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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

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Abstract

Background: Administering medication through an enteral feeding tube (FT) is a frequent cause of errors resulting in increased morbidity and cost. Studies on interventions to prevent these errors in hospitalized patients, however, are limited. *Objective:* The objective was to study the effect of a clinical decision support system (CDSS)–assisted pharmacy intervention on the incidence of FT-related medication errors (FTRMEs) in hospitalized patients. *Methods:* A pre-post intervention study was conducted between October 2014 and May 2015 in Catharina Hospital, the Netherlands. Patients who were admitted to the wards of bowel and liver disease, oncology, or neurology; using oral medication; and had an enteral FT were included. Preintervention patients were given care as usual. The intervention consisted of implementing a CDSS-assisted pharmacy check while also implementing standard operating procedures and educating personnel. An FTRME was defined as the administration of inappropriate medication through an enteral FT. The incidence was expressed as the number of FTRMEs per medication administration. Multivariate Poisson regression was used to calculate the incidence ratio (IR) comparing both phases. *Results:* Eighty-one patients were included, 38 during preintervention and 43 during the intervention phase. Incidence of FTRMEs in the preintervention phase was 0.15 (95% CI, 0.07–0.23) vs 0.02 (95% CI, 0.00–0.04) in the intervention phase, resulting in an adjusted IR of 0.13 (95% CI, 0.10–0.18). *Discussion:* Incidence of FTRMEs, as well as the IR, is comparable to previous studies. *Conclusion:* The intervention resulted in a substantial reduction in the incidence of FTRMEs. (*JPEN J Parenter Enteral Nutr.* 2021;45:625–632)

Keywords

clinical decision support; enteral feeding; enteral feeding tube; medication errors

Clinical Relevancy Statement

Administering medication through an enteral feeding tube remains a frequent cause of errors, resulting in increased morbidity and cost. A clinical decision support system–assisted pharmacy intervention can considerably help reduce the number of these errors with minimal additional workload.

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Introduction

A substantial number of hospitalized patients are temporarily dependent on enteral feeding [1] and are unable to swallow medication.[2] Liquid, transdermal, rectal, and even intravenous formulations are frequently unavailable or undesirable. As such, medication is frequently administered through the enteral feeding tube (FT). Previous studies demonstrated that incorrect administration of oral medication through an FT, like crushing formulations that may not be crushed, is a frequent cause of medication errors.[2,3] Medication errors can result in obstruction of the FT,[3,4] leading to increased morbidity[5-7] and cost.[8] Such medication errors can directly harm the patient[9-12] or constitute an health risk for medical personnel.[13,14]

Various approaches have been studied to reduce the number of FT-related medication errors (FTRMEs). In a study performed in an institution for individuals with intellectual disability (n = 11; 474 administrations), introducing a nurse training program reduced the number of FTRMEs significantly, 158 FTRMEs in 245 administrations compared to 69 FTRMEs in 229 administrations after the intervention, resulting in a estimated relative risk reduction (RRR) of 48% (adjusted odds ratio (OR) of 0.33).[15] A comparable study performed in nursing home patients (n = 197; 1317 administrations) added warning symbols on the unit dose for packaged and labeled medications, significantly reducing the number of FTRMEs, 21 FTRMEs in 681 administration compared to 3 FTRMEs in 636 administrations, resulting in a RRR of 85%.[16] In hospitalized patients (n = 16; 183 administrations), adding standard operating procedures and daily ward visits by pharmacy technicians and alerting in the computerized physician order entry (CPOE) decreased the number of FTRMEs even further, 73 FTRMEs in 96 administrations to 5 FTRMEs in 87 administrations, resulting in a estimated RRR of 93% (OR of 0.003).[2]

When using the Swiss cheese model[17] to analyze the process of medication use in patients with an FT, it is striking to observe that in current practice, the nurse administrating the medication is often the only layer of security to prevent an FTRME, meaning that errors are symptoms of a flawed system. Welie et al and Idzinga et al focused on improving this security layer,[15,16] but this still preserves a single point of failure. van den Bemt et al added 2 additional layers of security; however, it was at the expense of an increase in staffing, which could provide difficulties in scaling up.[2] Additionally, independently of the chosen approach, nurses and physicians were still responsible for choosing an appropriate alternative while frequently unaware that altering formulation may require a dose adjustment, a change in frequency of administration, or therapeutic drug monitoring.

A new security layer was developed, designed to be scalable and without the need for additional staffing. This extra layer was designated the "clinical decision support system (CDSS)–assisted pharmacy check." The pharmacy check consisted of a pharmacy technician autonomously switching medication to a liquid formulation, changing the route of administration, or outlining the correct administration method in the electronic administration instruction based on a tailored CDSS alert, making it suitable for oral as well as enteral administration. Added to this new component were components already known to be effective, including implementation of standard operating procedures and training of staff. The aim of the study was to evaluate the effect of the CDSS-assisted pharmacy intervention on the incidence of potential FTRMEs in hospitalized patients.

Methods

Setting, Study Population, and Design

This pre-post intervention study was performed on 3 wards of the Catharina Hospital Eindhoven, a 700-bed teaching hospital in the Netherlands. The 3 wards were bowel and liver disease with 32 beds, oncology with 28 beds, and neurology with 31 beds. The hospital used CS-EZIS (version 5.2, Chipsoft BV, Amsterdam, the Netherlands) as its electronic health record (EHR) system. All relevant medical data were ordered and stored in this system, including medication and usage of FT. To provide medication-related clinical decision support, including decision support during the study, the hospital used a separate CDSS, Gaston Pharma (version 2.8.2.100, Gaston Medical, Eindhoven, the Netherlands). To provide pharmaceutical services for these 3 wards, 3 pharmaceutical technicians were available on workdays. Pharmaceutical services included medication review, medication distribution, and medication preparation. There was also 1 pharmacist on duty dividing their attention among all wards.

Preintervention inclusion started October 2014 and lasted until December 2014. This was followed by a 3-month period of the implementation of the CDSS-assisted pharmacy intervention. The intervention focused on improving the medication process for patients with FT and consisted of implementing standard operating procedures, training of personnel, and the CDSS-assisted pharmacy check. The intervention is described in more detail in the section on implementing the intervention. Inclusion for the intervention phase started March 2015 and ended May 2015. All patients on the respective wards who had an FT for >24 hours and were prescribed oral medication were included. Patients could be included in only 1 of the phases. Rehospitalizations of patients during the same phase were cumulated and calculated as a single inclusion. Information on enteral FT status was based on the paper ward lists collected from the respective wards; FT status from the EHR was also collected but was found to be incomplete. The ward list stated basic

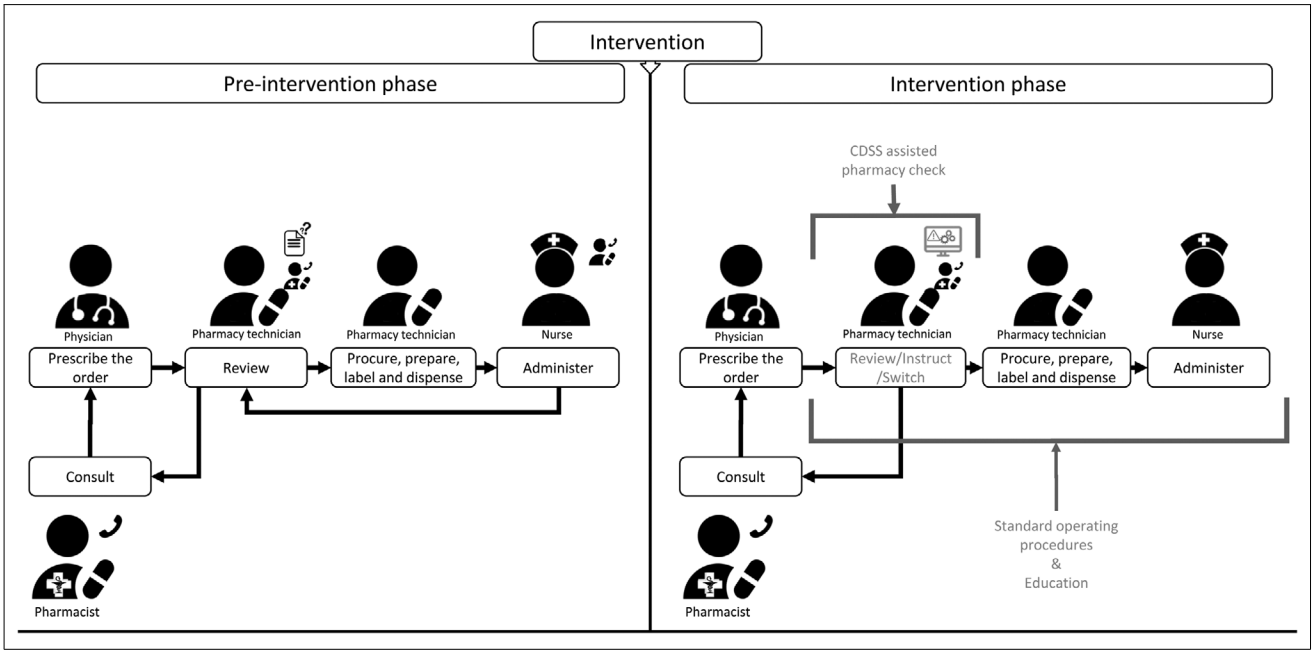

Figure 1. Graphical representation of the daytime medication process in the preintervention and intervention phases. The 4 steps correspond to the enteral nutrition use process as presented by Boullata et al and the medication use process.[18] On the right side, in gray, are the components of the intervention. The icon of a document represents a manual check of medication using local protocol. The icon of a monitor with an alert icon and turning gears represents the clinical decision support system (CDSS) with specific alerts. The telephone icon represents a telephonic consultation.

patient information such as name, patient number, reason of admission, comorbidities important for nursing, frequency of checking vital signs, mobility of the patient, enteral FT type and amount of feeding, do-not-resuscitate (DNR) order, and particularities of the medication. Figure S1 shows an example of such a ward list. The total of registered enteral FT days was equal to the sum of days that the enteral FT was mentioned on that ward list. General patient characteristics, tube characteristics, medication orders, and medication administrations were extracted from the EHR. When medication was listed as "when necessary" or 'p.r.n.' (as needed) in the EHR and was not "checked" as being administered or "checked" to be unnecessary by a nurse, it was counted as a medication administration. The study was approved by the local medical ethics committee.

Preintervention Phase

During the preintervention phase, care was provided as usual. The medication process for patients with an FT during this phase is graphically represented in Figure 1 on the left side. During the day, the nurse informed the pharmacy technician if an FT was placed. When informed, the pharmacy technician manually checked each medication order, using a local protocol, comparing the medication with a list of crushable medication. When the medication was not on the list of crushable medication, the pharmacy technician contacted the pharmacist. Subsequently, the pharmacist contacted the physician to discuss alternatives. The physician was eventually responsible for changing the medication order. After hours, the nurses themselves were responsible for manually checking each medication order, using the list of crushable medication, before administering medication. If the medication was not on the list, the nurse could consult the pharmacist.

Implementation of the Intervention

The intervention comprised implementing standard operating procedures on medication administration through an FT, training of pharmacy technicians and nurses on the subject, and implementing a CDSS-assisted pharmacy check. The standard operating procedures and training were based on American Society for Parenteral and Enteral Nutrition (ASPEN) recommendations and results from previous studies.[2,15,16,18] The input and recommendations for the CDSS were based on local guidelines and the Dutch Oralia VTGM database.[19] The recommendation on medication formulation was, if relevant to the recommendation, tailored to type, material, and position of distal tip of the enteral FT. Additionally, an expert team evaluated the medication orders of the included patients in the preintervention phase to identify common FTRMEs and formulate specific recommendations. These were used to improve the CDSS

content and alerts. Details on the expert team are provided in the section on FTRMEs.

Intervention Phase

The process during the intervention phase is graphically represented at the right side of Figure 1. The CDSS-assisted pharmacy check consisted of the CDSS generating tailored alerts for each patient and the pharmacy technician evaluating these alerts and acting accordingly. The CDSS generated alerts if 1 of the 2 following conditions were met: (1) an enteral FT was electronically ordered in the previous 24 hours and noncrushable medication was used or the medication used was not part of the CDSS database; (2) inappropriate medication was ordered in the previous 24 hours for a patient with an enteral FT. The CDSS alert text started with information on type, position of distal tip and date and time of placement of the FT. This was followed by a table with tailored recommendations for the most-encountered incorrectly prescribed medication. Moreover, the alert consisted of a list of medications with no specific recommendation, so the pharmacy technician had to check these medication orders manually making use of the Oralia VTGM database. (18) An example of a CDSS alert is shown in Figure S2. Alerts were generated once daily between 6:00 and 6:30 AM. Between 9:00 AM and 1:00 PM of the same day, the alerts were evaluated by the pharmacy technicians. The pharmacy technicians autonomously adjusted medication orders according to the alerts generated by the CDSS. All adjustments were double-checked by another pharmacy technician and later by a pharmacist. If the medication order other than formulation and/or frequency of administration needed to be adjusted, the pharmacy technician contacted the pharmacist. The pharmacist called the physician and advised on alternatives and/or necessary therapeutic drug monitoring.

Primary Outcome Measure

The primary outcome measure of the study was the number of FTRMEs per medication administration.

Feeding Tube–Related Medication Errors

An FTRME was defined as the administration of unsuitable medication through an FT (unsuitable being all medication formulations, according to Dutch Oralia VTGM database, that cannot be safely administered through an FT with or without modification of medication formulation, taking into account FT diameter, FT material, and position of distal tip). Medication prescribed orally and given enterally was not considered an FTRME, because the CPOE does not provide a possibility to choose an enteral administration route. The FTRMEs were categorized in 3 groups: errors leading to increased toxicity or decreased effectivity, errors leading to increased risk to medical personnel, or errors leading to increased risk of tube obstruction. Medication with an enteric-coated formulation, a modified-release formulation, or a liquid-filled hard-capsule formulation was categorized as an error leading to increased toxicity or decreased effectivity. Hazardous medication that led to increased risk for medical personnel was subcategorized into 1 of 4 categories: immunosuppressing, cytotoxic, sensitizing, and a residual category for otherwise harmful medicine. Medication described or known to increase risk of FT obstruction and not falling in the previous categories was classified as errors leading to increased risk of tube obstruction.

In addition to groups based on risk, FTRMEs were also classified as being easily preventable or hard to prevent. Easily preventable errors were FTRMEs that had one of the following alternatives: liquid or dispersible formulation suitable for enteral administration, normal-release formulations without coating that were known to be suitable for enteral administration, alternate route of administration (rectal or transdermal), or an available therapeutic alternative. Medication lists for all included patients were evaluated by an expert team to determine the presence and category of an FTRME based on the aforementioned criteria; no observations of medication preparation or enteral administration were performed as part of the study. The expert team consisted of 2 senior hospital pharmacists, a nurse specializing in enteral tube feeding, and a dietitian specializing in enteral nutrition. Evaluation of the medication lists was done independently by each expert. Differences in evaluation were discussed in a plenary meeting in which consensus was required to mark an administration as an FTRME.

Data Analysis

Patient characteristics were compared using the χ^2 test for differences in proportions, a t-test for differences in means, and a Mann-Whitney U test to compare medians. The incidence was calculated as the number of FTRMEs per medication administration. A multivariate Poisson regression was used to compare the incidence ratios (IRs) of the FTRMEs between both phases. Poisson distribution assumes that the number of events has a fixed time interval and that the events occur at random, independently in time, and at a constant rate. Because these assumptions were not necessarily true for this study, the number of administrations, the number of days at risk, FT days, and the number of unique drugs were tested as covariates to compensate for possible distortions in Poisson distribution. Forward selection was used to include variables in the multivariate model. If a covariate had $P < .05$ in the forward selection and final model, it was included in the multivariate

Table 1. Comparison of Patient Characteristics Before and After Intervention.

Variable	Preintervention n = 38	Intervention n = 43	*P*-value
Mean age in years (SD)	68.7 (13.8)	66.4 (15.0)	0.47[b]
Median hospitalization in days (IQR)	15 (12)	12 (18)	0.87[c]
Gender (%)			
Male	26 (68.4)	26 (60.5)	0.56[a]
Female	12 (31.6)	17 (39.6)	
Ward (%)			
Bowel and liver disease	11 (28.9)	14 (32.6)	0.81[a]
Oncology	15 (39.5)	14 (32.6)	
Neurology	12 (31.6)	15 (34.9)	
Medication			
Mean number of unique oral medication used (SD)	11.1 (5.7)	10.6 (5.9)	0.70[b]
Median number of oral medication administrations per patient (IQR)[d]	36.5 (56)	31 (74)	0.63[c]
Enteral feeding tube			
Median number of enteral feeding tube days (IQR)	4 (5)	4 (6)	0.71[c]
Type of enteral feeding tube, n[e] (%)			
Nasogastric	8 (21.1)	6 (14.0)	0.26[a]
Nasoduodenal	5 (13.2)	2 (4.7)	
PEG gastric/duodenal	2 (5.3)	4 (9.3)	
PEG-J	3 (7.9)	5 (11.6)	
Triple lumen[f]	0 (0.0)	4 (9.3)	
Unspecified	20 (52.6)	22 (51.2)	

Patient characteristics are shown for unique patients, hospitalized to the ward of bowel and liver diseases, oncology, or neurology in the period October 27, 2014, to May 15, 2015, with a least 1 day of enteral tube feeding as registered by the nursing staff on the ward list.
IQR, interquartile range; M, median; PEG-J, percutaneous endoscopic gastrostomy-jejunostomy.
[a] χ^2 Test.
[b] Unpaired 2-sample *t*-test.
[c] Mann-Whitney *U* test
[d] Median number of oral medication administrations per patient included after-hours administrations.
[e] As stated on ward list.
[f] Three-lumen dual-purpose air-vented assisted gastric aspiration and post–ligament of Treitz enteral feeding tube.[20]

analysis. Statistical analyses were performed using SPSS (IBM SPSS statistics version 25).

Results

Eighty-one patients were included into the study, 38 during preintervention and 43 in the intervention phase. Overall, of the included patients, 25 were admitted to the bowel and liver disease ward, 29 to the oncology ward, and 27 to the neurology ward. Table 1 shows the patient characteristics. There were no significant differences in any of the patient characteristics between the 2 phases. Patients included in the study had a mean age of 67.5 years. They were hospitalized for a median of 13 days (interquartile range [IQR] 15 days) and used a mean of 10.8 unique medications (SD 5.8) with a median of 36.5 oral medication administrations (IQR 70). It is worth mentioning that the ward list did not specify where the enteral FT ended in the gastrointestinal tract in >50% of the patients.

In the preintervention phase, there were 274 FTRMEs in 209 person-days with 2232 administrations; IR was 0.153 FTMREs per administration (95% CI, 0.07–0.23). In the intervention phase, there were 39 FTRMEs in 233 person-days with 2273 administrations, IR 0.02 FTMRE per administration (95% CI, 0.00–0.04). Univariate comparison of both IRs shows a significant difference in the number of FTRMEs. At least 1 FTRME occurred in 66% of the included patients preintervention compared with 12% in the intervention phase. Of the 39 FTRMEs in the intervention phase, 37 were due to human error by the pharmacy technician overlooking a part of the CDSS recommendation. The remaining 2 FTRMEs were due a technical error in which the CDSS did not generate a new alert when a patient with an enteral FT in situ was transferred from a ward not participating in the study to one of the study wards.

Table 2 shows the results from the multivariate Poisson regression comparing the IRs. There was a clear and significant reduction comparing the 2 phases, the IR being

Table 2. Multivariate Poisson Regression Comparing Feeding Tube–Related Medication Errors in the Intervention Phase With Preintervention.

Variable	IR[a] EXP(B)	95% CI(lower–upper)	*P*-value
Number of feeding tube–related medication errors	0.143	(0.102–0.200)	<0.001
Covariates			
Number of administrations	1.006	(1.005–1.008)	<0.001
Number of unique medications used	1.076	(1.051–1.101)	<0.001
Ward	1.865	(1.583–2.198)	<0.001

Multivariate Poisson regression is shown comparing feeding tube–related medication errors in the intervention phase with those in the preintervention, which is the reference population. The bottom part shows all included covariates, as well as their part in the calculated IR. Covariates were included into the analysis having a $P < .05$ when separately tested and $P < .05$ when tested in a single model.
EXP, expected count; IR, incidence ratio.
[a]Preintervention being the reference population.

Table 3. Type of FTRMEs.

Distribution in categories of FTRMEs	Preintervention (patients = 38)		Postintervention (patients = 43)	
	n	%	n	%
Total FTRMEs	274	(100)	39	(100)
Errors leading to increased toxicity or decreased effectivity	**191**	**(70)**	**35**	**(90)**
Enteric-coated formulation	88	(32)	8	(21)
Modified-release formulation	83[c]	(31)[c]	27[b]	(69)[b]
Liquid-filled hard-capsule formulation[a]	**20**	(7)	0	(0)
Errors leading to increased risk for medical personnel	**49**	**(18)**	**0**	**(0)**
Oral chemotherapy	12	(4)	0	(0)
Immunosuppressants	0	(0)	0[b]	(0)[b]
Sensitizing medication	35	(13)	0	(0)
Other	2[c]	(1)[c]	0	(0)
Errors leading to increased risk of tube obstruction	**34**	**(12)**	**4**	**(10)**

The table shows the different categories of FTRMEs for both phases. Major categories are shown as rows with bold font, together adding up to 100%. All other rows are subcategories, together constituting the major categories.
FTRME, feeding tube–related medication error.
[a]Liquid-filled hard-capsule formulation not suitable for administration through an enteral feeding tube, not falling apart in water, and having considerable loss when sucked up with a needle.
[b]There were 6 administrations of immunosuppressant, modified-release tacrolimus, which were included into the category of errors leading to increase toxicity or decreased effectivity and subcategory modified release instead of errors leading to increased risk for medical personnel and subcategory immunosuppressants.
[c]There was 1 administration of dutasteride/tamsulosin modified release that was included into the category of errors leading to increase toxicity or decreased effectivity and subcategory modified release instead of errors leading to increased risk for medical personnel and subcategory other.

0.128 (0.092–0.179), using preintervention phase as reference group, $P < 0.001$. The 3 covariates identified to contribute to the model are also shown in Table 2. It is interesting to observe that the number of administrations and number of unique medications used were independently associated with the risk of an FTRME. Univariate Poisson analysis and single covariates are shown in Table S1.

Table 3 shows the distribution of the different types of FTRMEs. Most errors (70% preintervention and 90% during the intervention phase) were those that led directly to increased toxicity or decreased effectivity. Within this group, the most common types of errors were crushing medication with an enteric coating (32% preintervention and 8% during intervention phase) and crushing medication with a modified-release formulation (31% preintervention and 69% during the intervention phase). Errors leading to increased risk to medical personnel were the cause of 18% of preintervention FTRMEs and were nonexistent during the intervention phase.

During the preintervention phase, 91% of the of the FTRMEs were easily preventable; during the intervention phase, it was 90%. Forty-two percent (42%) of the FTRMEs

were preventable because of the availability of a liquid or dispersible alternative; during the intervention phase, this was 76%. In 32% of the cases preintervention, choosing a therapeutic alternative, such as switching pantoprazol to esomeprazole, would have prevented an FTRME; during intervention, this was 20%. Another 14% were preventable by switching modified-release preparations to regular tablets given more frequently. In 3% of the cases, a transdermal alternative was available.

Discussion

Principal Findings

This study demonstrated that a CDSS-assisted pharmacy intervention resulted in an 87.2% reduction of FTRMEs in hospitalized patients. This FTRME reduction was achieved without additional staffing and is thought to be sustainable because of the additional layer of security provided by active alerting using an automated system. The preintervention incidence in the study was 1.34 FTMREs/person-day, showing that nurses are insufficiently aware that much medication may not be crushed, and in over 90% of the cases, alternatives were readily available. Seventy percent of the errors had the potential to directly harm the patient because of increased toxicity (for example, crushing of short-acting β-blockers, short-acting calcium antagonists, nitrates, opioids, and anti-epileptics) or loss of effectivity.

Implications

The results from this study combined with previous research indicates the necessity for each hospital to have a program to reduce the number of FTRMEs. Computerized support could provide an answer for staffing issues as well as relieve pressure on nurses to find correct ways of administering medicine through an enteral FT.

Comparison to Other Studies

The baseline IR of 0.15 FTRMEs per medication administration is comparable to previous studies (0.26 in hospitalized patients and 0.04 in nursing home patients).[2,16] The 87.2% reduction of FTRMEs is also in line with previous studies reporting estimated RRRs of 48%,[15] 85%,[16] and 93%.[2] Although a comparable IR and reduction were found, it is important to consider that these results were purely based on a reduction of unsuitable medication choice and did not take into account administration errors such as not flushing the enteral FT before and after administration, thus making it likely that there was an underestimation of true FTRME incidence in this study. van den Bemt et al added 2 additional layers of security; however, it was at the expense of an increase in staffing, which could provide difficulties in scaling up.[2]

Limitations

One of the limitations of the study is the chosen design. A randomized clinical trial design or a time series analysis would have ruled out bias due to different patient characteristics and time trends. However, no differences were identified in respect to patient characteristics, making selection bias unlikely. Moreover, the preintervention and intervention periods were in short succession, making a time trend also unlikely. Additionally, the measured effect was very substantial and in line with the effect measured in previous studies.[2,3,15,16] In over half the patients, FT entry point, position of distal tip, and diameter of the FT were not recorded on the ward list or in the EHR. Although this made FTRME estimation more difficult, if an administration was judged to be an FTRME then the chosen medication formulation was unsuitable for types and endings of FT. In contradiction to ASPEN recommendations, all medication was prescribed orally, and during prescribing, the physician was not alerted that medication might be administered through an FT. Another limitation of the study was that it was performed in a single center with a specific CDSS, which may restrict the generalizability of the results. Current intervention also did not change the enteral use process starting after hours.

Current Practice and Future Considerations

Despite the sizable reduction in FTRMEs, 37 errors were made during the intervention phase. All of these were attributable to human error, such as a pharmacy technician overlooking a suggested substitution and the nurse not being alerted when crushing a modified-release or enteric-coated formulation. To overcome these errors, a second evaluation of all alerts by a second pharmacy technician has become part of the standard operating procedures. Since the study's end, the CDSS-assisted pharmacy intervention has become part of routine care for all wards, 7 days a week. To aid nurses after hours, a nurse- and mobile-friendly version of the Dutch Oralia VTGM database has been made available. During the study, in over half the patients, FT registration in the EHR and on the ward list lacked important aspects of the FT. Knowing all aspects of the FT, however, is crucial to safely choose, prepare, and administer medication enterally. Moreover, it is also vital to generate the correct CDSS recommendations. Therefore, additional attention should be given during training to record all FT aspects correctly. Analysis of alerts and comments revealed that further improvements to the FT clinical rule were possible, such as extending the number of specific recommendations, which would reduce the time needed to handle the alerts.

Conclusion

The incidence of FTRMEs can be substantially reduced by a CDSS-assisted pharmacy intervention, consisting of implementation of standard operating procedures, training of personnel, and a CDSS-assisted pharmacy check.

Statement of Authorship

A. T. M. Wasylewicz, J. M. W. Bikker, M. H. M. Kerskes, and R. J. E. Grouls contributed to the conception/design of the research; R. J. B. van Grinsven, J. M. W. Bikker, and A. T. M. Wasylewicz contributed to acquisition of the data, A. T. M. Wasylewicz, R. J. B. van Grinsven, T. C. G. Egberts, and R. J. E. Grouls contributed to the analysis or interpretation of the data; A. T. M. Wasylewicz and R. J. B. van Grinsven drafted the manuscript; M. H. M. Kerskes, R. J. E. Grouls, E. M. Korsten, and T. C. G. Egberts critically revised the manuscript; and A. T. M. Wasylewicz, R. J. B. van Grinsven, J. M. W. Bikker, M. H. M. Kerskes, R. J. E. Grouls, E. M. Korsten, and T. C. G. Egberts agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors have read and approved the final manuscript.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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