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Unraveling medication errors in enteral tube administration: A cross-sectional study in geriatric patients receiving home health care

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ABSTRACT

Background: Medication administration through enteral feeding tubes requires careful consideration, as several medications are unsuitable for such administration due to interactions with feeding formulas or adverse effects when crushed. These errors can lead to feeding tube obstruction, reduced drug efficacy, or drug toxicity.
Objective: This study aimed to assess medication errors in geriatric patients using enteral feeding tubes who were enrolled in a home health care program.
Method: This was a cross-sectional observational study conducted at the Ministry of Health Government Hospital in Makkah City, Saudi Arabia. Medication errors related to chronic oral drugs in geriatric patients using enteral feeding tubes were evaluated, including inappropriate medications for enteral tube administration, inappropriate preparation, drug-nutrient interaction, and availability of liquid formulation, following established guidelines.
Results: Of the total 233 medications prescribed to 46 patients receiving enteral tube feeding at home, 49.3% exhibited at least one form of medication error, totaling 135 errors. Medication errors were highly prevalent among the patients (93.4%), with the leading cause being the administration of medications unsuitable for enteral feeding tubes (33.3%), predominantly due to the use of controlled release or enteric-coated formulations.
Conclusion: This study underscores the high prevalence of medication errors in older patients receiving enteral feeding at home. To ensure patient safety and optimal outcomes, healthcare professionals should utilize available resources and seek expert advice when selecting medications and dosage forms for tube-fed patients. Pharmacists play a critical role in promoting safe drug use and can greatly contribute by educating patient caregivers on proper medication preparation and administration techniques, thus preventing harm to patients.

1. Introduction

With advancing age, individuals are more susceptible to dysphagia, which is predominantly attributed to neurological disorders. A systematic review conducted in 2021 revealed that dysphagia was observed in 35.9% of older residents in nursing homes (Logrippo et al., 2017; Park et al., 2013). Consequently, a substantial proportion of this population requires enteral feeding tubes for nutritional support and medication.

Current options for administering medications through enteral feeding tubes often involve crushing pills, opening capsules, and mixing powders with water (Boullata, 2019). These methods, while common, pose various challenges and increase the potential for medication errors, ultimately endangering patient safety (Aronson, 2009). Moreover, modifying medication formulations for enteral administration may affect their pharmacokinetics, therapeutic efficacy, and adverse effects (Salmon et al., 2013). Medications with modified release profiles must never be broken or crushed due to higher risk of dangerous drug peaks and subtherapeutic troughs (Salmon et al., 2013). Tragic incidents highlight the importance of adhering to proper enteral medication administration protocols. (Hider et al., 2000; Schier et al., 2003).

Moreover, the interactions between medications and enteral nutrition may lead to decreased drug responsiveness or tube occlusions. Numerous cases have demonstrated a reduction in plasma phenytoin levels when administered via enteral tube feeding (Bauer, 1982; Cooper

Abbreviations: ASPEN, American Society for Parenteral and Enteral Nutrition; DNIs, drug–nutrient interactions; EHR, electronic health record; ISMP, Institute for Safe Medication Practices; MOH, Ministry of Health.

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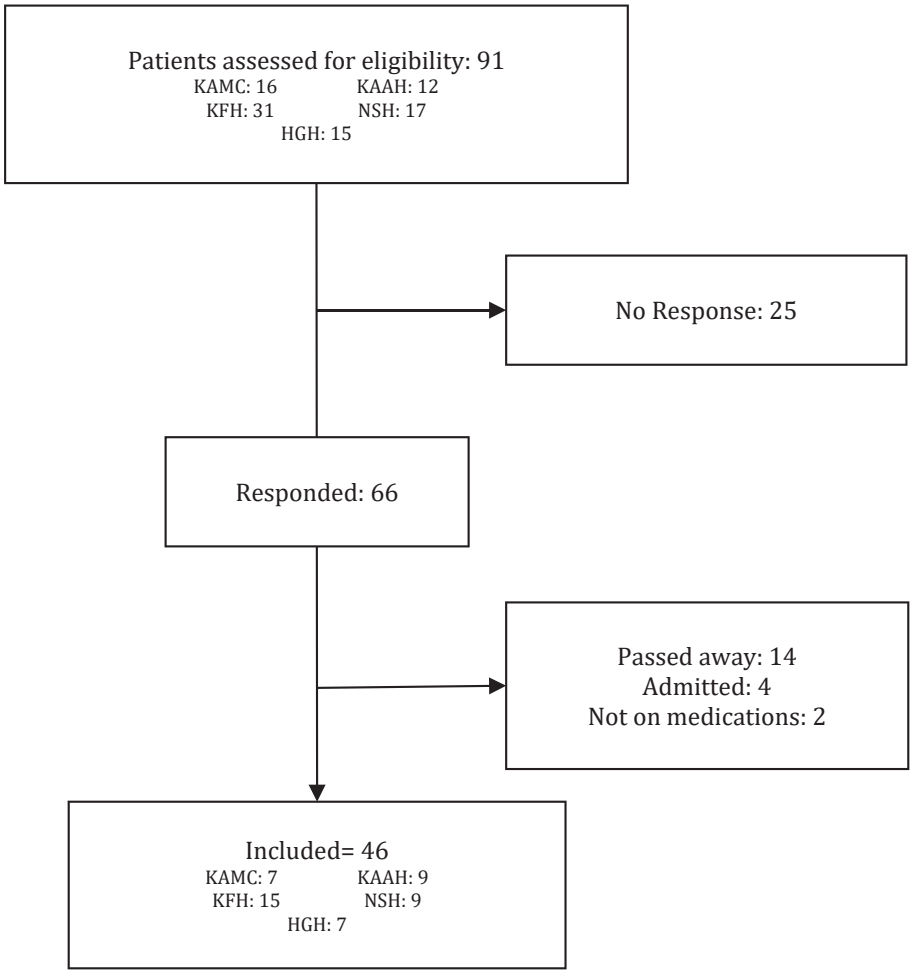

Fig. 1. Flow chart representing the selection of study participants. *KAMC: King Abdullah Medical City; KAAH: King Abdulaziz Hospital; KFH: King Faisal Hospital; NSH: Alnoor Specialty Hospital; HGH: Hera General Hospital.*

Table 1
Demographic characteristics of the study participants.

Characteristics			
Gender	Male 43%	Female 56.5%	
Age	65–75 (43.5%)	>75 (56.5%)	
Hospital	Tertiary (13%)	Secondary (87%)	
Type of enteral tube	NGT (73.9%)	PEG (26.1%)	
Educator	Doctor (84.8%)	Nurse (15.2%)	Pharmacist (0%)
Route of administration (based on the prescription)	PO (100%)	ET (0%)	

NGT: Nasogastric Tube; PEG: Percutaneous Endoscopic Gastrostomy; PO: Per Os; ET: Enteral Tube.

Table 2
Distribution of medication categories involved in medications error.

Medication category	N	%
Gastrointestinal	35	30.4%
Neurological	27	23.5%
Miscellaneous	17	14.8%
Antithrombotic	14	12.2%
Cardiac	10	8.7%
Hypertension	7	6.1%
Diabetic	4	3.5%
Psychiatric	1	0.9%

et al., 2008; Hatton, 1984). Therefore, meticulous planning of medication with enteral feeding is vital to mitigate drug–nutrient interactions (DNIs), improve clinical response and enhance absorption (Gilbar, 1999; Williams, 2008). However, information regarding drug compatibility with feeding formulas remains limited and may not be universally applicable to different formulations of the same medication or medications belonging to the same class (Boullata, 2021).

Several organizations offer valuable recommendations to reduce medication errors in enteral tube fed population, including "Oral dose forms that should not be crushed" from the "Institute for Safe Medication Practices (ISMP)"(Mitchell, 2018) and "Guidebook on Enteral Medication Administration" from the "American Society for Parenteral and Enteral Nutrition (ASPEN)" (Boullata et al., 2017). Furthermore, numerous studies have evaluated medication errors in enteral feed-tube patients, but the prevalence of these errors remains high (Demirkan et al., 2017; Fodil et al., 2017; Joos et al., 2015; Mandana et al., 2019; Sestili et al., 2014; Zhu et al., 2012). Notably, (Fodil et al., 2017) observed that 72.7% of errors in prescriptions related to drug preparation or administration occurred in geriatric wards. Similarly, in an ICU setting, (Sohrevardi et al., 2017) reported that approximately three-quarters of their patients experienced at least one type of medication error.

However, most studies investigating medication errors in tube-fed patients have primarily focused on those in patient settings who

Table 3
Distribution of medications based on causes of medication error.

Cause of Medication Error	Medications	N	%
Not appropriate for enteral administration	Aspirin	14	42.4%
	Pantoprazole	6	18.2%
	Gliclazide	3	9.1%
	Metoprolol	3	9.1%
	Tamsulosin	2	6.1%
	Indapamide	1	3.0%
	Metformin	1	3.0%
	Isosorbide dinitrate	1	3.0%
	Piribedil	1	3.0%
	Quetiapine	1	3.0%
Inappropriate preparation	Omeprazole	19	57.6%
	Esomeprazole	9	27.3%
	Memantine	4	12.1%
	Pregabalin	1	3.0%
Availability of liquid formulation	Ferrous Sulphate	5	23.8%
	Cholecalciferol	4	19.0%
	Levetiracetam	3	14.3%
	Spironolactone	2	9.5%
	Furosemide	2	9.5%
	Hydrochlorothiazide	1	4.8%
	Digoxin	1	4.8%
	Carbamazepine	1	4.8%
	Sodium Bicarbonate	1	4.8%
	Ferric hydroxide	1	4.8%
Drug–nutrient interaction (DNI)	Perindopril	5	45.5%
	Carbidopa/ Levodopa	4	36.4%
	Levothyroxine	2	18.2%
Not appropriate for enteral administration + Availability of liquid form	Levetiracetam	7	100.0%
DNI + Availability of liquid form	Phenytoin	3	60.0%
	Digoxin	1	20.0%
	Metoclopramide	1	20.0%
Not appropriate for enteral administration + DNI + Availability of liquid form	Sodium valproate	3	100.0%
Not appropriate for enteral administration + DNI	Tamsulosin	2	100.0%

Table 4
Distribution of medications error causes among patients.

Causes of medication error	No of patients	%
Not appropriate for enteral administration	28	60.8
Inappropriate preparation	30	65.2
Drug–nutrient interaction (DNI)	10	21.7
Availability of liquid formulation	16	34.7
DNI + Availability of liquid form	5	10.8
Not appropriate for enteral administration + Availability of liquid form	7	15.2
Not appropriate for enteral administration + DNI + Availability of liquid form	3	6.5
Not appropriate for enteral administration + DNI	2	4.3

received care directly from healthcare professionals (Demirkan et al., 2017; Fodil et al., 2017; Joos et al., 2015; Mandana et al., 2019; Sestili et al., 2014; Zhu et al., 2012). Consequently, there is a lack of research examining medication administration practices or patients with enteral feeding tubes in home settings, where they may face a higher risk of medication errors due to the absence of direct supervision from healthcare professionals. Therefore, this study aimed to assess medication errors in geriatric patients receiving enteral tube feeding at home by evaluating their medication records and obtaining additional information through caregiver interviews, aiming to shed light on this important aspect of patient care.

2. Material and methods

2.1. Study design, setting and duration

This prevalence observational cross-sectional study was conducted in Makkah, Saudi Arabia from April 2020 to January 2021.

2.2. Study population and sampling method

All geriatric patients aged $\geq$ 65 years, who were registered in the home health care program at the Ministry of Health (MOH) main hospitals in Makkah, were receiving enteral nutrition through feeding tubes and on chronic medications (medications prescribed for $>$ 3 months) were included. The hospitals included were King Abdullah Medical City, King Faisal Hospital, King Abdul-Aziz Hospital, AL-Noor Specialized Hospital, and Hera General Hospital as secondary centers. Hospitalized patients, those whose caregivers did not respond to the calls, passed away patients or patients not on chronic medications were excluded.

2.3. Data collection

Data were collected using an interviewer-administered data collection form, prepared by the second author and validated by three independent biostatisticians for accuracy and reliability.

The final version of the data collection form composed of three distinct parts. The first part was derived from the patients' hospital records, encompassing demographic information, details about the type of feeding tube, and the most recent medication prescriptions.

The second part involved direct communication with patients' caregivers, who were contacted via telephone after obtaining informed consent to participate in the study. Caregivers provided information regarding the drug administration educator (e.g., physician, nurse, or pharmacist). Furthermore, information on the brand name of the medications and the timing of medication administration in relation to feeding time was collected.

In the third part of the data collection process, each drug was evaluated by the first author and reviewed by the second author. This evaluation focused on determining the appropriateness of the drug for enteral tube administration, whether it was crushable or not, the potential for DNIs in term of appropriate medication administration time in relation to feeding time, and the availability of liquid formulations suitable for administration through enteral feeding tubes, as listed in the Saudi MOH formulary, as potential alternatives to solid form formulations.

To ensure accuracy and adherence to best practices, the evaluation of drug appropriateness and preparation was conducted according to a sequential reference check. These references included medication package inserts, the Handbook of Drug Administration via Enteral Feeding Tubes (White and Bradnam, 2015), facts and comparisons, new clinical drug reference databases, the ISMP publication on oral dosage forms that should not be crushed (Mitchell, 2018), the Handbook of Drug–Nutrient Interaction, and a literature review for specific medications. In cases where no pertinent data were available regarding the applicability of enteral tube feeding and no documented incidents of harm were reported using the specified medication for enteral tube patients, the drug was considered safe for enteral tube feeding (Tables A.1 and A.2).

Medication errors were classified based on specific criteria: (1) inappropriateness of a medication for enteral tube administration, (2) improper preparation of medication by caregivers, (3) administration of drugs at an inappropriate time in relation to feeding time, and (4) the availability of liquid formulation suitable for administration through enteral feeding tubes in the Saudi MOH formulary.

Table A1
Medication evaluation for appropriateness for enteral tube administration, presence of drug–nutrient interactions, and availability of liquid formulation in the Saudi MOH formulary.

Category		Generic Name	Brand name	Package insert	Handbook (White and Bradnam, 2015)	Micromedix/ Lexicomp	Pubmed	Appropriateness for Enteral administration	Comments	Availability of other formulations
HTN MED	1	Amlodipine (as besilate)	Lodipam ® Amlor® Amlodar® Amlocard®	NA	Most brands of tablets will disperse rapidly in water	_	Crushable (Allen, 2014)	Yes- Crushable		No
	2	Valsartan	Anginet® Tabuvan®	NA			Crushable (Zaid et al., 2014)	Yes- Crushable		No
	3	Valsartan-HCT	Co-Diovan®	NA				Yes- No data available		No
	4	Perindopril	Tenoryl®	NA						No
	5	Indapamide	Normalex®	Uncrushable	_			No– uncrushable “Modified release”		No
	6	Hydrochlorothiazide	Esidrex®	NA				Yes- No data available		No
	7	Hydralazine	–	NA			Crushable (Okeke et al., 2003)	Yes- Crushable		No
DM MED	1	Metformin	Omformin®	Crushable	_			Yes- Crushable		No
			Glucare®	Uncrushable	_			No– uncrushable “Extended release”		
	2	Linagliptin	Tragenta®	NA		Crushable	_	Yes- Crushable		No
	3	Sitagliptin	Januvia®	NA		Crushable	_			No
	4	Gliclazide	Diamicron®	Uncrushable	_			No– Uncrushable “Modified release”		No
	5	Glibenclamide	Glunil®	NA			Crushable (Estevez et al., 2016)	Yes- Crushable		No
CARDIAC MED	1	Atorvastatin	Atorva® Tovast®	NA			Crushable (Zaid et al., 2017)	Yes- crushable		No
	2	Rosuvastatin	Ivarin®	NA			Crushable (Ye, 2023)	Yes- crushable		No
	3	Aspirin	Bayer®	Uncrushable	_			No– Coated tablet Uncrushable		No
	4	Isosorbide dinitrate	Isobide®	Uncrushable	_			No– Uncrushable “Modified release”		No
	5	Digoxin	–	NA			Crushable (Grampian, 2023)	Crushable		Yes
	6	Metoprolol	Mitracin®	Uncrashable	_			No– Uncrushable “modified release”		No
			Lopresor®	Uncrashable	_			No– Uncrushable “modified release”		No
	7	Atenolol	Betaten®	NA		Crushable	Crushable (Garner et al., 1994)	Yes- crushable		No
	8	Bisoprolol	Cardicore®	NA	Crushable	_		Yes- Crushable		No
	9	Furosemide	Fusix®	NA			Crushable (Allen, 2017)	Yes- Crushable		Yes
	10	Spironolactone	Aldactone®	NA	Crushable	_		Yes- Crushable	Potential risk to caregiver, use double gloves	Yes
	11	Carvedilol	Riacavilol®	NA	NA	Crushable	_	Yes- Crushable		No
ANTI-COAGULANT MED	1	Apixaban	Eliquis®	Crushable	_			Yes- Crushable		No
	2	Rivaroxaban	Xalerto®	Crushable	_			Yes- Crushable		No
	3	Clopidogrel	Plavix®	NA	Crushable	_		Yes- Crushable		No

(*continued on next page*)

Table A1 (*continued*)

Category		Generic Name	Brand name	Package insert	Handbook (White and Bradnam, 2015)	Micromedix/ Lexicomp	Pubmed	Appropriateness for Enteral administration	Comments	Availability of other formulations
GI MED	1	Esomeprazole	Nexium®	Dissolve	_			Yes- Dissolve	"Disperse in water 25 ml and flush after administration"	No
	2	pantoprazole	Pantozol®	Uncrushable	_			No– Uncrushable "gastro resistant tablet"		No
	3	Omeprazole	Omedar®	Uncrushable, mix with applesauce	_			Yes- Uncrushable but "mix with applesauce"		No
	4	Lactulose	Duphalac®	_				Syrup	Very sticky "Dilute with water"	
	5	Mebeverine	Verine®	Crushable	_			Yes- Crushable	Medication leaflet "has bitter taste"	No
ANTI-EPILEPTIC MED	1	Levetiracetam	Keppra® Epitiam®	Crushable Uncrushable	_ _			Yes- Crushable No– Uncrushable "modifies release"		Yes
	2	Phenytoin	Epanutin®	NA		Crushable	_	Yes- Crushable	Potential risk to caregiver, use double gloves	Yes
	3	Sodium valproate	depakine®	Uncrushable	_			No– Uncrushable "modifies release"		Yes
	4	Carbamazepine	Tegretol®	Crushable	_			Yes- Crushable	Potential risk to caregiver, use double gloves	Yes
PSYCHIATRIC MED	2	Amitriptyline	Amirol®	NA			Crushable (Grampian, 2023)	Yes- Crushable		No
	3	Escitalopram	Cipralex® Citoxal®	Crushable (only bitter taste) Crushable (only bitter taste)	_			Yes- Crushable	Do not chew → bitter taste	No
	4	Quetiapine	Atapina® Quetta®	Crushable Uncrushable	_ _			Yes- Crushable No– Uncrushable "extended release"		No No
	5	Alprazolam	Xanax®	NA		Crushable	_	Yes- Crushable		No
MISCELLANEOUS	1	Vitamin D3	_	NA		Crushable (Fessler, 2009)	_	Yes- Crushable		Yes
	2	Ferrous sulphate	Feromin®	NA				Yes- No data against		Yes (oral drop)
	3	Ferric hydroxide	Ferose®	NA				Yes- No data against		No
	4	Folic acid	Befolvit®	NA				Yes- No data against		No
	5	Levodopa/ carbidopa	Credanil® Sinemet®	NA		Crushable	_	Yes- Crushable (Cooper et al., 2008)	Interaction between levodopa and enteral nutrition	No
	6	Piribedil	Trivastal®	Uncrushable	_			No– Uncrushable "Sustained release"		No
	7	Memantine	Dement®	NA			Opening capsule (Mitchell, 2018)	Yes- Uncrushable- entire contents of capsule may be sprinkled on applesauce and swallowed immediately		No
	8	Levothyroxine	Eltroxin® Euthyrox®	Crushable Crushable	_			Yes- Crushable		No
	9	Tamsulosin	Prosta-tab®	Uncrushable	_			No– Uncrushable "prolonged release"	Micromedex, Lexicomp	No
	10	Finasteride	Finiscar®	Crushable with caution	_			Yes- Crushable with caution	Potential risk to a caregiver who is pregnant, breast feeding, and male fetus	No

(*continued on next page*)

Table A1 (*continued*)

Category		Generic Name	Brand name	Package insert	Handbook (White and Bradnam, 2015)	Micromedix/ Lexicomp	Pubmed	Appropriateness for Enteral administration	Comments	Availability of other formulations
	11	Baclofen	Lioresal®	Crushable	-			Yes- Crushable		Yes
	12	Pregabalin	Nervax®	Open capsule	Open capsule	-		Yes- Open capsule		No
	13	Neurobion	–	NA	Crushable with caution "Coated tablet"	-		Yes- Crushable with caution "Coated tablet"	Stir for several minutes until sugar coating dissolves → high risk of tube blockage	No
	14	Sodium bicarbonate	–	NA	Crushable	-		Yes- Crushable		IV solution
	15	Metoclopramide	Primperan®	NA			Crushable(Grampian, 2023)	Yes- Crushable		Oral disintegrating tablets

NA: Not Available; HTN: Hypertension; Med: Medications; DM: Diabetic mellites; GI: Gastrointestinal.

2.4. Ethics approval and consent to participate

The current study was approved by the Institutional Review Board committee of the Makkah Health Affairs General Directorate, Ministry of Health, Saudi Arabia, in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use guidelines. The study was registered under the number H-02-K-076-1020-391. Verbal informed consent was obtained from each participant or their respective guardians, and this consent process was duly authorized and approved by the aforementioned committee.

2.5. Data analysis

Data analysis was performed using the Statistical Package for Social Sciences version 26. Mean and standard deviation were employed to characterize numerical variables. Additionally, nominal data were summarized using frequencies and percentages. To present the most significant findings comprehensively, tables were used as a visual aid.

3. Results

A total of 91 patients with enteral feeding tubes registered in the home healthcare program were contacted. Overall, the response rate was 72.5%, and 46 patients (50.5 %) were finally included in the study (Fig. 1).

Among the included patients, 57.8% were females, with a mean age of 77.4 ± 7.7 years, and approximately 56.5% of the patients were aged over 75 years. Approximately 84.8% of patients received instructions regarding medication from physicians, whereas 15.2% received these instructions from nurses. Notably, there was a lack of pharmacist participation in the education of patients' caregivers regarding medication administration. Table 1 summarizes the demographic and clinical characteristics of individuals receiving medication through an enteral feeding tube.

During the study period, a total of 233 medications were prescribed for all participants. The most commonly prescribed oral drugs are amlodipine capsules, omeprazole enteric-coated tablets, clopidogrel film-coated tablets, aspirin enteric-coated tablets, and atorvastatin tablets (Table A. 3). On average, each patient was prescribed 5 ± 2.5 medications. The seven oral formulations used included film-coated tablets (39.1%), tablets (25.3%), delayed-release tablets (21.9%), extended-release tablets (7.7%), capsules (2.1%), chewable tablets (1.7%), and hard capsules (0.9%).

A total of 135 errors were detected for 115 prescribed medications, indicating 49.3% medication error prevalence. Among the patients, 43 patients (93.4%) experienced medication errors, with an average of 3 ± 1.25 medications at risk of errors per patient. The most commonly involved medications in these errors were omeprazole, aspirin, levetiracetam, esomeprazole, and pantoprazole (Table A. 4). While the most medication category involved in medication error were Gastrointestinal and neurological medications (Table 2). The causes of errors were categorized as follows: medications not appropriate for enteral administration, 45 (33.3%); prescription of solid forms when liquid forms were commercially available, 36 (26.6%); inappropriate preparation by patients, 33 (24.4%); and DNI, 21 (17.5%) (Table 3). Inappropriateness of medication preparation stemmed from controlled-release forms, such as in levetiracetam, pantoprazole, and tamsulosin, or enteric-coated medications, as aspirin. The prevalence of tube-fed patients with medication errors based on the causes is illustrated in Table 4.

4. Discussion

This study highlights a concerning prevalence of medication errors in geriatric patients receiving enteral tube feeding at home, a population that has received limited attention in previous studies, with nearly half of the prescribed medications (49.3%) experiencing at least one form of

Table A2
Evaluation of drug-nutrient interactions.

Category		Generic Name	Brand name	Drug-Formula interaction	Comment
HTN MED	1	Amlodipine (as besilate)	Lodipam® Amlor® Amlodar® Amlocard®	No interaction (White and Bradnam, 2015)	_
	2	Valsartan	Anginet® Tabuvan®	No interaction (White and Bradnam, 2015)	_
	3	Valsartan-HCT	Co-Diovan®	–	No data available from the literature, medication leaflet, or Micromedex
	4	Perindopril	Tenoryl®	Interaction (White and Bradnam, 2015)	Reduce bioavailability by food ingestion
	5	Indapamide	Normalex®	–	No data available from the literature, medication leaflet, or Micromedex
	6	Hydrochlorothiazide	Esidrex®	–	No data available from the literature, medication leaflet, or Micromedex
	7	Hydralazine	–	Precaution (Semple et al., 1991)	Drug bioavailability will decrease with: Enteral bolus > Enteral infusion > Fasting
DM MED	1	Metformin	Omformin® Glucare®	No interaction	To be administered with meal to reduce GI adverse effect
	2	Linagliptin	Tragenta®		Micromedex, Lexicomp
	3	Sitagliptin	Januvia®		
	4	Gliclazide	Diamicron®	No interaction	Lexicomp
	5	Glibenclamide	Glibil®	No interaction	Lexicomp
CARDICIAC MED	1	Atorvastatin	Atorva® Tovast®	No interaction	Guideline for the administration of medicines to adult via enteral tubes within NHS Grampian
	2	Rosuvastatin	Ivarin®	No interaction	Medication leaflet, Micromedex
	3	Aspirin	Bayer®	No interaction	Micromedex
	4	Isosorbide dinitrate	Isobide®	–	No data available from the literature, medication leaflet, or Micromedex
	5	Digoxin	–	Interaction (White and Bradnam, 2015)	Absorption of digoxin is slowed and reduced by concurrent intake of high-fiber diet
	6	Metoprolol	Mitracin®	–	No data available from the literature, medication leaflet, or Micromedex
			Lopresor®	No interaction	Medication leaflet
	7	Atenolol	Betaten®	No interaction (Boullata and Armenti, 2011)	_
	8	Bisoprolol	Concor® Bistol®	No interaction (Boullata and Armenti, 2011)	_
	9	Furosemide	Fusix®	No interaction (White and Bradnam, 2015)	_
	10	Spironolactone	Aldactone®	No interaction	Lexicomp, Micromedex
	11	Carvedilol	Riacavilol®	No interaction (Boullata and Armenti, 2011)	_
ANTI-COAGULANT MED	1	Apixaban	Eliquis®	No interaction	Medication leaflet
	2	Rivaroxaban	Xalerto®	No interaction	Medication leaflet
	3	Clopidogrel	Clogrel®	No interaction	Medication leaflet
			Plavix®	No interaction	Dosing of Medications in Patients Receiving Continuous Enteral Feedings – Adult – Inpatient Clinical Practice Guideline
GI MED	1	Esomeprazole	Nexium®	Maximize efficacy (	Administer before meal by 30 min
	2	pantoprazole	Proton® Pantozol®	Boullata and Armenti, 2011)	
	3	Omeprazole	Omedar® Hyposec®		
	4	Lactulose	Duphalac®	No interaction	Medication leaflet
	5	Mebeverine	Verine®	No interaction	Medication leaflet
ANTI-EPILEPTIC MED	1	Levetiracetam	Keppra® Epitiam®	No interaction (Fay et al., 2005)	_
	2	Phenytoin	Epanutin®	Interaction (Williams, 2008) + Micromedex	Drug absorption reduced up to 70% + drug will adhere to the tube wall ↓ drug availability To be taken 2 h before or after the formula Flush the tube before and after drug administration
	3	Sodium valproate	depakine®	Interaction (Magnuson et al., 2005)	Narrow therapeutic index, Gastro irritant "ISMP"
	4	Carbamazepine	Tegretol®	Precaution (White and Bradnam, 2015)	Risk of tube blockage
PSYCHIATRIC MED	2	Amitriptyline	–	–	No data available from the literature, medication leaflet, or Micromedex
	3	Escitalopram	Cipralex® Citoxal®	No interaction	No data available from the literature, medication leaflet, or Micromedex
	4	Quetiapine	Atapina®	–	No data available from the literature, medication leaflet, or Micromedex
			Quetta®	–	No data available from the literature, medication leaflet, or Micromedex
	5	Alprazolam	Xanax®	–	No data available from the literature, medication leaflet, or Micromedex
MISCELLANEOUS	1	Vitamin D3	–		No data available from the literature, medication leaflet, or Micromedex
	2	Ferrous sulphate	Feromin®	No interaction (White and Bradnam, 2015)	_
	3	Ferric hydroxide	Ferose®		
	4	Folic acid	Befolvit®	No interaction	Lexicomp
	5	Levodopa/ carbidopa	Credanil® Sinemet®	Interaction (Cooper et al., 2008)	Drug absorption decreases with high protein diet → 30 min – 2 h prior to feeding or 2 h after feeding, total daily protein 0.8 g/kg, increase the dose of levodopa
	6	Piribedil	Trivastal®	–	No data available from the literature, medication leaflet or Micromedex

(*continued on next page*)

Table A2 (*continued*)

Category		Generic Name	Brand name	Drug-Formula interaction	Comment
	7	Memantine	Dement®	No interaction	Micromedex, Lexicomp
	8	Levothyroxine	Eltroxin® Euthyrox®	Interaction	Interaction between levothyroxine and soy protein "Soy polysaccharide is the most common fiber source in enteral formulas" change the formula, administer dose if possible after feeding and at least 1 h before feeding, Monitor the TFT
	9	Tamsulosin	Prosta-tab®	Interaction (White and Bradnam, 2015)	Reduced absorption
	10	Finasteride	Finiscar®	No interaction	Lexicomp, Micromedex
	11	Baclofen	Lioresal®	No interaction	Lexicomp
	12	Pregabalin	Nervax®	No interaction	Medication leaflet, Lexicomp, and Micromedex
	13	Neurobion	–	No interaction	Lexicomp
	14	Sodium bicarbonate	–	Spacing	1–3 h after meal "Lexicomp"
	15	Metoclopramide	Primperan®	Spacing	30 min prior to meal "Lexicomp"

HTN: Hypertension; Med: Medications; DM: Diabetic mellites; GI: Gastrointestinal.

Table A3
Distribution of medications administered to patients with enteral feeding.

Medication	N	%	Medication	N	%
Hypertensive medications			**Diabetic medications**		
Amlodipine	21	9.0%	Metformin	9	3.9%
Valsartan	7	3.0%	Gliclazide	3	1.3%
Valsartan + Hydrochlorothiazide	1	0.4%	Glibenclamide	1	0.4%
Perindopril	6	2.6%	Linagliptin	2	0.9%
Hydralazine	1	0.4%	Sitagliptin	0	0.0%
Indapamide	1	0.4%	**Gastric medications**		
Hydrochlorothiazide	1	0.4%	Pantoprazole	6	2.6%
Cardiac medications			Omeprazole	19	8.2%
Atorvastatin	14	6.0%	Lactulose	2	0.9%
Metoprolol	3	1.3%	Esomeprazole	10	4.3%
Digoxin	2	0.9%	Mebeverine	1	0.4%
Rosuvastatin	12	5.2%	Metoclopramide	1	0.4%
Isosorbide dinitrite	1	0.4%	**Neurological medications**		
Spironolactone	2	0.9%	Levetiracetam	10	4.3%
Furosemide	2	0.9%	Phenytoin	3	1.3%
Atenolol	2	0.9%	Sodium valproate	3	1.3%
Bisoprolol	4	1.7%	Levodopa/ carbidopa	5	2.1%
Carvidelol	1	0.4%	Baclofen	4	1.7%
Psychiatric medications			Memantine	4	1.7%
Carbamazepine	1	0.4%	Pregabalin	1	0.4%
Amitriptyline	2	0.9%	Piribedil	1	0.4%
Escitalopram	2	0.9%	**Miscellaneous**		
Quetiapine	2	0.9%	Cholecalciferol	4	1.7%
Alprazolam	1	0.4%	Levothyroxine	4	1.7%
Antithrombotic medication			Tamsulosin	4	1.7%
Apixaban	5	2.1%	Ferrous Sulphate	5	2.1%
Clopidogrel	15	6.4%	Folic acid	2	0.9%
Rivaroxaban	1	0.4%	Finasteride	3	1.3%
Aspirin	14	6.0%	Sodium Bicarbonate	1	0.4%
			Ferric hydroxide	1	0.4%

Table A4
Distribution of medications involved in medications error.

Medication	N	%	Medication	N	%
Omeprazole	19	16.5%	Digoxin	2	1.7%
Aspirin	14	12.2%	Spironolactone	2	1.7%
Levetiracetam	10	8.7%	Furosemide	2	1.7%
Esomeprazole	9	7.8%	Levothyroxine	2	1.7%
Pantoprazole	6	5.2%	Indapamide	1	0.9%
Perindopril	5	4.3%	Hydrochlorothiazide	1	0.9%
Ferrous Sulphate	5	4.3%	Metformin	1	0.9%
Levodopa/carbidopa	4	3.5%	Isosorbide dinitrate	1	0.9%
Memantine	4	3.5%	Metoclopramide	1	0.9%
Cholecalciferol	4	3.5%	Pregabalin	1	0.9%
Tamsulosin	4	3.5%	Piribedil	1	0.9%
Gliclazide	3	2.6%	Carbamazepine	1	0.9%
Metoprolol	3	2.6%	Quetiapine	1	0.9%
Phenytoin	3	2.6%	Sodium Bicarbonate	1	0.9%
Sodium valproate	3	2.6%	Ferric hydroxide	1	0.9%

error. Notably, these errors were prevalent among 93.4% of the patients, underscoring the significance of this issue.

The major cause of medication errors was the administration of medication unsuitable for administration through enteral feeding tubes (33.3%), particularly as most drugs were controlled-release or enteric-coated formulations. These findings align with previous research presented by Mandana et al., where gastrointestinal medications, specifically proton pump inhibitors such as omeprazole and pantoprazole, were commonly involved in incorrect medication administration due to their delayed-release sensitiveness to gastric acid, rendering crushing ineffective (Table 2) (Mandana et al., 2019).

Despite the commercially available liquid dosage forms for easier enteral tube administration that may have a lower risk of catheter obstruction, a considerable portion of prescribed medications were still administered in solid form (15.4%), with 8.7% of them prescribed as controlled-release formulations. This accounted for 30% of all medication errors, corroborating findings from Silva et al., who reported that of 49 medications administered in solid oral forms, 17 (34.7%) had equivalent oral liquid options (Silva et al., 2011).

DNI is another crucial factor to be considered in enteral feeding tube medication administration. DNI poses the risks of reduced pharmaceutical efficacy and catheter blockage. Medications like Levodopa/carbidopa, phenytoin, and sodium valproate are commonly involved in DNIs in patients. A previous study reported inappropriate administration of levodopa and phenytoin to 11.5 and 3.8% of patients in the emergency room, respectively (Spezia and Matheus, 2020). Considering the narrow therapeutic index of phenytoin and that the high-protein content of enteral feeding can inhibit levodopa absorption (Spezia and Matheus, 2020), extra caution and accurate coordination of drug administration with meals in enteral tube-fed patients are pivotal to ensuring safety and medication effectiveness.

Compared to findings in the literature, the prevalence of medication errors in this study was high (93.4%). In contrast, (Li et al., 2017) reported that only 43% of patients were prescribed at least one inappropriate medication. (Mandana et al., 2019) conducted a study on ICU patients and reported that approximately 80% of patients experienced medication errors during their hospital stay. This could be attributed to factors like the involvement of non-health care professionals in caregiving, the lack of sufficient instructions in most medication package inserts regarding enteral tube dosing, as only 55% of the medications provided complete information regarding the appropriateness of their dosing forms, inaccurate prescriptions regarding medication administration routes, and limited pharmacist engagement. Therefore, enhancing prescription accuracy and promoting pharmacists' involvement in education are crucial steps in reducing medication errors.

To address these challenges and reduce medication errors in enteral tube-fed patients, comprehensive initiatives must be implemented in Saudi Arabia. Establishing a multidisciplinary team to review the institutional drug formulary for enteral feeding tube restrictions using different resources, such as ASPEN (Boullata et al., 2017) and primary literature, could be a primary solution. Additionally, standardizing safe

drug administration techniques and conducting educational sessions for practitioners to safely prescribe, prepare, and administer medications via feeding tubes may also prevent some of these errors.

Furthermore, the adoption of electronic health record (EHR) systems is crucial to reducing the risk of medication errors. EHR systems can play a significant role by preventing the prescription of medications or formulations that are contraindicated for tube administration. Additionally, these systems can provide real-time alerts if an inappropriate formulation is ordered, prompting healthcare providers to reconsider the medication choice.

Prescribers should prioritize accuracy in prescriptions, including all required information, the accurate route of administration, and seek expert advice on the appropriate medication to be administered via an enteral feeding tube. Additionally, educating patients and caregivers on proper techniques, common issues, and best practices when administering medications via tubes is the most essential step (Billstein-Leber et al., 2018; ISMP, 2022). Future investigations should assess the impact of these initiatives on reducing medication errors and the knowledge and practices of healthcare professionals and caregivers with tube-fed older patients at home.

This study had some limitations. First, the findings of this study cannot be generalized since it was conducted only in one region and small number of patients were included. Second, the caregivers preparing and administering drugs at home were not visually observed due to the Coronavirus pandemic. Nevertheless, our study reveals a high incident of medication errors that should be investigated in other regions as well.

5. Conclusion

This study sheds light on the significant prevalence of medication errors among older patients enrolled in home health programs and receiving enteral feeding. To ensure patient safety and optimal outcomes, healthcare professionals must make informed decisions by leveraging available resources and seeking expert advice when selecting medications and appropriate dosage forms for tube-fed patients. Pharmacists should be involved in education of patients in home health care about proper medication preparation and administration techniques. By imparting this essential knowledge, healthcare professionals can collectively work towards preventing potential harm and enhancing the overall well-being of tube-fed patients.

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CRediT authorship contribution statement

Nisrin Bifari: Conceptualization, Validation, Visualization, Formal analysis, Writing – review & editing. **Ibtihaj Nasseraldeen Bifari:** Methodology, Investigation, Data curation, Resources, Project administration, Writing – original draft. **Yusuf Ahmed Alharbi:** Supervision.

Declaration of Competing Interest

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Appendix

(See Table A1-A4**).**

References

Allen Jr, L.V., 2014. Amlodipine 1 mg/mL Oral Liquid. US Pharm. 39, 55–56.
Allen Jr, L.V., 2017. Furosemide 10 mg/mL Oral Suspension. US Pharm. 42, 48–49.
Aronson, J.K., 2009. Medication errors: definitions and classification. Br. J. Clin. Pharmacol. 67, 599–604. https://doi.org/10.1111/j.1365-2125.2009.03415.x.
Bauer, L.A., 1982. Interference of oral phenytoin absorption by continuous nasogastric feedings. Neurology. 32, 570–572. https://doi.org/10.1212/wnl.32.5.570.
Billstein-Leber, M., Carrillo, C.J.D., Cassano, A.T., Moline, K., Robertson, J.J., 2018. ASHP Guidelines on Preventing Medication Errors in Hospitals. Am. J. Health. Syst. Pharm. 75, 1493–1517. https://doi.org/10.2146/ajhp170811.
Boullata, J.I., 2021. Enteral Medication for the Tube-Fed Patient: Making This Route Safe and Effective. Nutr. Clin. Pract. 36, 111–132. https://doi.org/10.1002/ncp.10615.
Boullata, J. I., Armenti, V. T., 2011. Handbook of Drug-Nutrient Interactions (Vol. 41). Emerald Group Publishing Limited. Doi: 10.1108/nfs.2011.41.6.448.1.
Boullata, J. I., Carrera, A. L., Harvey, L., Escuro, A. A., Hudson, L., Mays, A., McGinnis, C., Wessel, J. J., Bajpai, S., Beebe, M. L., Kinn, T. J., Klang, M. G., Lord, L., Martin, K., Pompeii-Wolfe, C., Sullivan, J., Wood, A., Malone, A., Guenter, P., Aspen Safe Practices for Enteral Nutrition Therapy Task Force, A. S. f. P., Enteral, N., 2017. ASPEN Safe Practices for Enteral Nutrition Therapy [Doi: 10.1177/0148607116673053]. J. Parenter. Enter. Nutr. 41, 0148607116673053. Doi: Doi: 10.1177/0148607116673053.
Boullata, J. I., 2019. Guidebook on enteral medication administration (J. I. Boullata, Ed. 2019 ed.). American Society for Parenteral and Enteral Nutrition.
Cooper, M.K., Brock, D.G., McDaniel, C.M., 2008. Interaction between levodopa and enteral nutrition. Ann. Pharmacother. 42, 439–442. https://doi.org/10.1345/aph.1K450.
Demirkan, K., Bayraktar-Ekincioglu, A., Gulhan-Halil, M., Abbasoglu, O., 2017. Assessment of drug administration via feeding tube and the knowledge of healthcare professionals in a university hospital. Eur. J. Clin. Nutr. 71, 164–168. https://doi.org/10.1038/ejcn.2016.147.
Estevez, P., Boscolo, O., Quiroga, E., Fernandez Penuto, R., Buontempo, F., Tripodi, V., Lucangioli, S., 2016. Development and stability study of glibenclamide oral liquid paediatric formulations for the treatment of permanent neonatal diabetes mellitus. Eur. J. Hosp. Pharm. 23, 213–218. https://doi.org/10.1136/ejhpharm-2015-000763.
Fay, M.A., Sheth, R.D., Gidal, B.E., 2005. Oral absorption kinetics of levetiracetam: the effect of mixing with food or enteral nutrition formulas. Clin. Ther. 27, 594–598. https://doi.org/10.1016/j.clinthera.2005.05.010.
Fessler, T., 2009. Vitamin D—new perspectives in enteral and parenteral nutrition practice. Retrieved 2023 Today. Dietit. 9, 6. https://www.todaysdietitian.com/newarchives/050409p18.shtml.
Fodil, M., Nghiem, D., Colas, M., Bourry, S., Poisson-Salomon, A.S., Rezigue, H., Trivalle, C., 2017. Assessment of Clinical Practices for Crushing Medication in Geriatric Units. J. Nutr. Health. Aging. 21, 904–908. https://doi.org/10.1007/s12603-017-0886-3.
Garner, S.S., Wiest, D.B., Reynolds Jr., E.R., 1994. Stability of atenolol in an extemporaneously compounded oral liquid. Am. J. Hosp. Pharm. 51, 508–511.
Gilbar, P.J., 1999. A Guide to Enteral Drug Administration in Palliative Care. J. Pain. Symptom. Manage. 17, 197–207. https://doi.org/10.1016/s0885-3924(98)00124-9.
Grampian, N., 2023. Guideline for the administration of medicines to adult via enteral tubes within NHS Grampian. . Grampian Medicines Information Centre. https://www.nhsgrampian.org/globalassets/foidocument/foi-public-documents1—all-documents/Guide_EnteralTubeA.pdf Retrieved 9.6.2023.
Hatton, R.C., 1984. Dietary interaction with phenytoin. Clin. Pharm. 3, 110–111.
Hider, J.D., Shehab, Z., Courteney-Harris, R., 2000. Effectiveness of modified release isosorbide mononitrate affected by incorrect use. Bmj. 320, 483.
ISMP, I. f. S. M. P., 2022. Preventing errors when preparing and administering medications via enteral feeding tubes. ISMP Medication Safety Alert! Acute Care. . 27(23):1-4.
Joos, E., Mehuys, E., Van Bocxlaer, J., Remon, J.P., Van Winckel, M., Boussery, K., 2015. Drug administration via enteral feeding tubes in residential care facilities for individuals with intellectual disability: an observational study. J. Intellect. Disabil. Res. 59, 215–225. https://doi.org/10.1111/jir.12129.
Li, T., Eisenhart, A., Costello, J., 2017. Development of a medication review service for patients with enteral tubes in a community teaching hospital. Am. J. Health. Syst. Pharm. 74, S47–S51. https://doi.org/10.2146/ajhp160519.
Logrippo, S., Ricci, G., Sestili, M., Cespi, M., Ferrara, L., Palmieri, G.F., Ganzetti, R., Bonacucina, G., Blasi, P., 2017. Oral drug therapy in elderly with dysphagia: between a rock and a hard place! Clin. Interv. Aging. 12, 241–251. https://doi.org/10.2147/cia.s121905.
Magnuson, B.L., Clifford, T.M., Hoskins, L.A., Bernard, A.C., 2005. Enteral nutrition and drug administration, interactions, and complications. Nutr. Clin. Pract. 20, 618–624. https://doi.org/10.1177/0115426505020006618.
Mandana, I., Negin, A., Farhad, S., Leila, K., Sepideh, S., Maryam, A., Maryam, H., 2019. Medication Administration through Enteral Feeding Tubes in Mechanically Ventilated Critically Ill Patients: Evaluation of the Potential Medication Errors. J. Pharm. Care. 7 https://doi.org/10.18502/jpc.v7i3.2351.

Mitchell, J.F., 2018. Oral dosage forms that should not be crushed. Retrieved 2023 Institute Safe Medicat. Practices 19, 6. https://www.ismp.org/sites/default/files/attachments/2018-02/DoNotCrush.pdf.

Okeke, C.C., Medwick, T., Nairn, G., Khuspe, S., Grady, L.T., 2003. Stability of hydralazine hydrochloride in both flavored and non- flavored extemporaneous preparations. Int. J. Pharm. Compd. 7, 313–319.

Park, Y.-H., Han, H.-R., Oh, B.-M., Lee, J., Park, J.-A., Yu, S.J., Chang, H., 2013. Prevalence and associated factors of dysphagia in nursing home residents. Geriatric. Nursing. 34, 212–217. https://doi.org/10.1016/j.gerinurse.2013.02.014.

Salmon, D., Pont, E., Chevallard, H., Diouf, E., Tall, M.L., Pivot, C., Pirot, F., 2013. Pharmaceutical and safety considerations of tablet crushing in patients undergoing enteral intubation. Int. J. Pharm. 443, 146–153. https://doi.org/10.1016/j.ijpharm.2012.12.038.

Schier, J.G., Howland, M.A., Hoffman, R.S., Nelson, L.S., 2003. Fatality from administration of labetalol and crushed extended-release nifedipine. Ann. Pharmacother. 37, 1420–1423. https://doi.org/10.1345/aph.1D091.

Semple, H.A., Koo, W., Tam, Y.K., Ngo, L.Y., Coutts, R.T., 1991. Interactions between hydralazine and oral nutrients in humans. Ther. Drug. Monit. 13, 304–308. https://doi.org/10.1097/00007691-199107000-00004.

Sestili, M., Ferrara, L., Logrippo, S., Ganzetti, R., 2014. Detection of medication errors in hospital discharge communications of patients on Enteral nutrition. Nutr. Ther. Metab. 32, 152–154. https://doi.org/10.5301/NTM.2014.12683.

Silva, M., Cava, C., Pedroso, P., Futuro, D., 2011. Evaluation of the profile of drug therapy administered through enteral feeding tube in a general hospital in Rio de Janeiro. Braz. J. Pharm. Sci. 47, 331–337. https://doi.org/10.1590/S1984-82502011000200014.

Sohrevardi, S.M., Jarahzadeh, M.H., Mirzaei, E., Mirjalili, M., Tafti, A.D., Heydari, B., 2017. Medication Errors in Patients with Enteral Feeding Tubes in the Intensive Care Unit. J. Res. Pharm. Pract. 6, 100–105. https://doi.org/10.4103/jrpp.JRPP_17_9.

Spezia, I., Matheus, F., 2020. Evaluation of prescription containing medication via enteral feeding tubes in an adult emergency unit. Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde 11, 497. https://doi.org/10.30968/rbfhss.2020.114.0497.

White, R., Bradnam, V., 2015. Handbook of drug administration via enteral feeding tubes. Pharma Press.

Williams, N.T., 2008. Medication administration through enteral feeding tubes. Am. J. Health. Syst. Pharm. 65, 2347–2357. https://doi.org/10.2146/ajhp080155.

Ye, A., 2023. Rosuvastatin 4 mg/mL Oral Suspension. US Pharm. 48, 59–60.

Zaid, A.N., Assali, M., Qaddomi, A., Ghanem, M., Zaaror, Y.A., 2014. Preparation and stability evaluation of extemporaneous oral suspension of valsartan using commercially available tablets. Int. J. Pharm. Compd. 18, 169–174.

Zaid, A.N., Assali, M., Zalmout, S., Basheer, A., 2017. Compounding and stability evaluation of atorvastatin extemporaneous oral suspension using tablets or pure powder. Eur. J. Hosp. Pharm. 24, 157–161. https://doi.org/10.1136/ejhpharm-2016-000913.

Zhu, L.L., Xu, L.C., Wang, H.Q., Jin, J.F., Wang, H.F., Zhou, Q., 2012. Appropriateness of administration of nasogastric medication and preliminary intervention. Ther. Clin. Risk. Manag. 8, 393–401. https://doi.org/10.2147/tcrm.s37785.