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Evaluation of Parenteral Opioid Analgesics Utilization in Patients Hospitalized in a Referral Teaching Hospital

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ABSTRACT

***Background*:** Opioid drugs are the most effective drugs for the treatment of moderate to severe pain. Rates of opioid use are influenced by a variety of factors. The aim of this study was to determine the pattern of use of parenteral opioid drugs in hospitalized patients in a referral teaching hospital.
***Methods*:** In a retrospective study, required data were extracted from medical records of adult patients who had received any parenteral opioid analgesic in the 6-month period from March 2013 to September 2013. The Anatomical Therapeutic Chemical Classification/Defined Daily Doses (ATC/DDD) system method was used for evaluation of opioid analgesic use in patients.
***Results*:** The overall usage of parenteral opioid analgesics was 730.51 DDDs with meperidine (Pethidine) having the most amounts of use (588.69 DDDs and 33.23 DDDs/100 bed-days). Overall, the male surgery ward and emergency department had the most amounts of use based on the number of DDDs (445.8 DDDs) and per 100 bed-days (1046 DDDs/100 bed-days), respectively. Methadone use was most in the infectious diseases ward.
***Conclusion*:** The trend of parenteral opioid analgesics consumption is increasing in this hospital. Therefore, better adherence to pain treatment guidelines by medical staff is necessary for rational use of these drugs.

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Introduction

Pain is prevalent in almost any medical field including surgery, internal medicine, general practice, oncology, and palliative care, and it concerns everyone from newborns to the elderly (1).

The use of potentially addictive medications such as narcotic analgesics continues to increase with time (2). Rates of opioid use are influenced by a variety of factors. First, the increased emphasis on pain control will increase analgesic opioid use; furthermore, the adverse effects of opioid drugs and the risk of addiction and diversion will decrease it (3). Although better pain control is desired, one always needs to be on guard for abuse and misuse of these potentially addictive medications. Because of the concerns about dependence or abuse, extra measures have been taken by the regulatory authorities of most countries. Even with these measures, abuse is known to occur (3). The global utilization of prescription opioid analgesics (POA) has sharply increased in recent years (4). For example, the production of morphine doubled 1992– 2011, and the production of oxycodone tripled

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2002– 2011 (5). However, the global distribution of POA utilization is highly inequitable (6). About 90% of all POAs are consumed in established market economies (EMEs), and >80% of the world's population have no or inadequate access to POAs, even though they have most of the world's cancer and HIV patients (6).

Reliable data on drug consumption are necessary and should ideally be based on the treatment of individual patients (7). However, as such data are seldom readily available, drug utilization studies are performed to analyze management data obtained over a certain period of time or to evaluate the effects achieved by therapeutic interventions. Moreover, the patterns of use in different settings or by different prescribers need to be compared in order to obtain the information necessary to devise and update prescribing policies as well as to provide proper feedback to the prescribers (7).

A methodology that is independent of sales prices and package size is preferable in order to obtain reliable and useful data on drug consumption. The Anatomical Therapeutic Chemical Classification/Defined Daily Doses (ATC/DDD system) is one such approach widely used. It provides a convenient tool that allows comparisons between different settings, regions, or even countries. The quality of the results is completely dependent upon strict adherence to the method. The ATC/DDD index is developed and updated by the World Health Organization (WHO) (8).

Very few studies have been performed about the pattern of opioid analgesic usage, especially in Iran. The aim of this study was to determine the utilization pattern of parenteral narcotic drugs including morphine, meperidine (also known as pethidine) (9), pentazocine, and methadone, in patients hospitalized in a referral teaching hospital.

Methods

This was a retrospective descriptive and analytic cross-sectional study performed in Taleghani hospital of Tehran, a teaching hospital affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran. The inclusion criteria were age > 18 years and receiving any parenteral opioid analgesic including morphine, meperidine, pentazocine, and methadone in the 6-month period from March 2013 to September 2013. Required data were extracted from medical records of adult patients using the computerized information profile of the hospital pharmacy unit. They included age, sex, hospitalization ward, reason for hospitalization (diagnosis), comorbidities and their interaction with the opioid analgesic, the current history of opioid addiction, the type of received parenteral opioid analgesic as well as its dosage, route of administration, and dosing interval, the concomitant drugs used by patient and their interaction with the opioid analgesic, the current history of opioid antagonist use, and the consistency of the nursing report with the physician order regarding the dose, route, and dosing interval for parenteral opioid analgesics. For determination of the cause of hospitalization, the 10th revision of International Classification of Diseases (ICD-10) recommended by WHO and available online at apps.who.int/classification/icd10 was used. To grading the severity of interaction of comorbidities and concomitant drugs with the analgesic, the website www.drugs.com was used. The comorbidity-drug interactions were classified as moderate (moderate potential hazard) or severe (severe potential hazard) while the drug-drug interactions were graded as minor, moderate, and major. The ATC/DDD system method was used for evaluation of opioid analgesic use in patients. For this, the used amounts of the drugs were calculated based on DDD (defined daily dose) and DDD/100 bed-days units using the following equations:

$$\text{Drug usage (DDDs)} = \frac{\text{the consumed amount of drug over the study period}}{\text{DDD recommended by WHO}}$$

$$\text{Drug usage (DDD/100 bed-days)} = \frac{\text{DDD} \times 100}{\text{Length of study period} \times \text{the full bed - days}}$$

Based on the last version of ATC/DDD system from WHO at the time of this study (version 2013), methadone had not any standard DDD. Therefore, the average amounts of usage per patient over the study period were calculated for this parenteral analgesic. The amounts of standard DDDs and ATC codes for evaluated analgesics are shown in Table 1.

SPSS 20.0 software was used for statistical analysis. In order to determine the possible effect of recorded independent variables on the used amounts of analgesics (based on DDD/bed-days), statistical analysis consisted of initial univariate screening for possible correlations by either Spearman's rank correlation (for quantitative variables), Mann-Whitney and Kruskal-Wallis (for nominal variables), or Kendal's rank correlation (for ordinal variables) tests. Finally, variables that were significantly associated with dependent variables ($P < 0.1$) were included into a multivariate ridge regression model with significance level of $P < 0.05$ to determine the most probable factors affecting the consumed amount of the analgesics.

Results

Of 1024 medical records of receipt of parenteral opioid analgesic during the evaluated time span, 910 (66% male) had the inclusion criteria for the study. The mean (± SD) age of patients was 37.23 (± 20.12) with the range of 19

Table 1. ATC codes and WHO recommended DDDs for parenteral opioid drugs.

Narcotic analgesic drug	DDD	ATC code
Morphine	30 mg	N02AA01
Meperidine	0.4 g	N02AB02
Pentazocine	0.2 g	N02AD01
Methadone	-	N07BC02

ATC: Anatomical Therapeutic Chemical Classification, DDD: Defined Daily Doses, WHO: World Health Organization

to 78 years.

External causes of morbidity and mortality (class XX in ICD-10), injury, poisoning and certain other consequences of external causes (class XIX in ICD-10), and diseases of the digestive system (class XI in ICD-10) were the most common causes of patients hospitalization (65%). The current histories of opioid addiction and opioid antagonist use were observed in 6% and 1% of patients, respectively.

Table 2 shows the consumed amounts of parenteral morphine, meperidine, and pentazocine based on DDD and DDD/100 bed-days units as well as the mean consumed dose of parenteral methadone per patient in different wards of the hospital. As shown, the overall usage of parenteral opioid analgesics was 730.51 DDDs with meperidine (Pethidine) having the most amounts of use (588.69 DDDs and 33.23 DDDs/100 bed-days). Overall, the male surgery ward and emergency department had the most amounts of use based on the number of DDDs (445.8 DDDs) and per 100 bed-days (1046 DDDs/100 bed-days), respectively. Methadone use was most in the infectious diseases ward.

Table 3 shows the percentage of different routes and intervals of administration of evaluated analgesics. As shown, the most cases of missed orders for administration route and dosage interval were observed for morphine and methadone, respectively.

In terms of the severity of comorbidity-opioid and concomitant drug-opioid interactions, the most cases were minor (76%) and moderate (54%; including interactions with antipsychotics, hydroxyzine, phenytoin, tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs], and hydrochlorothiazide), respectively.

Regarding the consistency of the nursing reports with the physician orders, 61% of evaluated profiles showed complete agreement, while the following errors were observed in the remaining profiles: drug administration without any physician order, 11%; wrong dosage, 9%; wrong dosage interval, 8%; no administration of the ordered drug, 8%; and administration of morhine instead of meperidine and vice versa, 3%.

Regarding the analysis of correlation between different independent variables and the amount of consumed analgesics, the initial univariate analysis, considering the significance level of 0.1, detected six variables (age, sex, severity of concomitant drug-opioid analgesic interaction, severity of comorbidity-opioid analgesic interaction, the reason of hospitalization, and the hospitalization ward) for the final multivariate analysis that showed only a weak significant reverse correlation for the severity of comorbidity-analgesic interaction ($r = 0.17$, $P<0.05$) meaning that the amount of consumed opioid analgesics (DDD/bed-days) has been lower for more severe interactions of comorbidity-analgesic.

Discussion

Opioid agonists are the most effective drugs for the treatment of moderate and severe pain (10); however, opioid production, consumption, and importation are strictly controlled at the international and country levels to avoid abuse, dependence, and diversion. Many countries, because of the fear of abuse, restrict their medical use (1). In addition to policy and legal barriers, professional barriers such as lack of training of medical staff also account for the inadequate medical use of opioids, as do some attitudes both among health care professionals and the general population (1). Therefore, studies about the rational use of these drugs are mandatory to detect and correct the wrong practices in their medical use.

The comparison of drug usage in different hospitals and different wards of a hospital is possible using determination of the amounts of drug usage based on DDD and DDD/100 bed-days (11). However, there are few DUE (drug utilization evaluation) studies about the parenteral opioids based on ATC/DDD system, especially in Iran. The comparison of our results with other studies shows high amounts of parenteral opioid use in our hospital. In the study of Salcedo et al., which evaluated the use of parenteral opioid analgesics in an university general hospital during 2004 – 2008, all consumed amounts of morphine (3.59, 3.73, 3.6, 4, and 4.3 DDD/100 bed-days in 2004 to 2008, respectively) and meperidine (0.39, 0.43, 0.4, 0.4, and 0.43 DDD/100 bed-days in 2004 to 2008, respectively) were lower than the amounts in our study (7.83 and 33.23 DDD/100 bed-days for morphine and meperidine, respectively) (12). In the study of Simo et al, the amounts of use for morphine, meperidine, pentazocine, and methadone were approximately 0.5, 0.5, 0.1, and 0.01

Table 2. The consumed amount of parenteral opioid analgesics in different wards of the hospital during the studied period.

Hospital Ward	Morphine		Meperidine		Pentazocine		Total opioid use		Methadone
	DDD	DDD/100 bed-days	DDD	DDD/100 bed-days	DDD	DDD/100 bed-days	DDD	DDD/100 bed-days	Mean Dose (mg)
Men surgery	102.8	9.1	343	30.48	0	0	445.8	39.61	67.5
Women surgery	12.33	7.44	76.85	46.42	0	0	89.18	53.87	55
Emergency	2.32	36.87	54.07	968.99	2	35.84	58.39	1046.415	5
Internal Medicine	1	1.1	41.4	46.37	0	0	42.4	47.49	157.5
CCU	2.73	3.331	30.76	37.58	0	0	33.49	40.92	77
ICU	8.44	3.572	9.25	3.91	0	0	17.69	7.48	50
GI diseases	1.5	5.55	15.83	60.79	0	0	17.33	66.55	150
Labor	1.5	21.43	9.53	170.783	0	0	11.03	160.273	5
Obstetrics	0.5	12.82	8	215.05	0	0	8.5	228.49	0
Infectious diseases	5.5	18.482	0	0	0	0	5.5	1.84	209
Total	**138.62**	**7.83**	**588.69**	**33.23**	**2**	**35.84**	**729.31**	**41.185**	-

ICU, intensive care unit; GI, gastrointestinal; CCU, coronary care unit, DDD: Defined Daily Doses.

Table 3. The administration routes and dosing intervals of parenteral opioid analgesics during the studied period.

Variable	Morphine	Meperidine	Pentazocine	Methadone
***Administration Route* (%)**				
IM	36	29	50	44
IV	22	34	50	37
SC	1	1	0	0
Blank	41	37	0	19
***Dosing Interval* (%)**				
Scheduled	27	7	50	30
As needed (PRN)	29	41	50	10
Blank	44	52	0	60

IM, intramuscular; IV, intravenous; SC, subcutaneous; Blank, without any order

DDD/1000 bed-days, respectively, in a general hospital in 1985 (13).

Higher use of opioid analgesics in surgery wards could be due to necessity of good control of postoperative pain in surgical patients as proper pain control after surgery is important to prevent negative outcomes such as tachycardia, hypertension, myocardial ischemia, decrease in alveolar ventilation, and poor wound healing (14). However, despite an increased focus on pain management programs and the development of new standards for pain management, many patients continue to experience intense pain after surgery (15).

Nowadays, use of meperidine as a first-line agent for pain relief is not recommended because of high potential for adverse effects such as tremor, twitching, anticholinergic effects, agitation, and convulsions due to its toxic metabolite, normeperidine (norpethidine); these effects increases with renal dysfunction and multiple dosing (16). However, our study showed that this drug was the most frequently prescribed parenteral opioid analgesic (588.69 DDDs). Therefore, it seems that more attention should be paid to more rational use of meperidine in our hospital. In contrast, the fact that pentazocine was the least frequently prescribed parenteral analgesic in our hospital, shows adequate attention of medical staff to this drug as it causes undesirable effects such as dysphoric and psychotomimetic effects and increase in blood pressure and heart rate (17).

The presence of discrepancy between physicians' order and nursing practice in 39% of cases observed in this study alarms about the risks of medical errors and treatment failure. So, more attention of medical staff and rational drug use committee of the hospital to strategies for reduction of these errors is mandatory.

The analysis of possible correlations showed that the severity of interaction of patient comorbidity with opioid analgesic has a significant reverse correlation with the amount of drug usage. This shows appropriate consideration of comorbidities for dosing of opioid analgesics by the physicians. Although no significant correlations were detected for other variables, adequate consideration of them especially age and the severity of concomitant drug-opioid interaction are yet recommended for prevention of possible serious adverse effects.

In conclusion, the trend of parenteral opioid analgesics consumption is increasing in this hospital. Therefore, better adherence to pain treatment guidelines by medical staff as well as development of new treatment guidelines for the hospital is necessary for rational use of these drugs.

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References

1. Duthey B, Scholten W. Adequacy of opioid analgesic consumption at country, global, and regional levels in 2010, its relationship with development level, and changes compared with 2006. J Pain Symptom Manage 2014;47(2):283-97.
2. Dhalla IA, Mamdani MM, Sivilotti ML, et al. Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone. Can Med Assoc J 2009;181(12):891-6.
3. Neutel CI, Skurtveit S, Berg C, Sakshaug S. Multiple prescribers in older frequent opioid users-does it mean abuse? J Popul Ther Clin pharmacol 2013;20(3):e397-405.
4. Fischer B, Jones W, Rehm J. Trends and changes in prescription opioid analgesic dispensing in Canada 2005-2012: an update with a focus on recent interventions. BMC Health Serv Res 2014;14(1):90.
5. International Narcotics Control Board (INCB): Narcotic Drugs Technical Report: Estimated World Requirements for 2013. New York, NY: United Nations; 2013.
6. Lohman D, Schleifer R, Amon JJ. Access to pain treatment as a human right. BMC Med 2010;8:8.
7. Natsch S, Hekster Y, De Jong R, et al. Application of the ATC/DDD methodology to monitor antibiotic drug use. Eur J Clin Microbiol Infect Dis 1998;17(1):20-4.
8. Wessling A, Boethius G. Measurement of drug use in a defined population. Eur J Clin Pharmacol 1990;39(3):207-10.
9. Russell JA, Leng G, Coombes JE, et al. Pethidine (meperidine) inhibition of oxytocin secretion and action in parturient rats. Am J Physiol 1991;261(2 Pt 2):R358-68.
10. The selection and use of essential medicines. World Health Organization technical report series. 2011 (965):i-xiv, 1-249.
11. World Health Organization, Group ISoHW. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. J Hypertens 2003;21(11):1983-92.
12. Gómez Salcedo P, Herrero Ambrosio A, Muñoz y Ramón JM. Estudio de utilización de analgésicos opiáceos en un hospital general universitario. Rev Soc Esp Dolor 2009;16(7):373-80.
13. Simó RM, Seijó F, Esteban MC. Evolución de la utilización de analgésicos en un hospital general. Comunicación XXXI Congreso Nacional de la Sociedad Española de Farmacia Hospitalaria. 1986.
14. Vadivelu N, Mitra S, Narayan D. Recent Advances in Postoperative Pain Management. Yale J Biol Med 2010; 83(1): 11–25.
15. Apfelbaum J, Chen C, Mehta S, Gan T. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg 2003;97(2):534-40.
16. McQuay H. Opioids in pain management. Lancet 1999;353:2229–32.
17. Brunton LL, Parker K, Blumenthal D, Buxton I. Goodman & Gilman's manual of pharmacology and therapeutics, 1st ed., 2008; New York, McGraw-Hill, p. 363.