

Original Article

Medication Errors in Patients with Enteral Feeding Tubes in the Intensive Care Unit

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INTRODUCTION

Critically ill patients in Intensive Care Units (ICUs) receive more drugs compared to patients of other wards. Thus, rates of medication errors are higher in these patients.^[1] Most patients admitted to ICU have problems in using oral medication or ingesting solid forms of drugs.^[2] Several medication errors can occur during enterally drug administration, including errors in dosage form selection, methods of oral medication administration, drug interactions, and incompatibility with nutrition formula.^[3] Although enteral feeding tubes are not suitable for administration of oral drugs, receiving crushed tablets is common through these tubes and can result in tube obstruction, an increase in adverse drug reactions, reduction in drug effectiveness, or drug-enteral nutrition (EN) incompatibility. Crushing many drugs

ABSTRACT **Objective:** Most patients admitted to Intensive Care Units (ICU) have problems in using oral medication or ingesting solid forms of drugs. Selecting the most suitable dosage form in such patients is a challenge. The current study was conducted to assess the frequency and types of errors of oral medication administration in patients with enteral feeding tubes or suffering swallowing problems. **Methods:** A cross-sectional study was performed in the ICU of Shahid Sadoughi Hospital, Yazd, Iran. Patients were assessed for the incidence and types of medication errors occurring in the process of preparation and administration of oral medicines. **Findings:** Ninety-four patients were involved in this study and 10,250 administrations were observed. Totally, 4753 errors occurred among the studied patients. The most commonly used drugs were pantoprazole tablet, piracetam syrup, and losartan tablet. A total of 128 different types of drugs and nine different oral pharmaceutical preparations were prescribed for the patients. Forty-one (35.34%) out of 116 different solid drugs (except effervescent tablets and powders) could be substituted by liquid or injectable forms. The most common error was the wrong time of administration. Errors of wrong dose preparation and administration accounted for 24.04% and 25.31% of all errors, respectively. **Conclusion:** In this study, at least three-fourth of the patients experienced medication errors. The occurrence of these errors can greatly impair the quality of the patients' pharmacotherapy, and more attention should be paid to this issue.

KEYWORDS: *Intensive Care Unit, medication errors, pharmaceutical preparations*

such as enteric coated tablets, controlled-release tablets, and mutagenic and teratogenic drugs can lead to a decrease in drugs effects, irritation of gastric mucosa, and harm to the nurse.^[4] Selection of the most suitable dosage form in such patients is a challenge. Liquid dosage forms are the best choices if possible because of easy absorption and no tube obstruction.^[5] Sometimes, other routes of administration exist for a drug and can be used as an alternative to solid forms.^[6] However, the challenging issue is that there is no liquid or injection substitution for many of drugs, and the only solution is using mortar and pestle for crushing tablets or opening

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capsules which can alter pharmacokinetic profile of the drug.^[7]

The aim of our study was to assess the frequency and types of errors of oral medication administration in patients with enteral feeding tubes or suffering from dysphagia who were admitted to the General ICU in Shahid Sadoughi Hospital (Yazd, Iran).

METHODS

A cross-sectional study was performed in the 16-bed ICU of the largest teaching hospital in Yazd, Iran, from January 2016 to April 2016. The study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences. ICU was selected because of high numbers of patients who cannot use solid forms of drugs or use EN. All patients with swallowing problems or feeding through nasogastric (NG) tube who were administered at least one oral drug were eligible to be enrolled in this study. All drugs were prepared and administered by nursing staff, and pharmacists had no intervention in this process. Nurses were not aware of the study's purpose and reason of pharmacist attendance as an observer. The needed information were collected including patient's age and gender, nurse's gender, type of disease, the length of hospital stay, number and frequency of oral drugs administered by enteral tube, and concomitant intravenous medications. Observations were performed during all work shifts and holidays. Oral pharmaceutical preparations that should not be crushed or administered through an enteral feeding tube were identified from the recommendations of the manufacturers and by reviewing articles and relevant references.^[8] Furthermore, the availability of liquid formulation for each drug was assessed to know if liquid substitutions for the solid dosage forms exist.

Then, the errors of drug administration through enteral tubes were evaluated and classified according to Table 1.^[9]

The data were analyzed using SPSS, V 16 (SPSS Inc., Chicago, IL, USA). The results were analyzed using descriptive statistics (frequency and percentage) and inferential statistics (Fisher's exact test and ANOVA). $P < 0.05$ was considered statistically significant.

RESULTS

During the study period, a total of 94 patients with a mean \pm standard deviation (SD) age of 58 ± 28.5 years (ranging from 2 months to 92 years) were evaluated. The main diagnoses were: cerebral (35.29%), respiratory (16.66%), and cardiovascular diseases (8.82%). The length of ICU stay varied from 2 to 57 days, with a mean \pm SD of 11.6 ± 11 days. The length of tube feeding or having swallowing difficulty varied from 1 to 55 days, with a mean of 10.7 ± 10.49 days. Totally, 10,250 administrations were observed during the study period. The average of drug administration for every patient was 109.04 (from 2 to 832). Moreover, 128 different types of drugs were prescribed for the patients. Five of the most commonly used oral drugs during the study period were pantoprazole tablet, paracetamol syrup, losartan tablet, lactulose syrup, and L-carnitine syrup. On average, every patient received 13.84 types of drugs, 5.84 types of oral drugs, and 4.7 types of solid drugs. Nine different oral pharmaceutical preparations were used, including tablets (51%), syrups (19%), coated tablets (11%), capsules (5%), oral suspensions (4%), effervescent tablets (3%), powders (3%), oral drops (3%), and oral solutions. In addition, 41 (35.34%) out of 116 different solid drugs (except effervescent tablets and powders) could be substituted by liquid or injectable forms. Preparation and administration errors occurred in 34 types of drugs while 76.59% of patients (72 patients) experienced these errors during their hospital stay. The most common error was the time error which included 19.25% of all administrations [Table 2]. The frequencies of wrong dose preparation and administration errors were

Table 1: Definition of errors

Error type	Definition
Omission	The drug is not given to the patient by the time of the next scheduled dose
Unordered drug	Receiving a drug which was not prescribed for the patient
Wrong drug	Administration of a drug instead of the drug prescribed by physician
Wrong formulation	Administration of a drug in wrong dosage form
Wrong dose preparation	Errors in preparation of a medicine before its administration, for example, crushing a sustained released or enteric coated tablet
Wrong technique of administration	Errors in administration of a medicine, for example, mixing the drug that should be administered with an empty stomach with EN
Wrong route of administration	The administration of the correct drug by a route or site that was not prescribed, for example, orally when prescribed through a NG tube
Wrong time	Administration of a medication earlier or later than 60 min from its scheduled administration time

NG=Nasogastric, EN=Enteral nutrition

Table 2: The twenty oral drugs most frequently prescribed which are non-crushable or can interact with enteral nutrition^[6,8,11]

Number	Drug	Labeled for administration by enteral feeding tube?	Number of this medication administration (%)	Number of patients receiving this medication (%)
1	Pantoprazole	No, because it is enteric coated or sustained released or should be crushed and dissolved in 8.4% sodium bicarbonate	597 (5.82)	32 (34.04)
2	Nitroglycerin	No, because it is sustained release	215 (11.7)	11 (2.09)
3	Calcium salts	Yes, but the tube should be adequately flushed to ensure that the calcium supplement does not come into contact with the feed	172 (1.67)	14 (14.89)
4	Phenytoin	Yes, but the presence of food can reduce the rate of absorption by 50%-75%	121 (1.18)	5 (5.31)
5	Furosemide	Yes, but food reduces the bioavailability of furosemide by 30%	114 (1.11)	5 (5.31)
6	Nimodipine	Yes, but should be administered quickly because is sensitive too light	96 (0.93)	4 (4.25)
7	Captopril	Yes, but the presence of food can reduce absorption by 30%-40%	89 (0.86)	6 (6.38)
8	Warfarin	Yes, but there is evidence of a physicochemical interaction between enteral feed and warfarin	76 (0.74)	5 (5.31)
9	Ciprofloxacin	Yes, but the concomitant administration of EN may reduce its absorption. It is recommended to stop the EN, especially dairy products 1 h before and 2 h after administration. Replace ciprofloxacin with another quinolone or use the injectable solution	76 (0.74)	2 (2.12)
10	Levofloxacin	Yes, but stop feed 1 h before dose and restart feed 2 h after dose	62 (0.06)	9 (9.57)
11	Coenzyme Q10	Yes, but soft capsules contents should be aspirated by a syringe	61 (0.59)	2 (2.12)
12	Levothyroxine	Yes, but after crushing the tablet, disperse in water and protect the solution from light. Concomitant administration with EN may reduce its absorption, especially if it is rich in fiber. It is recommended to stop the EN 1 h before and 2 h after administration. Monitor serum concentrations of the drug. Inhalation of crushed tablets should be avoided. Standard precautions apply	61 (0.059)	5 (5.31)
13	Rifampin	Yes, but care should be taken regarding contact sensitization. Feeding should be stopped at least 2 h before the dose; do not restart feed for 30 min after dose	45 (0.43)	3 (3.19)
14	Hydrochlorothiazide	Yes, but food can increase its absorption rate	45 (0.43)	3 (3.19)
15	Sucralfate	Yes, but sucralfate forms an insoluble protein-aluminum complex with enteral feeds, resulting in solid or semisolid agglomerates that can block feeding tubes, or even the stomach or esophagus. Enteral feed should be stopped at least 1 h before the dose and not restarted for 1 h postdose	45 (0.43)	1 (1.06)
16	Carbamazepine	Yes, but powder of the crushed tablet can adhere to the tube, and a less-than-optimal dose is absorbed	41 (0.4)	2 (2.12)

Contd...

Table 2: Contd...

Number	Drug	Labeled for administration by enteral feeding tube?	Number of this medication administration (%)	Number of patients receiving this medication (%)
17	Carbamazepine (Tegretol®)	No, because it is a sustained released dosage form	30 (0.29)	1 (1.06)
18	Omega-3	Yes, but soft capsules contents should be aspirated by a syringe	41 (0.4)	1 (1.06)
19	Metronidazole	Yes, but food reduces the bioavailability of metronidazole benzoate	38 (0.37)	3 (3.19)
20	Levodopa	Yes, but the protein in the diet and in the circulating system competes with levodopa for absorption and transport into the brain. Diets that do not exceed 0.8 g/kg of protein are reported to eliminate this problem. The timing of feed and dosing of levodopa should be as consistent as possible to reduce fluctuations in daily response. Administration after food delays the time to peak plasma concentration and reduces total bioavailability	34 (0.33)	3 (3.19)

EN=Enteral nutrition

about 11.15% and 11.73% of administrations, respectively. No omission, unordered drug, and wrong drug error was observed. The frequency of errors regarding the different work shifts, holiday and nonholiday shifts, and nurses' gender are shown in Table 3. The differences reached statistical significance just for work shifts.

DISCUSSION

In our study, it was found that most of the drugs were administered in solid dosage forms, and nearly 36% of them could be substituted by injection or oral liquid formulations. A study conducted by Barbosa *et al.* reported that 72.7% of studied cases were also receiving intravenous medications, and it was possible that some of the drugs could be substituted by intravenous formulations.^[6] Silva *et al.* reached the conclusion that among 49 drugs prescribed in solid oral pharmaceutical forms, 17 (34.7%) were also available in oral liquid form, implying that at least 290 prescriptions (21.8%) could have reduced the risk of catheter obstruction.^[10]

Among the administered medicines, pantoprazole was the most frequently prescribed and had the highest percent of wrong dose preparation. Pantoprazole is sensitive to gastric acid; therefore, crushing tablets and administering the pieces through NG tube have the possibility of degradation and therefore a decreased efficacy.^[3] Our results are different from those of Barbosa *et al.*, Presoti *et al.*, and Silva *et al.* They reported that the most frequently used drug was captopril.^[6,10,11] It seems that in these studies, proton-pump inhibitors are mostly used in their liquid dosage form (injectable dosage forms or oral suspensions), while in our country, oral suspension does not exist and only pantoprazole is used in injectable

dosage form which is much more expensive compared to its oral dosage forms and its use is not cost-effective for hospitals.

Digoxin and phenytoin were administered for 6.38% and 5.31% of patients. In another similar study conducted at a university hospital in Southern Brazil, the frequency of administrations of these two drugs was 9.8% and 6.3%, respectively.^[12] These drugs, especially phenytoin, need exclusive care for administration. Enteral feeding can decrease phenytoin absorption and hence reduce its serum concentrations.^[13] It is suggested that the serum concentrations of drugs with narrow therapeutic indices should be monitored regularly, especially when they are administered through a feeding tube.^[8]

Crushing sodium valproate enteric coated tablets is considered as an error in some studies because valproate is irritant for gastric mucosa and can cause nausea and vomiting. Therefore, its tablets should not be crushed for use through NG tube.^[3] We can use sodium valproate syrup instead of crushing tablets; however, using syrup will not solve the problem of nausea and vomiting. Thus, we did not consider crushing sodium valproate enteric coated tablets as an error in this study. For extended released products, it is recommended that doses be 8%–20% higher than non-extended release (ER) products; therefore, crushing them leads to a sudden release of high doses of valproate which can produce higher serum concentrations and effects than expected.^[14]

Considering the work shifts, our data showed that the rate of medical errors was so high at 8:00 a.m. Furthermore, most of the administrations occurred in this work shift (nearly 23%). The high number of

Table 3: Correlation between the nurses' demographic data and work shifts with the frequency of errors occurrence

Error type	Wrong route	Wrong preparation	Wrong administration	Wrong time	Wrong dose	Total
Weekly days						
Holiday	36 (1.75)	226 (11.01)	257 (12.52)	409 (19.93)	56 (2.72)	984 (47.95)
Nonholiday	145 (1.76)	917 (11.18)	946 (11.53)	1565 (19.09)	196 (2.39)	3769 (45.97)
<i>P</i>	0.96	0.82	0.21	0.08	0.37	0.10
Sex						
Male	47 (1.98)	254 (10.71)	303 (12.78)	436 (18.39)	67 (2.82)	1107 (43.62)
Female	134 (1.70)	889 (11.28)	900 (11.42)	1538 (19.51)	185 (2.34)	3646 (48.19)
<i>P</i>	0.36	0.44	0.07	0.22	0.18	0.70
Work shifts						
(1) 8:00-14:00	23 (0.68)	475 (14.09)	494 (14.66)	1217 (36.12)	119 (3.53)	2328 (69.10)
(2) 14:00-20:00	46 (2.45)	58 (3.09)	147 (7.84)	36 (1.92)	34 (1.81)	321 (17.13)
(3) 20:00-8:00	112 (2.23)	610 (12.18)	562 (11.22)	721 (14.39)	99 (1.97)	2104 (42.01)
<i>P</i> value between						
(1) and (2)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
(1) and (3)	<0.001	0.016	<0.001	<0.001	<0.001	<0.001
(2) and (3)	0.81	<0.001	<0.001	<0.001	0.921	<0.001

Data are presented as the frequency (%) of errors occurrence

administrations and changes in the nurses' shifts at this time plays an important role in errors occurrence. Indeed, 8:00 a.m. is the pick time for nursing distractions and lack of concentration due to telephone calls, educational rounds, physicians' visits, higher nurse workloads, ordering necessary drugs to pharmacy center, and drug distribution from there leading to increased risk of errors.^[15,16]

According to the UK standards for ICUs, a minimum nurse/patient ratio of 1:1 together with additional nurses according to patient needs, training requirements, the total number of beds, and the geographical arrangements within the unit should exist. Nonetheless, in this ward, every nurse is responsible for two patients and nursing workload is high. Thus, this ICU is particularly prone to medical errors and one solution for this problem is to employ more nurses.

In this ICU, medication preparation and administration are carried out by nurses and each nurse does it on the basis of their experience, habit, and personal information, not according to standard protocols. Unfortunately, no standard protocol was defined in this ICU. In-hospital education of nurses by clinical pharmacists can significantly increase their knowledge and profession in the aspects of medication preparation, tube flushing, recognizing drug-drug or drug-feed interactions, and recognizing dosage forms characteristics.^[17] Pharmacists can help treatment team by providing useful information on selecting the correct drug, dosage form, and route of administration. Moreover, pharmacists are able to decrease some drug-drug interactions by administrating them separated by an appropriate time interval (generally 2–4 h).^[18]

It is suggested that a routine checklist must be followed including: (1) never add medications directly to the enteral formula, (2) clean the enteral tube by flushing water under pressure, and (3) observe the patient for unexpected changes in clinical response and evolution.^[12]

It was observed that most of the time all the drugs administered at the same time were crushed and mixed together which is completely wrong. Drugs should not be mixed together for administration through NG tube and each drug should be administrated separately; otherwise, physical and chemical incompatibility, tube occlusion, or changes in drug pharmacodynamics will possibly occur.^[19]

Our study indicated that the frequency of drug administration and preparation errors in patients who cannot use solid forms of drugs in this ICU was high. Close cooperation between medical teams including pharmacists or pharmacotherapists, physicians, and nurses can result in administration of drugs through enteral catheters correctly.^[17]

AUTHORS' CONTRIBUTION

Dr. Seyed Mojtaba Sohrevardi contributed in study design and revising manuscript. Dr. Mohammad Hossein Jarahzadeh contributed as the head of the ICU and treating physician. Mahtabalsadat Mirjalili contributed in data gathering, manuscript writing and data analysis. Dr. Ehsan Mirzaei contributed in study idea and data gathering. Arefeh Dehghani Tafti contributed in data analysis. Dr. Behrooz Heydari contributed as scientific advisor and has revised the manuscript critically.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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