Incompatible intravenous drug combinations and respective physician and nurse knowledge: a study in routine paediatric intensive care

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ABSTRACT

Objectives To identify incompatible intravenous drug combinations in routine paediatric intensive care and evaluate physician and nurse knowledge.

Methods In a university paediatric intensive care unit, intravenous drug incompatibilities were analysed using a database and physician and nurse knowledge of incompatibilities was assessed using a questionnaire.

Results We analysed 665 prescriptions in 87 patients. Incompatible drug administration was identified in 9 (10%) of the 87 patients with a median of 3 different incompatibilities per patient (Q25/Q75: 1/3). We found 26 incompatible combinations. The most frequently involved drugs were cefotaxime, pantoprazole and vancomycin. A median of 10 of the 15 drug combinations were correctly assessed as compatible or incompatible (Q25/Q75: 8/11). Pantoprazole had a low number (20%) of correct answers.

Conclusions One in 10 patients in paediatric intensive care was affected by drug incompatibility, with knowledge deficits seen in a third of assessed combinations. This indicates quality improvement strategies should be urgently implemented by pharmacists.

questionnaire survey was performed with the consent of the staff committee.

Study design, setting and participants

We carried out the study without performing any interventions in the paediatric ICU of a university hospital. In this unit, central venous catheters with up to three lumens and monoluminal peripheral venous catheters were used. Information on incompatibilities in this unit was available in the form of an ebook edited by the German Society of Hospital Pharmacists, a paediatric intensive care handbook, three different posters checked by the hospital pharmacists or unit physicians, and the Summaries of Product Characteristics. Electronic clinical decision support systems or a unit-based pharmacist were not available, but it was always possible to call a pharmacist who had access to further information such as standard literature or specific databases. An electronic system was available in the study unit for comprehensive documentation of prescriptions and drug administration. Although we found high documentation quality, we could not completely rule out the possibility that nurses interrupted infusions and flushed the line before they administered another drug. The data of consecutive patients hospitalised in the study unit and treated with at least two different intravenous drugs were analysed. The study lasted nine weeks.

Data collection and analysis

► We first collected physicians' prescriptions and nurses' administration documentation once daily from patient charts. We evaluated the incompatibility of intravenous drug combinations (considering only pairs of drugs) using a database (Kompatibilität im Katheter – KiK 4; oData, Rastede, Germany). We focused on combinations for which an incompatibility has been documented several times. The database is based on brand names, and a choice of diluent is not possible. We used the name of the active ingredient when presenting our results in order to increase comprehensibility as brand names vary internationally. Each prescription was counted only once per patient to avoid the over-representation of patients who had been hospitalised for a longer time. As the risk for harm caused by incompatibilities increases with the frequency of administration, we analysed both the number of patients affected by the

INTRODUCTION

With frequencies of 25%, incompatibilities were reported to be the most common intravenous medication errors in hospital.¹ Many incompatibilities of intravenous drug combinations are not visible, which might promote limited awareness of the issue even though drug losses can reduce effectiveness. Additionally, adverse drug effects such as thrombotic events and systemic inflammatory response syndrome have been reported.² Tissot *et al*³ classified one in four of all incompatibilities occurring on intensive care units (ICUs) as serious or life-threatening. Children and adolescents are particularly vulnerable to the serious consequences of incompatibility.⁴

In our paediatric ICU we therefore aimed to identify incompatible intravenous drug combinations and to evaluate physician and nurse knowledge of drug incompatibilities in order to improve quality.

METHODS

Ethics approval

The local ethics committee approved the study according to the Declaration of Helsinki. The

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administration of incompatible drugs and the frequency of incompatible drug combinations administered.

- We invited all physicians and nurses in the paediatric ICU to voluntarily participate in a questionnaire survey concerning the (in)compatibility of drugs used in the study unit. We developed a multiple-choice questionnaire addressing identification of the compatibility of drug combinations based on our analysis of drug prescription and administration. The physicians and nurses had to indicate whether they assumed a given intravenous drug combination was (in)compatible. The 15 drug combinations included incompatible drug combinations frequently administered in the study unit (six combinations), incompatible drug combinations not administered in the study unit (three combinations), and drug combinations considered safe (six combinations).

Statistics

Frequencies are shown as numbers and percentages. Continuous data are presented as the median with the first (25%) and third (75%) quartiles (Q25/Q75) and minimum/maximum (min/max).

RESULTS

- Of 109 patients hospitalised in the paediatric ICU during the study period, 87 were prescribed at least two drugs for intravenous administration. The 87 patients were a median of 3.9 years old (Q25/Q75: 0.9/9.3; min/max: 0.02/18.9), and 40 (46%) were female. We analysed 665 prescriptions for intravenous administration with 74 different active ingredients. Of the 665 prescriptions, 217 (33%) concerned central and 70 (11%) peripheral intravenous administration, 4 (0.01%) were ambiguous, and for 374 (56%) the specific intravenous administration route was not given. Of the prescriptions without a specified route, 67 (18%) were prescriptions for PRN ('pro re nata') use. Administered incompatible intravenous drug combinations were identified in 9 (10%) of the 87 patients. We found a median of three different incompatibilities per patient (Q25/Q75: 1/3; min/max: 1/15) in these nine patients. Altogether, 18 different intravenous drugs were involved in 26 different incompatible drug combinations (table 1). The most frequently involved drugs were cefotaxime, pantoprazole and vancomycin.
- A total of 21 nurses with a median age of 40 years (Q25/Q75: 36/44) and median professional experience of 21.5 years (Q25/Q75: 15.75/25.25) and seven physicians with a median age of 33 years (Q25/Q75: 28/34.5) and median professional experience of 5 years (Q25/Q75: 2.05/7.5) filled in the questionnaire regarding the (in)compatibility of 15 given drug combinations (table 1). Results showed that a median of 10 drug combinations were correctly assessed (Q25/Q75: 8/11) corresponding to 272 (65%) correct assessments among all 420 drug combinations. Pantoprazole had one of the lowest numbers of correct answers (20%, 11/56) of all drugs assessed.

DISCUSSION

Incompatibilities pose the risk of ineffectiveness and severe and sometimes even fatal adverse events.³ However, incompatibilities are generally avoidable. We found that we needed to more closely examine the 10% of patients affected by drug combinations that should not be co-administered under any circumstances.

Pantoprazole in particular was frequently administered in incompatible combinations. This may be because pantoprazole

Table 1 Drugs and drug combinations involved in incompatibilities

Drug/drug combination	Prescribed to patients (n)	Incompatibly administered to patients (n)	Total of incompatible administrations (n)
Acetylcysteine	7	1	7
Ambroxol	2	2	7
Caspofungin	3	1	9
Cefotaxime	6	3	110
Ciprofloxacin	1	1	2
Dobutamine	4	1	23*
Furosemide	11	4	38
Gentamicin	1	1	3
Heparin	7	3	28
Levofloxacin	1	1	9
Meropenem	3	3	12
Midazolam	15	3	52
Pantoprazole	7	6	113
Phenobarbital	1	1	44
Piperacillin/tazobactam	7	2	2
Potassium canrenoate	10	4	35
Ranitidine	15	1	6
Vancomycin	6	3	174
Administered incompatible combinations			
Ambroxol–potassium canrenoate		2	6
Cefotaxime–antoprazole		1	20
Cefotaxime–potassium canrenoate		2	21
Cefotaxime–vancomycin		2	56
Dobutamine–heparin		1	23*
Furosemide–midazolam		1	17
Heparin–pantoprazole		2	2
Meropenem–pantoprazole		2	5
Pantoprazole–piperacillin/tazobactam		2	2
Pantoprazole–vancomycin		2	76
Phenobarbital–vancomycin		1	42
Drug combinations correctly judged as (in)compatible (correct answers)			
	n (% of 7 physicians)	n (% of 21 nurses)	
Caspofungin–furosemide (incompatible)	6 (86)	20 (95)	
Cefotaxime–metronidazole (compatible)	6 (86)	16 (76)	
Cefotaxime–pantoprazole (incompatible)	4 (57)	2 (10)	
Cefotaxime–potassium canrenoate (incompatible)	3 (43)	5 (24)	
Clonidine–ketamine (compatible)	5 (71)	17 (81)	
Dexamethasone–pantoprazole (incompatible)	2 (29)	3 (14)	
Dobutamine–heparin (incompatible)	6 (86)	14 (67)	
Dobutamine–norepinephrine (compatible)	5 (71)	21 (100)	

Continued

Table 1 Continued

Drug combinations correctly judged as (in)compatible (correct answers)	n (% of 7 physicians)	n (% of 21 nurses)
Furosemide–levofloxacin (incompatible)	6 (86)	19 (90)
Furosemide–midazolam (incompatible)	7 (100)	17 (81)
Lorazepam–ranitidine (compatible)	3 (43)	8 (38)
Morphine–ranitidine (compatible)	3 (43)	11 (52)
Phenobarbital–vancomycin (incompatible)	7 (100)	15 (71)
Piperacillin/tazobactam–ranitidine (compatible)	4 (57)	12 (57)
Propofol – vancomycin (incompatible)	7 (100)	18 (86)

*Administered as a continuous infusion, thus counted once per day.

In the top section of the table, we present the number of patients who were prescribed the respective drug, the number of patients to whom the concerned drug was administered in at least one incompatible combination, and the frequency of administration of the concerned drug in incompatible combinations. Drugs not involved in incompatibilities are not shown. In the middle section of the table, we show the respective incompatible drug combinations administered either to more than one patient or at least ten times. In the lower section of the table, we present drug combinations correctly judged as (in)compatible in the questionnaire by nurses. All drugs are listed in alphabetical order.

has a lower potential for interactions than omeprazole,⁵ suggesting that pantoprazole is generally safer in combinations with others drugs as seen in the frequent incorrect answers concerning pantoprazole in the questionnaire. However, pantoprazole is well known to be frequently involved in incompatibilities in ICUs.⁶ Vancomycin and cefotaxime were also among the three drugs most frequently administered in incompatible combinations. Incompatible combinations with these drugs increase the risk of decreased antibiotic plasma levels and thus lower effectiveness in critically ill paediatric patients.⁷

The incompatible drug combinations cefotaxime–potassium canrenoate and cefotaxime–pantoprazole were judged as compatible by the vast majority of participants. This indicates a major knowledge gap that should be addressed in teaching sessions. Most of the nurses had extensive work experience, indicating a need to regularly refresh and update their existing knowledge. Thus, we recommend teaching sessions to generally increase awareness of drug-related problems, especially as regards intravenous administration. To maintain knowledge gained in the teaching sessions, handouts or posters could be provided. Additionally, sources of information should highlight drugs frequently involved in incompatibilities.

Moreover, attention should be paid to further strategies to prevent incompatibilities such as the use of multiple-lumen infusion devices, pausing continuous drug therapy to allow administration of a bolus injection and flushing of the intravenous line with isotonic saline solution, in-line filtration, or colour-coded use of compatible drug classes.^{2,8,9} However, especially in paediatric patients, some of these strategies have limited feasibility, for example, because of the limited number of intravenous lumens and the low amount of infusion solution that can be administered. Therefore, knowledge and availability of information on

drug (in)compatibilities is crucial. The physicians were generally well aware of incompatible combinations, but knowledge of compatible combinations could be improved. Use of lumens for infusing compatible combinations allows other lumens to be used for incompatible drugs, so the total amount of infusion solution can be reduced. As reported earlier,¹⁰ sustainable results can be achieved by involving pharmacists in tailored prevention strategies.

Limitations and generalisability

In almost half of the intravenous prescriptions the number catheter lumens to be used was not specified, so the actual event rate might even higher than found. For PRN drugs, it might be better to not predefine a lumen for administration but to consider the infusions administered at the point of need and then decide accordingly. In paediatric patients, the number of lumens available is usually lower than in adults. Thus, the situation might be worse in children than in adults. However, especially in the case of pantoprazole, the potential for incompatibilities is underestimated and thus might result in patient harm in other patient groups as well.

CONCLUSIONS

In a university paediatric intensive care, intravenous incompatibilities were found in one in 10 patients. This was accompanied by knowledge deficits regarding a third of the assessed combinations. Pantoprazole, cefotaxime and vancomycin were identified as the drugs most frequently involved in intravenous drug incompatibilities. Our results indicate that quality improving strategies by clinical pharmacists are urgently required.

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