1: Schematic representation of study procedure**

**Statistics:** Interpreted data obtained from cases were statistically analyzed by using 'GraphPad Instat' software. Analysis of variance test (ANOVA)<sup>[11]</sup> and Tukey-Kramer multiple comparison tests were performed to analyze the data of various parameters to obtain the final result with statistical significance.

## RESULTS

A total of 104 cases were collected during the study period and various data obtained were interpreted and analyzed to acquire the final result. Demographic characteristics of patients are shown in **table 1**. About 66% of them are male and mostly belong to the age group of 21-40 yrs. **Table 2** demonstrates that majority of admission in orthopedics department were diagnosed with fractures (n=54, 51%), followed by trauma (n=15, 14%), surgical procedures (n=9,

8%), dislocation (n=6, 5%). Commonly prescribed antibiotic was found to be Ceftriaxone (n= 76, 24%) followed by Cephalexin (n= 73, 23%), Amikacin (n= 71, 22%) and Cefotaxime (n= 32, 10%). Analgesics most frequently used were Paracetamol (n= 90, 40%) and Diclofenac (n=87, 39%) **Table 3**. Commonly preferred route of administration for antibiotic and analgesic include both Oral and Parenteral. Major number of antibiotics prescribed per prescription is three (n=44, 42%). Analgesics prescribed per prescription shows higher incidence for two (n= 61, 58%) **Table 4**. The frequency of prescriptions of antibiotics and analgesics are shown in **Table 5**. Overall, 104 cases containing 311 antibiotics and 222 analgesics were reviewed. Antibiotic therapy was found to be rational in 257 cases (82.64%) and analgesic therapy was rational in 195 cases (87.84%). Whereas 54 cases (17.36%) of antibiotic was

irrational and analgesic therapy was irrational in 27 cases (12.16%) **Table 6**. Most common reason for irrationality was due to lack of serology test data and others include improper dose, duration and route of administration. There were also switches in antibiotic and analgesic from parenteral to oral form, this is due to tolerability of the patient to oral form without GI disturbances and upon discharge. Whereas switch from oral to parenteral route was observed only in analgesics based on situations i.e. surgery, non-responsiveness or poor response to oral therapy. A total of 143 drug switches were found in antibiotics of which 1-1 drug type switch (n=97) mainly Ceftriaxone to Cephalexin (n=30, 31.91%) was

mostly common followed by 1-2 type of switch (n=12) i.e., Cephalexin to {Ceftriaxone + Amikacin}, 2-1 type of switch (n=33) i.e., {Ceftriaxone + Amikacin} to Cephalexin and 3-1 type of switch (n=1) i.e., {Ceftriaxone + Amikacin + Metronidazole} to Cephalexin. In analgesics all the drug switches are of 1-1 type (n=146) of which the most common was Diclofenac to Paracetamol, **Table 7**.

Out of total 104 cases, only two ADRs were detected, those are Amikacin induced loose motion and Cephalexin induced vomiting. A distinct medical condition Anxiety induced loose motion was also observed, which was managed by administering Ofloxacin, Alprazolam, ORS and IVF.

**Table 1: Demographic profile of cases (n=104).**

Age Distribution	Number (%)
1. 0-20 years	13 (12.5%)
2. 21-40 years	48 (46.2%)
3. 41-60 years	32 (30.8%)
4. > 60 years	11 (10.5%)
Sex Distribution	Number (%)
1. Male	69 (66.5%)
2. Female	35 (33.6%)

**Table 2: Diagnosis wise distribution of cases (n=104).**

Diagnosis Distribution	Number (%)
1. Fractures	54 (51.9%)
2. Trauma	15 (14.4%)
3. Surgical procedures	9 (8.6%)
4. Dislocation	6 (5.7%)
5. Rotator cuff tears	4 (3.8%)
6. Arthritis	3 (2.8%)
7. Avascular necrosis	3 (2.8%)
8. Prolapsed intervertebral disc	3 (2.8%)
9. Spondylothesis	3 (2.8%)
10. Others	4 (3.8%)

**Table 3: Detail distribution of Analgesic and Antibiotic**

Antibiotic	Number (%)
1. Ceftriaxone	76 (24.4%)
2. Cephalexin	73 (23.4%)
3. Amikacin	71 (22.8%)
4. Cefotaxime	32 (10.2%)
5. Metronidazole	17 (5.4%)
6. Cefixime	12 (3.8%)
7. Amoxicillin + Clavulanic acid	10 (3.2%)
8. Piperacillin + Tazobactam	8 (2.5%)
9. Azithromycin	3 (0.9%)

10. Cefuroxime	3 (0.9%)
11. Ciprofloxacin	3 (0.9%)
12. Imepenam	1 (0.3%)
13. Levofloxacin	1 (0.3%)
14. Ofloxacin	1 (0.3%)
<b>Analgesic</b>	<b>Number (%)</b>
1. Paracetamol	90 (40.5%)
2. Diclofenac	87 (39.2%)
3. Tramadol	40 (18%)
4. Ibuprofen	5 (2.2%)

**Table 4: Route of administration and number of drugs per prescription**

Route of administration	Antibiotic (Number&%)	Analgesic (Number&%)
Oral	7 (6.7%)	11 (10.5%)
Parenteral	9 (8.6%)	4 (3.8%)
Both	88 (84.6%)	89 (85.5%)
No. of drug(s)/prescription	Antibiotic (Number & %)	Analgesic (Number & %)
One	8 (7.6%)	13 (12.5%)
Two	26 (25%)	61 (58.6%)
Three	44 (42.3%)	28 (26.9%)
More than Three	26 (25%)	2 (1.9%)

**Table 5: Antibiotics and Analgesics with rationality& irrationality**

Name of the drug	Rationality	Irrationality	Total
<b>Antibiotics</b>	<b>Number (%)</b>	<b>Number (%)</b>	<b>n =311</b>
Ceftriaxone	45 (14.4%)	31 (9.9%)	76 (24.4%)
Cephalexin	68 (21.8%)	5 (1.6%)	73 (23.4%)
Amikacin	67 (21.5%)	4 (1.2%)	71 (22.8%)
Cefotaxime	30 (9.6%)	2 (0.6%)	32 (10.2%)
Metronidazole	11 (3.5%)	6 (1.9%)	17 (5.4%)
Cefexime	12 (3.8%)	0 (0.00)	12 (3.8%)
Amoxicillin + clavulanic acid	7 (2.2%)	3 (0.9%)	10 (3.2%)
Piperacillin + Tazobactam	5 (1.6%)	3 (0.9%)	8 (2.5%)
Others	12 (3.8%)	0 (0.00)	12 (3.8%)
<b>Average</b>			3.06
<b>SEM</b>			0.12
<b>SD</b>			2.71
<b>P- Value</b>			<0.0001
<b>Analgesics</b>			<b>n= 222</b>
Paracetamol	86 (38.7%)	4 (1.8%)	90 (40.5%)

Diclofenac	69 (31%)	18 (8.1%)	87 (39.1%)
Tramadol	36 (16.2%)	4 (1.8%)	40 (12.8%)
Ibuprofen	4 (1.8%)	1 (0.4%)	5 (2.2%)
<b>Average</b>			2.15
<b>SEM</b>			0.06
<b>SD</b>			0.61
<b>P-Value</b>			<0.0001

**Table 6: Reasons for irrationality of antibiotic (n= 54) and analgesic therapies (n=27)**

Reason for irrationality	Number (%)	P-value
<b>Antibiotics:</b>		
Unjustified use (indication)	2 (3.7%)	<0.0001
Improper dose	3 (5.5%)	<0.0001
Improper duration	12 (22.2%)	<0.0001
Insufficient lab data	37 (68.5%)	<0.0001
<b>Analgesics:</b>		
Unjustified use (indication)	5 (18.5%)	<0.0001
Improper dose	0	-
Improper duration	6 (22.2%)	<0.0001
Insufficient lab data	16 (59.2%)	<0.0001

**Table 7: Description of type drug switches**

Drug switch		
<b>Antibiotics (n=143)</b>		
1-1 type	97 (67.8%)	<0.0001
1-2 type	12 (8.3%)	<0.0001
2-1 type	33 (23%)	<0.0001
3-1 type	1 (0.6%)	<0.0001
<b>Analgesics (n=146)</b>		
1-1 type	146 (100%)	

Inter comparisons of variables among following parameters – No. of AB, ROA AB, IV-PO AB, PO-IV AB, DS AB, No. of Anal, ROA Anal, IV-PO Anal, PO-IV Anal, DS Anal, Diagnosis, LOS, and

No. of drugs. (AB- antibiotics, ROA- route of administration, IV- intra venous, PO- per oral, DS- drug switch, Anal- Analgesic, LOS- length of stay)**Table 8.**

**Table 8. Inter comparisons of variables among various parameters**

Comparison	Mean difference	P value
No. of AB Vs IV-PO AB	1.971	P < 0.001**
No. of AB Vs PO-IV AB	2.067	P < 0.001**
No. of AB Vs DS AB	0.6827	P < 0.001**
ROA AB Vs IV-PO AB	1.692	P < 0.001**
ROA AB Vs PO-IV AB	1.788	P < 0.001**
ROA AB Vs DS AB	0.4038	P < 0.01*
IV-PO AB Vs DS AB	-1.288	P < 0.001**
PO-IV AB Vs DS AB	-1.385	P < 0.001**
No. of Anal Vs ROA Anal	-0.5962	P < 0.001**
No. of Anal Vs IV-PO Anal	0.8269	P < 0.001**
No. of Anal Vs PO-IV Anal	0.9808	P < 0.001**
No. of Anal Vs DS Anal	-0.2500	P < 0.05*
ROA Anal Vs IV-PO Anal	1.423	P < 0.001**
ROA Anal Vs PO-IV Anal	1.577	P < 0.001**
ROA Anal Vs DS Anal	0.3462	P < 0.001**
IV-PO Anal Vs DS Anal	-1.077	P < 0.001**
PO-IV Anal Vs DS Anal	-1.231	P < 0.001**
Diagnosis Vs LOS	-13.337	P < 0.001**
Diagnosis Vs No. of Drugs	-6.135	P < 0.001**
LOS Vs No. of Drugs	7.202	P < 0.001**
LOS Vs No. of AB	13.298	P < 0.001**
LOS Vs No. of Anal	14.212	P < 0.001**
No. of Drugs Vs No. of AB	6.096	P < 0.001**
No. of Drugs Vs No. of Anal	7.010	P < 0.001**

## DISCUSSION

Key finding of this study was occurrence of rational use of antibiotics, analgesics and drug switch. Although several literatures have demonstrated rational use of Analgesics and rational Antibiotics prescription in Orthopedics Departments throughout the world, their irrational use is still rampant, especially in developing countries like India<sup>[12]</sup>.

In this study Cephalosporins and Aminoglycosides were the most frequently used antibiotics. Ceftriaxone is considered as the drug of choice in orthopedics because of its broad spectrum activity. These antibiotics were continued to be main stay of therapy in the orthopedics department because of their broad spectrum of activity, clinical efficacy and favorable tolerability.

Paracetamol and Diclofenac was mostly prescribed analgesic in orthopedics department mainly because of their clinical efficacy and tolerability.

Most of the cases presented in orthopedics department were fractures and trauma which supports previous study conducted by **Muraraiah S (2014)**<sup>[13]</sup> and **Hassan AM (2009)**<sup>[14]</sup>.

Second to Ceftriaxone, Cephalexin was the drug of choice as antibiotic mainly in discharge medication. Mostly prescribed Aminoglycoside was Amikacin mainly prescribed during surgical procedure.

Analgesic choice was restricted to only 4 drugs i.e., Paracetamol, Diclofenac, Tramadol and Ibuprofen, of these Ibuprofen was prescribed based on type of disease and patient condition only thus came out as least prescribed.

Paracetamol and Diclofenac were equally prescribed in this study, which is mainly due to intensity of pain & depending upon type of disease. These finding also supported by previous study conducted by **Das BP (2000)**<sup>[15]</sup>, **Kumarasingam T (2014)**<sup>[16]</sup>, **Kuttichira P (2008)**<sup>[17]</sup> and **Maheshwari P (2014)**<sup>[18]</sup>.

In our study we found that number of antibiotic prescribed per prescription are 3 (42.31%), contradicted by **Reji S (2015)**<sup>[19]</sup> which reports single antibiotic use. Number of analgesic prescribed per prescription are 2 (58.66%) in this study which is supported by **Vallano A (2007)**<sup>[20]</sup>.

Switch of drug therapy i.e. change from parenteral (I.V&I.M) to oral treatment, has been studied by several investigators over the past few years and has been shown to save costs, shorten the length of stay and decrease adverse reactions of parenteral administration, all with equal therapeutic outcome. This study demonstrated that both oral and parenteral route are preferred for administration of both antibiotic and analgesic, similar finding was

previously reported by **Ubedulla S (2013)**<sup>[21]</sup> and **George SS (2013)**<sup>[22]</sup>. Parenteral to oral switch was found in both antibiotics and analgesics whereas oral to parenteral switch was found only in analgesics. This is mainly due to severity of the condition and need of faster drug effect, once the condition get stabilize or normalized, drugs switch to oral route.

Even drug switches were observed in this study i.e. switching from one antibiotic/analgesic to another due to unavailability of a drug or poor therapeutic response. This finding was also supported by **NHS policy**<sup>[23]</sup>.

We found that antibiotic therapy was appropriate in 83 % cases and that of analgesic was 88%. Little irrationality were also there, those mainly due to insufficient/lack of laboratory test results. Lab tests play a key role during antibiotic prescription decision as their report helps in deciding the type of antibiotic for a particular disease & make it more rational. Analgesic prescription was also found to be mostly rational in our study. Similar finding was also reported by **Raveh D (2001)**<sup>[11]</sup>.

Several limitations of this study need to be mentioned also. First, a continuous study with longer duration & regular collection & analysis of case will be more applicable to make a final comment or judgment. We also encountered difficulties in assessment due to lack of lab data on antibiotic resistance.

## CONCLUSION

In conclusion, our results revealed that over all utilization of both Antibiotic & Analgesic were almost in rational manner in orthopedics department. Little irrationality were also present but based on the present scenario like, Govt. Institution, heavy patient load and limitation of drug has led to this condition. Inclusion of various lab tests like; complete blood picture, culture & sensitivity test, renal function test and liver function test will be more useful in selecting antibiotic & analgesic which will ultimately lead to better patient care.

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