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Prescribing Pattern and Drug–Drug Interactions of Analgesics Prescribed For Pain Management in a Pakistani Tertiary Hospital

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Introduction Pain remains one of the top five reasons for consultations in general practice, presenting either alone or as co morbidity [1]. Pain can be defined as "unpleasant sensory and emotional experience associated with actual or potential tissue damage" [2,3]. Reports show that, more than 1.5 billion people undergo chronic pain, globally [4]. New data show that a 20% world's population suffers from moderate to severe chronic pain. Moreover, due to pain, about a 35% world's population cannot sustain an independent life style [5]. Although pain cannot be completely abolished, yet if proper treatment plan is made initially after assessing the intensity of pain, it can be relieved in more appropriate way. The primary goal of analgesic therapy is to decrease the intensity of pain to bearable one in order to restore the physical functions. The World Health Organization (WHO) established guidelines that physicians should follow in prescribing analgesics [6]. Moreover, a 10-point scoring system was developed to assess pain intensity, in order to assist physicians while developing therapeutic strategy for pain management [7]. However, several reports have highlighted the problems linked with pain management, such as assessment of pain intensity, side-effects management and use of concomitant drugs [8]. The magnitude of irrational prescribing of medicines in Pakistan has been highlighted in many reports [9-12]. This study is aimed at analyzing the prescribing pattern of analgesics for patients with different degree of pain admitted in Oncology and General Surgery wards of a tertiary care hospital in Peshawar. The duration of analgesic therapy is correlated with the therapeutic outcome thereof (reduction in degree of pain with prescribed analgesics). Furthermore, prescriptions are analyzed for compliance of standard guidelines in analgesic therapy and interactions of analgesics with other prescribed drugs. Methodology This non interventional, cross sectional study was conducted from 16th August 2015 to 15th October 2015 at Rehman Medical Institute, Peshawar, a tertiary care 400 bedded hospital. Data were collected from General Surgery Ward and Oncology Ward. Data collection Data were collected using specified Performa designed for the purpose of the study. The Performa was divided into four main parts i.e., Patient's demographic data, patient medical history and tools for analyzing prescriptions. Inpatients included in study were continuously interviewed throughout their stay at hospital in order to evaluate the effectiveness of advised analgesic therapy. Prescriptions were reviewed for analgesic preferences and potential drug–drug interactions. Adult patient prescribed with analgesics, hospitalized in oncology and general medicine ward, were included in the study. Patients below age of 10, or hospitalized for short duration, or undergone major surgeries were also excluded from the study. Assessment of pDDIs pDDIs were analyzed using Stockley drug interactions book [13] and Medscape Multi Drug interaction checker [14]. Data Analysis The data was statistically analyzed using SPSS software, version 17 (SPSS, Inc., Chicago, IL, USA). Results A total of 45 inpatient prescriptions (53.3% male and 46.6% female) were analyzed. Demographic information of the patients is given in Table 1. Around 22% of the patients are from 31–40 years age group, while 41–50 years age group is around 20%. Similarly, 21–30 years and 51–60 years age groups are each 18% in the study. As shown in Table 1, the predominant reason for hospitalization was found to be cholelithiasis (17.8%), liver and stomach cancer (11.1% each). While breast cancer, choriocarcinoma and portal vein thrombosis accounted for about 7% of the hospitalization. The duration of hospitalization might reflect the severity of complication. For instance, around 29% of the patients were hospitalized for 3 days, while 4 days and 5 days hospitalization was seen for 27% and 18% of the patients. Duration longer duration than 5 days was less common. While analyzing the prescriptions for polypharmacy, it was observed that 51% cases had 11–15 drugs per prescription, while 6–10 drugs per prescription was observed in 35.6% patients (Table 1). Moreover, 16– 30 drugs per prescription were observed in 11% patients. As for as the number of analgesics prescribed per prescription, 55.6 % prescriptions had two analgesics per prescription, while 3 and 4 analgesics per prescription were seen in 24.4 % and 17.8 % prescriptions, respectively. Only 2.2% cases had received a single analgesic (Table 1). As shown in Figure 1a–c, the most favored analgesic was tramadol, which was present in 25% of prescription, while nalbuphin was the second most frequently prescribed analgesic (seen in 16.38% prescription). Moreover, ketorolac and ibuprofen was observed in only in 11.21 and 9.48% prescription, while morphine was prescribed to 3.45% patients. Interestingly, the selected therapeutic regimen of analgesics was ineffective in pain management. For instance, as shown in Table 1, 53.3% patients had intense pain post analgesic therapy, while complete relief from pain was observed only in 28.9% cases. Moreover, 17.8% cases had mild pain after analgesic therapy. Furthermore prescriptions were analyzed for the extent of pDDIs (Figure 2). Each prescription had some extent of pDDIs. More Variables N (%) Gender Male Female 24 (53.3) 21 (46.7) Age groups (years) 10-20 21-30 31-40 41-50 51-60 61-70 71-80 81-90 3 (6.7) 8 (17.8) 10 (22.2) 9 (20.0) 8 (17.8) 4 (8.9) 1 (2.2) 2 (4.4) Duration of hospitalization (days) 3 4 5 6 7 8 9 10 12 13 (28.9) 12 (26.7) 8 (17.8) 1 (2.2) 5 (11.1) 2 (4.4) 2 (4.4) 1 (2.2) 1 (2.2) Number of drugs prescribed per prescription 1-5 6-10 11-15 16-30 1 (2.2) 16 (35.6) 74.1 (51.1) 16 (11) Main Reason for Hospitilization Liver Cancer Stomach Cancer Breast Cancer Nasopharynx Cancer Cervical Cancer Choriocarcinoma Acute Lymphoblastic Leukemia Lymph Node Cancer Cancer Esophagus Endometrial Carcinoma Testsicular Cancer Cerebral Mets Neuro Endocrine Cancer Rhabdomyo Sarcoma Prostate Cancer Cholelithiasis Lipoma Portal Vein Thrombosis Bile Peritonitis Hydated Liver Cyst Irritable Bowel Syndrome Gallbladder Cancer 5 (11.1) 5 (11.1) 3 (6.7) 1 (2.2) 2 (4.4) 3 (6.7) 1 (2.2) 1 (2.2) 1 (2.2) 1 (2.2) 1 (2.2) 1 (2.2) 2 (4.4) 1 (2.2) 1 (2.2) 8 (17.8) 1 (2.2) 3 (6.7) 1 (2.2) 1 (2.2) 1 (2.2) 1 (2.2)

Table 1: Demographic and hospitalization information of patients. Citation: Khan SA, Afridi R, Afridi UK, Sadozai S (2016) Prescribing Pattern and Drug–Drug Interactions of Analgesics Prescribed For Pain Management in a Pakistani Tertiary Hospital. J App Pharm 8: 230. doi: 10.21065/1920-4159.1000230 Page 3 of 4 Volume 8 • Issue 4 • 1000230 J App Pharm, an open access journal ISSN: 1920-4159 specifically, the most predominant case was that of 5-6 pDDIs per prescription (i.e., 22%). Moreover, 18% patients received prescriptions having 7–8 pDDIs. Similarly, 1–2 and 3–4 pDDIs were observed in 18% and 20% prescriptions, respectively. Nevertheless, total of 276 interactions were found in 45 prescriptions, in which 60% were of major or moderate nature, while minor pDDIs were around 40 % (Table 2). Most of the major pDDIs were because of concomitant prescription of tramadol with dexamethasone and ondansteron, which was 25% and 19% of the major pDDIs, respectively. Similarly, simultaneous use of Ondansteron with dexamethasone and flouroquinolones resulted in 13% and 18% of the major pDDIs found, respectively. Discussion Our study identifies that in most of the patients, pain is undertreated. The analgesic prescribing pattern remained same for all patients regardless of their pain intensity. Murnion Gnjidic et al., reported same kind of results in orthopedic and cancer patients and attributed it to the poor health care provider's knowledge as main cause of incomplete analgesia [15]. Lack of assessment of intensity of pain was identified in our study as a major cause of incomplete analgesia in majority of patients. Our study has also identified many pDDIs which might have resulted in reduced plasma levels of prescribed analgesics, hence posing a barrier to achieve desired analgesia. Patients self-report is most valuable measure of pain intensity, which should be properly evaluated and analgesic selection, should be based on that evaluation [16]. For proper pain assessment there should effective communication between patient and health care provider. The WHO analgesic ladder is easy tool for righteous selection of analgesic according to the intensity of pain. The pain assessment numerical score is a standard tool used in many advanced countries for analgesic selection [16]. However, these guidelines were not followed, as per our observations. Patients employed in our study showed mean pain score in the range of 6–7 (data not shown), which is considered as moderate to severe pain, yet it did not affected the prescribers choice in selecting analgesic. For instance, Morphine and Fentanyl were scarcely used. Moreover, the choice of dosage form was also not rigorously managed, such as, morphine and many other potent analgesics were administered only intravenously, even though these drugs are available in oral dosage forms. Tramadol and Ketrolac were common analgesics prescribed, while other analgesics were seldomly prescribed. Similarly, the of adjuvant analgesic were rare, although dexamethasone was present but it was indicated for other purpose rather than as adjuvant analgesic. We also encountered several pDDIs frequently found in patients prescribed with numerous drug combinations, and 60% of these pDDIs were of major severity. Analgesic combination with other drugs were identifies as major cause of pDDIs. Similar results are also reported by Riechelmann et al., [17] and van Leevun et al., [18], where almost 34 % noted pDDIs were of major severity. One of the poor pain management in Pakistani hospital may be the lack of pharmacist involvement in health care team. Pain management is a collaborative team work, in which pharmacist work with physicians to determine optimal analgesic regimen according to the needs of patient [19]. It is pharmacist's understanding and knowledge of drugs– drug interactions, drug pharmacokinetics and mechanism of action that can help to individualize analgesic regimen so that complete analgesia can be achieved with minimal adverse drug reaction [16]. Conclusion This study identified that limited number of analgesic both opioids and NSAIDs are used in management of acute and chronic pain. The 0 5 10 15 20 25 Fre q u e n c y (%) No. of pDDIs/prescription Figure 2: Prevalence and extent of pDDIs per prescription. 2.2 55.6 24.4 17.8 Frequency (%) 4 analg./prescr. 3 analg./prescr. 2 analg./prescr. 1 analg./prescr. 25% 16% 3% 11% 7% 3% 10% 6% 1%1% 3% 7% 1% 5% 1% Tramadol Nalbuphin Morphine Ketorolac Paracetamol Paracetamol + Orphenadrine Ibuprofen Meloxicam Naproxen Fentanyl Mefanamic Acid Dexamethasone Piroxicam Alprazolam Gabapentin 28.9 53.3 17.8 Post analgesic therapy response (%) No Pain Sever Pain Mild Pain (a) (b) (c) Figure 1: Diagrammatic Representation of (a) number of analgesics/prescriptions (b) Frequency of analgesics prescribed (c) Effectiveness of analgesics therapeutic regimen. Citation: Khan SA, Afridi R, Afridi UK, Sadozai S (2016) Prescribing Pattern and Drug–Drug Interactions of Analgesics Prescribed For Pain Management in a Pakistani Tertiary Hospital. J App Pharm 8: 230. doi: 10.21065/1920-4159.1000230 Page 4 of 4 Volume 8 • Issue 4 • 1000230 J App Pharm, an open access journal ISSN: 1920-4159 Nature of pDDIs N (%) Total Number pDDIs 271 Minor 106 (40) Major/Moderate 165 (60) Distribution of Major pDDIs Dexamethsone + Tramadol 25 (15) Ondansetron + Tramadol 19 (11) Benzodiazepines + Opioids 13 (7.8) Dexamethasone + Ondansetron 18 (10.9) Flouroquinolones + Ondansetron 7 (4.2) NSAIDS + Flouroquinolones 5 (3) Dexamethasone + Benzodiazepines 10 (6) Antihistamines + Opioids 13 (7.8) Dexamethasone + Flouroquinolones 6 (3.6) Levofloxacin + tropisetron 6 (3.6) Table 2: Nature of pDDIs and Common interacting drug-combinations. use of potent opioids in post-operative and cancer pain management is nearly negligible. Severe pain is even treated with analgesic like tramadol and ketorolac, which are not sufficient to reduce the intensity of pain up to bearable scale; consequently, pain is under treated in majority of patients. Moreover, analgesic was prescribed without assessing the pain intensity. Improper analgesic regimen is often selected and too many interacting drugs are prescribed simultaneously.