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Concurrent intravenous drug administration to critically ill children: Evaluation of frequency and compatibility

Melany Gaetani, M.B., B.Ch., BAO [a], Helena Frndova, Dipl.-Ing. [a,e,h], Winnie Seto, BScPhm, PharmD, MSc, R.Ph [a,e,g], Christopher Parshuram, MB.ChB DPhil [a,b,c,d,e,f,g,h,*]

[a] Child Health Evaluative Sciences, The Hospital for Sick Children, Peter Gilgan Centre for Research & Learning [PGCRL], 686 Bay Street, 11th floor, Toronto, Ontario M5G 0A4, Canada
[b] Institute of Medical Science, The Hospital for Sick Children, Peter Gilgan Centre for Research & Learning [PGCRL], 686 Bay Street, Toronto, Ontario M5G 0A4, Canada
[c] Departments of Health Policy, Management, and Evaluation, University of Toronto, 27 King's College Cir, Toronto ON M5S, Canada
[d] Interdepartmental Division of Critical Care Medicine, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
[e] Department of Critical Care Medicine, 555 University Ave, Toronto, ON M5G 1X8, Canada
[f] Department of Pediatrics, 555 University Ave, Toronto, ON M5G 1X8, Canada
[g] Department of Pharmacy, 555 University Ave, Toronto, ON M5G 1X8, Canada
[h] Center for Safety Research, The Hospital for Sick Children, Peter Gilgan Centre for Research & Learning [PGCRL], 686 Bay Street, 11th floor, Toronto, Ontario M5G 0A4, Canada

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ABSTRACT

Purpose: To evaluate the frequency of concurrent drug administration and drug-drug incompatibility of concurrently administered drugs in critically ill children based on available references.
Materials and methods: We retrospectively evaluated concurrent intravenous drug administration in children admitted to a single centre. Eligible patients included those admitted to the critical care unit for at least 6-hours in the ten-year period ending 30 July 2015 and received two or more IV drug administrations. Compatibilities were classified using local reference documents.
Results: The 16,863 eligible patients were admitted to ICU for 2,212,326 h and received 3,664,667 concurrent administrations. Concurrent infusions ran for 6,263,600 h. There were 2,284,066 (62%) concurrent administrations; 334,144 (9%) were compatible, 293,856 (8%) were incompatible, 293,856 (8%) required pharmacist consultation, and 752,601 (21%) had 'unknown' compatibility. Individual patients received a median (IQR) of 33 (10 − 132) concurrent administrations, comprised of 7 (1 − 30) concurrent injections 1 (0–5) concurrent infusions and 13 (0–74) concurrently administered injections and infusions.
Conclusions: Concurrent IV-drug administration is frequent in critically ill children. Known incompatible concurrent administration occurs, however the compatibilities of many drug-drug pairs were unknown - adding complexity to routine bedside management and identifying information gaps for future research.

1. Introduction

Physical or chemical drug incompatibility results in patient complications, including fatalities [1-3]. Concurrent administration of incompatible drugs has been described in critically ill adults and neonates in intensive care units (ICU) [1-4], however compatibility information for intravenous drugs that are commonly administered in adult ICU and neonatal ICUs is incomplete [4,5]. A recent systematic review of 820 drug pairs from 41 drugs commonly used in adult ICU found no physical compatibility data for 47% of combinations, and no chemical compatibility data for 93% [4]. Compatibility data may be similarly lacking in children.

Critically ill children receive many drugs. We found 68% of 4419 orders written for 100 critically ill children were for intravenous medications, and that each patient received a median (interquartile range) of 58 (28–129) administrations during their ICU stay. Each additional ICU day was associated with 11 additional administrations [6].

Drug-drug co-administration arises as a consequence of the high volume of administrations observed and finite vascular access in critically ill children. Anecdote and our experience suggest concurrent administration is common and that consideration of drug-drug compatibility is an important bedside practice in pediatric ICU. We sought to better understand this aspect of pharmacotherapy in the pediatric ICU. The objective of this study was to evaluate the frequency of concurrent

* Corresponding author at: The Hospital for Sick Children, Department of Critical Care Medicine, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada.
E-mail addresses: melany.gaetani@gmail.com (M. Gaetani), helena.frndova@sickkids.ca (H. Frndova), winnie.seto@sickkids.ca (W. Seto), christopher.parshuram@sickkids.ca, chris@sickkids.ca (C. Parshuram).

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drug administration and describe the nature of the compatibilities of concurrently administered drugs in critically ill children.

2. Materials and methods

A retrospective cohort study, of critically ill children at the Hospital for Sick Children, Toronto, was performed. Eligible patients were admitted to either the pediatric or cardiac ICU for at least 6 h, during the period from 31 July 2006 to 30 July 2015 and received two or more intravenous drug administrations while in ICU.

Eligible drug administrations were included in the 347 drugs listed in the hospital formulary and were administered by intravenous route to eligible patients. Each intravenous drug administrations were classified as either an intermittent injection or a continuous infusion. A continuous infusion began and ended as documented, and was separated by at least 4 h from other documented infusion(s) of the same drug in the same patient.

The main study outcomes were concurrent administration of intravenous drugs and the compatibilities of these drug-drug pairs. A concurrent administration was defined as administration of two intravenous drugs to the same patient in one of three situations: [1] when two infusions were administered at the same time. This was counted as one concurrent administration and the duration of concurrent administration of the two infusions was measured in hours [2]. When an injection was administered during an infusion episode; and [3] when two injections were administered within 60 min of each other. The latter definition was chosen as a practical reflection of varied precision of documentation of times, and in recognition that lines may be incompletely purged of drug after small volume flushes.

Secondary outcomes were the frequency that drug-drug pairs were concurrently administered; the numbers of: concurrently administered injections; injections that were administered during infusions; concurrently administered infusions; the number of hours that infusions were concurrently administered; and the number of concurrent infusions that were being administered in each hour of ICU.

We described the patients in terms of age at ICU admission (in months), the ICU of admission (pediatric versus cardiac), ICU length of stay, PELOD score (maximum throughout ICU-stay), the duration of mechanical ventilation, veno-venous haemodialysis, and ExtraCorporeal Membrane Oxygenator support and their ICU survival.

2.1. Drug compatibility information

Compatibility of co-administered drugs was determined using data from The Hospital for Sick Children, Pharmacy Department, Critical Care Unit Intravenous Ad-mixtures charts and documents, Lexi compatibility software and The Hospital for Sick Children eFormulary. An amalgamated compatibility document was prepared using Microsoft Excel (Microsoft Corporation, Redmond, CA, USA) containing combinations of co-administered intravenous drugs with the corresponding, available, compatibility information. All drug combinations were classified as either Incompatible (I), Compatible (C), consult a pharmacist (Rx), or unknown compatibility information as none available (U).

2.2. Data acquisition and management

Data was obtained from the clinical database housed in the Department of Critical Care Medicine. The PELOD score, and the durations of ICU stay, ECMO, dialysis and mechanical ventilation were directly abstracted. Documentation of intermittent and continuous administrations was reviewed to identify eligible drugs, and correct variations in drug naming conventions and to correct spelling errors.

Infusions and periods of infusion were identified from administration data. Intra-arterial administrations were identified and excluded. Gaps of >4 h between consecutive administrations in the same patient were identified and used to define the beginning and end of infusion periods for infusions of each unique drug in each patient. This 4-hour period was chosen to incorporate a reasonable period of delayed documentation for a given infusion (standard practice is every hour), and to exceed the likely time during which any residual drug would have been flushed from the line by which it was administered.

Next, the total number of hours that each infusion was administered during the patient-admission was calculated. The maximum number of concurrent infusions running in each patient was determined by evaluating each hour the patient was in the ICU and counting the number of infusions running in that hour. This data was tabulated and was represented in a histogram. In recognition that more than one heparin infusion (2 units/ml) may be concurrently administered to maintain line patency of different intravenous lines, low dose heparin infusions were regarded as separate infusions in descriptions of the numbers of infusions, but were counted as one drug for determinations of the number of concurrent drugs infused.

2.3. Analyses

The unique concurrently administered drug-drug pairs were identified for each patient and the frequency that each pair occurred for each of infusion-infusion, infusion-injection, and injection-injection types of concurrent administration was counted and ranked. These frequencies were tabulated for the entire dataset for each ICU, by length of stay and the maximum number of infusions running.

Data were presented as median and interquartile range (IQR) for counts of administration, concurrent administrations per patient day, per patient-admission and per calendar day, or as the number of affected patients.

3. Results

3.1. Patient population characteristics and length of stay

There were 17,482 patients admitted between July 31st 2006 and July 31, 2015. We excluded 619 who received 1 or fewer intravenous drug administrations, did not receive any intravenous drug administrations or were admitted to the ICU for <6 h. The 16,863 eligible patients who were studied had a median (IQR) age of 35 (6–131) months at ICU admission (Table 1), and were in ICU for 2,198,446 h (Table 2). The median (IQR) length of stay was 45 (21–119) hours; 9375 (54%) patients were admitted for <48 h, and 2961 (17%) were admitted for >7 days. The median (IQR) PELOD score was 11 (1 — 13); 7811 (46%) patients were mechanically ventilated, 318 (2%) received ECMO; and 351 (2%) received continuous veno-venous hemofiltration. Survival to ICU discharge was 97% (Table 1).

3.2. Concurrent administrations and compatibilities

There were 3,664,667 concurrent administrations comprised of 850,301 (23%) concurrent injections; 2,692,437 (74%) injections given concurrently with infusions and 121,929 (3%) concurrent infusions that ran for 6,263,600 h (Table 2). Concurrent injections were most likely to occur within the first 10 min and at 50 to 60 min after the first injection (Fig. 1). A total of 2,284,066 (62%) concurrent administrations were compatible, 334,144 (9%) were incompatible, 293,856 (8%) required pharmacist consultation, and 752,601 (21%) had unknown compatibility information (Table 3).

Each patient received a median (IQR) of 33 (10–132) concurrent administrations during their ICU stay. These were comprised of 7 (1–30) concurrent injections, 1 (0–5) concurrent infusions and 13 (0–74) injections and administered during an infusion (Table 2); 17 (3–79) were compatible; 0 (0–7) were incompatible; 2 (1 — 10) required pharmacist consultation, and 3 (0–17) had no compatibility information (Table 3). The largest number of concurrent infusions running in a single patient in a single hour was 11 (Fig. 2).