Medication incompatibility in intravenous lines in a Paediatric Intensive Care Unit (PICU) of Indonesian hospital

Suci Hanifah, Patrick Ball, Ross Kennedy

Abstract

***Objectives*: Currently, little is documented concerning the patterns of multiple concurrent medication use utilising single intravenous line. The in-line compatibility issues in Paediatric Intensive Care Units (PICUs) are not as well documented as in adult patients either. This study closely examined the combination of medications used concurrently in a PICU, recorded how medications were used, and then investigated the in-line potential compatibility.**

***Methods*: This study was a mixed model designed first to identify retrospectively the patterns of multiple medication use at any single time of administration (STA). Secondly, a questionnaire was distributed to practitioners to elucidate their perceptions about incompatibility.**

***Results*: From a single lumen peripheral line in-vitro simulation, it was observed that three infusions typically met in sequential Y-sites and had the potential to interact. The combinations identified were morphine+midazolam, midazolam+fentanyl+morphine, morphine+fentanyl+dobutamine, morphine+midazolam+ketamine, and midazolam+dobutamine+norepinephrine. Compatibility data covering simultaneous administration of three-or-more intravenous drugs was not found in 97.5% (n=120) of the cases. Most practitioners (92.9%) recognized incompatibility. Many (46.4%) said they observed >3-10 in-line incompatibilities in a month. Most nurses (78.5%) reported using the manufacturer as their reference source for compatibility data. Flushing with clear fluid between doses was the most used method to prevent incompatibility (45.5%).**

***Conclusions*: It was a common practice to concurrently administer three or more medications: analgesics, sedatives, inotropes, and others, through the same port with major potential for incompatibility issues. Most of the literature is based on two drug comparisons with minimal information on using combinations of three or more. Most practitioners' understanding of the implications of the terminology of "incompatibility not known or possible" for their patients appeared lacking.**

Key words: Intravenous, drug utilization, drug incompatibility, critical care, paediatrics.

Introduction

In critical care, the majority of medications (>70%) are administered parenterally for faster action or due to patient's inability to swallow oral medications. It is known that many patients will receive an average of 10 different medications in multiple doses during a single admission. (1) In paediatric practice, the requirement for multiple parenteral medications with limited venous access and fluid volume restriction frequently leads to concurrent administration of combinations of intravenous (IV) medications through a single line. Based on pharmaceutical formulation principles, this has the potential for physical and chemical reactions, which when occurring in-line and directly entering the patient circulation, may lead to morbidity or mortality. (2,3) Anecdotal evidence suggests that insufficient attention is paid to this, which seems to be multifactorial and may include knowledge, time, workforce, and cost constraints. (4)

Literature reports on medication use have concentrated on a single agent and infusion fluids or perhaps in combination with another, making it difficult to evaluate in the context of multiple medications being added at different access points into a single infusion system. (5,6) Also, laboratory mod-

From Pharmacy Department, Faculty of Science, Universitas Islam Indonesia (UII), Yogyakarta, Indonesia (Suci Hanifah), School of Pharmacy, Faculty of Science and Engineering, Wolverhampton University, England, UK (Patrick Ball), and School of Biomedical Science, Charles Sturt University, New South Wales, Australia (Ross Kennedy).

Address for correspondence:
Suci Hanifah
Jalan Kaliurang Km 14.4 Sleman, Yogyakarta 55582, Indonesia
Tel: +6285643958700
Emails: suci.hanifah@gmail.com, suci.hanifah@uii.ac.id

els where two medications have been mixed together at fixed concentrations in a test tube poorly reflect the way in which medications may also interact with residuals of another before or after, the IV fluids, and the infusion system (tubing, connectors, etc.), or for various periods of time at variable concentration gradients resulted from flow effects. Also, the role of pharmaceutical excipients in the formulation makes it impossible to extrapolate information from one manufacturer's formulation to an alternative product from a different manufacturer. (7) A recent study has suggested that pharmacists, who are usually consulted when information about incompatibility is not available, need to be aware of medication compatibility issues and that "no data available" should not be interpreted as safe to minimize such errors in their hospitals. (8)

This preliminary study was used as the basis for identifying the problem of incompatibility in paediatric critical care setting in in-vitro real time simulated IV lines by closely observing and recording the practice and gathering information about ward staff experiences and reactions to what has been observed by pharmacists as incompatibility.

Methods

Study approach

The setting of this research was the PICU in a teaching hospital in Java, Indonesia, which is considered a centre of excellence within the province. It is a leading centre from which other hospitals look for guidance. After a comprehensive review of literature, a retrospective prescription chart review was conducted to establish the most common combinations of medications and the problems incurring during their administration. This was followed by a prospective observational study of medication administration practice and administration of a simple questionnaire on the perceptions of nursing and medical staff in relation to the problem of drug incompatibility.

Ethics approval for this study was obtained from the Charles Sturt University Human Research Ethics Committee (CSU HREC) on 18 September 2013 (2013/173). In addition, approval was also granted by Universitas Gadjah Mada Human Ethics Committee (GMU HEC) on 31 July 2013 (KE/FK/733/EC). Hospital staff participation was voluntarily, and the return of completed questionnaire was considered as an implied consent to participate.

Data collection

As an initial step, medical records for the period between 1 June 2012 and 30 September 2013 were reviewed to gain an adequate sample of medication usage patterns in the PICU and any recorded issues regarding incompatibility. Then, bedside observations were undertaken for one month to confirm patterns of how medications were prescribed, prepared and administered as well as where medications were administered simultaneously. No staff information or identifiers were collected, and only the process sequence was recorded. Thirdly, a questionnaire was administered to nurses and resident doctors involved in drug preparation and administration. This was used to understand their perspective on incompatibilities and to identify whether they perceived them as serious problems. The collected information was then analysed to establish an understanding of the level of incompatibility problem and current prevention strategies in the PICU facility. All data collected in this phase was anonymous and no personal identifiers were used.

Operational definitions adopted for drug administration

"Single time of administration (STA)" refers to the administration of more than one medication at a specific timing, such as 8.00 o'clock in the morning or in the evening. The term "infusion-infusion" refers to the simultaneous administration of two medications by infusion via a two-way connector. At any STA, if an intermittent or single bolus IV medication is injected sequentially through a port into infusion tubing, the term "infusion-injection" will be used.

Data analysis

Data collected from the medical records was transcribed into a Microsoft Excel™ spreadsheet. To ensure that there was no missing data, the spreadsheet was crosschecked several times in sequence and randomly. The data regarding medication use and questionnaire responses were qualitatively analysed.

Results

The retrospective medical record search yielded information on 231 patients. There were 19 patients excluded due to missing measurable data fields in their records, and 212 patient records were considered for further analysis, including the name of the medication, route, dose, administration time, and any reported incompatibility medication-related problems.

Profile of multiple intravenous

Patients in this PICU were administered an average of 1-6 drugs at one STA, mostly (89%) through a

peripheral venous cannula (PVC). Over one third of the patients (32.5%) received three infused medications concurrently through one line with other medications administered by a bolus injection merged into the infusion line at a 'Y'-site. Therefore, a medication group was defined as the combination of medications administered simultaneously through one line (infusion-infusion) or consecutively at one STA through one extension (infusion-injection). From a review of the medical records, it was found that there were more than 100 different groups of infusion-infusion and infusion-injection amongst the 212 sample patients. **Figure 1** shows the frequency of the top 20 groups of drugs by frequency of occurrence among the study samples.

The top 20 medication groups included various analgesic, sedative, and inotropic drugs. The most frequent groups were morphine+midazolam (15.6% frequency), morphine+fentanyl+midazolam (9.4% frequency), and morphine+fentanyl+dobutamine (6.6% frequency).

In one STA, infusions met injections (intermittent medications) in the following descending order of frequency: paracetamol, cefotaxime, furosemide, ranitidine, meropenem, ampicillin, phenobarbital, phenytoin, metronidazole, chloramphenicol, acyclovir, fluconazole, gentamicin, and methylprednisolone.

Potential problem of incompatibility

Incompatibility is defined as the potential for a chemical reaction, displacement of particles, precipitation, jell formation, or other interactions arising from medications coming together in the tubing, such as drug-solution or drug-drug including infusion-infusion and infusion-injection or drug-equipment. Using recent literature, a two-dimensional compatibility chart could be developed (**Figure 2**), which shows that 73.6% of medications had their information available on the PICU hospital website database; of these, 57.3% appeared compatible, while 16.2% were incompatible in solution.

To identify the compatibility of co-infusions with simultaneous administration in a 'Y'-site, a chart was developed which more closely resembled the practice. **Table 1** was developed to represent a possible compatibility chart (infusion-injection) based on actual experience in practice. Unlike the two-dimensional chart, using recent literature, many frames were missing (97.5%; n=120) from this chart.

Problem of IV drug incompatibility faced by health practitioners

During the one-month period of bedside observation of practitioners' practice in administering parenteral infusion, it was found that practitioners did not appear to pre-consider IV drug compatibility, including definitions, prior to commencing administration. Some nurses asked for an explanation of what incompatibility is and how it occurs. Other nurses asked how to distinguish incompatibility from thrombophlebitis and the differences between incompatibility and drug interaction. There were also questions about when flushing should be used in relation to medication administration.

The questionnaire was administered to nurses (n=22) and resident medical doctors (n=6) who were in charge of the preparation and administration of IV drugs in PICU for more than a month, and all staff (n=28) returned the completed survey. There was no consultation with or input from clinical pharmacists in the ward on the preparation or administration of drugs. The answers from nursing staff and resident medical doctors to the questionnaire are shown in **Table 2**.

All the nurses reported that they had observed drug incompatibilities during their employment at PICU. Only four of the doctors reported observing incompatibilities. The doctors reported that they had observed less than three incompatibilities in the month prior to the survey, whereas about 59% of nurses reported observing 3-10 incompatibilities in the same period. In this context, incompatibility refers to a visible colour change in the line or the appearance of a 'flash' of powder, as medications come together, but not other possible incompatibility, which does not cause physical characteristic changes.

Although the doctors reported observing less than three occlusions in the previous month, about 45.5% of nurses observed 3-10 occlusions and about 54.5% observed more than 10 occlusions. However, all the doctors and nurses had reported that their perceived occlusions were not due to drug incompatibilities. The staff had linked the occlusion to having been caused by a technical problem or blood clotting occlusion.

With respect to prevention of incompatibility, practitioners (78.6%) usually referred to pharmaceutical manufacturers although some (21.4%) reported that they used the "Handbook on Injectable Drugs" (Trissel, 2014) instead; however, on investigation, the book was found to be located in the pharmacy not readily accessible in the ward. Most (45.5%) managed incompatibility by flushing with sodium chloride 0.9%. However, most nurses (68%) and all the medical doctors reported that they considered drug incompatibility issues as beyond their responsibilities.

A range of drugs was reported to be involved in the

incompatibilities observed (**Figure 3**). The most frequent medications involved, reported by both doctors and nurses, were phenytoin and phenobarbital. Interestingly, inotropic drugs were also viewed as problematic by the doctors (66.7%) but less so by the nurses (22.7%).

Discussion

The likelihood of incompatibility increases with the increasing number of medications at any STA. Reducing the number of drugs per STA may be possible by spacing the administration of injections, but this may fit poorly into nursing routines and is complicated for slow or continuous concurrent infusions. This is more complicated in paediatrics population when only a small volume of fluids can be infused and multiple access sites are not possible due to the age of patients. This may increase cost and workload of ward staff and lead to medication errors. (9)

When a single lumen PVC is utilized, a rule to use separate lumen for each drug may become impossible. Additionally, in one single PVC, several infusions flow in each piece of tubing and meet with the other infusions or injections at a 3-way stopcock or other connector where incompatibility reactions can occur. In contrast, incompatibility seems rarely to be reported when two IV drugs are administered concurrently in critical care. The potential for incompatibility between consecutive IV injections appears to be avoidable if practitioners are accustomed to flushing with clear fluid before and after medication delivery provided that the solution and volume used have been validated for the system in use; however, in small infants, the volume and electrolyte administered with the flushes may be significant. Though rare, it may still occur as a fixed route for three common groups: amine/cardioactive drugs, analgesic/sedative, and parenteral nutrition in separated lumen that cannot be implemented because of the non-availability of multi lumen catheters in this unit. However, the frequency of this occurrence is not known and missing from the chart mimicking practice (**Table 1**). This study's finding regarding the increased risk of incompatibility between three or more medications concurs with that of other works being understudied. (7,10) Therefore, the development of a three-dimensional (or more) chart for each infusion group administered in conjunction with an injection is a benefit to the current body of knowledge in the area of parenteral therapy for paediatric patients.

Based on the questionnaires, nurses were more likely to encounter and observe drug incompatibilities and occlusion of the infusion line than doctors as this is an inherent part of their practice responsibilities as drug administration specialists. However, most of the nurses felt that, even though they are drug administration specialists, managing compatibility is beyond their expertise and responsibility. Therefore, the lack of ward pharmacy services in this PICU appears to be an integrated part of the incompatibility problems. Fahimi (2015) found that drug incompatibility problems are frequent and need to be dealt with as they are one of the leading medication errors. (11)

On further investigation, it was found that manufacturer information sheets were commonly used as a reference by nurses though they actually provided insufficient information on compatibility. This is also in accordance with a previous study which discovered that many practitioners lacked awareness of compatibility and how to source trusted information about it. (8) In addition, Kanji (2010) stated that nurses often ran concomitant drugs without sufficient understanding of drug compatibility. (12)

Another finding was that the PICU practitioners have insufficient training on how to manage incompatibility issues effectively. This study also identified vast variation in medication groups and administration protocols, which seems to be confusing for nurses, leaving them at the risk of causing administration errors. Camire (2010) found a correlation between a higher level of knowledge and a reduction in errors. (13)

Incompatibility is commonly classified by nurses as relating to the medication injected rather than the process. Most injections, such as acyclovir, ampicillin, furosemide, phenobarbital, phenytoin and meropenem, have a basic pH (>7) or high pKa and will theoretically cause precipitation when in low pH solutions such as 5% glucose (pH 4-4.5). It is well known that the high pKa of these drugs means that relatively high pH levels are required to sustain drugs in solution and they are very prone to precipitation during dilution if the pH is allowed to drift too low. (14) Considering this, it is deemed necessary to undertake assays of compatibility to fill in the missing frame of the chart (**Table 1**). Bertsche (2008) found that having a protocol reduced incompatibility from 5.8% to 2.4%. (8) Thus, the provision of IV compatibility data is a fundamental pharmacy service in critical care. (15)

Overall, these present findings have illustrated the recurrent problems of incompatibility and lacked recognition and understanding. The lack of a ward pharmacist in PICU may contribute to the low awareness level. This appears to differ from hospitals in some developed countries where pharmacist contribution is considered helpful in two-thirds of

compatibility cases (16) and can reduce errors by 66%. (17) Accordingly, the current study supports the need for clinical pharmacists to be involved in the development of infusion protocols in PICU. The role of pharmacists should be extended to critical care services. (18,19) According to the international guidance on competency from the Society of Critical Care Medicine, the prevention of incompatibility falls within the competency and responsibility of clinical pharmacists. (20)

This study has provided preliminary information on the incompatibility problems in PICU and addressed the urgency of incompatibility assays for three and more concurrent medications. The identification of incompatibility must be interpreted with caution as the numbers and percentages do not express the actual frequency of incompatibility in every single case, but they are based on the most frequently listed medications and conditions, which have the potential for incompatibility. This study may be limited to reflect incompatibility problems in Indonesia, which can be different from other countries.

Based on the findings, the current study proposes that hospitals should provide staff with education sessions in the area of parenteral drug compatibility to raise the level of awareness regarding this critical issue. Appropriate professional development short courses can also relay information, refresh the knowledge, and increase awareness of practitioners concerning incompatibility. (21)

Conclusions

Based on the medical records of 212 paediatric patients, the majority were administered multiple medications using three simultaneous infusions and an injection. The five main drug groups in this PICU were morphine+midazolam, midazolam+fentanyl+morphine, morphine+fentanyl+dobutamine, morphine+midazolam+ketamine, and midazolam+dobutamine+norepinephrine. Additional medications may also be administered as bolus or intermittent, including ampicillin, acyclovir, cefotaxime, chloramphenicol, gentamicin, phenytoin, methylprednisolone, metronidazole, meropenem, phenobarbital, phenytoin, and ranitidine.

'Y'-site incompatibility occurred during the dwell time with other infusions and injections as they were administered with a one-lumen catheter (no separate line). Based on a review of the literature, much information (97.5%, n=120) is missing from the infusions-injections compatibility chart with regard to the most frequently administered combinations.

The responses from the questionnaires have shown that most practitioners (92.9%) encountered incompatibility during observation, mainly with phenytoin, although most did not have sufficient understanding of incompatibility problems and management. The 78.5% practitioners used manufacturer information to check the compatibility data. To prevent incompatibility, flushing was used by 45.5% nurses, while 39.3% chose to change drugs, and 17.9% reported to the doctors.

Table 1. Compatibility amongst medication groups, infusion with injection

Infusion Drug groups	Without injection	Injection drugs											Intermittent		
		Acyclovir	Ampicillin	Cefotaxime	Chloramphenicol	Dexamethasone	Furosemide	Gentamicin	Meropenem	Phenobarbital	Phenytoin	Ranitidine	Paracetamol	Metronidazole	Fluconazole
Midazolam, morphine	C	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Morphine, midazolam, fentanyl	C	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Morphine, fentanyl, dobutamine	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Midazolam, morphine, ketamine	C	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Fentanyl, dobutamine, norepinephrine	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
Midazolam, dobutamine, norepinephrine	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?

Legend: C=compatible; ?=no data available (no recent compatibility study or information in the literature to answer).

Table 2. Incompatibility problem according to health practitioners based on questionnaires

Questions and choice of answers	Responses to questions	
	Nurses (n=22)	Doctors (n=6)
Duration of work in PICU		
- <1 year - 1 to <5 years - 5 to <10 years - ≥10 years	0 2 13 7	6 0 0 0
Occurrence of incompatibility		
- Have you ever observed drug incompabilities at PICU Sardjito?		
• Yes • No	22 0	4 2
- How often have you observed drug incompatibilities within the last month?		
• <3 • 3-10 • >10 • No answer	4 13 4 1	6 0 0 0
- Have you observed an infusion line occlusion?		
• Yes • No	22 0	5 1
- How often did you observe an occlusion within last month?		
• <3 • 3-10 • >10	0 10 12	6 0 0
- Were those occlusions associated with incompatibility?		
• Yes • No	0 22	0 6
- What medications have you observed drug incompatibilities with?	Various answers given; see Figure 3	
- What incompatibilities have proved hard to manage?	Phenytoin (22)	Phenytoin (4)
	Phenobarbital (20)	No answer (2)
	Diazepam (2)	
Prevention of incompatibility		
- Is there any protocol for preventing incompatibility?	Yes (10), flushing No (12) Did not know (0)	Yes (0) No (6) Did not know (0)
- What reference do you use to have a look at information regarding incompatibility?	Manufacturers (16) Book* (6)	Manufacturers (6)
- How can you manage the incompatibility or line occlusion?	Spooling or aspiration (10)	Spooling or aspiration (0)
	Changing with the other (8)	Changing with the other (3)
	Reporting to senior or doctor (4)	Reporting to senior or doctor (1)
		No answer (2)

Legend: *=Trissel's "Handbook on Injectable Drugs".

Figure 1. Top 20 simultaneous infusions in PICU

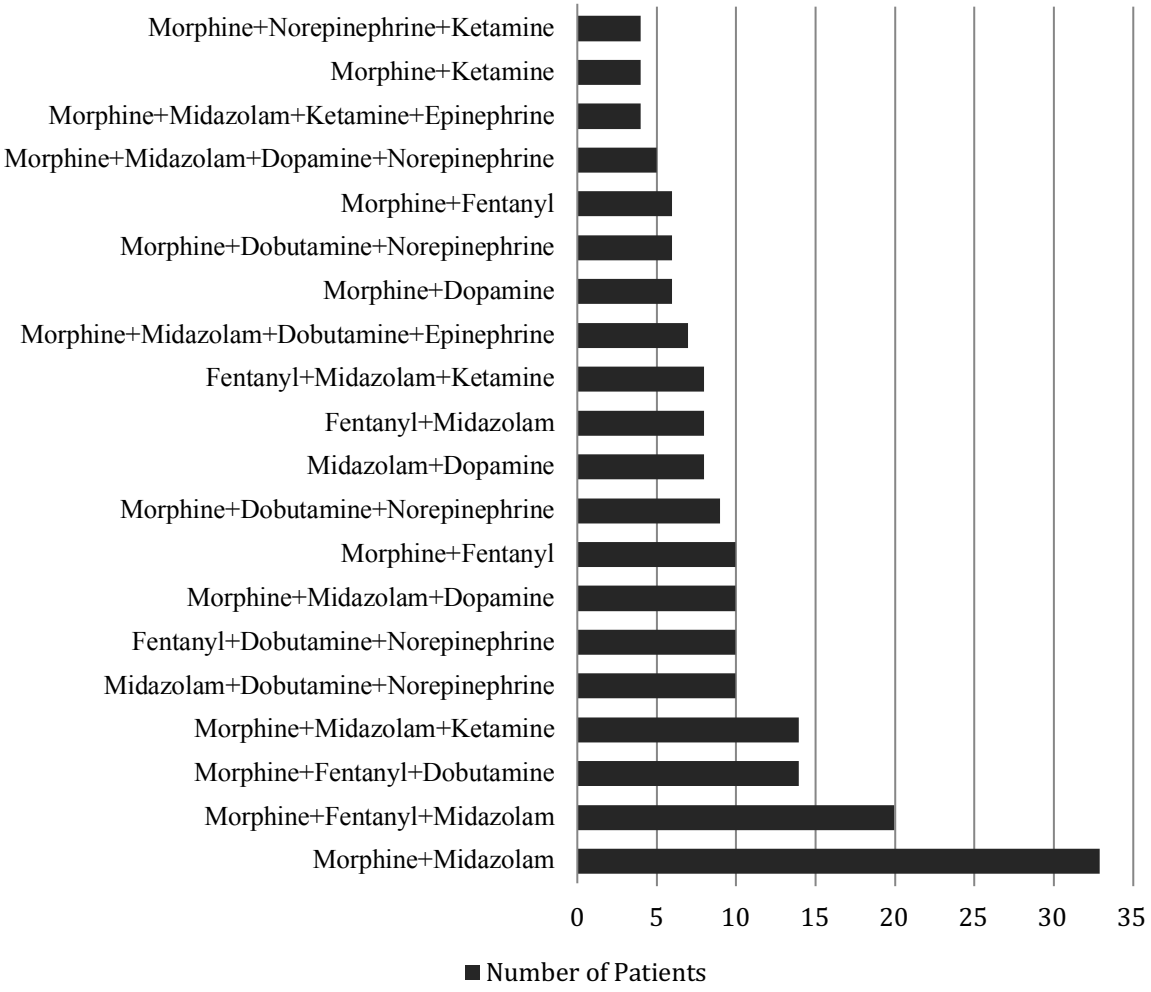
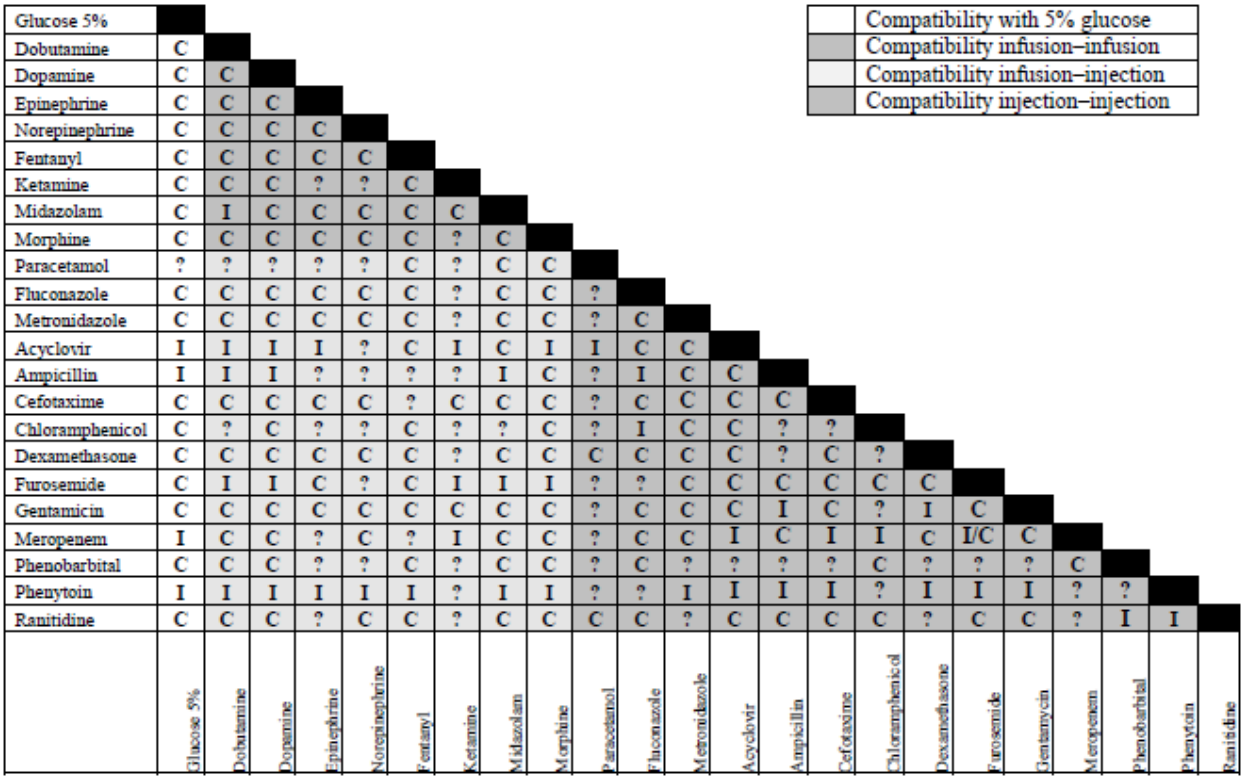


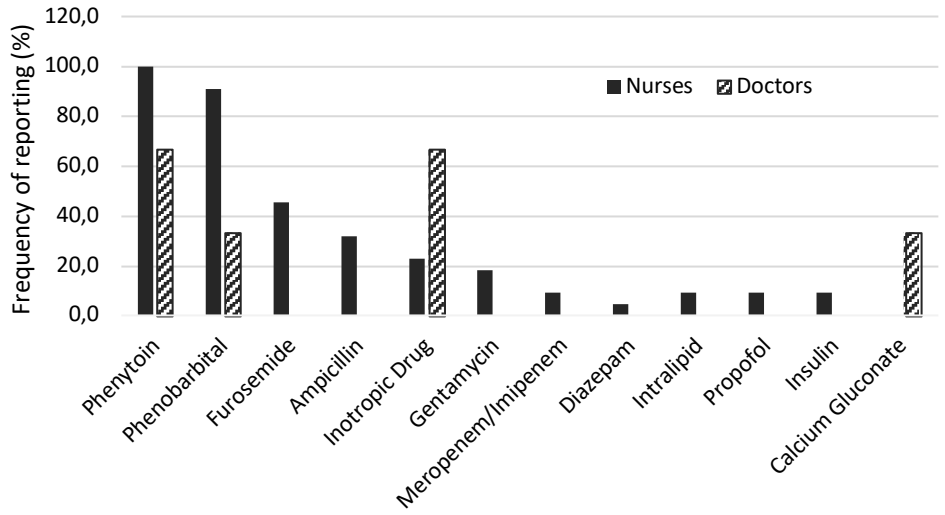
Figure 2. Two-dimensional compatibility chart of the 22 top drugs in PICU



	Glucose 5%	Dobutamine	Dopamine	Epinephrine	Norepinephrine	Fentanyl	Ketamine	Midazolam	Morphine	Paracetamol	Fluconazole	Metronidazole	Acyclovir	Ampicillin	Cefotaxime	Chloramphenicol	Dexamethasone	Furosemide	Gentamycin	Meropenem	Phenobarbital	Phenytoin	Ranitidine
Glucose 5%																							
Dobutamine	C																						
Dopamine	C	C																					
Epinephrine	C	C	C																				
Norepinephrine	C	C	C	C																			
Fentanyl	C	C	C	C	C																		
Ketamine	C	C	C	?	?	C																	
Midazolam	C	I	C	C	C	C	C																
Morphine	C	C	C	C	C	C	?	C															
Paracetamol	?	?	?	?	?	C	?	C	C														
Fluconazole	C	C	C	C	C	C	?	C	C	?													
Metronidazole	C	C	C	C	C	C	?	C	C	?	C												
Acyclovir	I	I	I	I	?	C	I	C	I	I	C	C											
Ampicillin	I	I	I	?	?	?	?	I	C	?	I	C	C										
Cefotaxime	C	C	C	C	C	?	C	C	C	?	C	C	C	C									
Chloramphenicol	C	?	C	?	?	C	?	?	C	?	I	C	C	?	?								
Dexamethasone	C	C	C	C	C	C	?	C	C	C	C	C	C	?	C	?							
Furosemide	C	I	I	C	?	C	I	I	I	?	?	C	C	C	C	C	C						
Gentamicin	C	C	C	C	C	C	C	C	C	?	C	C	C	I	C	?	I	C					
Meropenem	I	C	C	?	C	?	I	C	C	?	C	C	I	C	I	I	C	I/C	C				
Phenobarbital	C	C	C	?	?	C	?	C	C	?	C	?	?	?	?	C	?	?	?	C			
Phenytoin	I	I	I	I	I	I	?	I	I	?	?	I	I	I	I	?	I	I	I	?	?		
Ranitidine	C	C	C	?	C	C	?	C	C	C	C	?	C	C	C	C	?	C	C	?	I	I	

Legend: C=compatible; I=incompatible; ?=no data available.

Figure 3. Frequency of reported drug incompatibility occurrences



References

1. Di Paolo ER, Hirschi B, Pannatier A. Quantitative Determination of Particulate Contamination in Intravenous Administration Sets. Pharm Weekbl Sci 1990;12(5):190-5.
2. Taxis K, Barber N. Incidence and Severity of Intravenous Drug Errors in a German Hospital. Eur J Clin Pharmacol 2004;59(11):815-7.
3. Bradley JS, Wassel RT, Lee L, Nambiar S. Intravenous Ceftriaxone and Calcium in the Neonate: Assessing the Risk for Cardiopulmonary Adverse Events. Paediatrics. 2009;123(4): e609-13.
4. Almasdy D, Siregar CJP. Evaluasi Teknik Penggunaan Sediaan Parenteral dan Pencampuran Intravena pada Ruangan Rawat bedah di Suatu Rumah Sakit Pemerintah. Jurnal Sains dan Teknologi Farmasi 2002;7:36-43.
5. Biswal S, Mishra P, Malhotra S, Puri G, Pandhi P. Drug Utilization Pattern in the Intensive Care Unit of a Tertiary Care Hospital. J Clin Pharmacol 2006;46(8):945-51.
6. Tavallaee M, Fahimi F, Kiani S. Drug-Use Patterns in an Intensive Care Unit of a Hospital in Iran: an Observational Prospective Study. Int J Pharm Pract 2010;18(6):370-6.
7. Hanifah S, Ball P, Kennedy R, Lambert K. Mapping of Incompatibility Assay: Bringing Method to Problem in Critical Care. Int J Pharm Pharm Sci 2014;6(4):171-3.
8. Bertsche T, Mayer Y, Stahl R, Hoppe-Tichy T, Encke J, Haefeli WE. Prevention of Intravenous Drug Incompatibilities in an Intensive Care Unit. Am J Health Syst Pharm 2008;65(19): 1834-40.
9. Dabaghzadeh F, Rashidian A, Torkamandi H, Alahyari S, Hanafi S, Farsaei S, et al. Medication Errors in an Emergency Department in a Large Teaching Hospital in Tehran. Iran J Pharm Res 2013;12(4):937-42.
10. Trissel LA. Handbook on Injectable Drugs. 16th ed. Maryland: Bethesda MD, American Society of Health-System Pharmacists; 2011.
11. Fahimi F, Forough AS, Taghikhani S, Saliminejad L. The Rate of Physicochemical Incompatibilities, Administration Errors. Factors Correlating with Nurses' Errors. Iran J Pharm Res 2015;14:87-93.
12. Kanji S, Goddard R, Donnelly R, McIntyre L, Turgeon A, Coons P, et al. Physical Compatibility of Drug Infusion used in Canadian Intensive Care Units: A Program of Research. Canada: Canadian Patient Safety Institute and Institut Canadien pour la securite des patients; 2010 May 31. 32 p.
13. Camiré E, Moyen E, Stelfox HT. Medication Errors in Critical Care: Risk Factors, Prevention and Disclosure. CMAJ 2009;180(9):936-43.
14. Newton DW. Drug Incompatibility Chemistry. Am J Health Syst Pharm 2009;66(4):348-57.
15. Mühlebach S. Incompatibility Reactions in IV Drug Therapy: Preventable Medication Errors. Paper presented at: The 12th EAHP Congress; 2007 Mar 21-23; Bordeaux, France.
16. Delestras S, Kabiche S, Guignard B, Sigrist T, Fonzo-Christe C, Bonnabry P. CP-049 Are Pharmacist's Recommendations on Drug Compatibility Applied by Healthcare Professionals? A Randomised Controlled Study. Eur J Hosp Pharm Sci Pract 2014;21:A20.
17. Leape LL. Errors in Medicine. Clin Chim Acta. 2009;404(1):2-5.
18. Chuang L, Sutton JD, Henderson GT. Impact of a Clinical Pharmacist on Cost Saving and Cost Avoidance in Drug Therapy in an Intensive Care Unit. Hosp Pharm 1994;29(3):215-8, 21.
19. LaRochelle JM, Desselle B. Critical Care Pharmacotherapy: Description of an Innovative Pediatric Residency Elective Experience Unitlizing Clinical Pharmacy Faculty as Preceptor. Crit Care Shock. 2015;18:52-4.
20. Rudis MI, Brandl KM. Position Paper on Critical Care Pharmacy Services. Society of Critical Care Medicine and American College of Clinical Pharmacy Task Force on Critical Care Pharmacy Services. Crit Care Med 2000;28(11): 3746-50.
21. Shah A. Pharmacy Intervention in the Medication-use Process. The Role of Pharmacist in Improving Patient Safety. Den Haag, The Netherlands: International Pharmaceutical Federation (FIP); 2009.