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Original Article

Importance of Appropriate Medication Administration in Patients with Nasogastric Feeding Tube

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ABSTRACT

Solid dosage forms like modified release and enteric coated formulations are considered inappropriate for nasogastric feeding tube (NGFT) administration due to varying pharmacokinetics which could lead to inadequate therapeutic responses or toxicity. An analysis was conducted to assess the appropriateness of prescribed medicines for NGFT administration in hospital inpatients so that physicians can be sensitized to the importance of this. In this cross-sectional study conducted in a large tertiary care centre, prescription data of in-patients with nasogastric feeding tube (NGFT) were retrieved through electronic pharmacy transactions. Adult patients who were admitted in the hospital for more than one day and were dispensed a NGFT were included. The appropriateness of medicines administered through NGFT was assessed using standard published literature. Details of medicines that were categorized as inappropriate were collated and analysed. In case of inappropriate prescribing, availability of appropriate dosage forms was also determined. A total of 510 patients were found eligible for analyses. Majority of the patients were dispensed at least one inappropriate dosage form. Among the dispensed oral solid dosage forms, 16.38% were found to be inappropriate for NGFT administration. Of these, 21.41% were dispensed on same day as the NGFT, 34.67% were dispensed before the NGFT and were continued throughout the hospital stay and 43.92% were dispensed within or after 24 hours of NGFT dispensation. These findings will improve awareness among healthcare professionals about the need for appropriate administration of oral formulations in patients intubated with NGFT.

Keywords: Inappropriate Dosage Forms; Nasogastric Feeding Tube; Appropriate Dosage Forms; Modified Release Formulations

INTRODUCTION

It is a common occurrence to find medicines being administered via nasogastric feeding tube (NGFT) in hospital settings. Patients who are unable to swallow medicines whole as a result of conditions like dysphagia or others who may require sedation or intubation require oral solid dosage forms to be crushed and administered via the enteral route. Not all medications can be safely administered via NGFT. Crushing certain solid dosage forms could result in an array of problems like NGFT obstruction, higher rates of adverse drug events, decreased medicine efficacy or incompatibility with enteral feeds.

Due to advances in the pharmaceutical industry, several types of oral medication exist in the market. Conventional oral dosage forms such as tablets and capsules are designed to release the active ingredient immediately after reaching the stomach. Modified-release (MR) medicines are dosage forms that alter the timing and/or the rate of release of the active pharmaceutical ingredients and are advantageous compared to the former agents since they result in either a reduction in the frequency of administration or improvement in patient compliance[1].

Various MR formulations have been approved for therapeutic uses in the market such as extended-release (ER), delayed release (DR), and targeted-release (TR) formulations[2]. ER formulations are superior than conventional formulations since they reduce the frequency of administration by at least two-fold. Controlled-release (CR),

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sustained-release (SR), and long-acting formulations are a few examples of ER formulations. Delayed-release (DR) formulations like enteric-coated (EC) or gastro-resistant (GR) tablets are dosage forms that release a specific amount of drug promptly after administration. TR dosage forms selectively and preferentially release drugs at the target site. All MR formulations have their individual releasing properties and different therapeutic efficacy at different times to produce therapeutic action.

MR formulations are considered inappropriate for nasogastric feeding tube (NGFT) administration due to varying pharmacokinetics and pharmacodynamics when crushed. For instance, the doses of MR formulations are reported to be 8%–20% higher than corresponding immediate-release tablets [3].

Crushing MR formulations could lead to a sudden release of a high dose of the active ingredient which could contribute to potential toxicity as well as decreased clinical effectiveness [4]. Likewise, crushing enteric-coated tablets for the sake of administration through NGFT changes the original purpose of enteric coating. Therefore, it is essential to study different treatment practices with orally ingested medicines among patients intubated with NGFT. The results of this study will help sensitize healthcare professionals regarding the risks as well as stimulate hospitals to put in place policies and protocols to minimize this risk. With this in mind, we conducted a study to assess the types of medicines administered to hospital in-patients with NGFT, to assess the appropriateness of prescribed medicines for NGFT administration, and identify safer alternatives for medicines that are inappropriate for NGFT administration.

MATERIALS AND METHODS

This study was conducted in a large tertiary care hospital in India. Adult in-patients 18 years and older who were administered medicines through NGFT in the month of March, 2018 were included in the study. We retrospectively collected data including patient demographics, the reason for admission, comorbidities, length of hospital stay, number of oral drugs prescribed during the hospital stay, the day when NGFT was dispensed, and drugs dispensed before and after NGFT dispensation. Details of other formulations such as parenteral, liquid, topical, nasal, otic and ophthalmic preparations dispensed were also collected from the hospital electronic medical records. Electronic pharmacy transactions of patients were used to retrieve data pertaining to medicines dispensed on or after NGFT dispensation during the same hospital stay. Any MR, enteric-coated, or other solid oral drugs that were not meant to be crushed but administered through NGFT were considered inappropriate. We restricted our study population to those who received NGFT 16 Fr (French gauge) which is commonly prescribed for adult patients in the study centre.

For those medicines administered inappropriately, safer alternatives were identified using manufacturer's recommendations and by reviewing respective drug monographs, published literature, local hospital guidelines, and relevant textbooks. The required sample size to identify the appropriateness of prescribed medicines for NGFT administration was found to be 260 when the anticipated co-relation was found to be 0.65 with 80% power and 5% level of significance [3]. The study was approved by the Institutional Review Boards (Research and Ethics Committees) of Christian Medical College, Vellore, Tamil Nadu, India (IRB 12023 [Retro] dated 24 April 2019).

Statistical Analysis

The data were collected, entered, and stored in the Research Electronic Data Capture (REDCap®), an online database manager. The collected data were exported into an Excel spread sheet and the variables were analysed using descriptive statistics.

RESULTS

A total of 1024 NGFTs were dispensed during the study period. Out of these, 200 NGFTs were dispensed in an outpatient setup and hence excluded from further analysis. The remaining 824 NGFTs were dispensed to 557 in-patients. After excluding 47 patients who were less than 18 years old and others who were dispensed NGFTs before the study period, 510 patients were included in the final analysis, of these 76.5% (n=390) were dispensed at least one inappropriate dosage form. Table 1 shows the full demographic characteristics of patients.

A total of 13,213 drugs were dispensed during the entire hospital stay. Of these, 7795 (59%) were parenteral and 4420 (33.5%) were oral solid dosage forms. The remaining 7.5% included other formulations like oral liquids, inhalers, nebulizers, topical products, eye-drops, and ear-drops.

Among the oral solid dosage forms, 16.38% (n=724) were found to be inappropriate for NGFT administration during the hospital stay. Of these, 21.41% (n=155) were dispensed on the same day as the NGFT, 34.67% (n=251) were dispensed before the NGFT dispensation and 43.92% (n=318) were dispensed within or after 24 hours of NGFT dispensation. Of the 724 inappropriate oral solid dosage forms, 29.14% (n=211) were switched to an appropriate dosage form during the course of their stay.

Actions taken by the physicians after observing the inappropriateness of the dosage forms given via the NGFT was assessed. Of the 390 patients who were dispensed inappropriate dosage forms, 15% (n=59) were completely changed to an appropriate dosage form, 23.1% (n=90) were partially changed (switched at least one inappropriate dosage form) and a vast majority (61.8%, n=24) continued without any changes.

Inappropriate dosage forms were switched to appropriate forms after a median of 3 days (IQR 1, 4) of NGFT dispensation. Nearly half of the inappropriate dosage forms dispensed before or within 24 hours of NGFT dispensation were switched to appropriate dosage forms on the same day as NGFT dispensation.

Majority of the inappropriate dosage forms had suitable alternatives that could be administered through a NGFT or another appropriate route of administration (Table 2). 85% of the dosage forms that were dispensed inappropriately could have been switched to appropriate alternate dosage forms that were available in the hospital formulary, the exceptions include Ranolazine ER, Serratiopeptidase EC, Sulfasalazine EC and Trypsin and chymotrypsin EC. Pantoprazole EC was the most commonly dispensed inappropriate dosage form (41.44%).

Table 1: Demographic Characteristics

Characteristics	Value (n=510)
Sex, n (%)	
Male	369(72)
Female	141(28)
Mean age ± SD (years)	**49 ± 15.5**
Median (IQR) length of the hospital stay	**10 days (5-16 days)**
Speciality (%)	
Surgical stream	52.0
Medical stream	48.0
Diagnosis (%)	
Malignant disorder	123(24.1)
Cardiovascular disorder	101(19.8)
Nervous disorder	76(14.9)
Infections	‘68(13.3)
Gastrointestinal disorder	52(10.2)
Renal disorder	27(5.3)
Respiratory disorder	27(5.3)
Others*	36(7.1)
Patients with at least one co-morbidity, No. (%)	296 (58.0)

*Others included hepatic, musculoskeletal, endocrine, blood, skin, reproductive, immune disorders, and trauma

DISCUSSION

A study conducted in a Dutch hospital reported that 70% of medications crushed and administered through NGFT by the nurses had the tendency to cause harm to the hospitalized patients because of increased toxicity or loss of efficacy[5]. This study revealed that at least one inappropriate dosage forms was dispensed alongside a NGFT in 76.5% of patients. Similarly, another study conducted in France reported inappropriate dosage forms in up to 72.7% of prescriptions among hospital in-patients with NGFT[6]. Among all the oral formulations (n=4420) dispensed in our study, we found 16.38% (724) to be MR formulations which were inappropriate for nasogastric administration. Administering the inappropriate dosage forms through the NGFT by crushing may distort the coating mechanism or the technology that allows the slow release of the drug over a specific period of time. This may lead to sudden exposure to a high dose that may increase the risk of adverse outcomes[7].

Harmful consequences due to altering the MR formulations have been reported in the literature. In a case report, the unresponsiveness of a patient due to sedation and respiratory depression was associated with crushing and administering SR oxycodone hydrochloride tablets through NGFT. The rapid absorption of the entire dose led to this untoward response in this patient. In another case, a patient died due to concomitant administration of labetalol with crushed ER nifedipine through NGFT[8,9].

In our study, EC proton pump inhibitors (PPIs) were the most common inappropriate dosage form dispensed, EC pantoprazole tablet was dispensed the most (41.44%) followed by EC tablet esomeprazole. PPI’s can become unstable if crushed or broken due to the acidic pH in the stomach which could potentially inactivate the drug[10]. In a case report, a patient who had severe heartburn due to reflux esophagitis failed to respond to treatment after one-month of continuous intake of omeprazole which was crushed and administered through NGFT[8]. Drugs with alternative dosage forms such as lansoprazole dispersible tablets are preferred in such instances. The appropriate alternatives substituted instead of inappropriate formulations are listed in Table 2 .

A Pharmacokinetic study that compared EC Mycophenolate sodium with Mycophenolate mofetil (Film-coated) in patients who underwent kidney transplants revealed that the former achieved quicker systemic exposure, higher levels of systemic availability and a decreased risk of gastrointestinal toxicity resulting in minimal dosing changes[11]. Likewise, improved gastrointestinal tolerance has been observed with EC sulfasalazine when compared to its uncoated counterpart[12]. Destroying this enteric coating could be disadvantageous and nullify the positive effects.

A review of experimental and clinical evidence comparing steady-state properties of trimetazidine immediate-release (IR), modified release (MR) formulations have shown similar total exposure but delayed time to peak and increased mean absorption time. The latter showed a 31% increase in trough concentration, decreased peak-trough fluctuation, and increased plateau time[13]. The conventional IR formulation is designed to be administered as 20 mg thrice a day and the MR formulation, 35 mg twice a day. Crushing the MR formulations could cause a sudden increase in bioavailability, lead to unintended drug exposure and possible adverse events. It is essential to conduct a medication review to stop or change inappropriate dosage

Table 2: Details of the Proportion of Formulations Dispensed and Suitable Alternatives Available in the Hospital Formulary

Sl No.	Inappropriate drugs (dosage forms) prescribed	No. of patients dispensed	Proportion of inappropriate dosage forms dispensed (%)	Appropriate alternative drug/therapeutic alternatives available in the hospital	Alternative appropriate dosage forms
1	Pantoprazole (EC)	300	41.44	Ranitidine HCl	Film coated tablet, Injection
				Famotidine	Film coated tablet
				Pantoprazole	Injection
				Lansoprazole	Mouth disintegrating tablets
2	Aspirin (EC)	126	17.4	Aspirin	Uncoated tablet
3	Diclofenac (SR)	49	6.77	Diclofenac	Injection, Uncoated tablet
4	Bisacodyl (EC)	45	6.22	Bisacodyl	Suppository
				Lactulose	Solution
				Ispaghula	Powder for suspension
				Milk of magnesia, liquid paraffin	Emulsion
5	Trimetazidine HCl (MR)	36	4.97	Trimetazidine HCl	Film coated tablet
6	Ranolazine (ER)	29	4.01	Not Available	
7	Metformin HCl (SR)	26	3.59	Metformin HCl	Uncoated tablet
8	Glyceryl trinitrate (TR)	26	3.59	Glyceryl trinitrate	Injection
9	Metoprolol (ER)	17	2.35	Metoprolol	Uncoated tablet
10	Tamsulosin HCl (MR)	12	1.66	Tamsulosin HCl	Film coated tablet
11	Etofylline and Theophylline (SR)	10	1.38	Etofylline+theophylline	Uncoated tablet, Injection
12	Sodium valproate (CR)	9	1.24	Sodium valproate	Syrup, solution
13	Esomeprazole (EC)	6	0.83	Ranitidine HCl	Film coated tablet
				Famotidine	Film coated tablet
				Pantoprazole	Injection
				Lansoprazole	Dispersible tablet
14	Nifedipine (SR)	6	0.83	Nifedipine	Capsule, uncoated tablet
15	Prazosin HCl (GITS)	6	0.83	Prazosin HCl	Uncoated tablet
16	Mycophenolate Sodium (EC)	4	0.55	Mycophenolate Mofetil	Film coated tablet
17	Serratiopeptidase (EC)	3	0.41	Not Available	
18	Alfuzosin HCl (MR)	2	0.28	Silodosin	Capsule
				Tamsulosin HCl	Film coated tablet
19	Sulfasalazine (EC)	2	0.28	Not Available	
20	Dutasteride and Tamsulosin HCl (MR)	2	0.28	Dutasteride and Tamsulosin HCl	Film coated tablet
21	Trypsin and Chymotrypsin (EC)	2	0.28	Not Available	
22	Carbamazepine (CR)	1	0.14	Carbamazepine	Uncoated tablet, Suspension
23	Gliclazide (MR)	1	0.14	Gliclazide	Uncoated tablet
24	Indapamide (SR)	1	0.14	Not Available	
25	Indomethacin (SR)	1	0.14	Indomethacin	Capsule
26	Mesalazine (EC)	1	0.14	Mesalazine	Uncoated, film coated tablet

EC: Enteric coated, SR: Sustained release, MR: Modified release, ER: Extended release, CR: Controlled release, GITS: Gastro-intestinal therapeutic system

forms at the time of NGFT insertion. In our study, 29.1% of inappropriate medicines were switched to appropriate dosage forms at some time during the patient's hospital stay. Half of these were switched on the same day as NGFT dispensation. For those whose inappropriate medications were not switched on the same day as NGFT insertion, there is a chance of potential harm due to drug overdose or loss of efficacy.

The risk of overdose was reported with sustained release formulations containing biperiden, levodopa/carbidopa, alfuzosin, tamsulosin, oxycodone, and venlafaxine. Potential loss of efficacy with EC medications such as divalproex sodium, valpromide and esomeprazole has also been reported[6].

Increasing age can further aggravate the harm caused by the administration of inappropriate dosage forms due to pharmacokinetic variability. A study that compared the pharmacokinetics of SR theophylline administered through NGFT with oral administration in elderly patients found a significant reduction in the trough levels and Cmax in the NGFT group[14] 20% of our study population were elderly (≥65 years) who were commonly prescribed pantoprazole, tamsulosin hydrochloride, aspirin, trimetazidine hydrochloride, ranolazine etc.

Two third of the inappropriate formulations dispensed in our study were not switched to appropriate alternatives throughout the entire hospital stay. A lack of understanding of the pharmaceutical dosage forms could be attributed to the inappropriate prescribing in patients with NGFT. Identifying a rational drug formulation that can be administered through NGFT will essentially prevent potential harm. In order to achieve this, the selection of the ideal formulation of the drug is as important as the selection of the drug itself. In patients with NGFT, the primary goal should be to prevent drug toxicity and maintain desired therapeutic effect. It is essential that healthcare workers are made aware of the differences in pharmaceutical dosage forms that could influence the administration of the drug and ultimately, the bioavailability.

This study has made an attempt to explain the importance of considering alternate drug options, preferable routes of administration, and pharmaceutical formulations type to ensure the safety and therapeutic benefits for the patients on NGFT. Alternate drug options are available for most of the drugs administered inappropriately in our study population.

Few drugs such as sulfasalazine and indapamide were administered inappropriately because suitable alternative formulations were not available in the hospital formulary. However, suitable alternatives for these drugs are available in the market. Drugs without suitable alternatives are very minimal in our study. Only Indapamide SR, Ranolazine ER, Serratiopeptidase EC, Sulfasalazine EC and Trypsin and chymotrypsin EC were not found to have suitable alternatives in the hospital formulary.

This study has a few limitations, firstly, this is a single centre study and the data reported is mainly based on the practices being followed by the study centre which could differ from other settings. Secondly,we only included patients with NGFT 16 Fr (French gauge) which is commonly prescribed for adult patients in the study centre. However, 8, 10, and 14 Fr NGFTs were also prescribed for adult patients. In addition, we included only hospitalized patients whereas NGFT is also commonly prescribed in outpatient settings. However, the medication history is often incomplete for outpatients in the hospital electronic medical records and hence we excluded them. Also, Additionally, we were unable to determine if there was any potential harm in patients who were prescribed inappropriate dosage forms. Future prospective studies on similar patients could help identify clinical consequences of administering inappropriate dosage forms, in addition to providing cumulative data regarding this vital issue in the healthcare setting.

CONCLUSION

Use of inappropriate dosage forms among hospital inpatients with NGFT is common. The use of inappropriate dosage forms may result in an inadequate therapeutic response or toxicity. A combined effort from healthcare professionals to minimize this issue is warranted. It would be helpful if physicians could conduct a medication review in situations where a NGFT may need to be initiated to ensure that appropriate medication/dosage forms are prescribed. Another way to prevent this problem would be for the physician to mention that the patient is on a NGFT on the prescription so that pharmacist could also remind physicians about potential inappropriate dosage forms before dispensing them. Educating nurses to improve their understanding of NGFT and medication that could be inappropriate if administered via the nasogastric route could also prove beneficial. The findings of our study will help create awareness among healthcare professionals about the need for appropriate administration of oral formulations in patients intubated with NGFT.

REFERENCES

1. Shargel L, Wu-Pong S, Yu A. Modified-Release Drug Products. In: Applied Biopharmaceutics & Pharmacokinetics;vol. 17. 2012. Available from: https://accesspharmacy.mhmedical.com/content.aspx?bookid=513&sectionid=41488035.
2. Zaid AN. Comprehensive Review on Pharmaceutical Film Coating: Past, Present, and Future. *Drug Design*. 2020;14:4613–4636. Available from: https://doi.org/10.2147/DDDT.S277439.
3. Sohrevardi SM, Jarahzadeh MH, Mirzaei E, Mirjalili M, Tafti AD, Heydari B. Medication Errors in Patients with Enteral Feeding Tubes in the Intensive Care Unit. *Journal of Research in Pharmacy Practice*. 2017;6(2):100–105. Available from: https://doi.org/10.4103/jrpp.JRPP_17_9.
4. Grissinger M. Preventing Errors When Drugs Are Given Via Enteral Feeding Tubes. *Pharmacy and Therapeutics*. 2013;38(10):575–581. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3875244/.

5. Wasylewicz ATM, Van Grinsven RJB, Bikker JMW, Korsten HHM, Egberts TCG, Kerskes CHM, et al. Clinical Decision Support System-Assisted Pharmacy Intervention Reduces Feeding Tube–Related Medication Errors in Hospitalized Patients: A Focus on Medication Suitable for Feeding-Tube Administration. *Journal of Parenteral and Enteral Nutrition*. 2021;45(3):625–632. Available from: https://doi.org/10.1002/jpen.1869.
6. Fodil M, Nghiem D, Colas M, Bourry S, Poisson-Salomon AS, Rezigue H. Assessment of clinical practices for crushing medication in geriatric units. 2017. Available from: https://doi.org/10.1007/s12603-017-0886-3.
7. Hdaib NA, lbsoul Younes A, Wazaify M. Oral medications administration through enteral feeding tube: Clinical pharmacist-led educational intervention to improve knowledge of Intensive care units' nurses at Jordan University Hospital. *Saudi Pharmaceutical Journal*. 2021;29(2):134–176. Available from: https://doi.org/10.1016/j.jsps.2020.12.015.
8. Cornish P. Avoid the crush: hazards of medication administration in patients with dysphagia or a feeding tube. *Canadian Medical Association Journal*. 2005;172(7):871–872. Available from: https://doi.org/10.1503/cmaj.050176.
9. Schier JG, Howland MA, Hoffman RS, Nelson LS. Fatality from Administration of Labetalol and Crushed Extended-Release Nifedipine. *Annals of Pharmacotherapy*. 2003;37(10):1420–1423. Available from: https://doi.org/10.1345/aph.1D091.
10. Norman A, Hawkey CJ. What you need to know when you prescribe a proton pump inhibitor. *Frontline Gastroenterology*. 2011;2(4):199–205. Available from: https://doi.org/10.1136/flgastro-2011-100006.
11. Behrend M, Braun F. Enteric-coated mycophenolate sodium: tolerability profile compared with mycophenolate mofetil. *Drugs*. 2005;65(8):1037–1050. Available from: https://doi.org/10.2165/00003495-200565080-00001.
12. Weaver A, Chatwell R, Churchill M, Kastanek L, Beyene J, Garceau R, et al. Improved Gastrointestinal Tolerance and Patient Preference of Enteric-Coated Sulfasalazine Versus Uncoated Sulfasalazine Tablets in Patients with Rheumatoid Arthritis. *JCR: Journal of Clinical Rheumatology*. 1999;5(4):193–200. Available from: https://doi.org/10.1097/00124743-199908000-00003.
13. Dézsi CA. Trimetazidine in Practice: Review of the Clinical and Experimental Evidence. *American Journal of Therapeutics*. 2016;23(3):871–880. Available from: https://doi.org/10.1097/MJT.0000000000000180.
14. Berkovitch M, Dafni O, Leiboviz A, Mayan H, Habut B, Segal R. Therapeutic Drug Monitoring of Theophylline in Frail Elderly Patients: Oral Compared With Nasogastric Tube Administration. *Therapeutic Drug Monitoring*. 2002;24(5):594–597. Available from: https://doi.org/10.1097/00007691-200210000-00003.