

Systematic Steps to Diminish Multi-Fold Medication Errors in Neonates

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Tenfold and other multiple-of-dose errors are particularly common in the neonatal intensive care unit (NICU), where the fragility of the patients increases the potential for significant adverse outcomes. Such errors can originate at any of the sequential phases of the process, from medication ordering to administration. Each step of calculation, prescription writing, transcription, dose preparation, and administration is an opportunity for generating and preventing medication errors. A few simple principles and practical tips aimed at avoiding decimal and other multiple-dosing errors can be systematically implemented through the various steps of the process. The authors describe their experience with the implementation of techniques for error reduction in a NICU setting. The techniques described herein rely on simple, inexpensive technologies for information and automation, and on standardization and simplification of processes. They can be immediately adapted and applied in virtually any NICU and could be integrated into the development of computerized order entry systems appropriate to NICU settings. Either way, they should decrease the likelihood of undetected human error.

KEYWORDS: medication errors, neonates

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INTRODUCTION

Errors owing to prescription and administration of medication are particularly common in pediatric patients,¹⁻³ given the need to calculate individualized, weight-adjusted doses. Calculation errors comprise about 15% of all prescription errors in a regional academic hospital.⁴ Incorrect equations are used in about 1:200 prescriptions in a pediatric service, accounting for 35% of errors in pediatrics, whereas decimal point errors account for 15% of pediatric errors.¹ Significant morbidity is most likely to occur with decimal point or other several-fold dosing errors.^{5,6} In neonatal (NICU) and pediatric (PICU) intensive care units, where patient weights may vary over a 10-fold range or more, neither large nor small doses will, *per se*, appear unusual.

Errors, particularly multiple-of-dose errors, may originate at any step of the order-to-administration process.² Thus, each step of calculation, prescription writing, transcription, dose preparation, and administration provides an opportunity for generating or preventing medication errors. Systematic application of a few principles can diminish the likelihood of such errors (Table).

STANDARDIZATION

The principle of standardization aims to simplify and minimize variation in methods of calculation, in order to enhance familiarity with both the methods and the expected range of results. Standardization can be applied at any step in the healthcare system, from dose calculation to administration.

The simultaneous use of English and metric units in the United States is the source of many errors in pharmacological treatment. For example, a birth weight of "four-eight" reported by telephone from a referring hospital can be translated into 4.8 kg by a NICU clerk; the same

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weight can be recorded as 3.742 kg (instead of 2.041 kg), when the rows and columns representing pounds and ounces on the conversion chart are inadvertently transposed. In either case, erroneous weights might be used for calculation of emergency drug dosages. Hospital policies removing English units from clinical documentation and communication could abolish this problem.

Standardization can also be applied to the numeric format of weights that are used in calculations. In pediatric patients >9 kg, no decimals are needed. In NICU, the format #.# kg should be adopted (exactly 2 digits separated by a decimal point) for all weight entries in calculations. A trailing zero would be permissible in this instance *only*; this exception applies to weight values, not prescribed doses. Thus, 0.7 kg, replaces 675 grams or 0.675 kg; 1.2 kg should be used instead of 1.235 kg, 1.0 kg instead of 1.040 kg. A small and constant number of significant digits simplifies calculations, making decimal point errors less likely; it also helps in error detection.

Using fewer significant digits might result in a 10% variation from actual weight, in the smallest neonates; however, this imprecision is unlikely to cause biologically significant changes in doses administered, particularly for extremely low birth weight (ELBW) infants. The minuscule volumes involved in dose delivery to ELBW patients cannot be measured precisely, so that actual dose administered frequently varies by more than 10% from the target dose. Measurements show substantial variation between the prescribed and actual concentrations of catecholamines in clinical infusates.⁷ Similarly, large differences exist between assumed and actual infusion rates of insulin, owing primarily to its adsorption to plastics.⁸ These factors, combined with low, inconstant fluid delivery rates by infusion pumps,⁹ make drug delivery to neonates an intrinsically imprecise endeavor. Additionally, many drugs that are used in critically ill neonates are titrated to effect, obviating the need for dose "precision". By rounding off doses to correspond to measurable volumes, errors relating to dose preparation and administration can be avoided, without adding to existing imprecision.

Since some calculations are unavoidable and about one third of medication errors involving calculations results from the use of the wrong

Table. Steps used to minimize decimal and other multiple dosing errors

Principle	Example/Comment
Use standard language and units of measure, across services	Morphine written as mg/kg/hr (NICU) and µg/kg/hr (PICU), confuses housestaff. Abolish use of "pounds/ounces" in clinical setting
Use standard weight (e.g., #.# kg) in NICU	0.7 kg, instead of 675 grams or 0.675 kg; 1.2 kg instead of 1.235 kg
Minimize the use of calculations	Use pre-printed medication dosing sheets
Use computer applications with built-in error checks, to generate patient-specific medication sheets	Automated "code cards"; weight and name are the only entries required; range of allowable values is restricted
Use decimals in dose formats only when necessary (i.e., when of clinical consequence)	Round off prescribed doses, particularly if within ~10% of "exactly" calculated amounts
Always use a leading zero to the left of a decimal	Some decimals can't be seen in print
Don't use trailing zeros (to the right of a decimal)	Beware of invisible decimals
Clarify illegible or otherwise unclear orders fully and explicitly, directly with the prescriber or supervisor	Reiterate all details of the order, from patient weight to final dose, including indication
When double-checking a dose or volume calculated by someone else, start from scratch; obtain results independently. Estimate mentally, then use calculator	Seeing prior miscalculations, either an incorrect equation or incorrect computation, can misguide subsequent recalculations
When entering fluid rates in programmable infusion pumps, verify that numbers displayed are exactly as intended. Independently confirm settings for critical infusions	Digit inversions, transposition of time and volume entries, misplaced or missed decimals - a final opportunity for serious errors

dose equation,¹ standardization can be applied to the calculation process itself. Stepwise calculation procedures have been recommended to minimize errors; ideally, the weight factor is entered in the last step.¹⁰

By standardizing concentrations of drugs used for continuous infusion, equations are no longer necessary to calculate the concentration of drug in infusates (see below). Thus, another opportunity for error is bypassed. Standardized concentrations can now be used for most neonatal infusions since modern infusion pumps can deliver smaller fluid rates more precisely than in the past.

Standardized dosing may also be used for medications that are given intermittently. Such methods coupled with specification of volumes to be drawn up by the nursing unit (or by the pharmacy, in unit-dose dispensing systems) further diminish the chances of error. Drugs that are highly concentrated and thus difficult to measure (e.g., dexamethasone) and those that are part of the unit's floor stock (e.g., controlled substances) are ideal for standardized dosing.

CALCULATIONS

Miscalculations were a frequent cause of prescribing errors in recent studies of pediatric hospital pharmacy services.^{1,4} They ranged from use of the wrong equation to arithmetical errors, including misplaced decimal.⁶ Following are some of the techniques we have used to remove calculations from the prescribing process and thus prevent miscalculation errors.

Some calculations can be avoided by using standard concentrations of drugs in conjunction with dosing charts for prescribing potentially life-threatening drugs such as vasopressors or insulin (Appendix); only the drug infusion rate (amount/kg/time unit) needs to be ordered - no calculations are necessary. Alternatively, these charts can be used to doublecheck calculations. Design features such as paper color-coding, background shading color or text font variations facilitate the distinction of adjacent rows and columns. Limiting weight and dosage increments to clinically significant changes also minimizes clutter.

Computer-generated code cards and other medication dosing sheets decrease the need for repeated manual calculations and consequent human errors. Alas, computers also automate and magnify errors. In the early days of using an automated code card-generating spreadsheet, a weight of "700" (grams) was entered instead of 0.7 (kg), such that all resulting doses were incor-

rect by ~100-fold. A subsequent user overcame maximum value warnings and restrictions by entering the weight value as text, which has a numerical value of zero; all resulting medication doses equaled zero. Both sheets appeared signed at the bedside, and the errors went unnoticed for several days! To prevent this type of error, the application can be customized to restrict the range of input values for the cell containing body weight, and to return a warning message when values likely outside of common weight ranges are entered. For example, using Excel[®] to generate a "code card" in NICU, the *weight* cell can be formatted to display one decimal. Then, values can be restricted by using the Data/Validation feature (Allow: *Decimal* / Data between: 0.2 and 9.9 / Input message: *Enter weight in kg, with ONE significant digit* / Error Alert: Style: *Stop*; Title: *Error! Weight not likely in NICU patient*; Error Message: *Weight must be between 0.2 and 9.9 kg*). The cells for the patient's name and weight must remain unlocked; the remainder of the spreadsheet, particularly cells containing formulas, should be locked and password-protected, before the form is placed into general use. As further verification, we require the weight value to be handwritten next to the prescriber's signature, to ensure that the weight entered is actually looked at after it is printed. In recent years, no errors in calculation have been detected on the NICU code sheets.

PRESCRIPTION WRITING

Using a standard weight format in NICU and writing this weight on every order sheet, allows for easy crosschecking of prescribed doses. This is further facilitated by entering the amount/kg per "day" (spelled out) or, preferably, per "dose" (also spelled out), and the total dose ordered (with units of measurement). Units should be separated by a space from the number, and clearly spelled out: writing "mcg" (better yet, "micrograms"), not "µg"; "unit", not the abbreviated form "U" or "u", which can look like a zero. Also, all writing should be legible. For substances whose quantification can be expressed in more than one type of unit, bilateral communication among prescriber, nurse, and pharmacist should be expected to ensure that the units ordered were written as intended - writing "mmol" or "mEq" instead of "mg" can result

in fatal overdoses.¹¹ When residents rotate through various pediatric services, it is helpful to use the same standard language and units of measure for medication dosages across services; using micrograms/kg/hr as dosage units for morphine infusions in a PICU and mg/kg/hr in a NICU at the same institution can confuse housestaff and pharmacists. Standard prescription language can be defined by institutional Pharmacy and Therapeutics committees.¹²

Final prescribed doses or volumes should be rounded off when possible. The ability of newer infusion pumps to deliver fractions of an mL/hr has created an illusion of precision in our ability to predict, specify, and deliver the exact needs of micro-patients. If the delivery of 60 mL/kg/day of fluids would require 4.3 mL/hr, using 4 mL/hr would yield a clinically equivalent intake of 56 mL/kg/day. The "4" is easier to add up repeatedly in the fluid intake columns of bedside flowsheets than "4.3", and thus more likely to result in error-free totals; errors of addition also become easier to detect by visual inspection. In this setting, it may be preferable to be imprecisely correct than precisely incorrect.

Poor lettering and numbering, made more illegible by carbon copy or facsimile renditions of original orders, can make decimals disappear; decimals written on existing page lines can also be invisible. This is another reason for always using a zero to the left of the decimal point and for dropping zeros to the right of the decimal when writing medication or fluid doses as decimals. When writing out a large number (e.g., 150,000), spelling it (one hundred and fifty thousand) prevents misinterpretation as 1,500,000 - we find it necessary to apply this rule when writing bank checks! Lettering style has also been the source of tenfold error when the decimal point is omitted and replaced by a superscripted digit (Figure) or exaggerated by a line which can be mistaken for a "1". Again, only a standard style should be used for writing decimal points.

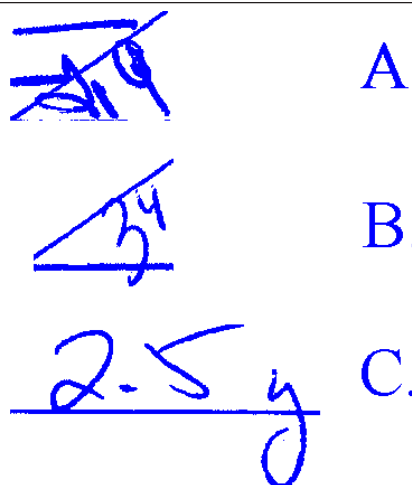
Drugs may also be delivered as multiples of the intended dose if they are available as multiple different salt forms (e.g., phosphate salts, iron, calcium, erythromycin). Other drugs have multiple ingredients (e.g., Polycitra, trimethoprim-sulfamethoxazole, acetaminophen with codeine). When prescribing compounded drugs, the intended amount of at least one of the components must be specified explicitly, such

that the prescribed amount refers clearly to a particular component (elemental form, base, salt, or ingredient). Unambiguous language is essential. Furthermore, the corresponding units must be entered correctly. In the authors' experience, "caffeine" has been ordered literally, while using caffeine citrate dosing guidelines. Pharmacists then incorrectly assumed that the prescribers meant "caffeine base" and converted ordered amounts to be delivered as caffeine base. For a period of several months, all infants received twice the intended dose, albeit without observable consequences. When 2 mEq of Polycitra are prescribed, does this refer to 2 mEq of Na⁺, K⁺, or citrate? An incorrect assumption in this situation was catastrophic. Similarly, prescribing "mmol" instead of "mg" of phosphorus could prove fatal.¹¹

TRANSCRIPTION PHASE

Prescribers should entirely re-write orders that are messy or potentially confusing. Often, direct communication with nursing and pharmacy helps prevent potential confusion, *a priori*. When nurses or pharmacists decipher an order, if it is illegible or in any way unclear, full clarification should be requested from the prescriber. This includes all the data essential for indepen-

Figure. Non-standard calligraphy style as sources of tenfold errors.



A. Decimal point exaggerated as a line which was mistaken for a "1" (number intended was 2.9, interpreted as 219). B. Decimal point omitted and replaced by a superscripted digit (number intended was 3.4, used as 34). C. The order intended was "2.5 mg", and it was interpreted correctly; however, renditions of "mg" by this writer are easily read as "g".

dent recalculation of doses (patient's weight, dose/kg, total dose, frequency, units of measurement) and possibly, indication.

Transcription of telephone or verbal orders, whether to a nurse or pharmacist, is prone to errors that can be minimized by using systems such as a "5 Rs" checklist sticker (i.e., right patient, right drug, right dose, right time and right route). Furthermore, when a verbal order is taken, the individual taking the order should write it down immediately, and then read it back to the caller. Using a standard institutional mechanism for order clarification helps to overcome conflicts based on "rank" and serves as a mechanism for providing education and feedback to prescribers. Errors in the phases from calculation to transcription are expected to decrease with implementation of computerized physician order entry (CPOE) systems in the next few years. CPOE removes problems of interpretation and calculation from clinicians, and it can also add decision support, range restrictions, and logical checks appropriate to NICU patients. For example, mechanisms must be implemented to ensure that weights of newborns are updated at appropriate intervals and that they are consistent with gestational and postnatal age.

CPOE has decreased medication errors in adults,¹³ and it has the potential to minimize dosing errors in pediatric inpatients.¹⁴ However, ten-fold dosing errors still occurred despite the use of CPOE in pediatric emergency rooms,¹⁵ and the effectiveness of this tool has not been demonstrated in a NICU setting. Additionally, if the system is not "fool-proof," erroneous values displayed on a computer may be considered "correct" by caregivers who assume that results of electronic computations cannot be wrong.

DRUG PREPARATION

Additional errors can occur when volume of stock solution must be calculated. Physicians and nurses, regardless of experience, perform poorly at this task.¹⁶ More "precise" original orders (i.e., with excessive significant digits or non-standard values such as 142 mg of ampicillin), are more complicated to compute and, thus, are more likely to result in erroneously calculated volumes. At this step, calculations could be minimized, and standardization of drug preparation is an effective method of minimizing errors.

One method of standardizing volume calculations is the use of pre-printed dose/volume charts, which are a rough, yet useful guide to accurate dosing. When critical calculations are needed and once they are double-checked by a coworker, the second set of calculations should be started anew, without seeing any part of the prior calculations or equation, so that the results are arrived at independently.

Those who prepare the dose should exert the effort to read vial labels carefully in order to avoid confusing concentration with vial size, color or total amount of drug. This is a step where systematic error is common. Predictably, pharmacy departments that have instituted unit dosing have greatly minimized the numbers and consequences of errors at this level.¹⁷⁻²⁰

ADMINISTRATION

Punching an incorrect number sequence into a programmable infusion pump may result in rapid and precise delivery of a very incorrect and potentially toxic dose – a process sometimes called "death by decimal".²¹ These are new types of errors, which have not been the subject of systematic study, except in a newspaper report.²¹ Recent discussions on the NICU-net, regarding unintended boluses of fat emulsion, suggest that pump programming errors are common in at least some NICUs. We are aware of at least some internal underreporting of infusion pump incidents in our NICU, particularly when the errors are relatively harmless, as when continuous orogastric feedings are unintentionally infused as a bolus.

Different devices are prone to be associated with unique types of data entry errors, dependent on how numbers are input. For example, pumps that require direct numerical keypad entry may be prone to number transposition errors (e.g., 60 instead of 06, for an intended 0.6). Pumps that have a mode for entry of volume over time (rather than hourly rate) can be incorrectly programmed by transposing volume and time values or by entering incorrect units of time (e.g., minutes instead of hours).

Staff education, stressing visual review and confirmation of number entry, is most important. Some NICUs require double-checking of initial infusion rates by another caregiver. Some pumps can also be programmed to limit the types and

ranges of data entered; having pumps dedicated to specific types of infusions could enhance safety, but it would be too inflexible and expensive.

The likelihood of errors at this step may be decreased by a policy of ordering and entering particular types of infusion in standardized formats. For example, a NICU might choose to routinely order fat emulsion infusions either as a total volume to be given over a number of hours or as a volume/hr, but not either way, arbitrarily. The chosen practice should be congruent with equipment capabilities, staff experience, and related clinical practices. In our NICU, we further standardized infusion rates for fat emulsions, such that prescribing between 5 and 10 mL/d will automatically result in an infusion rate of 0.5 mL/hr, 21–30 mL/d corresponds to 1.5 mL/hr, etc. We have found that “non-standard” rates are rarely necessary, and, by this simple intervention, we have essentially eliminated unintended rapid infusions of Intralipid, compared to a baseline of 8 to 12 unintended bolus infusions per year previously reported to the NICU’s incident reporting system.

CONCLUSION

Drug prescription errors will likely persist, even with increased vigilance, given the average levels of stress and workload.^{20,22,23} Tenfold drug dosing errors still occur despite the use of both computerized order entry and unit-dose dispensing.¹⁵ The nature of medication errors committed will likely change as the systems for prescribing and administering drugs evolve. Accurate quantification of the frequency of these errors at all levels is extremely difficult and resource intensive.^{2,15} Therefore, as in our case, one cannot confidently measure the number of errors nor the results of implementing multiple changes throughout a drug administration system to eradicate similar errors.

These difficulties should not dissuade practitioners and institutions from developing and adapting methods for error minimization. Application of the principles and practices outlined herein requires customization to the needs and environment of each unit of patient care. One may approach multiple-of-dose errors systematically through monitoring (reports plus observations), followed by multidisciplinary analyses

of patterns and root causes. These will necessarily result in standardized modifications of multiple steps in the prescription-to-administration sequence, aimed at minimizing the frequency and consequences of prescription errors.^{12,20,24-26}

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PATIENT NAME _____ ACCT # _____

ALBANY MEDICAL CENTER CONTINUOUS INFUSION DOSING CHART

SUGGESTED STARTING DOSE-	
(Splenic/Renal):	1-5 mcg/kg/min
(Inotrope):	6-10 mcg/kg/min
(Pressor):	>10 mcg/kg/min
INCREMENTAL CHANGES:	2.5 mcg/kg/min
DOSAGE RANGE- (USUAL):	3-10 mcg/kg/min
(MAXIMUM):	20 mcg/kg/min

DOPAMINE 1mg/ml D5W "Pink"
(1mg/ml = 1000mcg/ml)

CENTRAL LINE ONLY

Weight	Doses as mcg/kg/min							
	3	5	7.5	10	12.5	15	17.5	20
0.5 kg	0.1	0.2	0.2	0.3	0.4	0.5	0.5	0.6
0.6 kg	0.1	0.2	0.3	0.4	0.5	0.5	0.6	0.7
0.7 kg	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
0.8 kg	0.1	0.2	0.4	0.5	0.6	0.7	0.8	1
0.9 kg	0.2	0.3	0.4	0.5	0.7	0.8	0.9	1.1
1 kg	0.2	0.3	0.5	0.6	0.8	0.9	1.1	1.2
1.1 kg	0.2	0.3	0.5	0.7	0.8	1	1.2	1.3
1.2 kg	0.2	0.4	0.5	0.7	0.9	1.1	1.3	1.4
1.5 kg	0.3	0.5	0.7	0.9	1.1	1.4	1.6	1.8
1.8 kg	0.3	0.5	0.8	1.1	1.4	1.6	1.9	2.2
2 kg	0.4	0.6	0.9	1.2	1.5	1.8	2.1	2.4
2.5 kg	0.5	0.8	1.1	1.5	1.9	2.3	2.6	3
2.8 kg	0.5	0.8	1.3	1.7	2.1	2.5	2.9	3.4
3 kg	0.5	0.9	1.4	1.8	2.3	2.7	3.2	3.6
3.5 kg	0.6	1.1	1.6	2.1	2.6	3.2	3.7	4.2
3.8 kg	0.7	1.1	1.7	2.3	2.9	3.4	4	4.6
4 kg	0.7	1.2	1.8	2.4	3	3.6	4.2	4.8
4.5 kg	0.8	1.4	2	2.7	3.4	4.1	4.7	5.4
4.8 kg	0.9	1.4	2.2	2.9	3.6	4.3	5	5.8
5 kg	0.9	1.5	2.3	3	3.8	4.5	5.3	6

Values appear as ml/h

COMPATIBLE INTRAVENOUS FLUIDS:

D5W, NS, and any combination of the two including those containing potassium.
 Do NOT use any other IV solutions.

Provided by the Departments of Pharmacy/Pediatrics