Comparing Three Methods for Dilution Accuracy of Intravenous Preparations

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Purpose: *Dilutions of intravenous medications may be inaccurate. The mixing technique may be a crucial factor.*
Design: *Three factors of dilution were tested: volume for dilution (large vs small), method for mixing (shaking vs inversion), and number of maneuvers (3 times vs 10).*
Methods: *Dilutions of glucose in saline solution were made by nurses, after a random factorial plan. The judgment criteria were the comparison between measured (Cmes) and expected (Cexp) concentration.*
Finding: *Cmes (n = 40) ranged from 89.5% to 123.6% of Cexp and was more accurate when made with a large volume (98.4% of Cexp vs 106.5%) and when mixed by inversion (100.6% of Cexp vs 104.6%).*
Conclusions: *Inversion rather than shaking and dilution in a large volume is a simple procedure for bedside medication preparation that allows better accuracy. The 3 versus 10 mixing procedures resulted in the same accuracy, which may be important for these time-consuming procedures. These results should be confirmed in clinical situations.*

Keywords: *pharmaceutical solutions/administration & dosage, administration, intravenous, syringes, research.*

ADDED TO THE RISK OF ERROR, inaccuracy of bedside preparation of intravenous (IV) medications is known to be higher[1-10] than in manufactured products, with a larger difference between the intended and delivered doses. To our knowledge, the first report of inaccuracy of bedside preparation in the medical literature showed that a very common procedure (supplementation of potassium in a normal saline container), made without standardized protocol,[9] led to life-threatening situations. The second report concerned acetylcysteine preparation,[2] where 10% of preparations had 50% or more variation from the expected concentration. Since then, several publications issued from adult[3,4] or pediatric[5,6] intensive care units have also reported inaccuracies ranging from 10% to 25% for electrolytes,[4] antibiotics,[5,6] vasopressors,[3] and sedative drugs.[3,4] Although these inaccuracies are clearly differentiated from errors,[8,9] the time-consuming nature of preparing IV solutions may predispose them to true errors.[10]

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Inaccuracy of diluted medications is inherent to any bedside preparation and would not be diminished by any politic in error prevention. Furthermore, the lack of pharmaceutical formulations fitted to the patient frequently requires bedside dilutions, especially in operating rooms, intensive care units, and pediatric nursing. Pediatric and neonatal nursing are particularly at risk as reconstitution of the medication most often requires only a fraction of the formulation. The magnitude of this inaccuracy may have pharmacokinetic, pharmacodynamic, and moreover, clinical consequences as the concentration (and so the amount) of medications actually delivered to the patient may differ more than 20% of the expected concentration.

Drug preparation is a complex and time-consuming task[10] and needs to be better analyzed.[3] The task requires the implementation of several different and complex steps: dose calculation, volume measurement, and mixing of the solutions. Mixing may be the most crucial step[7] as it should be assumed that for each other step of the process, the solution is already homogenous. Although poorly studied, the mixing technique can explain the main component of the observed inaccuracy.[1,3,8] To our knowledge, there are neither recommendations nor guidelines for nurses, and no systematic and rational approach has yet been published. The only available French basis are the International Organization for Standardizations norms,[11] which states that syringes should not be used for volume inferior to the half of their nominal capacity. Because of this lack of recommendations, nurses face too many choices for bedside preparations to obtain the required dose.

To test three of the several factors involved in dilution (volume of the dilution, mode of mixing, and number of repetition of mixing), we choose to dilute glucose in a saline solution.

This study focused only on the accuracy of the obtained concentration, analyzing the difference between the expected and measured concentrations.

Materials and Methods

Preparations were made by nurses of our unit over a 1-month period in June 2011, after a random pre-established three-factor factorial plan. We mimicked preparations commonly made in our unit. Observations of actual practices in the unit and several interviews of experienced nursing staff led us to the conclusion that three factors were always considered: volume of dilution, mixing modality, and number of maneuvers for mixing.

The objective of this study was to compare the measured concentration (Cmes) to the expected concentration (Cexp) of glucose in a dilution of a glucose solution in an isotonic saline solution, with analysis of the effect of three factors:

- volume for dilution: a 10-mL syringe versus a 100-mL bag
- mode of mixing: shaking versus inversion
- times of mixing: 3 versus 10.

The needed number of measurements was calculated from a previous study conducted in our unit, for an expected difference of accuracy of 10%, with an α risk of 0.05 and a β risk of 0.80.

For the first factor (volume of dilution), two different one-step preparations were compared, with two different volumes for dilution:

- 5 mL of 10% glucose mixed in 100-mL infusion bags full of 0.9% saline solution, for an expected glucose concentration of 23.8 mmol/L.
- 1 mL of 5% glucose mixed with 9 mL 0.9% saline solution quantum satis 10 mL, for an expected glucose concentration of 25 mmol/L

The second (shaking vs inversion) and third (3 vs 10 times) factors were made for each preparation after a random pre-established factorial plan. About 2 mL of each preparation was sampled, and glucose concentration was then measured (Rapidlab 1265; Siemens, Erlangen, Germany).

Results for each preparation were expressed as percentage of the expected concentration. Comparisons were made with a multivariate analysis of variance.

Results

In the 40 preparations (ie, five repetitions in a factorial plan with three factors: $2^3 \times 5$), the measured concentrations of glucose (expressed as the percentage of the expected one) were widely distributed, ranging from 89.5 to 123.6 (median, 100.3; first and third quartiles, 97.0 to