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ORIGINAL RESEARCH ARTICLE

Utilization, availability of analgesics and quality of pain control for post-operative pain in surgical patients

Ya Min[1] · Thida Tun[1] · Ye Htut Linn[1] · Nu Nu Aye[1] · Nang Hla Hla Win[1]

Abstract

Background Effective post-operative pain control can provide patient comfort and satisfaction and also improve quality of life.

Objectives The study aimed to determine the amount of opioid and non-opioid analgesics used during the 24-h post-operative period, as well as the effectiveness of pain control, in the general surgical wards of Thingangyun Sanpya General Hospital and Yangon General Hospital in Yangon, Myanmar.

Methods We conducted this hospital-based, prospective, cross-sectional descriptive study over a period of 5 months (May to September, 2016). World Health Organization (WHO) Anatomical Therapeutic Chemical classification (ATC)/Defined Daily Dose (DDD) methodology and drug utilization (DU) 90% segments were used to determine the amount of opioid and non-opioid analgesics used during the 24-h post-operative period. The effectiveness of pain control was determined using a numerical rating scale (NRS) and the pain Management Index (PMI).

Results Among total 233 post-operative patients, 161 patients (69%) received combined opioids and non-opioid analgesics, 36 patients (15.5%) received opioid analgesics only and 36 patients (15.5%) received non-opioid analgesics only. Total analgesic usage was 11.04 DDD/1000 inhabitants/days. Diclofenac was the most frequently prescribed analgesic (5.9 DDD/1000 inhabitants/days), followed by tramadol (1.9), and ketorolac (1.75); fentanyl was the least frequently prescribed (0.04). Diclofenac, tramadol and ketorolac were included in the DU 90% segment. Six hourly NRS records reveal 7–25% of patients suffered moderate pain and 0.9–2.1% suffered severe pain. By using PMI, 208 patients (89.3%) received adequate pain medication and 25 patients (10.7%) received ineffective pain medication. All analgesics listed in the 2016 Myanmar National List of Essential Medicines were available on these wards.

Conclusion The results of this study can provide information to the prescriber about to what extent analgesics were being used and to policy makers or administrators for planning services on management of post-operative pain.

Introduction

Drug utilization research is a very important part of pharmacoepidemiology in determining the extent, nature and determinants of drug exposure [1]. The World Health Organization (WHO) has defined drug utilization as the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences [2]. Drug utilization research can be used to estimate the numbers of patients exposed to specified drugs within a given time period.

Drug utilization is measured with the WHO Anatomical Therapeutic Chemical classification (ATC)/Defined Daily Dose (DDD) methodology. The Anatomical Therapeutic Chemical Classification System categorizes the active pharmaceutical ingredient of a drug by its therapeutic use and targeted organ or system, for example, the heart or circulatory system. Once the drug has been classified and assigned an ATC code, a DDD is determined in order to accurately measure utilization. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults, and can only be assigned for drugs that already have an ATC code. The DDD is purely a technical unit of

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✉ Ye Htut Linn
dryehtutlinn@gmail.com

[1] Department of Pharmacology, University of Medicine 1, Yangon, No. 245, Myoma Kyaung Street, Yangon, Myanmar

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measurement and comparison and provides a rough estimate of the proportion of patients within a community that would receive the drug treatment [3]. The ATC/DDD system is intended to serve as a tool for drug utilization research in order to improve the quality of drug use. It is usually used for the presentation and comparison of drug consumption statistics at international and other levels.

Drug Utilization 90% (DU 90%) identifies the drugs accounting for 90% of the volume of prescribed drugs after ranking the drugs used by volume of DDD [4]. The remaining 10% may contain specific drugs used for rare conditions in patients with a history of adverse effects or intolerance to a drug, complex co-morbidities and/or therapy prescribed by others [5]. The DU 90% segment may be used to evaluate adherence to local or national prescription guidelines.

Pain has been defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage [6]. As the feeling of pain is subjective, there is inter-individual variation, and dosage of analgesics needs to be adjusted for each individual to get adequate pain control. The goal of effective pain management is to provide relief and satisfaction to patients, expedite recovery and functional ability, reduce morbidity and minimize hospital stay.

Opium and its synthetic derivatives are the most effective analgesics in the immediate post-operative period [7]. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used drugs for the management of pain and inflammation, have good efficacy, represent the most widely used class of medications in the world, and are available as over-the-counter drugs [8]. The combined use of opioid and non-opioid analgesics is currently popular. A study done in India found that the combined use of analgesics was 36.9% and the use of opioid as a sole analgesic agent was 26.6% for post-operative pain [9]. Among them, tramadol was the most consumed analgesics in two studies conducted in India [9, 10], as well as in developed countries such as Finland, Norway, Denmark, Spain and Australia [11]. In contrast, a study conducted in 15 countries (including Australia, the People's Republic of China, Malaysia, Taiwan, Canada and the UK) reported that diclofenac was the most consumed analgesic in the DU 90% segment [12]. The World Federation of Societies of Anesthesiologists have developed the "Analgesic Ladder" to treat acute pain [13]. According to this ladder, immediately after an operation, pain can be expected to be severe and may require treatment with strong parenteral opioids together with local anesthetic blocks and peripherally acting drugs. A German study found that the pain score of patients is often high [numerical rating scale (NRS) score > 4] on the day after surgery [14]. Other studies in the Netherlands and Sweden reported that, on the first post-operative day, 30–43% of patients had moderate or severe pain (NRS score > 4) [15, 16]. Optimizing pain management can improve the outcome of patient care after any surgical interventions.

Quality of pain control is evaluated by the Pain Management Index (PMI). It is a useful indicator of adequacy in evaluating the range and appropriateness of pain treatment for hospitalized post-operative patients [17, 18].

Globally, the consumption of opioid analgesics has increased considerably between 1991 and 2013; however, their consumption is significantly low in developing countries compared to the developed ones due to legal and resource limitations [19]. According to a study conducted in Ethiopia, 80.1% of patients received ineffective pain medication during their post-operative period, indicating insufficient and inappropriate management of post-operative pain, which is partly due to the high cost of opioids [20]. A survey of anesthetic officers in Uganda showed that only 45% always had either pethidine or morphine available; 21% never had these drugs available [21]. A study done in India stated that potent opioids, such as morphine and pethidine, were not used in their hospital due to their non-availability [10].

There are very few data for the utilization of analgesics in the post-operative period in Myanmar. This study can provide data for analgesics utilization, availability and quality of pain control in surgical wards of teaching hospitals in Yangon, and this may help to improve post-operative pain management and analgesic drugs supply and procurement.

Materials and methods

This hospital-based, prospective, cross-sectional descriptive study was conducted from May 2016 to September 2016 in Surgical Unit 1 of Yangon General Hospital (YGH) and the General Surgical ward of Thingangyun Sanpya General Hospital (TSGH).

Patient selection

The inclusion criteria are as follows: (1) both male and female patients aged ≥ 13 years, (2) patients who underwent elective major operations with spinal, general anesthesia or epidural anesthesia, and (3) patients who gave informed consent. Patients who were seriously ill, had a mental disorder, were unable to respond to verbal questions, or had undergone an operation under local anesthesia were excluded from the study.

Data collection

Complete patient demographic data and the type of surgery were recorded. Different types of analgesic, prescribed dose of analgesics, routes of administration and other co-administered analgesics were noted. The availability of analgesics listed in the Myanmar 2016 National List of Essential Medicines (NLEM) was checked with the stocks of each ward.

Assessing pain score using a numerical rating scale

Patients' pain scores were determined by pain assessment score on the NRS at 6-h intervals during the 24-h post-operative period. The patients were asked to rate their pain intensity on a scale from 0 to 10, with 0 indicating no pain at all, 1–3 mild pain, 4–6 moderate pain and 7–10 the worst possible pain [17].

Determining Pain Management Index scores

PMI scores are based on patients' level of worst pain intensity, which is categorized into 0 (no pain), 1 (1–3: mild pain), 2 (4–6: moderate pain) and 3 (7–10: severe pain) [17], which is then subtracted from the most potent level of analgesic drug therapies prescribed, which is categorised as 0 (no analgesic drug), 1 (non-opioids), 2 (weak opioids) and 3 (strong opioids) [18]; i.e. PMI score = pain score − most potent level of analgesic drug prescribed. The PMI score can range from − 3 to + 3. Negative scores indicate inadequate pain medication.

Data analysis

Data were coded, cleaned and analyzed using SPSS version 16. Analgesics utilization data were described with number and percentage and compared using the Chi-square test. Repeated measure analysis of variance (ANOVA) was used for comparing pain scores in different post-operative periods.

Determining DDD/1000 inhabitants/day

Total numbers of DDDs for each analgesic were calculated from collected data by DDD formula with DDDs of ATC index 2015 [22].

$$\text{Drug usage (DDDs)} = \frac{\text{Items issued} \times \text{Amount of drug per item}}{\text{DDD}}$$

$$\text{DDD/1000 inhabitants/day} = \frac{\text{Total consumption in DDDs} \times 1000}{\text{Covered inhabitants} \times \text{Days in the period of data collection}}.$$

Determining DU 90%

DU 90% segment was obtained by ranking analgesics as volume of DDD, summing the DDD for these drugs and then determining how many drugs accounted for 90% of drug use.

Results

Data from a total of 233 post-operative patients were analyzed in this study. Among them, 102 were male and 131 were female. Patient age ranged from 13 to 88 years, with most (68.3%) being aged between 40 and 70 years.

Table 1 shows the utilization of types of analgesics (opioids or non-opioids alone or combined) in the two hospitals for management of post-operative pain. Overall, analgesic utilization differed significantly ($p < 0.001$) between the YGH and the TSGH. The combined use of analgesics was more common in the YGH than in the TSGH, and the use of opioid analgesics alone was more common in the TSGH than in the YGH. The use of non-opioid analgesic did not differ between these hospitals.

Of the post-operative analgesics used in the 233 patients in the surgical wards of YGH and TSGH, tramadol was most commonly used (84.5% of patients), followed by paracetamol (54.2%), diclofenac (50.2%), ketorolac (21.5%) and fentanyl (7%).

Total utilization of analgesics in the post-operative period was 11.04 DDD/1000 inhabitants/day. Diclofenac (suppository, injection or oral formulations) was the most prescribed analgesic, tramadol was the second, ketorolac was the third and fentanyl was the least (Table 2). Diclofenac, tramadol and ketorolac were included in DU 90% segment.

The severity of pain during the 24-h post-operative period is described in Fig. 1. During the immediate post-operative

Table 1 Utilization of analgesic type in post-operative patients in surgical wards of the YGH and TSGH

Type of analgesic	No. of patients using analgesic (%)		
	YGH ($n = 151$)	TSGH ($n = 82$)	Total ($n = 233$)
Opioid alone	12/151 (7.9)	24/82 (29.3)	36/233 (15.5)
Non-opioid alone	24/151 (15.9)	12/82 (14.6)	36/233 (15.5)
Combined opioid + non-opioid	115/151 (76.2)	46/82 (56.1)	161/233 (69.1)

Chi-square = 18.785; $p < 0.001$

TSGH Thingangyun Sanpya General Hospital, *YGH* Yangon General Hospital

Table 2 Drug utilization 90% segment of analgesics in post-operative patients

Serial number	Drugs (strength)	ATC code	DDD (mg)	DDD/1000 inhabitants/day	Percentage
1.	Diclofenac suppository (100 mg/1 suppository)	M01AB05	100	4.55	41.2
2.	Diclofenac injection (25 mg/ml)	M01AB05	100	1.22	11.1
3.	Diclofenac oral (50 mg/tab)	M01AB05	100	0.13	1.2
4.	Tramadol (50 mg/ml)	NO2AX02	300	1.9	17.2
5.	Ketorolac (30 mg/ml)	M01AB15	30	1.75	15.8
6.	Paracetamol (500 mg/tab)	N02BE01	3000	1.45	13.1
7.	Fentanyl (0.05 mg/ml)	NO2AB03	0.6	0.04	0.4

ATC anatomical therapeutic chemical, *DDD* defined daily dose [22]

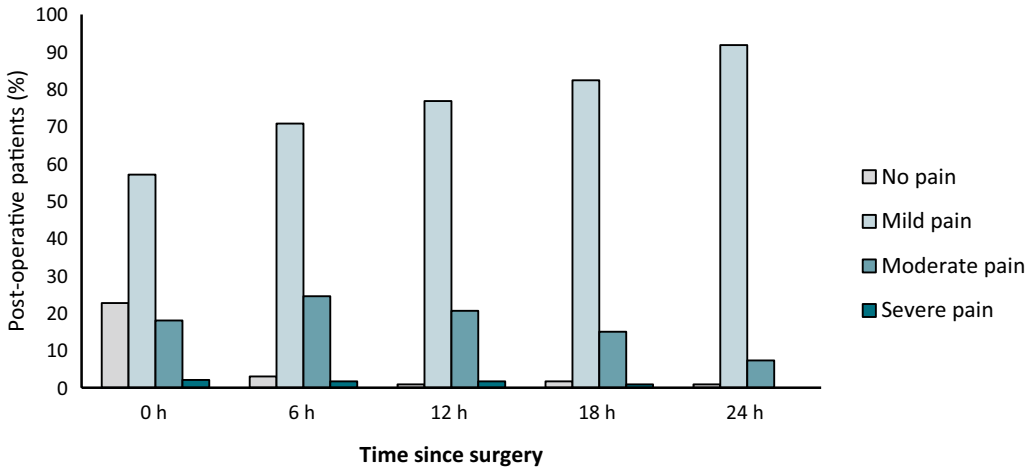

Fig. 1 Comparison of pain at different post-operative period by using NRS score. *NRS* numerical rating scale

period, 22.7% of patients reported having no pain. Patients suffered more moderate pain during the 6-h post-operative period than during any of the other periods. Most of the patients rated pain as mild during the 24-h post-operative period. At 24-h after operation, no patients reported severe pain.

Table 3 shows the post-operative NRS pain scores of surgical patients at baseline and every 6-h up to 24-h. Pain scores differed to a significant extent between cancer and non-cancer patients ($p = 0.001$) and between TSGH and YGH patients ($p < 0.001$), but not between genders, epidural in situ and patient-controlled analgesia, and types of analgesics used.

According to the PMI, 208 of the 233 patients (89.3%) received adequate pain medication, and the remaining 25 (10.7%) received ineffective pain medication.

All analgesics listed in the 2016 NLEM of Myanmar were available in these wards. (See the Electronic Supplementary Material, File 1.)

Discussion

The current study found that the majority of patients (69.1%) received combined analgesics (opioids + non-opioids) and only 15% of patients received opioid or non-opioid as sole analgesic agent for their post-operative pain control. In contrast, a study in our neighboring country of India found that the combined use of analgesics was not as high (36.9%) as that in our country, and that the use of opioids as a sole analgesic agent was very much higher (26.6%) than in the current study [9].

In the present study, tramadol (alone or in combination) was the most commonly prescribed analgesic (accounted for the use of 84.5% of all analgesics), followed by paracetamol and diclofenac. Likewise, tramadol was the most consumed analgesic in two studies conducted in India [9, 10], as well as in developed countries such as Finland, Norway, Denmark, Spain and Australia [11].

Table 3 Numerical rating scale pain scores at baseline and every 6-h up to 24 h, in post-operative patients

Pt group (number)	Mean post-operative NRS pain scores ± SD					*p* value
	0 h	6 h	12 h	18 h	24 h	
All pts (233)	2.22 ± 1.72	3.08 ± 1.51	2.98 ± 1.45	2.73 ± 1.21	2.49 ± 0.90	
Pts at TSGH (82)	2.58 ± 1.52	3.46 ± 2.01	3.42 ± 1.86	2.92 ± 1.42	2.77 ± 1.16	< 0.001
Pts at YGH (151)	2.03 ± 1.79	2.87 ± 1.12	2.75 ± 1.11	2.64 ± 1.08	2.34 ± 0.69	
Cancer pts (105)	1.82 ± 1.58	2.72 ± 1.48	2.66 ± 1.18	2.65 ± 1.27	2.43 ± 0.77	0.001
Non-cancer pts (128)	2.53 ± 1.76	3.35 ± 1.48	3.24 ± 1.58	2.80 ± 1.17	2.53 ± 0.99	
Male pts (102)	2.19 ± 1.78	3.18 ± 1.67	2.90 ± 1.40	2.67 ± 1.30	2.47 ± 0.96	0.420
Female pts (131)	2.24 ± 1.67	2.99 ± 1.37	3.05 ± 1.49	2.78 ± 1.14	2.50 ± 0.85	
Pts receiving epidural in situ (23)	2.04 ± 1.91	2.78 ± 1.44	3.22 ± 1.38	3.00 ± 1.34	2.70 ± 0.76	0.462
Pts using PCA (8)	2.26 ± 1.70	3.15 ± 1.50	2.94 ± 1.46	2.73 ± 1.20	2.48 ± 0.91	
Pts using only opioids (36)	2.00 ± 1.54	2.53 ± 1.71	2.75 ± 1.64	2.72 ± 1.54	2.44 ± 0.99	0.346
Pts using only non-opioids (36)	2.00 ± 1.56	2.94 ± 1.37	3.11 ± 1.34	2.58 ± 0.80	2.50 ± 0.84	
Pts using both (161)	2.32 ± 1.79	3.23 ± 1.47	3.01 ± 1.43	2.77 ± 1.21	2.49 ± 0.90	

NRS numerical rating scale, *PCA* patient-controlled analgesia, *pt* patient, *SD* standard deviation, *TSGH* Thingangyun Sanpya General Hospital, *YGH* Yangon General Hospital

In the present study, tramadol utilization was 17.2% in post-operative patients, compared with 35% in Norway and 72% in Slovakia [11]. In developing countries, such as Myanmar, opioid utilization and availability are generally restricted, because of legal limitations (e.g. tightly controlled access) and limited resources. In general, the availability and utilization of opioids as analgesics in developed countries are much higher than that in developing countries [19].

In the present study, only three drugs (diclofenac, tramadol and ketorolac) were included in the DU 90% segment. This was similar to the finding of a study conducted in 15 countries (including Australia, the People's Republic of China, Malaysia, Taiwan, Canada and the UK) in which diclofenac was the most consumed analgesic in the DU 90% segment [12].

In Croatia, utilization of morphine increased from 0.05 DDD/1000 inhabitants per day in 2007 to 0.06 DDD/1000 inhabitants per day in 2013, fentanyl from 0.56 to 0.62, tramadol from 2.5 to 2.61, diclofenac from 15.06 to 12.82, and paracetamol from 3.51 to 4.46 [23]. In Israel, consumption of five strong opioids increased by 47% over a 9-year period, from 2.46 DDD/1000 inhabitants per day in 2000 to 3.61 DDD/1000 inhabitants per day in 2008. This rise was mainly due to a fourfold increase in fentanyl consumption from 0.32 DDD/1000 inhabitants per day in 2000 to 1.28 DDD/1000 inhabitants per day in 2008. Oxycodone and methadone consumption levels rose moderately, and buprenorphine and dextropropoxyphene consumption increased significantly, whereas morphine, pethidine and codeine use significantly fell [24]. In Malaysia, by 2005, morphine utilization was 0.1094 DDD/1000 population/day, fentanyl utilization was 0.0065 DDD/1000 population/day and tramadol utilization was 0.3696 DDD/1000 population/day [25].

Globally, the consumption of opioid analgesics increased considerably between 1991 and 2013; however, their consumption is significantly low in developing countries, with Myanmar being no exception [19]. Apart from tramadol, there was a lower consumption of strong opioids like morphine (0.15 DDD/1000 inhabitants/day) and fentanyl (0.04 DDD/1000 inhabitants/day) in the present study.

In the present study, most patients did not suffer moderate and severe pain immediately after the surgery, which is probably due to the effects of anesthesia and intra-operative analgesics. Only a small proportion of patients suffered severe pain during the immediate and 6-h post-operative periods. According to a study done in German hospitals, the pain score of patients undergoing various types of surgery is often high, as indicated by NRS scores of > 4 on the day after surgery [14]. Another two studies done in the Netherlands and Sweden reported that on the first post-operative day, 30–43% of patients had moderate or severe pain (NRS score > 4) [15, 16].

Pain management was significantly ($p = 0.001$) better in cancer patients than in non-cancer patients in our study. This may be due to good pain management and acceptable pain during the intra-operative and post-operative periods. Pain control in non-cancer patients, therefore, needs to be improved. In our study, there was no significant association between gender and post-operative pain. Similar results have been reported by one study [26], but other studies have reported that females are more susceptible to post-operative pain [27, 28].

In our study, nearly 90% of the patients received adequate pain medication according to PMI results. In a study conducted in Ethiopia, 194 participants (80.1%) received ineffective pain medication during their post-operative period, and only 48 patients (19.9%) received adequate to good pain medication, indicating insufficient and inappropriate management of post-operative pain [20]. Their study stated that the high cost of opioids in developing countries added to this problem [20]. In many places, opioid analgesia is unavailable intra-operatively and post-operatively. A survey of anesthetic officers in Uganda showed that only 45% always had either pethidine or morphine available; 21% never had these drugs available [21]. A study done in India stated that potent opioids, such as morphine and pethidine, that are useful and effective for pain control following major surgical procedures were not used in their hospital due to their non-availability [10]. In our study, morphine and pethidine were stocked in the teaching hospitals in Yangon. But the exact availability of these opioids in the whole country has not been determined. There may be low usage of strong opioids because of the strict rules and regulations for medical use of such drugs.

In the future, we should encourage the use of pain charts as part of the routine assessment of patients (together with fever, heart rate and blood pressure records), which may improve the quality of pain control, as well as assessing the quality of post-operative care. To improve post-operative pain management, the continuing education of health care professionals is also an important intervention. The data obtained from our study can contribute to the evaluation of health care in the hospital setting and can provide a reference for the future evaluation of intervention measures aimed at improving the management of post-operative pain. In this study, the study population was the post-operative surgical patients from tertiary hospitals. Similar data from the other specialties and hospitals from district or township levels is still required.

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Compliance with Ethical Standards

This study was approved by the Postgraduate Board of Studies (Pharmacology), University of Medicine 1, Yangon (an institutional review board). The trial was registered at Thai Clinical Trial registry with the trial registration number TCTR20180808006. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare that they have no conflict of interest.

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