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Drug-Food Interactions in Hospitalised Patients

Methods of Prevention

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Summary

Drug-food interactions in hospitalised patients may result in decreased drug efficacy or increased drug toxicity. The increasing complexity of drug therapy regimens has increased the potential for drug-food interactions to occur, reinforcing the need to develop methods to prevent clinically significant drug-food interactions.

Before selecting the optimal method, in terms of feasibility of implementation and successful outcome, drugs with the potential for clinically significant interactions with food must be identified. From an analysis of the literature, 6 methods to prevent drug-food interactions have been suggested as useful tools. Each method has its own advantages and disadvantages. Most have been developed in response to guidelines from the most well recognised agency for quality review in the US, the Joint Commission on Accreditation of Healthcare Organisations (JCAHO). Based on those recommendations, an ideal programme to prevent drug-food interactions would be a combined patient counselling and label system to select the most appropriate drug administration times and increase nurse and patient awareness of the potential for drug-food interactions. However, because of time constraints and limited resources, a label system or the provision of a drug-food interaction pamphlet to the patient before discharge would be a more practical method. Newsletters and educational inservices combined with patient counselling or a label system would be a valuable method to prevent drug-food interactions in hospitalised patients.

1. Drug-Food Interactions: Scope of the Problem

Drug-food interactions may occur by different mechanisms and result in a decrease in drug efficacy or an increase in drug toxicity in hospitalised patients. As a consequence, patient care may be adversely affected and hospital stay prolonged. Healthcare providers should develop methods for identifying and preventing clinically significant drug-food interactions.

Despite the publication of several informative reviews on drug-food interactions,[1-4] the actual incidence and clinical significance of such interactions are still being investigated. Most importantly, very limited data exist on practical and efficient methods to prevent drug-food interactions in different clinical settings. Most methods published so

far have been applied in programmes implemented in response to guidelines from the most well recognised agency for quality review in the US healthcare systems, the Joint Commission on Accreditation of Health Care Organisations (JCAHO), which authorises pharmacists and dieticians to monitor drug-food interactions in hospitalised patients.[5]

The purpose of this article is to review and assess the published methods to prevent drug-food interactions and make recommendations based on this evaluation.

2. Types and Clinical Significance of Drug-Food Interactions

As described in the literature, drug-food interactions may be mediated by pharmacokinetic or pharmacodynamic mechanisms.[6]

2.1 Pharmacokinetic Interactions

An alteration in the extent of drug absorption represents the most common type of pharmacokinetic interaction.[7] For instance, taking lovastatin without a meal[8] may result in a significant decrease in bioavailability and efficacy. Similar results can occur when taking azithromycin with food[9] or ciprofloxacin with dairy products.[10] An increase or decrease in the hepatic clearance of theophylline secondary to low carbohydrate-high protein or high carbohydrate-low protein diets, respectively, can occur and usually requires close monitoring of serum drug concentrations.[11]

Changes in the *extent* of drug absorption due to interactions with food can be clinically significant for a number of drugs, especially for those with narrow therapeutic ranges such as cyclosporin, phenytoin and slow-release theophylline preparations. On the other hand, changes in the *rate* of absorption are rarely clinically significant, provided that a rapid onset of drug action is not required.

2.2 Pharmacodynamic Interactions

Drug-food interactions may occur by pharmacodynamic mechanisms, resulting in an excessive potentiation or antagonism of the desired pharmacological effect of a given drug. For example, the concomitant intake of dietary salt substitutes with potassium-sparing diuretics or ACE inhibitors can potentiate the increase in serum potassium level caused by these drugs, resulting in hyperkalaemia. By directly affecting the activation of clotting factors, diets with a high content of vitamin K may counteract the anticoagulant effect of warfarin, thereby resulting in undesired thromboembolic events.[12,13] Another important pharmacodynamic drug-food interaction is that between tyramine-rich foods and monoamine oxidase inhibitors, which can result in a hypertensive crisis.[14]

Many other drug-food interactions have been described elsewhere in the literature.[1-4] Table I summarises drug-food interactions reported as clinically significant and that should be potential targets of any programme aimed at preventing drug-food interactions in hospitalised patients.

3. Methods to Prevent Drug-Food Interactions

After having identified the significant drug-food interactions that can occur in an institution, by in-house surveys or drug utilisation evaluations, the next step is to select the optimal method to prevent such interactions in the most feasible and efficient manner. Six methods to prevent drug-food interactions have been suggested.[33-41] These are listed in table II, with their respective advantages and disadvantages.

3.1 Standard Drug Administration Schedules

Lewis et al.[33] assessed the risk of drug-food interactions in 3 long term-care facilities. The final goal of their study was to identify strategies for the intervention and prevention of these interactions. Establishing standard drug administration schedules was considered an option, as it should ensure that medications are administered appropriately relative to mealtime and would thereby decrease the incidence of gastrointestinal interactions. However, because some drugs are optimally administered with food and others are best given on an

Table I. Mechanisms and recommendations for the prevention of clinically significant drug-food interactions in hospitalised patients

Drug	Food type	Effect on drug action/disposition	Recommendation	Reference
ACE inhibitors	Salt substitutes (potassium-containing)	Potentiation of the ↑ of serum potassium level	Avoid use of salt substitute	3
Atovaquone	High-fat meals	↑Plasma concentrations	Give with meal containing fat	3,4,15
Azithromycin (not tablet)	Regular meal or snack	↓Bioavailability (40%) and peak concentration (50%)	Give 1h before or 2h after a meal or snack	3,4,9
Captopril	Regular meal or snack	Possible ↓ absorption	Give 1h before or 2h after a meal or snack	3,4,16,17
Ciprofloxacin	Dairy products or enteral feedings	↓Absorption	Do not give within 2h of dairy products or enteral feedings	3,4,10
Cyclosporin	Grapefruit juice, milk, regular meal	↑Absorption	Give with a regular meal or at the same time in relation to meals and with the same drink	4,18
Didanosine	Regular meal or snack	↓Absorption	Give 1h before or 2h after a meal or snack	3,19
Digoxin	Bran fibre	↓Absorption	Give 0.5-1h before or 4h after bran fibre	3,20
Erythromycin stearate	Regular meal or snack	↓Absorption	Give 1h before or 2h after a meal or snack	3,4
Fluoroquinolones	Iron, magnesium, zinc and calcium supplements	↓Absorption of fluoroquinolones due to complexation with divalent cations	Do not give within 2h of supplements	4,21
Isoniazid	Regular meal or snack	Delayed or ↓ absorption	Give 1h before or 2h after a meal or snack	4,22
Levodopa	High-protein diet	Competition from amino acids for absorption and transport into the CNS	Avoid high-protein diet, if appropriate, and monitor; give 0.5h before or 1-2h after meals	3,23,24
Lovastatin	Regular meal	↑Absorption	Give with regular meal, but avoid large amount of pectin	4,8,25
MAOIs	Food rich in tyramine	Hypertensive crisis	Avoid foods rich in tyramine	3,4,14
Misoprostol	Regular meal or snack	↓Incidence of gastrointestinal adverse effects due to a ↓ in peak serum concentrations	Give with a meal or snack	4,26
Nifedipine	Regular meal or snack	↓Incidence of adverse effects due to a ↓ in peak serum concentrations	Give with a meal or snack	4
	Grapefruit juice (concentrated)	Significant ↑ in serum concentrations, possibly due to inhibition of nifedipine metabolism	Give with an alternative fluid or use other calcium antagonists, such as amiodipine	27
NSAIDs	Regular meal or snack, milk	↓Incidence of gastrointestinal effects	Give with a meal, snack or milk	4,28
Penicillins	Regular meal or snack	↓Absorption	Give 1h before or 2h after a meal or snack	3,4
Phenytoin	Enteral feedings	↓Absorption	Withhold the enteral feed 2h before and after administration	3,29,30
Potassium-sparing diuretics	Salt substitute	Potentiation of the ↑ in serum potassium level	Avoid salt substitute	3
Rifampicin (rifampin)	Regular meal or snack	↓Absorption with <150mg, unaffected at >700mg	Give 1h before or 2h after a meal or snack	3
Sucralfate	Regular meal or snack	↓Effect due to binding to protein components of food	Give 1h before or 2h after a meal or snack	4
Tetracyclines (except doxycycline and minocycline)	Regular meal, dairy products, iron	↓Absorption due to chelation	Do not give within 2h of a meal, dairy products or iron	3,4,31
Theophylline (regular)	High carbohydrate, low protein diet	↓Hepatic clearance	Monitor serum concentrations	3,4,11
Theophylline (sustained release)	Regular meal	Interference with the design of formulation, resulting in sudden elevation of serum concentrations	Avoid taking with meal and monitor serum concentrations	32
Warfarin	Food high in vitamin K	Antagonism of the effect of warfarin	Maintain diet balanced in vitamin K content	3,4,12,13
	Enteral feedings	↓Absorption	Do not give within 3h of enteral feedings	
Zidovudine	Regular meal or snack	↓Absorption	Give 1h before or 2h after a meal or a snack	4

Abbreviations and symbols: MAOIs = monoamine oxidase inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs; ↑ = increased; ↓ = decreased.

Table II. Advantages and disadvantages of suggested methods to prevent drug-food interactions in hospitalised patients

Advantages	Disadvantages	Reference
Standard drug administration schedules		
Automatic process not requiring knowledge from nurses The least time consuming	Drug administration mistiming not always avoided No impact on nurses' and patients' awareness	33
Hospital newsletters		
Impact on health care professionals' awareness Not labour intensive Reinforces other methods	Not read by everybody Information may be forgotten at the time of drug administration No impact on patients' awareness	34-35
Educational inservices		
Impact on health care professionals awareness Reinforces other methods	Low attendance, could be improved by targeting appropriate audience Often labour intensive for a modest benefit Indirect impact on patients' awareness: depends on impact on health care professionals' awareness and subsequent patient education	34-35
Label systems		
Impact on nurses' awareness, especially at times of administering the drug to the patient Inexpensive and not labour intensive for the gained benefit	No impact on patients' awareness Annoying for nurses who do not pay attention to the labels any more	35-36
Computerised drug-food interaction screening and warning systems		
If it is capable of printing the directions to prevent drug-food interactions onto labels dispensed with patient medications and/or on nursing medication administration records, will have all advantages of any label system and is less labour intensive than a noncomputerised label system	Expensive If not capable of printing the directions to prevent drug-food interactions on medication labels or nurses' medication administration records, has the same disadvantages as establishing a standard drug administration schedule (i.e. the information is not available at the time of drug administration)	37
Patient counselling		
Written information and verbal information		
Impact on patients' awareness	Labour intensive Possible under-appreciation of counselling by patients	36, 38-41
Written information only		
Not labour intensive	Not necessarily received, read or well understood by patients. It is therefore best used in combination with patient counselling for reinforcement	36, 38-41

empty stomach, this option does not necessarily achieve an optimal timing of drug administration for all drugs at all administration times. Furthermore, a standard drug administration schedule does not always coincide with a mealtime schedule, which may vary daily from one hospital floor to another. Setting standard administration times per drug might represent a more accurate method, but from a nursing perspective, may become complicated and labour intensive. Establishing standard drug administration times without providing nursing education may compromise patient care.

3.2 Hospital Newsletters

The use of newsletters distributed to the hospital staff was investigated by Franse et al.[34] in a Veterans Administration Medical Center and by Garabedian-Ruffalo et al.[35] as part of a more comprehensive drug-drug and drug-food interactions prevention programme in a large teaching hospital (see section 3.3).

When used as a single method of prevention, a newsletter was associated in an incidence of clinically significant drug-food interactions of 0.4%.[34] Since the authors did not evaluate the baseline in-

cidence of interactions before sending their newsletters, it remains impossible to attribute the low incidence of drug-food interactions to any impact of their programme. Nevertheless, these authors reported that this method proved to be a valuable option for preventing drug-food interactions when adopted by clinical pharmacy services in 2 different hospitals.

Since newsletters should be designed as quick references for the busy healthcare professional, a list of the most common drug-food interactions in a given institution should be displayed concisely, with a description of the interaction and the corresponding recommendations for its prevention. This method requires the effort of writing and sending the newsletter at a specific point in time, but does not involve any extra workload for the pharmacy department on a daily basis. However, in order to be successful as a sole method, all nurses and physicians would have to read the newsletter, retain the information included and, most importantly, use this knowledge at the time of prescribing or administering the drug to the patient. Unfortunately, this is unlikely to happen. However, when used in combination with other methods, a newsletter represents a valuable and easy educational tool to reinforce the need to prevent drug-food interactions in hospitalised patients.

3.3 Educational Inservices

As mentioned in section 3.2, Garabedian-Ruffalo et al.[35] implemented a very comprehensive programme including a drug-interaction alert label system reinforced by educational inservices, i.e. educational programmes implemented within a hospital, and departmental newsletters. Educational inservices on drug-drug and drug-food interactions were given by the clinical pharmacists to all staff pharmacists 1 week prior to the programme implementation.

Educational inservices should be provided periodically to nurses and pharmacists of all work shifts. While it is recognised that they require more time and effort than newsletters, inservices offer an opportunity for providing knowledge and answering questions through direct communication between the lecturer and the audience. However, inservices are often poorly attended and are more likely to provide successful outcomes when they are used in combination with other methods and the target audience is appropriately selected.

3.4 Label Systems

This system may be designed and operated by the pharmacy and nursing departments. Garabedian-Ruffalo et al.[35] developed a system consisting of drug interaction alert cards for each of the drug-drug or drug-food interactions that were considered clinically significant among the most widely used drugs in their institution. Each card was addressed to either the physician or nurse, described the nature and mechanism of the interaction, and provided a recommendation on how to monitor and prevent the interaction. A poster of all interactions included in the programme was posted in each satellite pharmacy, to serve as a quick reference for the pharmacists who screened for potential interactions daily as they verified the content of the patient medication drawer. If they thought that there was the potential for an interaction to occur, they completed a drug interaction card, which they placed in the medication cassette drawer or on the front of the patient's chart to capture nurses or physicians' attention, as appropriate. They also recorded and documented each drug interaction alert card sent in a special binder.

Six months after implementation, the authors measured the impact of their programme through a quality assurance chart review. This indicated that 95 of the 279 (34%) cards provided to nurses and 40 of the 49 (82%) cards provided to physicians resulted in a change in drug administration time or prescription. The authors considered their programme successful in terms of a positive response from pharmacists, nurses and physicians who adopted the programme and participated in its further development and the biannual review for its continuous improvement. The nursing and medical staff felt that the programme increased their awareness of potential drug-drug and drug-food in-

teractions and appreciated the fact that the information received from the pharmacy was consistent, relevant and complete.

Such a label system, reinforced by newsletters and education programmes, increases the likelihood of achieving a successful outcome, but requires significant commitment from the clinical and staff pharmacists. Although newsletters and education programmes may not be considered a permanent extra pharmacy workload, as they are used only to introduce the programme to the hospital personnel, they could become significantly time-consuming when reused biannually to update the ongoing system. Also, placing the drug interaction alert card in the medication cassette drawer without the need for card completion and process documentation would become simpler and faster.

Our group[36] experimented with a label system, in which directions about the optimal time to administer a given drug were written on a highly coloured label placed in the patient's medication drawer. As a reminder, another label listing medications to monitor for drug-food interactions was permanently placed on the cover of the nursing medication card flip-chart. This method differs from that of Garabedian-Ruffalo et al.[35], in that their labels were placed in patient medication drawers at the initiation of treatment and left in place every time the drug was dispensed to the patient for the whole treatment period. From the pharmacy viewpoint, this method was simpler than completing a card once and documenting the process in a special binder. From the nursing viewpoint, the constant presence of the label at the time of administering the drug was considered an excellent reminder of potential drug-food interactions.

As reported by others,[35] our label system was well accepted and considered helpful by nurses. Interestingly, we obtained this successful outcome without the reinforcement of newsletters and in-service education programmes.

Following our positive experience with the pilot project, our label system was expanded to include more drugs and additional hospital floors. Based on the recommendations of pharmacists and nurses, we adjusted our method: for each hospital floor, the pharmacy provided nurses with a list of drugs requiring optimal timing of administration and the corresponding labels designed to fit in the patient medication administration records. Nurses became more involved by placing the list of drugs to monitor on the front of the nursing medication card flip-chart and the labels right next to the appropriate medications on the patient medication administration records.

Periodic quality assurance reviews of medication administration records would help to assess the appropriateness of utilisation and the impact of such a label system. Overall, the label system appears to be an efficient method to prevent drug-food interactions in terms of feasibility, positive healthcare professional acceptance and response, thus improving patient care. However, this method may lack optimal impact on patients' outcome if patients are never directly informed about the potential of drug-food interactions before discharge.

3.5 Computerised Drug Interaction Screening and Warning Systems

Poirier and Gludici[37] evaluated 8 computer software programs for the detection of drug-food interactions according to determined criteria including: (i) the scope of drug-food interaction coverage or ability to screen for drug-food interactions; (ii) the quality of clinical documentation in terms of reference to primary literature; and (iii) quality performance based on the accuracy and relevance of the drug-food interaction and the frequency of updates. Three programs were considered to provide reasonable information with supportive reference citations. The authors concluded that the design of an excellent program is still limited by the lack of a core evaluative reference source to validate the information, such as a drug-food interactions compendium developed and published by a group of experts.

Computer systems are incomplete and usually minimally helpful if the information provided is not connected to the current drug delivery system, especially if the recommendations about the opti-

mal administration time of a given drug are not printed on a label dispensed with the patient's medication. The ideal system would be a computerised system that detects the potential for an interaction and prints out the appropriate message directly onto the medication administration records used by the nurses on a daily basis. The challenge is to prove that the extra cost of such an automated system would outweigh the cost of pharmacy and nursing times spent on screening patients who are receiving medications with the potential to interact with food, and in operating any effective label system where the information warning of the interaction is available at the time of administering the medication to the patient.

3.6 Patient Counselling: Written and/or Verbal Information

In response to a recommendation from the JCAHO, which stated that, before discharge, patients should be given instructions about and be counselled on potential drug-food interactions, 3 surveys were conducted in US hospitals.[38-40] The objectives were to: (i) characterise current drug-food interaction counselling programmes; (ii) determine which drugs initiated the process and which healthcare professional provided the patient counselling; and (iii) solicit opinions on these programmes from pharmacists and dieticians.

The first survey took place in 1986 among 5 upper Midwestern general hospitals with a bed capacity for 175 patients or more.[38] A 75% response rate was achieved and the survey revealed that 64% of responding hospitals provided patient counselling on drug-food interactions. The details on methods of counselling patients or opinions on the counselling programmes were not described. However, the authors reported that dieticians were the professionals who provided the counselling in more than 50% of cases. Since the survey was sent to dieticians only, the contribution of other healthcare professionals in providing patient counselling may have been underestimated.

In 1992, when the JCAHO recommendation became a determinant in the accreditation process, a second survey on drug-food interaction counselling programmes was conducted nationwide among teaching hospitals with a capacity of between 200 and 500 beds.[39] 320 of 396 hospitals responded to the questionnaire survey. Over half of the respondents reported that patients were counselled either immediately before discharge or at some time during the day of discharge. From those patients who were counselled, 14% received verbal counselling, 9% written information and 77% received both verbal and written information on drug-food interactions. The written information was mostly preprinted and prepared by the pharmacy or dietetic department in the institution. The American Hospital Formulary Service Drug Information and Drug Interaction Facts were the main reference sources used by the pharmacists and dieticians to prepare the leaflets.

As in the first survey, dieticians were the professionals most frequently reported to perform the patient counselling. However, in some institutions, pharmacists were sharing the responsibility of the patient counselling programme with the dieticians. Pharmacists provided reference materials on potential drug-food interactions and identifying drugs for which patient counselling was required. Some pharmacists were involved in activities such as developing policies and procedures and identifying patients to be counselled. Only a few of them reported providing patients with written information or performing patient counselling at the time of discharge.

According to the majority of pharmacists and dieticians who responded to the survey, most teaching institutions appeared to be deficient in comprehensive, formalised drug-food interaction counselling programmes. Most respondents believed that a drug-drug rather than a drug-food interaction programme had a more significant impact on quality of patient care. When interpreting these survey data, the fact that the characteristics of a formal drug-food interaction programme were not specified in the questionnaire should be consider and, consequently, it was left to the respondents to

classify their programme as formal or not, based on their own perceptions.

Teresi and Morgan[40] performed a third survey that was addressed to pharmacists, dieticians, nurses and physicians directly involved in clinical nutrition support. Among all respondents, 12% provided drug-food counselling in more than 50% of patients, and 72% felt pharmacists were in the best position to provide the counselling. As in the 2 previous surveys, the good response rate does not eliminate the possibility of nonrespondent bias when interpreting survey results.

Ideally, all patients should be counselled about potential drug-food interactions and the appropriate timing of administration of their medications before being discharged from the hospital. However, because of time constraints and limited resources, a drug-food interaction counselling programme targeting patients at greatest risk for clinically significant interactions seems to be a more realistic option. All surveys revealed that the most difficult challenge in operating a drug-food interaction counselling programme was to find an ideal method for detecting such higher risk patients.[38-40] All of the studies reported monoamine oxidase inhibitors, warfarin, antibacterials and cardiovascular drugs as the most targeted drugs in their drug-food interaction counselling programmes.[38-40]

Reviewing patients' charts or physician orders, and relying on pharmacists or nurses to detect drug-food interactions while dispensing or administering a given drug, may be time consuming and has the potential to miss patients. Using a computer programme generating a daily list of patients per each drug targeted for drug-food interaction intervention programmes is a more efficient method to identify patients for counselling. Given the usual circumstances of constrained resources, the successful implementation of a drug-food interaction counselling programme requires the selective monitoring of the most common clinically significant drug-food interactions in a given setting. This consequently limits the required counselling to a reasonable number of patients who will potentially attain the greatest benefit.

Lasswell and Loreck[41] developed and reported on a programme set up according to the JCAHO standards for counselling on potential drug-food interactions. This programme was designed and implemented by a committee including members from the clinical nutrition, nursing and pharmacy departments. Six drugs with the potential for drug-food interactions were selected, based on both a literature review and the drugs most commonly prescribed in the institution. A retrospective survey estimated that a mean of 3 patients per day were receiving 1 of the designated drugs for which they needed counselling. Pharmacists were responsible for screening and indicating the potential drug-food interaction on the computer-generated medication administration record and on the first label identifying the medication dispensed to the patient for the first time. Since the mean number of patients to counsel per day was still compatible with a reasonable nursing workload, nursing staff provided the counselling and documented the instructions given to the patient in the medication administration record, the progress notes of the medical record or the patient discharge summary. Dieticians provided additional education during diet counselling sessions, when more detailed nutrition information was indicated.

The authors reported some subsequent steps in their programme development, including the generation of research questions from the monitoring activities and the assessment and adjustment of their programme through a continuous quality assurance process. Even though primarily descriptive, the report of this high calibre programme contributes significantly to the literature on methods to prevent drug-food interactions in hospitalised patients, especially in institutions that can afford such a programme to fulfil JCAHO criteria.

In our study[36] that compared programmes for preventing drug-food interactions in hospitalised patients, we described and assessed the use of patient counselling. Based on the importance of the drug administration time in relation to food intake

and a drug use evaluation in our institution, 5 drugs were selected. Patients receiving these drugs were monitored and/or counselled for potential drug administration mistiming or drug-food interactions. From a possible 6 to 10 patients per day, 3 to 5 patients were randomised to be counselled by the pharmacist. The patient counselling was of a mean duration of 5 minutes and was structured according to a standardised approach that was applied consistently to each patient. The impact of such counselling on the actual drug administration times and patient awareness of the potential for and consequences of a drug-food interaction was assessed by reviewing patients' medication administration records and an interviewer-based questionnaire administered to the patient.

We found that patient counselling decreased the possibility of drug-food interactions and increased patients' awareness about the appropriate time of their drug administration. However, the significant increase in patients' awareness may have been the result of patient recall bias. Since the patient questionnaire was usually administered between day 3 and day 5 after counselling, the improved patient awareness may have been an overestimate of the real impact of patient counselling by reflecting patients' short term recall rather than understanding of the counselling information. Furthermore, the same unblinded investigator interviewed the patients and performed the patient counselling, so interviewer bias might have occurred.

When compared with a label system, patient counselling did not significantly enhance the appropriate time of drug administration or decrease the possibility of drug-food interactions. Our study revealed that more than 60% of patients who were not counselled were not interested in receiving any information about their drugs while in the hospital. Most of them stated that they were relying on nurses and physicians to manage their drug regimens appropriately while they were hospitalised and that they were not interested in taking responsibility for the administration of their drugs. Others indicated that they had no need for information about their medication during their time in the hospital, as they usually interacted with their community pharmacist when they are at home. This last finding may discourage health professionals from expending effort to counsel hospitalised patients about drug-food interactions.

A less labour intensive counselling programme would consist of giving a pamphlet containing information about drug-food interactions and optimal timing of administration of selected drugs to the patient before discharge. The pamphlet should contain information on specific drugs, and the written information should be brief, concise and readable. In our study,[36] drug-food interaction pamphlets were distributed to our control patients only when the pamphlet was requested from the pharmacy by the nursing staff. As a result of this method, which reflected the usual hospital policy, no pamphlet was requested for any of the 34 patients screened for potential drug-food interactions over a 2-week period and, as a result, the impact of providing information for counselling could not be assessed.

The successful implementation of a pamphlet distribution programme would be dependent on the recognition, by patients, of the importance of one piece of paper amongst the many pieces given on discharge. A second but equally important concern would be to ensure that the information was read and understood by the patient.

4. Conclusion

When deciding on a method to prevent drug-food interactions, an institution should select the method that is appropriate to its resources and patient population. Establishing standard drug administration schedules becomes a complex method when trying to eliminate the inappropriate timing of drug administration. An ideal programme would integrate both verbal patient counselling and a computerised label system. The latter should involve the transfer of information on optimal drug administration times that is documented in nursing medication administration records to labels for patients' medications. While being labour intensive, a noncomputerised label system operated by phar-

macists and nurses is a less expensive option in terms of material, but not necessarily human, resources.

Based on the estimated number of patients to counsel per day, verbal patient counselling may be performed by a pharmacist or the nurse who is directly administering the drug to the patient, as appropriate. The feasibility and success of any programme depends on the monitoring of a limited number (between 5 to 10) of drugs known to have clinically significant drug-food interactions and, where possible, targeted according to the results of a drug utilisation survey performed before programme implementation.

Given the usual restrictions in material and human resources, the initial programme implemented by the average hospital may consist of an effective label system that prevents drug administration mistiming and increases awareness of potential drug-food interactions among the healthcare professionals directly involved in dispensing or administering the drug to the patient. If possible, a pamphlet containing information and recommendations about significant drug-food interactions should be provided to the patient before discharge. This represents a more feasible alternative to verbal patient counselling. In today's context of pharmaceutical care, patient counselling, either verbally or with written information, is recommended to improve patients' awareness of and facilitate optimal management of their pharmacotherapy. Newsletters and educational inservices can reinforce, or at least introduce, any new drug-food interaction prevention programme to healthcare professionals.

Finally, a continuous quality assurance processes, that measures the impact of any programme and readjusts the process throughout its development and implementation, is a necessary part of any research programme.

References

1. Neuvonen PJ, Kivisto KT. The clinical significance of food-drug interactions: a review. Med J Aust 1989 Jan 2; 150: 36-40
2. Thomas JA. Drug-nutrient interactions. Nutr Rev 1995 Oct; 53 (10): 271-82
3. Yamreudeewong W, Henann NE, Fazio A, et al. Drug-food interactions in clinical practice. J Fam Pract 1995 Apr; 40 (4): 376-84
4. Kirk JK. Significant drug-nutrient interactions. Am Fam Phys 1995 Apr; 51 (5): 1175-82
5. Accreditation Manual for Hospitals. Chicago: Joint Commission on Accreditation of Hospitals, 1997
6. Williams L, Davis JA, Lowenthal DT. The influence of food on the absorption and metabolism of drugs. Med Clin North Am 1993 Jul; 77 (4): 815-29
7. Welling PG. Interactions affecting drug absorption. Clin Pharmacokinet 1984; 9: 404-34
8. Illingworth DR. Comparative efficacy of once versus twice daily mevinolin in the therapy of familial hypercholesterolemia. Clin Pharmacol Ther 1986; 40: 338-43
9. Hopkin S. Clinical toleration and safety of azithromycin. Am J Med 1991; 91 Suppl. 3A: 40S-5S
10. Neuvonen PJ, Kivisto KT, Lehto P. Interference of dairy products with the absorption of ciprofloxacin. Clin Pharmacol Ther 1991 Nov; 50 (5): 498-502
11. Fagan TC, Walle T, Oexmann MJ, et al. Increased clearance of propranolol and theophylline by high-protein compared with high-carbohydrate diet. Clin Pharmacol Ther 1987; 41: 402-6
12. Scott AK. Warfarin usage. Can safety be improved? Pharmacol Ther 1989; 42: 429-57
13. Karlson B, Leijd B, Hellstrom K. On the influence of vitamin K-rich vegetables and wine on the effectiveness of warfarin treatment. Acta Med Scand 1986; 220 (4): 347-50
14. Lippman S. Monoamine oxidase inhibitors. Am Fam Phys 1986; 34 (1): 113-9
15. Artymowicz RJ, James VE. Atovaquone: a new antipneumocystis agent. Clin Pharm 1993; 12: 563-70
16. Mantyla R, Mannisto PT, Vuorela A, et al. Impairment of captopril bioavailability by concomitant food and antacid intake. Int J Clin Pharmacol Ther Toxicol 1984; 22: 626-9
17. Singhvi SM, McKinstry DN, Shaw JM, et al. Effect of food on the bioavailability of captopril in healthy subjects. J Clin Pharmacol 1982; 22: 135-40
18. Gupta SK, Manfro RC, Tomlanovich S, et al. Effect of food on the pharmacokinetics of cyclosporine in healthy subjects following oral and intravenous administration. J Clin Pharmacol 1990; 30: 643-53
19. Hartman NR, Yarchoan R, Pluda JM, et al. Pharmacokinetics of 2′,3′-dideoxyinosine in patients with severe human immunodeficiency infection: II. The effect of different oral formulations and the presence of other medications. Clin Pharmacol Ther 1991; 50: 278-85
20. Rodin SM, Johnson BF. Pharmacokinetic interactions with digoxin. Clin Pharmacokinet 1988; 15: 227-44
21. Lomaestro BM, Bailie GR. Quinolone-cation interactions: a review. DICP Ann Pharmacother 1991; 25: 1249-58
22. Mannisto P, Mantyla R, Kilnge E, et al. Influence of various diets on the bioavailability of isoniazid. J Antimicrob Chemother 1982; 10: 427-34
23. Nutt JG, Woodward WR, Hammerstad JP, et al. The 'on-off' phenomenon in Parkinson's disease. Relation to levodopa absorption and transport. N Engl J Med 1984; 310: 483-8
24. Baruzzi A, Contin M, Riva R, et al. Influence of meal ingestion time on pharmacokinetics of orally administered levodopa in parkinsonian patients. Clin Neuropharmacol 1987; 10: 527-37
25. Richter WO, Jacob BG, Schwandt P. Interaction between fibre and lovastatin [letter]. Lancet 1991; 338: 706

26. Karim A, Rozek LF, Smith ME, et al. Effect of food and antacid on oral absorption of misoprostol, a synthetic prostaglandin E1 analog. J Clin Pharmacol 1989; 29: 439-43
27. Bailey DG, Munoz C, Spence JD, et al. Interaction of citrus juices with felodipine and nifedipine. Lancet 1991; 337: 268-9
28. Soll AH, Weinstein WM, Kurata J, et al. Nonsteroidal anti-inflammatory drugs and peptic ulcer disease. Ann Intern Med 1991; 114; 307-19
29. Longe RL, Smith OB. Phenytoin interaction with an oral enteral feeding results in loss of seizure control. J Am Geriatr Soc 1988; 36: 542-4
30. Baurer LA. Interference of oral phenytoin absorption by continuous nasogastric feedings. Neurology 1982; 32: 570-2
31. Leyden JJ. Absorption of minocycline hydrochloride and tetracycline hydrochloride: effect of food, milk, and iron. J Am Acad Dermatol 1985; 12: 308-12
32. Jonkman JH. Food interactions with sustained-release theophylline preparations: a review. Clin Pharmacokinet 1989; 16: 162-79
33. Lewis CW, Frongillo EA, Roe DA. Drug-nutrient interactions in three long-term-care facilities. J Am Diet Assoc 1995 Mar; 95 (3): 309-15
34. Franse VL, Stark N, Powers T. Drug-nutrient interactions in a Veterans Administration Medical Center teaching hospital. Nutr Clin Pract 1988; 3: 145-7
35. Garabedian-Ruffalo SM, Syrja-Farber M, Lanius PM, et al. Monitoring of drug-drug and drug-food interactions. Am J Hosp Pharm 1988 Jul; 45: 1530-4
36. Gauthier I, Malone M, Lesar TS. Comparison of programs for preventing drug-nutrient interactions in hospitalized patients. Am J Health Syst Pharm 1997 Feb 15; 54: 405-11
37. Poirier TI, Gludici RA. Evaluation of drug-food/nutrient interactions microcomputer software programs. Hosp Pharm 1991 Jun; 26: 533-40
38. Jones CM, Reddick JE. Drug-nutrient interaction counseling programs in upper midwestern hospitals: 1986 survey results. J Am Diet Assoc 1989 Feb; 89 (2): 243-5
39. Wix AR, Doering PL, Hatton RC. Drug-food interaction counseling programs in teaching hospitals. Am J Hosp Pharm 1992 Apr; 49: 855-60
40. Teresi ME, Morgan DE. Attitudes of healthcare professionals toward patient counseling on drug-nutrient interactions. Ann Pharmacother 1994 May; 28: 576-80
41. Laswell AB, Loreck ES. Development of a program in accord with JCAHO standards for counseling on potential drug-food interactions. J Am Diet Assoc 1992 Sep; 92 (9): 1124-5

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