REVIEW ARTICLE

Role of Pharmacists and Nurses to Avoid Physicochemical Drug Interactions to Ensure Patient Safety

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Abstract

Healthcare professionals such as nurses and pharmacists play a vital role in patient care. The paper underscores the roles of nurses and pharmacists in reducing physicochemical drug interaction and improving patient safety thereby improving the overall healthcare system. A comprehensive literature analysis was done to investigate the impact of physicochemical drug interactions, the responsibilities of nurses and pharmacists in minimizing these interactions, and the value of multidisciplinary teamwork. The study also contains therapeutic recommendations for avoiding drug-drug, drug-food, and drug-nutrient interactions. There has been an increasing rate of medication error due to the physicochemical interaction of the drugs. The unexpected side effects during patient treatment are particularly concerning, as they can elevate mortality and morbidity rates while driving up therapeutic costs. The data show that approximately 50% of pharmaceutical mistakes are caused by physicochemical interactions, particularly in intravenous dose forms. Nurses and pharmacists can work together to prevent these errors by checking medication compatibility, continuously monitoring patient reactions, and revising compatibility recommendations. As a team, pharmacists can examine prescriptions to avoid contraindicated drug combinations, while nurses, as frontline caretakers, ensure that drugs are administered correctly and the food administered to the patient does not negatively interact with the medications. Both experts must work together to discover and avoid physicochemical incompatibilities, which improves patient safety and lowers healthcare costs. This coordinated approach is critical for reducing prescription mistakes while improving the overall stability and efficacy of pharmacological formulations in patient care.

Key words: Collaboration, drug interaction, nurse, patient safety, pharmacist

INTRODUCTION

The need to enhance the patient care system globally has seen an immense rise within the healthcare community. With ever-increasing demand in the healthcare department, there have been numerous challenges associated with the healthcare system, which include limited resources, high surge in healthcare costs, increased medical errors, lack of trained professionals, etc. which eventually hampers the healthcare system.[1] The two most common challenges linked with the healthcare system are medication errors and unanticipated side effects during patient treatment, which can raise the mortality and morbidity rate while also increasing therapeutic costs. One crucial aspect of these challenges is

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the prevention of physicochemical drug interactions.[2] Both the pharmacist's and the nurse's roles become paramount to identify these physicochemical interactions and eradicate them to avoid any pernicious effect on a patient's life. Nurses and pharmacists together can be a robust team in preventing redundancies and improving the safety of patients.[3]

Physicochemical interactions of medications are how pharmaceuticals interact with one another or with biological systems depending on their chemical and physical qualities. These interactions can have an impact on medication pharmacokinetics (absorption, distribution, metabolism, and excretion) as well as pharmacodynamics (body effects). Incompatibilities might be physical (precipitation, effervescence, and color changes) or chemical (≥10% degradation of a produced component within 24 h). One of the most common and severe physicochemical interactions is observed in the intravenous (IV) route of drug administration.[4,5] Physicochemical interaction in IV preparations may also result in venous catheter occlusion, toxic compound formation, embolism, or local/systemic inflammatory reactions. Thus, compatibility must be assured before the co-administration of medicines.[6]

Another major cause of physicochemical interaction is the co-administration of various medications and foods. Healthcare providers, such as nurses and pharmacists can play a vital role in addressing the safety of medications and avoiding any contra-indications.[7]

UNDERSTANDING PHYSICOCHEMICAL INCOMPATIBILITY

Drug incompatibility can be defined as the unwanted interaction between the ingredients of the pharmaceutical dosage form between the 2 co-administered drugs or between food and drug which results in a change in the physical, chemical, or therapeutic effect of the drug.[8] It can also be defined as the unintentional change in the pharmacokinetic or pharmacodynamic properties of the drug when co-administered with other incompatible substances. These incompatibilities affect the safety, appearance, and overall stability of pharmaceutical preparation.[9] Hence the nurse and pharmacist should use their knowledge to overcome such incompatibility. Some key physicochemical interactions that can occur include drug-drug interaction, drug-food interaction, and drug-nutrient interaction.

Drug-drug interaction

A drug-drug interaction is defined as the unwanted interaction between two or more drugs when co-administered. The interaction can result in altered drug levels in the body or lead to severe side effects. For instance, mixing blood thinners like warfarin with non-steroidal anti-inflammatory drugs medicines like ibuprofen can raise the risk of bleeding.[10] Similarly, certain antidepressants known as selective serotonin reuptake inhibitors can combine with other drugs that influence serotonin levels, resulting in a potentially fatal condition known as serotonin syndrome.[11]

Many such interactions have been observed and the clinical implications of such interactions are significant and require careful management by healthcare professionals [Table 1]. Pharmacists and nurses can work together to reduce such implications. Pharmacists can thoroughly review patients' prescriptions and ensure no contra-indicated drugs are administered together.[12,13] Nurses who are frontliners in patient care can ensure the correct dosing of the drug and ensure no contraindicated drugs are administered to the patients.[14]

From the above table, we can infer the role of nurses and pharmacists in avoiding different interactions. Nurses play a critical role in avoiding medication interactions by closely monitoring patients for signs and symptoms of side effects. They should have a thorough awareness of typical medication interactions, especially those involving pharmacokinetic and pharmacodynamic incompatibilities. Proactive measures include a thorough medication history review, vigilant monitoring throughout administration, and prompt reporting of any unexpected symptoms or evidence of drug incompatibility.[21] Nurses must also be able to recognize medication incompatibilities, such as precipitation or discoloration in IV fluids. Effective communication with chemists is critical for resolving questions, receiving professional advice, and ensuring prompt intervention. By following established standards, nurses can help to reduce the likelihood of adverse medication events.[14]

Pharmacists play a critical role in medication safety by aggressively reducing drug interactions. Their thorough understanding of pharmacology allows them to detect probable incompatibilities during drug assessment and prescription evaluation. Pharmacists should understand pharmacokinetic and pharmacodynamic interactions to predict and reduce hazards.[22] Creating and updating thorough compatibility charts is critical for directing healthcare practitioners. Furthermore, chemists may help by teaching healthcare providers about medication interactions and stressing the significance of monitoring patients for side effects. Collaboration with nurses to optimize drug regimens and swiftly resolve issues is critical.[23] Taking a proactive approach to medication safety allows chemists to drastically minimize the possibility of drug interactions while also improving patient outcomes.

Drug-food interaction

The consequences of food-drug interactions are serious, ranging from treatment failure to severe adverse reactions.

Table 1: Examples of drug-drug interactions

Interaction type	Mechanism	Potential outcome	Examples	Role of nurses and pharmacists
Pharmacokinetic incompatibility[15,16]	Changes in the absorption, distribution, metabolism, or excretion of a drug	The altered concentration of the drug in the blood leads to decreased efficacy or toxicity	Antacids reduce the absorption of tetracyclines. Warfarin metabolism is affected by enzyme inducers/ inhibitors	Pharmacists: Conduct comprehensive medication reviews, use interaction-checking tools, and adjust doses based on drug levels. Nurses: Monitor patients for signs of altered drug effects and report to pharmacists or physicians
Pharmacodynamic incompatibility[17]	Increase or decrease in the therapeutic effect of the drug leading to synergistic or antagonistic effects	Enhanced or diminished therapeutic effects or increased risk of adverse effects	Concurrent use of opioids and benzodiazepines leading to excessive sedation. Non-steroidal anti-inflammatory medicines and anticoagulants increase bleeding risk	Pharmacists: Guide safe medication combinations, and monitor for therapeutic efficacy and adverse effects. Nurses: Observe patients for any adverse reactions and effectiveness of therapy, and report issues promptly
Pharmaceutical incompatibility[18]	Physical or chemical incompatibility	Formation of precipitates or inactivation of drugs	Calcium gluconate and sodium bicarbonate	Pharmacists: Ensure proper drug compatibility before mixing, and educate on proper administration techniques. Nurses: Follow guidelines for mixing and administering medications, and report any issues with drug solutions
Synergistic effect[19]	The combined effect of two drugs leads to a greater effect than the sum of their individual effects	Enhanced therapeutic effect	Combination of antibiotics (e.g., penicillin and gentamicin) for improved bacterial killing	Pharmacists: Assess the potential benefits and risks of drug combinations, and ensure the appropriateness of the therapy. Nurses: monitor patient response to combination therapies and report any significant changes or side effects
Antagonistic effect[20]	One drug reduces or counteracts the effect of another drug	Reduced therapeutic efficacy	Opioids and naloxone	Pharmacists: Advise on appropriate timing and dosing schedules, and consider alternative treatments. Nurses: Ensure correct timing of drug administration, and communicate any concerns about drug interactions to pharmacists.

Alcohol, for example, might extend the effects of insulin or oral diabetic medications, resulting in dangerously low blood sugar levels.[24] It may also combine with acetaminophen, raising the risk of serious liver damage, or with antihistamines such as Benadryl, causing greater drowsiness. Understanding these interactions is critical for patients seeking to manage their medicines efficiently and safely. Health professionals, such as nurses and pharmacists, play an important role in educating patients about these interactions and offering advice on how to reduce risks. To avoid possible hazardous interactions, it is advised to the patients to contact their healthcare professionals before changing their diet or drug routine.[25]

In addition to absorption, drug-food interaction can also affect the metabolism of the drug. The presence of certain nutrients or food compounds can inhibit or enhance the metabolism of the drug thereby affecting the drug clearance rate. For example, the flavonoids in grapefruit juice inhibit P-glycoprotein and CYP3A4, which can lead to elevated plasma levels of drugs metabolized by these pathways, increasing the risk of toxicity. Conversely, foods rich in Vitamin K, such as leafy greens, can counteract the effects of anticoagulants like warfarin, reducing their efficacy and potentially leading to thromboembolic events.[21,26] An intelligent collaboration between healthcare professionals can help in avoiding such unnecessary interactions. Table 2 highlights some important drug-food interactions.

Table 2: Examples of drug-food interaction

Drug-food interaction	Type of interaction	Type of effect	Reason behind the interaction	Potential outcome	Examples	Clinical implications
Grapefruit juice and statins[27]	Increased drug levels in the blood	Enhanced statin effects	Grapefruit juice contains furanocoumarin which inhibits CYP3A4, affecting drug metabolism	Increased risk of statin-related side effects (e.g., muscle pain)	Simvastatin, atorvastatin with grapefruit juice	Dose adjustment of the drug - Avoid grapefruit juice 2 h before and after drug administration
Vitamin K-rich foods and warfarin[28]	Reduced anticoagulant effect	Diminished warfarin efficacy	Vitamin K is a cofactor for clotting factors, reducing warfarin's effectiveness	Increased risk of thromboembolic events, potential for clot formation	Leafy greens (e.g., spinach, kale) with warfarin	Do not administer vitamin K along with warfarin
Tyramine-rich foods, such as aged cheese, pickles, yeast extracts, fermented food, and MAO inhibitors[29]	Increased tyramine	Hypertensive crisis	MAO inhibitors prevent the breakdown of tyramine, leading to a fatal increase in blood pressure	Risk of hypertensive crisis and related complications	Aged cheese, pickles, yeast extracts, fermented food administered with MAO inhibitors, such as linezolid.	Potential for severe hypertensive episodes so might require urgent medical attention, avoid tyramine-rich food
Dairy products and tetracyclines/ ciprofloxacin/ levofloxacin[30]	Reduced drug absorption	Decreased efficacy of tetracyclines/ ciprofloxacin/ levofloxacin	Calcium in dairy binds to tetracyclines, reducing their absorption	Reduced effectiveness of tetracycline antibiotics	Milk, Cheese, and other dairy products with tetracycline/ciprofloxacin/ levofloxacin	Take tetracyclines/ ciprofloxacin/levofloxacin with water and avoid dairy products for at least 2 h before and after
Alcohol and acetaminophen[31]	Decrease drug metabolism	Increased risk of hepatotoxicity	Alcohol induces liver enzymes, increasing the risk of acetaminophen toxicity	Risk of liver damage and potential for acute liver failure	Beer, wine with acetaminophen	Limit alcohol intake and avoid excessive use of acetaminophen
High-fiber foods like bran and digoxin[32]	Reduced drug absorption	Decreased efficacy of digoxin	Fiber binds to digoxin, reducing its absorption in the gut	Decreased therapeutic effect of digoxin	Whole grains, beans, bran with digoxin	Monitor digoxin levels and maintain consistent fiber intake
Caffeine and theophylline[33]	Increased drug levels	Enhanced theophylline effects	Caffeine can inhibit the metabolism of theophylline, increasing its levels	Increased risk of theophylline toxicity	Coffee, Tea, energy drinks	Potential for adverse effects such as tremors, and palpitations, monitor theophylline levels closely. Limit caffeine intake
Alcohol and antihistamines[34]	Enhanced sedation	Increased sedative effects	Alcohol enhances the central nervous system effects of antihistamines	Increased risk of drowsiness, sedation, and impaired cognitive function	Diphenhydramine, loratadine with alcohol	Increased risk of accidents and impaired daily functioning, avoid alcohol intake

(Contd...)

Table 2: *(Continued)*

Drug-food interaction	Type of interaction	Type of effect	Reason behind the interaction	Potential outcome	Examples	Clinical implications
Soybean formulas with thyroid supplements[35]	Decrease absorption	Decreased effect	Soybean has phytoestrogens and fiber, which decreases absorption and increases elimination of thyroid supplements	Decrease the effect of the thyroid medication	Levothyroxine and soybean	Avoid consuming soybean-related food.

MAO: Monoamine oxidase

Drug-nutrient interactions

Nutrient-drug interactions occur when a nutrient in the ingested meal influences the medicine. To avoid adverse effects, factors such as the timing of drug administration and the kind of food consumed must be regulated. Certain long-term medications can also affect the nutritional health of the patient and may lead to vitamin and mineral deficiencies.[36,37] For instance, laxatives can reduce absorption of several vitamins and minerals by forcing food to pass quickly through the body, resulting in poor nutritional uptake.[38,39] Furthermore, several anticonvulsants can reduce folate absorption.[40] Medications can also lower nutrient synthesis. For example, bacteria in the intestines create Vitamin K, but antibiotics, in addition to killing bad bacteria, can also kill beneficial bacteria, including those that make Vitamin K. Furthermore, drugs might impair the body's capacity to metabolize nutrients. Some anticonvulsants, for example, change the activity of liver enzymes, increasing the metabolism of folate, Vitamin D, and Vitamin K.[41,42] Details of specific nutrients affecting the absorption of drugs are given in Table 3.

ROLE OF NURSE AND PHARMACIST TO REDUCE PHYSICOCHEMICAL INCOMPATIBILITY IN INTENSIVE CARE UNIT (ICU)

ICUs are high-risk environments, with medication mistakes common due to the complexity of patient care. Critically ill patients frequently require numerous high-alert drugs, including opioids, sedatives, and insulin, raising the risk of adverse drug events. According to research, there is a high association between patient severity and medication mistake rates in ICUs.[51] For example, studies have shown that ICU patients are given twice as many drugs as normal ward patients, and the rate of avoidable medication mistakes is proportionally greater. The use of weight-based dosage for drugs such as antibiotics, vasopressors, and anticoagulants complicates matters even further, as estimating mistakes might result in pharmaceutical dose problems.[52]

Nurses are the frontier in the healthcare system and play a critical role in the management and reduction of physicochemical incompatibilities in the ICU as they closely monitor and manage the medication administration of critically ill patients. They are typically responsible for ensuring the compatibility of the drug before administrating to the patients.[52] Their job also involves checking for any physical-chemical or therapeutic incompatibilities between co-administered drugs. To make educated selections, they frequently consult with pharmacists, use compatibility tables, and follow rules.[53] Proper labeling, timely administration, and timely vigilant observation for signs of incompatibility (such as color changes or precipitate formation) are essential nursing responsibilities that help prevent adverse drug

Table 3: Drug-nutrient interactions

Nutrient in food	Medicine	Type of effect	Reason behind the interaction	Potential outcome	Clinical implications	Management strategies
Calcium[43]	Ciprofloxacin	Reduced absorption	Calcium binds with ciprofloxacin, forming insoluble complexes	Decreased drug efficacy	Potential for treatment failure or infection	Hold enteral feeding 1 h before and 2 h after administration of the drug
Potassium[44]	Diuretics, thiazide, chlortalidone	Electrolyte imbalance	Causes loss of potassium and magnesium	Rapid heart rate and arrhythmias	Risk of cardiac complications	Administer potassium/magnesium supplements or foods such as apricots, bananas, cantaloupe, dairy foods, dried beans, lentils, oranges, and tomatoes
Vitamin D supplements[45]	Gastrointestinal medications	Hypercalcemia	Vitamin D increases calcium absorption	Calcium toxicity and kidney failure	Risk of nephrocalcinosis and renal impairment	Avoid milk; restrict milk products and calcium supplements
Aluminum[46]	Levofloxacin	Reduced absorption	Aluminum binds with levofloxacin, reducing its bioavailability	Decreased drug efficacy	Potential for treatment failure	Avoid meals that contain aluminum and aluminum supplements
Iron[47]	Norfloxacin	Reduced absorption	Iron forms insoluble complexes with norfloxacin	Decreased drug efficacy	Potential for treatment failure	Avoid meals that contain iron and iron supplements
Zinc[48]	Various medications	Reduced absorption	Zinc binds with certain medications, reducing their absorption	Decreased drug efficacy	Potential for treatment failure	Avoid meals that contain zinc and zinc supplements
Vitamin K[49]	Warfarin	Anticoagulant effect reduction	Vitamin K is essential for clotting factor production	Reduced efficacy of warfarin	Increased risk of clotting	Limit foods high in Vitamin K such as broccoli, spinach, and turnip greens
Iodine[50]	Metformin	Decreased absorption and increased elimination	Iodine affects absorption and increases fecal elimination of metformin	Reduced drug efficacy	Potential for poor glycemic control	Limit foods high in iodine, such as cabbage, soybeans, and Brussels sprouts.

reactions and ensure patient safety. The nurses can also take care of the diet of the patient based on the drug being administered to the patient.[54] This would help avoid any food-drug interaction and improve the healthcare system.

Contrary, pharmacists have a very specialized role in preventing drug incompatibility in the ICU through their intensive knowledge of the drugs. Pharmacists can play a vital role in drafting a medication routine for an ICU patient keeping in mind the possible drug interactions and avoiding co-prescribing such drugs. The pharmacist also keeps track of any nutrient supplement or any other disease the patient has and therefore can prescribe the drugs accordingly. They play an integral part in developing and updating compatibility guidelines and protocols that nurses and other healthcare providers follow.[53] They along with nurses and physicians can help in providing alternative treatment regimens in case of any incompatibilities detected and therefore provide total care to the ICU patients.

Effective interdisciplinary collaboration between the pharmacist and the nurses is critical in mitigating unintentional physicochemical incompatibilities. The duo has shown tremendous improvement in reducing the healthcare cost of individuals and reduction in unnecessary side effects due to medication errors. The duo's complimentary expertise leverages the treatment. Their teamwork can help in the identification of any issue promptly and addressing them for smooth treatment.[55] Regular multidisciplinary meetings, as well as the usage of electronic health records to document and share medication compatibility data, can help to improve collaboration. Pharmacists may give training sessions and updates on new medication incompatibility discoveries, while nurses can provide their views and experiences for smooth collaboration.[56]

This combined effort would in turn help in providing extensive and improved care to ICU patients. By preventing drug incompatibilities, healthcare professionals can provide more stable care to the patient without weighing any unnecessary financial burden on the patients. It can also help in avoiding any life-threatening cases such as occluded IV lines, therapeutic failures, or toxicities.[57] This proactive strategy not only improves the safety and effectiveness of patient care but also contributes to the optimization of overall healthcare delivery in the ICU.[58] Patients benefit from a more simplified and safe medicine delivery method, resulting in speedier recovery periods and better overall health results.

PHARMACIST AND NURSES IN PROVIDING PARENTERAL NUTRITIONAL SUPPORT

The administration of several IV products through the same catheter is a regular occurrence in ICU patients, where the stakes are high and the consequences are not always apparent to nurses. When certain terminally ill patients are unable to tolerate oral feeding, they are given IV nutritional formulations to provide them with essential nutrients, either to sustain life in the event of a critical illness or to maintain their health by providing nutrients in which they are deficient. This is referred to as parenteral nutrition (PN) treatment.[59] The PN formulations are complex combinations containing both macronutrients (amino acids, dextrose, and injectable fat emulsions) and micronutrients (electrolytes, vitamins, and minerals).[60] This formulation can be tailor-made by the pharmacist as per the needs of the patient. To ensure the safety of the patient, nurses can be vigilant during the PN therapy and ensure no drug interacts with these nutrients.[61] Both pharmacist and nurses can monitor their drug prescriptions to ensure no drug-nutrition interactions take place.

CONCLUSION

The prevention of physicochemical drug interactions is critical for improving patient safety and lowering the risks associated with medication mistakes in healthcare systems. The complexity of these interactions particularly drug-drug interaction, drug-food interaction, and ICU requires vigilant monitoring and proactive measures. Pharmacists play an important role in evaluating prescriptions to avoid inappropriate drug combinations and ensure that pharmaceutical pharmacokinetics and pharmacodynamics are not compromised. Nurses, as frontline caretakers, are responsible for the proper administration of these medications, monitoring the diet of the patient, and continuously monitoring for symptoms of incompatibility. Hence collaboration among the healthcare team is essential. Nurses can collaborate with doctors, pharmacists, and other healthcare professionals to coordinate care, review treatment plans, and address any concerns or changes in the patient's condition. By working in collaboration, healthcare professionals contribute to safer and more effective treatment leading to better patient outcomes and a more efficient healthcare system.

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ETHICAL DISCLOSURE

None required.

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