Teaching undergraduate students appropriate dose calculations in relation to intravenous infusion

Medical emergencies such as cerebral malaria, diabetic coma, cardiogenic shock and many more require immediate treatment with parenteral drug administration. Intravenous (I.V.) infusion is one of the commonly preferred routes for this purpose. As one of the goals of undergraduate training is to train students in managing patients,[1] it is mandatory that the students acquire a sound knowledge of certain basic steps of intravenous drug infusion. These include dose calculation (viz., based on body weight and body surface area) and clinical skills (viz., proper collection of drugs from ampoule/vial, introduction of drug into suitable diluting fluid, i.v. drip setting, etc.). One of the ways to achieve such a goal is by including many exercises on calculation of infusion rates in the undergraduate pharmacology practicals curriculum.

As dose calculation is an important initial step in such clinical procedures, we have emphasized it in relation to different aspects such as the following:

**Total dose**: The infusion rate will not differ in case of total dose administration (e.g., infusion rate of quinine will remain the same for a 30, 50 or a 70 kg patient since it is given in the dose of 10 mg/kg in 500 ml of 10% dextrose solution which is to be administered over 4 h). In contrast to this, the infusion rate will differ when drugs are to be given at the specified rates (e.g., infusion rate of aminophylline will differ for a 30, 50 or a 70 kg patient since it is to be given in the dose of 1 mg/kg/hr in 500 ml of normal saline).

**Weight (mg/kg)**: The weight-based dose calculation (mg/kg) is more popular despite certain disadvantages, viz., one needs to know the different doses according to body weight (mg/kg) as well as according to the age of the patient.[2]

**Body surface area**: Body surface area (BSA) is another method which is considered as a more accurate basis for dose calculation.

The following comparison will provide a better understanding of the problems which may arise due to a mistake in calculating the infusion rate. [Please refer to next page]

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**1. Dose calculation of Inj. quinine required:**

i.e. \( \frac{500 \text{ mg}}{10 \text{ mg/kg}} \)

**2. Calculate the required volume of Inj. quinine:**

One ampoule Inj. quinine contains 300 mg/ml (2 ml amp)

So, 500 mg of quinine will be present in \( \frac{1}{300} \times 500 = 1.67 \text{ ml} \).

**3. Selection of fluid**

10% dextrose solution

**4. Calculate the rate of quinine infusion.**

Introduce 1.67 ml of Inj. quinine into 500 ml of 10% dextrose solution, which is to be administered over 4 h.

So, the desired rate of administration will be:

\[
\text{500 ml} \text{ to be given in } 4 \text{ h} \\
\text{125 ml to be given in } 1 \text{ h (60 min)} \\
\text{i.e.} \frac{125}{60} = 2.08 \text{ ml/min} \\
\text{Thus, in 1 min, 2.08 ml (approx. 2 ml) is to be given} \\
1 \text{ ml} = 16-20 \text{ drops in normal i.v. set} \\
\text{So, the rate of quinine administration will be 32–40 drops/min.}
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**1. Dose calculation of Inj. aminophylline required:**

i.e. \( \frac{30 \text{ mg}}{1 \text{ mg/kg}} \)

**2. Calculate the required volume of Inj. aminophylline:**

One ampoule Inj. aminophylline contains 25 mg/ml (10 ml amp, 2.5% W/V)

So, 30 mg of aminophylline will be present in \( \frac{1}{25} \times 30 = 1.2 \text{ ml} \).

**3. Selection of fluid**

Normal saline solution

**4. Calculate the rate of aminophylline infusion.**

Introduce 1.2 ml of Inj. aminophylline into 500 ml normal saline, which is to be administered over 1 h.

So, the desired rate of administration will be:

\[
\text{500 ml} \text{ is to be given in 1 h (60 min)} \\
\text{i.e.} \frac{500}{60} = 8.33 \text{ ml} \\
\text{Thus, in 1 min, 8.33 ml is to be given} \\
1 \text{ ml} = 16-20 \text{ drops in normal IV set} \\
\text{So, the rate of aminophylline administration will be 133–167 drops/min.}
\]
calculation since total body water, extracellular fluid volume and metabolic activity are better paralleled by it. The BSA of an individual can be calculated from the formula of Dubois

\[ \text{BSA (m}^2\text{)} = \text{Body weight (kg)}^{0.425} \times \text{Height (cm)}^{0.725} \times 0.007184 \]

or obtained from chart-form/slide-rule nomograms based on body weight and height. Dose recommendations in terms of BSA are available only for a limited number of drugs (e.g., anticancer drugs) as this method is more cumbersome in clinical practice.[3]

**Average adult body weight:** The dose can also be calculated by using the average adult body weight (60–70 kg) basis from the formula: [Individual dose = Body weight (kg)/70 × average adult dose].[3]

**Diluting fluid:** Selection of a suitable diluting fluid is necessary for i.v. infusion. For example, 10% dextrose solution is being used for quinine infusion, which prevents hypoglycemia due to hyperinsulinemia caused by the powerful stimulatory effect of quinine on pancreatic beta cells,[14] whereas dopamine infusion is given with 5% dextrose (acidic pH) solution for its compatibility and stability with the latter (i.e., 5% dextrose).[3]

Some problems that may be encountered during dose calculation are listed below.

1. **Following the same steps of dose calculation for different drugs**

   To calculate the rate of quinine infusion is simple since quinine is to be given in 500 ml of 10% dextrose solution, to be administered over 4 h (i.e., we have to administer 500 ml of 10% dextrose solution with the required dose of quinine over 4 h).

   But students can make mistakes if they follow this step of rate calculation for calculating the infusion rate of other drugs that are to be administered by their specified infusion rates (e.g., aminophylline: 1 mg/kg/hr). Therefore, the students should be taught these aspects as well since many drugs come under this category (e.g., dopamine, insulin and oxytocin). [Please refer comparison given on page 1]

   Thus, it is obvious that such an infusion rate for aminophylline (133–167 drops/min) is not practically feasible.

   The correct calculation for the rate of aminophylline infusion is given below.

   ➢ **Exercise:** You have decided to give i.v. infusion of aminophylline for a child (10 years old, 30 kg) suffering from acute bronchial asthma (Dose: 1 mg/kg/hr). Set an i.v. drip for this patient.

   ➢ **Answer:**

   A. Calculate the required dose of Inj. aminophylline:
   - i.e. 30 mg of Inj. aminophylline (1 mg/kg)

   B. Selection of fluid:
   - i.e. Normal saline

   C. Aminophylline is available as 2.5% W/V in 10 ml ampoule, i.e. 250 mg/10 ml.

   Introduce all 10 ml of Inj. aminophylline into 500 ml of normal saline solution.

   Now we have 250 mg in 500 ml of normal saline solution, i.e. 30 mg will be present in 30/250 × 500 = 60 ml, which is to be administered in 1 h.

   So, the desired rate of administration will be:
   - 60 ml to be given in 1 h (60 min),
   - i.e. 60/60 = 1 ml/min

   Thus, in 1 min, 1 ml is to be given
   - i.e. 60–67 drops/min

   So, the rate of aminophylline administration will be 16–20 drops/min.

   OR

   Introduce all 10 ml of Inj. aminophylline into 500 ml of normal saline solution.

   i.e. 500 ml of normal saline solution contains 250 mg of aminophylline

   So, 1 ml will have 1/500 × 250 = 0.5 mg of aminophylline.

   So, 30 mg will be present in 30/0.5 × 1 = 60 ml, which is to be administered in 1 h.

   Therefore, the desired rate of administration will be:
   - 60 ml to be given in 1 h (60 min)
   - i.e. 60/60 = 1 ml/min

   Thus, in 1 min, 1 ml is to be given
   - i.e. 60–67 drops/min

   So, the rate of aminophylline administration will be 16–20 drops/min.

2. **Dose calculation by different methods**

   **Problem:** Calculate the required dose for aminophylline infusion for a child suffering from acute bronchial asthma (12 years old, 37 kg, BSA 1.25 m²; Dose: 1 mg/kg/hr).

   **Solution:**

   A. **mg/kg basis:**
   - i.e. 37 mg/hr

   B. **Average adult body weight (60–70 kg) basis:**
   - Formula: [Individual dose = Body weight (kg)/70 × average adult dose]
   - i.e. 37/70 × 70 = 37 mg/hr

   C. **BSA-based rule:**
   - Formula: [Individual dose = BSA (m²)/1.7 × average adult dose]
   - i.e. 1.25/1.7 × 70 = 51 mg/hr

   **D. Salisbury rule (proposed for children):**[8]

   • Less than 30 kg: (Weight × 2) percentage of the adult dose of a drug
   • More than 30 kg: (Weight + 30) percentage of the adult dose of a drug

   According to this, (37 + 30) percentage of the adult dose of a drug
   - i.e. 67% of 70 mg of aminophylline,
   - i.e. 47 mg/hr

   This shows that there is no difference in doses calculated by mg/kg and average adult body weight-based rules, but there is a definite difference when both are compared with the BSA-based rule. The dose calculated by the Salisbury rule is closer to the BSA-based value.
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Metabolism of theophylline (aminophylline) is often faster in children, after the first year of life, than in adults; and there is a marked interindividual variation in the rate of its elimination (average half-life is about 3.5 h in young children as compared to 8-9 h in adults).[3, 4] Considering these pharmacokinetic parameters as well as the narrow safety margin of aminophylline, the more accurate BSA-based rule may be preferred for dose calculation, keeping in mind its limited application in a clinical set-up.

3. Dose calculation in relation to time duration

Paclitaxel (an anticancer drug) is to be given in different schedules [Schedule 1: 175 mg/m² over 3 h (infusion rate: 58 mg/m² per hour, plasma clearance: 212 ml/min per m²) and Schedule 2: 175 mg/m² over 24 hours (infusion rate: 7 mg/m² per hour, plasma clearance: 393 ml/min per m²)]. A practical problem may arise if one calculates the dose of paclitaxel for schedule 2 from schedule 1. The dose and infusion rate will become 1400 mg/m² and 58 mg/m² respectively, which appear very different from the actual schedule 2 for 24 h. As clearance of paclitaxel is saturable and decreases with an increasing dose or dose rate, such probable mistakes will definitely affect the clinical response.

To conclude, during undergraduate pharmacology practicals, different aspects, such as total dose, weight (mg/kg and average adult body weight basis), BSA, time duration and diluting solution, as well as likely practical problems that may arise during dose calculation, should be highlighted by demonstrating different exercises on the calculation of infusion rates.

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