

Pharmacoepidemiology of Drugs Used in Indoor Patients of Orthopaedic Department at a Tertiary Care Hospital

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Abstract

Background: Globally, with the increasing orthopaedic admissions, the management modalities have also been evolving. With the focus mainly on reducing hospital stay and improving quality of life, pharmacotherapy is a keystone in management. Thus, the present study was undertaken to assess the drug utilization in orthopaedic inpatients.

Methods: This is a cross sectional, observational study carried out over a period of one year from April 2021 to April 2022. Data was collected from prescriptions of 200 patients admitted in the Orthopaedic ward and evaluated for WHO Drug Use Indicators and potential drug-drug interactions (pDDI) and prescription pattern was noted. Adverse Drug Reactions (ADR) were noted and assessed.

Results: A total of 2046 drugs were prescribed in 200 prescriptions. Average number of drugs per prescription is 10.23. Antimicrobials (25.76%) was the most common class of drug prescribed followed by supplements (20.28%) and analgesics (16.13%). 79.42% drugs were prescribed by generic name, 82.06% were from the National List of Essential Medicines (NLEM) and 99.9% drugs were from hospital pharmacy. Antibiotics prescribed were as per WHO AWaRe guidelines. ADR noted in 4 patients with drug being discontinued in one case. pDDI were seen in 98% prescriptions with 95.8% being Pharmacokinetic interactions.

Conclusion: Current study provides insight into the drug utilisation pattern, highlighting the extensive use of antibiotics and analgesics in orthopaedic inpatients. Adherence to WHO guidelines helps reduce antibiotic resistance and promotes better patient care.

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Keywords: Drug Utilization Research; Orthopaedic; Cephalosporins

Introduction

Globally, in 2019, there were 178 million new fractures, 455 million prevalent cases of acute or long-term symptoms of a fracture that led to work absence, impaired quality of life, and high health-care expenditure (1). With the increasing orthopaedic admissions, the management modalities have also been evolving. The focus is mainly on reducing hospital stay and improving quality of life, with pharmacotherapy being a keystone in management (2). It includes frequent prescribing of antibiotics, prophylactically and therapeutically to treat infection, as well as analgesics for pain management (3,4). Rational prescribing of drugs is therefore very important to

prevent resistance, adverse drug reactions and to decrease cost of treatment along with reducing length of hospital stay. Drug utilization study is defined by WHO in 1977 as the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences (5,6,7). Pharmacoepidemiology refers to the epidemiological methods to study the clinical use and effects/side-effects of drugs in large numbers of people with the purpose of supporting the rational and cost-effective use of drugs in the population. Timely evaluation of drug utilization pattern is required to enhance therapeutics, decrease adverse effects, promote rational use of drugs and provide feedback to the prescribers (8). With these facts

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in consideration, the present study was planned with the aim of studying the drug utilisation in patients admitted in orthopaedics ward of a tertiary care hospital. The objective was to evaluate the prescriptions according to WHO drug use indicators, to study the occurrence of adverse drug reactions (ADR) and to study potential drug-drug interactions (pDDI).

Methods

This was a cross sectional, observational study conducted in Orthopaedic ward of a tertiary care teaching hospital over a period of one year from April 2021 to April 2022. After obtaining approval from Institutional Ethics Committee (Reference number D-0121020-020 dated 22-1-2021) patients of either gender and all ages admitted in Orthopaedic ward and those voluntarily willing to give written informed consent were included in the study. Demographic details, prescription pattern that includes the class of drugs, strength, dose, frequency and route of administration of drugs prescribed, WHO prescribing indicators (9), adverse drug reactions and potential drug-drug interactions (pDDI) were studied in 200 patients. Also, the use of antibiotics as per WHO AWaRe guidelines (10) were studied which classifies antibiotics into Access, Watch, Reserve (AWaRe) group. "Access group includes antibiotics having activity against a wide range of common susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Watch group antibiotics include most

of the highest priority agents, have higher resistance potential, that should be reserved for the treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics are last resort options, use of which, should be tailored to highly specific patients when all other alternatives have failed or are not suitable" (10). Data was entered in Microsoft Excel Software and assessed using descriptive statistics. Potential drug-drug interactions, that are possible variations in response to a drug when it is co-administered with another drug were studied using Medscape drug interaction checker (11).

Results

Of 200 patients enrolled in the study, there were 148 males (74%) and 52 females (26%). The mean age was 45.62 years with range of 21-80 years. 26% were in the age group of 31-40 years followed by 22% above 60 years. Patients admitted were of fractures (170), total hip replacement (17), total knee replacement (3), implant removal (5), ligament tear (3), septic arthritis (1), osteomyelitis (1). Important risk factors predisposing to fractures observed were advancing age, that is 33 patients were above 65 years of age, 31 females with postmenopausal status, alcohol consumption seen in 15 patients and 1 patient had osteoporosis. Out of 170 patients with fractures 102 patients (60%) were of open fractures and 68 (40%) were closed fractures with fracture related infection seen only in 4 patients (2.35%).

Table 1. WHO prescribing indicators.

| Prescribing Indicator | Results | |
|---|-----------|--------|
| Average number of drugs per encounter | 2046/200 | 10.23 |
| Percentage of drugs prescribed by generic name | 1625/2120 | 79.42% |
| Percentage of encounters with an antibiotic prescribed | 200/200 | 100% |
| Percentage of encounters with an injection prescribed | 200/200 | 100% |
| Percentage of drugs prescribed from essential drug list | 1679/2046 | 82.06% |

Table 2. Drugs prescribed in Orthopaedic inpatients.

| Sr No | Types of drugs prescribed | Total number of encounters | Percentage |
|-------|------------------------------|----------------------------|------------|
| 1 | Tramadol | 130 | 6.35% |
| 2 | Diclofenac | 200 | 9.78% |
| 3 | Pantoprazole | 200 | 9.78% |
| 4 | Ondansetron | 200 | 9.78% |
| 5 | Calcium lactate | 200 | 9.78% |
| 6 | Iron sulphate + Folic acid | 12 | 0.59% |
| 7 | MVBC | 200 | 9.78% |
| 8 | Vitamin D3 | 3 | 0.15% |
| 9 | Amoxicillin- Clavulanic acid | 5 | 0.24% |
| 10 | Cefotaxime | 95 | 4.64% |
| 11 | Ceftriaxone | 105 | 5.13% |
| 12 | Metronidazole | 152 | 7.43% |
| 13 | Piperacillin- Tazobactam | 5 | 0.24% |
| 14 | Gentamicin | 156 | 7.62% |
| 15 | Vancomycin | 5 | 0.24% |
| 16 | Co-trimoxazole | 3 | 0.15% |
| 17 | Teicoplanin | 1 | 0.05% |
| 18 | Paracetamol | 60 | 2.93% |
| 19 | Metformin | 15 | 0.73% |
| 20 | Insulin | 8 | 0.39% |
| 21 | Amlodipine | 15 | 0.73% |
| 22 | Atorvastatin | 1 | 0.05% |
| 23 | Atenolol | 2 | 0.10% |
| 24 | Bupivacaine | 189 | 9.24% |
| 25 | Clonidine | 45 | 2.20% |
| 26 | Fentanyl | 5 | 0.24% |
| 27 | Lignocaine | 6 | 0.29% |
| 28 | Aspirin | 2 | 0.10% |
| 29 | Rivaroxaban | 2 | 0.10% |
| 30 | LMWH | 18 | 0.88% |
| 31 | Warfarin | 1 | 0.05% |
| 32 | Tetanus immunoglobulin | 2 | 0.10% |
| 33 | Teriparatide | 2 | 0.10% |
| 34 | Bisacodyl | 1 | 0.05% |

Table 3. Antibiotics classified as per WHO Access, Watch, Reserve (AWaRe) classification.

| Antibiotics classified as per WHO AWaRe classification | Total number of encounters (x) | Percentage = x/ Total no of antibiotics prescribed (527) *100 |
|--|--------------------------------|---|
| Access | 316 | 59.96% |
| Amoxicillin- Clavulanic acid | 5 | 0.95% |
| Metronidazole | 152 | 28.84% |
| Gentamicin | 156 | 29.60% |
| Co-trimoxazole | 3 | 0.57% |
| Watch | 211 | 40.04% |
| Cefotaxime | 95 | 18.03% |
| Ceftriaxone | 105 | 19.92% |
| Piperacillin- Tazobactam | 5 | 0.95% |
| Vancomycin | 5 | 0.95% |
| Teicoplanin | 1 | 0.19% |
| Reserve | 0 | 0% |
| None | | |

A total number of 2046 drugs were prescribed over 200 prescriptions. Prescriptions were analysed according to WHO indicators and summarised in Table 1. 99.9% drugs were prescribed from hospital pharmacy. Polypharmacy (Prescriptions having 5 or more than 5 drugs) was seen in 100% prescriptions. Fixed dose combinations (FDCs) included Multivitamin B complex (200), Amoxicillin clavulanic acid (5), Ferrous sulphate folic acid (12), Cotrimoxazole (3) and Piperacillin Tazobactam (5). The details of drugs prescribed are shown in Table 2 and class-

Antibiotics (25.76%) was the most common class of drug prescribed followed by Supplements (20.28%) and Analgesics (16.13%).

Average number of antibiotics per prescription was 2.635. Antibiotics were classified as per WHO Access, Watch, Reserve (AWaRe) classification and summarised in Table 3. Most common analgesic prescribed was Diclofenac (9.78%). Drugs given parenterally accounted for 63.29 % and 36.71% drugs were given orally.

$$\begin{aligned} \text{Average number of antibiotics per prescription} &= \frac{\text{Total number of antimicrobials prescribed}}{\text{Total number of prescriptions}} \\ &= 527/200 = 2.635 \end{aligned}$$

$$\begin{aligned} \text{Average number of analgesics per prescription} &= \frac{\text{Total number of analgesics prescribed}}{\text{Total number of prescriptions}} \\ &= 330/200 = 1.65 \end{aligned}$$

Of 200 patients, adverse drug reactions were observed in 4 patients (2%) as seen in Table 4.

Causality assessment for Adverse drug reactions was done with Naranjo Scale (12).

Of 200 prescriptions, 196 (98%) prescriptions had the potential for possible drug interactions. 95.8% of DDI were due to Pharmacokinetic (PK) interactions and 4.2% were Pharmacodynamic (PD) interactions.

Table 4. Drugs causing ADRs, Causality Assessments and Management

| Drug Prescribed | ADR | No. of patients with ADR | Causality assessment as per Naranjo Scale | Drug continued/ discontinued | Management |
|-----------------|-------------------------------|--------------------------|---|------------------------------|---------------------------------------|
| Vancomycin | Red man syndrome | 1 | Probable | Discontinued | Inj. Pheniramine, Inj. Hydrocortisone |
| Aspirin | Gastritis | 1 | Possible | Continued | Injection Pantoprazole |
| Metronidazole | Nausea, Vomiting Diarrhoea | 1 | Possible | Continued | Symptomatic |
| Diclofenac | Nausea, epigastric pain | 1 | Possible | Continued | Injection Pantoprazole |

Discussion

A total of 200 patients admitted in Orthopaedic ward were selected and their prescriptions were analysed. The mean age of patients was 45.62 years as compared to 51.84 years seen in another study (13). Patients above 60 years constituted 22% similar to the 20.3% observed by Abhilash et al., (14) emphasizing the fact that age related bone changes in the geriatric population makes them prone to fractures even after trivial trauma. Male preponderance was higher 148 (74%) as compared to females 52 (26%), like in the study done by Muraraiiah et al., where 73% patients were males, while 27% were females (15). Out of 52 female patients 31 were postmenopausal and 21 were premenopausal. None of the postmenopausal women received hormone replacement therapy. Higher percentage of postmenopausal females is in adherence with standard literature, that postmenopausal osteoporosis increases risk of fragility fractures (16). In our study fractures (170 patients, 85%) was the most common condition admitted in the Orthopaedic ward similar to Choudhury et al., study wherein fractures were the most common condition comprising 72% of patients (17). Advancing age, that is age more than 65 years was seen in 33 participants (16.5%) and postmenopausal status in females in 31 participants (15.5%) were found to be the most common risk factors. Diabetes was the most common co-morbidity noted, similar to study done by Srividya et al., (3) where hypertension and diabetes were the most common associated comorbidity in majority of study population. It was seen that 102 patients (60%) admitted in the Orthopaedic ward were of open fractures and 68 (40%) were closed fractures. Fracture related infection was seen in 4 patients only (2.35%) which was lesser as compared to 5% observed in a study done by Radhamony et al., (18). Fracture related infection was seen due to resistant organisms – Staphylococcus aureus (Methicillin resistant), Klebsiella pneumonia, Coagulase

negative staphylococcus aureus, E coli. Thus, 97.65% patients who did not show any fracture related infection, were probably benefitting from good infection control practices and antimicrobial prophylaxis.

A total of 2046 drugs were prescribed in the 200 case files that were analysed for

WHO Prescribing Indicators. Average number of drugs per prescription was 10.23, slightly higher than 8.86 seen in study by Baghel et al., (6) suggesting that polypharmacy (seen in all prescriptions) is common in orthopaedic inpatients due to factors like infection, immobility, combination of risk factors and comorbidities, all requiring pharmacological intervention. In the present study, the most commonly prescribed class of drug was Antimicrobials (25.7%) followed by Supplements (20.28%) and Analgesics (16.13%) which is different from study done by Srividya et al., where analgesics (31.81%) followed by antibiotics (22.24%) were most commonly prescribed (3). In this study, 79.42% of the drugs were prescribed by the generic name which was higher than 60% observed in another study. Promoting generic drugs enables patients to get affordable health care and reduces economic burden on patients (15). 99.90 % of the prescribed drugs were available in hospital pharmacy. This is a good indicator as maximum drugs were available in the tertiary care hospital where the study was conducted. According to WHO 100% drugs should be prescribed from NLEM. In the present study 82.06 % of the prescribed drugs were mentioned in National List of Essential Medicine 2021 (NLEM) similar to 85% seen in study done by Muraraiiah et al., (15). Prescribing maximum drugs from NLEM ensures affordable and accessible healthcare for all. In our study percentage of encounters with antibiotics prescribed was 100% similar to study by Anjani Teja et al., probably because the study was done in orthopaedic wards where surgical intervention warranted the use of antibiotics for

prophylaxis and treatment (7). In the present study only 11% drugs were prescribed as a fixed dose combination (FDC), all FDCs being rationale and justified. In a study done by Abhilash et al., 40.3% drugs prescribed were FDCs which is much higher as compared to our study (14). It is of utmost importance that FDC prescribed are rational since irrational FDCs not only produce undesirable adverse effects but also increase economic burden on patients and healthcare as a whole.

Average number of antimicrobials used was 2.635. Antibiotics prescribed meticulously followed the WHO Access, Watch, Reserve (AWaRe) classification keeping in mind the need to reduce antimicrobial resistance. In our study, 59.96% of antibiotics were from access group which is in accordance with the WHO recommendation that at least 60% antibiotics should be from the Access group. Watch group antibiotics, consisted of 40.04% and Reserve group antibiotics that is “last resort” antibiotics were not used at all in our study. This highlights the judicious use of antibiotics, which is extremely important to prevent drug resistance (10).

Diclofenac was the most common analgesic prescribed our study (60.61%) which was similar to study done by Choudhury et al., (43.49%) (12). Average number of analgesics per prescription was 1.65 which was lesser as compared to a study done by Baghel et al., (6) where it was 2.24 and similar to study done by Choudhury et al., (17) where average number of analgesics per prescription was 1.46. In patients where pain was not relieved with diclofenac, top ups of tramadol were given to relieve severe pain. Among the 200 patients, adverse drug reactions were observed in 4 patients.

Red Man Syndrome was seen in 1 patient who received Vancomycin after which drug was discontinued. Sivagnanam et al., mentions it to be the most common hypersensitivity reaction associated with vancomycin (19). Polypharmacy predisposes patients to develop ADRs and DDI, thus their identification, prevention and treatment is vital to patient safety (20). 196 (98%) prescriptions had the potential for possible drug interactions, 4 prescriptions had no potential drug interaction, whereas 3 pDDI were noted in majority of prescriptions (114). This finding was different as compared to a study done by Solanki and Patel et al where maximum number of prescriptions (60) showed 4 pDDI. The maximum number of possible drug interactions in prescriptions was 4 and minimum number of interactions was 1. In study done by Solanki and Patel et al maximum number of drug interactions in a prescription was 5. A total of 500 possible drug interactions were noted, out of which 479 (95.8%) were Pharmacokinetic drug interactions and 21(4.2%) were Pharmacodynamic drug interactions. Similar findings were seen in study done by Solanki and Patel et al., where out of 660, 613

(92.87%) were Pharmacokinetic and 47 (7.13%) were Pharmacodynamic drug interactions (20). A study by Yadav et al., also showed Pharmacokinetic interactions to be higher (88.2%) than Pharmacodynamic ones (11.8%) (21). In our study, a few potential drug interactions were such that they would require close monitoring of therapy to prevent adverse effects (Aspirin and diclofenac which had potential to increase chances of bleeding) while others did not have any significant clinical consequence (Pantoprazole (oral) and Ferrous sulfate, Pantoprazole (oral) and cyanocobalamin). Some interacting drugs showed pharmacodynamic synergism, that increased the effect of drugs and was beneficial in therapy. No serious drug interaction requiring modification in therapy was noted.

The study was done in a single tertiary care teaching hospital with small sample size, extrapolation of results would be better with a large sample and multicentric studies.

Current study provides insight into the drug utilisation pattern, highlighting the extensive use of antibiotics and analgesics in orthopaedic inpatients. A high percentage of the drugs were prescribed from the Hospital pharmacy and National List of Essential Medicines (NLEM), encouraging the idea of accessible and affordable healthcare for all. Our study highlighted the adherence to WHO AWaRe guidelines while prescribing antibiotics, be it for prophylaxis or treatment as a key in reducing antibiotic resistance which is a massive healthcare concern today. Although polypharmacy is usually unavoidable in orthopaedic inpatients, it is advisable to limit the number of drugs per prescription to as low as possible, to minimize the risk of potential DDI and adverse drug reactions that may occur subsequently. Study of pDDI enables to timely catch any serious drug interaction that may require therapy modification and early identification and management of ADR helps ensure better clinical outcomes thereby reducing economic burden on health care system.

Conflict of Interest

There are no Conflict of Interest.

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