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Original Article

A Drug Utilization Evaluation of Intravenous Acetaminophen in Neurology Ward of a Teaching Hospital: A Retrospective Single-Center Cohort Study

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Abstract

Background: The administration of intravenous (IV) acetaminophen is increasing worldwide, due to the higher costs of oral and rectal administration; hence, appropriate prescription of IV acetaminophen is highly important. The aim of this study was to check the compliance of injectable acetaminophen prescription based on the patient's conditions with health protocols in the neurology ward of hospitalized adults in Hamadan, Iran.

Methods: A total of 97 patients with the age range of 17-88 years hospitalized in the neurology ward of Shahid Beheshti hospital in Hamadan from April 2021 to September 2021, who received at least 1 dose of IV acetaminophen, were examined in this retrospective single-center cohort study. Demographic information and clinical parameters such as blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, international normalized ratio, the reason for administration, administration dose and intervals, and the number of administration doses with national guidelines underwent an investigation. The data of the study were extracted from the medical records of the patients and analyzed with SPSS software at a confidence level of 95%.

Results: The results demonstrated that the indications for injecting acetaminophen were pain (62.9%), fever (32%), and simultaneous pain and fever (5.2%). The average dose of injectable acetaminophen, the duration of administration (minutes), and the administration intervals (hours) were 5.05 ± 0.66, 67.50 ± 6.62, and 12.34 ± 5.37, respectively. The frequency of compliance with the instructions was 21.6% and 72.2% of non-compliance due to the lack of a need for an injectable form while there was the possibility of using an oral or rectal form.

Conclusion: Based on the results of this study, the majority of IV acetaminophen in patients admitted to the neurology ward did not comply with national guidelines, and the most common cause of non-compliance was the use of the injectable form of acetaminophen. Moreover, improper administration of IV acetaminophen is not economically beneficial for the healthcare system.

Keywords: Acetaminophen, Intravenous, Drug utilization evaluation

Introduction

Drug utilization evaluation (DUE) is defined as an advanced and appropriate program that investigates and analyzes drug use patterns in comparison with standard criteria in a medical center (1). According to the definition of the World Health Organization (WHO), DUE studies include the study of the growth and distribution, as well as prescription and consumption of drugs in the community with an emphasis on medical, social, and economic results (2,3). The successful implementation of a DUE study will ensure the appropriate, safe, and effective use of drugs. Among the goals of the implementation of DUE programs are ensuring the rationality of the quality of drug use, ensuring the health of patients, predicting and

preventing side effects timely, drawing the pattern of drug use in society, and reducing unnecessary costs (4). The appropriate dosage form and route of administration are fundamental steps in drug administration to achieve optimal clinical results from limited financial resources (5).

Trying to rationalize drug use has always been considered one of the important issues of drug policies (6). According to the WHO, to achieve the rational use of drugs, it is necessary to use drugs with appropriate therapeutic effects that can meet the clinical needs of patients in a specific geographical area with the least complications and the least cost (7,8). In addition, it is highly important to pay attention to the dose and duration of drug use.

Acetaminophen (paracetamol) is an antipyretic and

pain reliever. This drug is a non-narcotic pain reliever that is used in cases of mild to moderate pain such as headache, toothache, mild osteoarthritis pain, and pain from minor surgeries (9,10). It was believed that acetaminophen causes analgesia by inhibiting cyclooxygenase enzymes (11). However, the main analgesic mechanism of acetaminophen is its metabolism to N-acylphenolamine (AM404), which then acts on the transient receptor potential vanilloid type-1 (12).

Acetaminophen can be prescribed orally, rectally, or intravenously (IV). The main difference between the pharmaceutical forms of acetaminophen includes pharmacokinetic properties, classification of pregnancy, and indication in children (13,14). The cerebrospinal fluid concentration of acetaminophen is significantly higher following IV injection compared to oral and rectal forms (15). The maximum plasma concentration of 1 gram of injected acetaminophen after 15 minutes is 30 mg/L, and its bioavailability is 89.4% (16). One of the potential benefits of IV administration is bypassing the hepatic first pass (17).

The side effects of IV acetaminophen include nausea, vomiting, constipation, itching, abdominal pain, hyperammonemia, hyperchloremia, hyperuricemia, a decrease in serum bicarbonate, sodium, and calcium, an increase in serum glucose, bilirubin, and alkaline phosphatase (ALP). Picetti et al reported that the administration of paracetamol is effective but exposes patients to episodes of hypotension that must be recognized and treated quickly to prevent further damage to the affected brain (18).

In the treatment system, drug use should be evaluated in a systematic and planned process (6). Considering that this process is performed by collecting data, it can be considered an evidence-based analysis (19). However, in the current study, we checked the compliance of injectable acetaminophen prescription based on the conditions of patients who were hospitalized in the neurology ward of Shahid Beheshti hospital (Hamadan, Iran) from April 2021 to September 2021 via a retrospective single-center cohort study.

Materials and Methods

Study Design and Data Sampling

In the present retrospective single-center cohort study, 97 patients within the age range of 17-88 years hospitalized in the neurology ward of Shahid Beheshti Hospital in Hamadan from April 2021 to September 2021, who received at least 1 dose of IV acetaminophen were examined to evaluate the appropriateness of IV acetaminophen prescribing.

Demographic, laboratory, and clinical data were retrieved from the patient's files. The desired information in the checklist that was designed for this purpose, included age, gender, weight, prescription indication, dose, duration of administration, administration intervals, comorbidities, liver enzymes (alanine aminotransferase

[ALT], aspartate aminotransferase [AST], ALP), creatinine (Cr) level, and international normalized ratio (INR). The information was compared with the national guidelines for the administration of injectable acetaminophen issued by the Ministry of Health and Medical Education. All data were extracted by clinical pharmacist supervision. The limitations of this study were the non-availability of some files and defects in the information of the files.

Statistics

All data were expressed as the mean ± standard deviation (SD) and analyzed with SPSS software at a confidence level of 95%. Nominal and continuous variables were compared using an independent t-test and chi-square test, respectively.

Results

Age and Gender Distribution of Patients

Table 1 lists the frequency of gender distribution of patients. Overall, 43 male (44.32%) and 54 female (55.67%) patients participated in this study. The average age of patients according to gender distribution in male and female patients was 54.44 ± 2.99 and 53 ± 3.08, respectively.

Compliance of Age and Gender Distribution With the Guideline

Table 2 summarizes data on the frequency of gender and age distribution of patients if they comply with the guidelines. Out of the 97 cases of injectable acetaminophen administration, 21 cases (21.6%) complied with the guidelines, while 76 cases (78.4%) did not. However, the frequency of matching of acetaminophen administration

Table 1. Age and Gender Distribution of the Study Participants

Age, years	Mean ± SD	53.74 ± 1.92
	Range	17-88
Age category, N (%)	17-28 years	14 (14.43)
	29-40 years	14 (14.43)
	41-52 years	15 (15.46)
	53-64 years	27 (27.83)
	65-76 years	16 (16.49)
	77-88 years	11 (11.34)
Gender, N (%)	Male	43 (44.32)
	Female	54 (55.67)
Gender, Mean ± SD	Male	54.44 ± 2.99
	Female	53 ± 3.08

Note. SD: Standard deviation.

Table 2. Compliance of Age and Gender Distribution With the Guideline

Gender	Yes	No	P Value
Male, N (%)	7 (16.3)	36 (83.7)	>0.05
Female, N (%)	14 (25.9)	40 (74.1)	>0.05
Total, N (%)	21 (21.6)	76 (78.4)	>0.05
Age, mean ± SD	49.67 ± 20.83	54.86 ± 2.15	<0.05

Note. SD: Standard deviation.

in patients hospitalized in the neurology ward was not significant according to gender ($P>0.05$), while a significant difference was observed according to age ($P<0.05$).

Indication of Pain and Fever in the Gender Distribution of Patients

Pain and fever indications in the gender distribution of male and female patients underwent examination. In this study, 35 female (36.08%) and 26 male (25.22%) patients, as well as 5 female (15.46%) and 16 male (16.49%) patients had pain indications and fever indications, respectively. Furthermore, 4 female patients (4.12%) and 1 male patient (1.03%) had indications of pain and fever at the same time (Table 3).

Comorbidities

Table 4 presents the comorbidities of patients in this study. The examination of comorbidities revealed that most male and female patients had hypotension (22.78%), and only 4 patients suffered from renal disease (5.06%).

Dose, Duration, and Intervals of Acetaminophen Administration

Table 5 compares the results of the average variables of dose, duration, and intervals of acetaminophen administration in the neurology ward. The mean variables of dose, duration, and intervals of acetaminophen administration were 5.05 ± 0.66, 67.5 ± 52.5, and 12.18 ± 0.76, respectively. Moreover, the results of INR, Cr, urea, ALP, ALT, and AST factors in patients during hospitalization are provided in Table 6.

Discussion

The current study evaluated the administration of IV acetaminophen in the neurology ward of hospitalized patients in Shahid Beheshti Hospital (Hamadan, Iran) from April 2021 to September 2021 in a retrospective single-center cohort study to investigate the appropriateness of IV acetaminophen prescribing via the Ministry of Health and Medical Education. Overall, our results revealed that from 97 cases who received IV acetaminophen, only 21 cases (21.6%) complied with the guidelines, whereas the remaining 76 cases (78.4%) did not comply with them. However, the frequency of matching of acetaminophen administration in patients had a significant difference according to age.

The average age of the patients whose pattern of injecting acetaminophen was in accordance with the national guidelines was 49.67 ± 20.83 years, and that of those who did not conform was 54.86 ± 2.15 years (Table 2). Thus, the age of the patient is mentioned as the best indicator of the need for acetaminophen. According to our data, the average consumption of IV acetaminophen decreased with the increasing age of the patients. In this regard, Nejati et al (17) reported the rational use of injectable analgesics in the emergency and surgical wards. In addition, out of a total of 1181 cases, 23.62% of the prescriptions were rational in terms of indications, dosages, time intervals, and drug interactions and 76.38% of the prescriptions were irrational. It seems that there should be an intervention regarding more education to the medical staff regarding the rational prescription of injectable analgesics according to the guideline.

Among the solutions that can be proposed to improve the existing conditions related to the pattern of injectable analgesic drug consumption and rationalize the prescription and consumption of these drugs are the formulation and implementation of standard protocols for pain control, training of nurses and medical staff regarding drug management and evaluation, and recommendation of the use of therapeutic protocols. The other solutions include reforming the distribution system of injectable

Table 4. Examining Patients for Comorbidities

Comorbidities, N (%)	Male	Female	Total
Hypertension	10 (12.65)	8 (10.12)	18 (22.78)
Hypotension	2 (2.53)	3 (3.79)	5 (6.32)
Diabetes mellitus	5 (6.32)	6 (7.59)	11 (13.92)
Coronary artery disease	4 (5.06)	6 (7.59)	10 (12.65)
Pulmonary disease	9 (11.39)	5 (6.32)	14 (17.72)
Renal disease	3 (3.79)	1 (1.26)	4 (5.06)
Depression/anxiety	3 (3.25)	4 (4.33)	7 (7.59)
Other diseases	6 (8.61)	5 (6.56)	11 (15.18)

Table 3. Indication of Pain and Fever in the Gender Distribution of Patients

Indication	Male	Female
Pain, N (%)	26 (25.22)	36 (35.08)
Fever, N (%)	16 (16.49)	15. (15.46)
Pain and fever, N (%)	1 (1.03)	4 (4.12)
Total, N (%)	43 (43.32)	54 (55.67)

Table 5. Dose, Duration, and Intervals of Acetaminophen Administration

Variable	Mean±SD	Minimum	Maximum
Administration dose (g)	5.05 ± 0.66	1	31
Duration (min)	67.5 ± 52.5	15	120
Intervals (h)	12.18 ± 0.76	6	24

Note. SD: Standard deviation.

Table 6. The Results of INR, Cr, Urea, ALP, ALT, and AST

INR	Cr	Urea	ALP	ALT	AST
1 ± 6.19	1 ± 17.99	1 ± 17.99	228.13 ± 46.36	39.01 ± 93.07	40.12 ± 90.51

Note. SD: Standard deviation; INR: International normalized ratio; Cr: Creatinine; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase. Data were reported as means±SDs.

narcotic drugs and adequate supervision from the distribution stage to the stage of prescribing to the patient, monitoring the prescription of injectable narcotic drugs, and creating awareness among patients and medical staff (20). Moreover, studies have shown that the correct implementation of drug administration protocols can reduce costs for patients and health service providers and provide health benefits to patients through appropriate drug use (21).

In this study, approximately 62% of patients received IV acetaminophen because of pain. It seems that the injectable form of acetaminophen had superiority to other forms (oral or rectal) for rapid pain relief in patients via time-saving. However, in clinical trials, the use of IV acetaminophen has been associated with better clinical results in terms of fewer overall complications, shorter hospital stays, and lower treatment costs (22). In contrast, studies indicated that there was no strong evidence for the superiority of IV acetaminophen administration over oral routes. For example, the cost of IV acetaminophen is about 100 times the cost of oral formulations and twice the cost of rectal formulations, and the non-compliance of IV acetaminophen prescription with the guidelines imposes an additional cost to the hospital health care system in Australia (23).

Conclusion
Most of the cases of injectable acetaminophen administration in patients admitted to the neurology ward of Shahid Beheshti hospital in Hamadan did not comply with the national guidelines, and the most common cause of non-compliance was the use of the injectable form of acetaminophen, while it was possible to use the oral and rectal forms. Injectable acetaminophen appears to provide rapid pain relief. Nonetheless, to reduce the unnecessary cases of injecting acetaminophen in hospitalized patients and save resources, it is suggested that the personnel in the field of national guidelines for injecting acetaminophen should be retrained, and the way of administering the drug according to the guidelines requires further monitoring.

Authors' Contribution
Mohammad Ali Mohseni: Data collection, data analysis, writing of manuscript. Maryam Etminani Esfahani: Study design, Manuscript editing and proofreading. Sara Ataei: Study design, Pari Tamri: Study design and supervision of research.

Competing Interests
There is no conflict of interest.

Ethical Approval
The study was approved by the Ethics Committee of Hamadan University of Medical Sciences (ethical code: IR.UMSHA.REC.1400.746).

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