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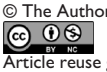

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Quantitative assessment of required separator fluid volume in multi-infusion settings

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Abstract

Background: Administering a separator fluid between incompatible solutions can optimize the use of intravenous lumens. Factors affecting the required separator fluid volume to safely separate incompatible solutions are unknown.

Methods: An intravenous tube (2-m, 2-mL, 6-French) containing methylene blue dye was flushed with separator fluid until a methylene blue concentration ⩽2% from initial was reached. Independent variables were administration rate, dye solvent (glucose 5% and NaCl 0.9%), and separator fluid. In the second part of the study, methylene blue, separator fluid, and eosin yellow were administered in various administration profiles using 2- and 4-mL (2 × 2 m, 4-mL, 6-French) intravenous tubes.

Results: Neither administration rate nor solvent affected the separator fluid volume ($p = 0.24$ and $p = 0.12$, respectively). Glucose 5% as separator fluid required a marginally smaller mean ± SD separator fluid volume than NaCl 0.9% (3.64 ± 0.13 mL vs 3.82 ± 0.11 mL, $p < 0.001$). Using 2-mL tubing required less separator fluid volume than 4-mL tubing for methylene blue (3.89 ± 0.57 mL vs 4.91 ± 0.88 mL, $p = 0.01$) and eosin yellow (4.41 ± 0.56 mL vs 5.63 ± 0.15 mL, $p < 0.001$). Extended tubing required less separator fluid volume/mL of tubing than smaller tubing for both methylene blue (2 vs 4 mL, 1.54 ± 0.22 vs 1.10 ± 0.19, $p < 0.001$) and eosin yellow (2 vs 4 mL, 1.75 ± 0.22 vs 1.25 ± 0.03, $p < 0.001$).

Conclusion: The separator fluid volume was neither affected by the administration rate nor by solvent. Glucose 5% required a marginally smaller separator fluid volume than NaCl 0.9%, however its clinical impact is debatable. A larger intravenous tubing volume requires a larger separator fluid volume. However, the ratio of separator fluid volume to the tubing's volume decreases as the tubing volume increases.

Keywords

Infusions, intravenous, infusion pumps, disposable equipment, vascular access devices, spectrophotometry, ultraviolet

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Introduction

Flushing procedures to clean intravenous (IV) tubing and catheters are common practice whenever solutions are administered intravenously.[1] IV tubing, which connects an IV bag or syringe to the patient's IV access, is flushed to make sure all drugs present in the tubing are delivered into the bloodstream of the patient.[2] IV catheters need to be flushed and locked at the end of infusion to clear or prevent obstruction and thrombus formation, or to reduce bacterial colonization during the period when the catheter is idle.[3,4] Normal saline (NS; NaCl 0.9%) and glucose 5% (G5) are commonly used as a flushing fluids as they are compatible with many IV drugs.[5]

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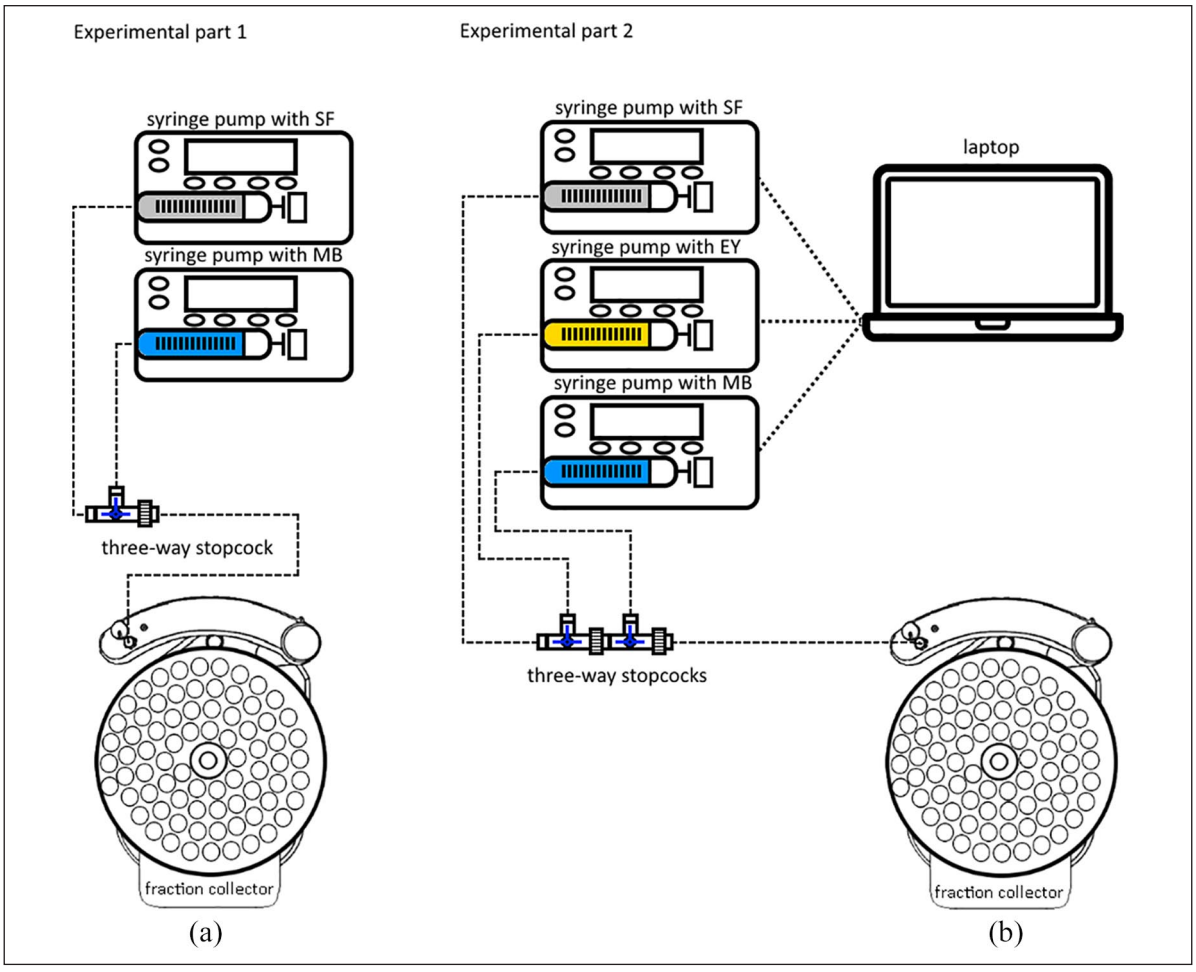

Figure 1. (a) Experimental setup used to investigate whether and how the administration rate, solvent, and separator fluid (SF) affect the required SF volume (SFV). A 2-m (2-mL) IV tube runs between the three-way stopcock and the fraction collector. (b) Experimental setup used to investigate whether and how IV line volume affects the required SFV in different administration profiles. MB: methylene blue, EY: eosin yellow. Depending on the administration profile, either a 2-m (2-mL) IV tube or 2 × 2 m tubes (4-mL) run between the stopcocks and the fraction collector.

Another function of flushing is to separate two incompatible drug solutions that are sequentially administered. A separator fluid (SF) serves to avoid the contact of the incompatible solutions before they reach the bloodstream. When two drug solutions are physically or chemically incompatible, precipitation or inactivation may occur when they are mixed.[5] When incompatible IV solutions must be administered continuously, a common way to address this problem is the use of multiple catheters or multi-lumen catheters that allow for a separated flow of each solution.[6,7] However, even with such systems, the number of incompatible solutions may still exceed the number of available lumens.

In such a case sandwiching a SF between the incompatible solutions facilitates the use of a single lumen for the administration of these solutions.[8] When administering a SF between incompatible solutions it is important to know what minimal separator fluid volume (SFV) is required so that no relevant interaction takes place between the constituents of these solutions.

This volume must be sufficient to avoid mixing, but should not be excessive as patients may have a limited fluid intake regimen.[9,10] The administration rate, drug solvent, choice of SF, and IV tubing volume may also be factors affecting the required SFV.[11–13] However, to our knowledge there is no literature on the requirements of flushing.

In this study we aimed to investigate whether and how the administration rate, drug solvent, choice of SF, its administration rate, and the IV tubing volume affects the SFV required for the safe separation of incompatible drug solutions. Please see Appendix 1 for a list of key-definitions.

Methods

Experimental procedure

Part 1: influence of administration rate, solvent, and SF. In this part of the study we investigated to which extent the administration rate, solvent, and SF affected the required SFV.

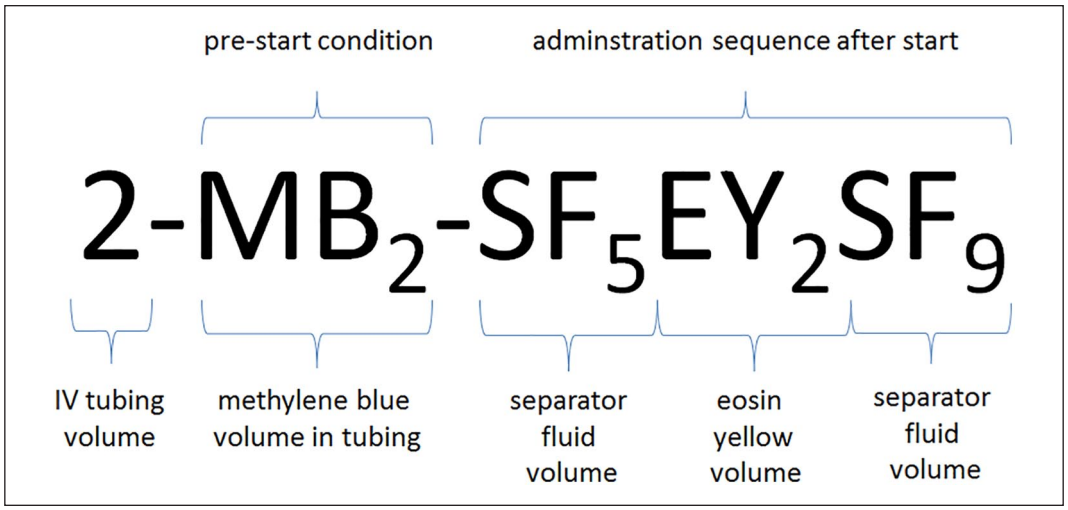

Figure 2. The coding of administration profiles. The three segments (separated by a horizontal line), respectively, represent the IV tubing volume in mL, pre-start condition, and the administration sequence. MB: methylene blue, EY: eosin yellow, SF: separator fluid. Numbers trailing the substance indicators in subscript indicate the volume of the indicated substance in mL.

The experimental setup is shown in Figure 1(a). Three different rates were used: 50, 100, and 200 mL/h.

Quantitative measurements were carried out using ultraviolet−visible (UV-Vis) spectrophotometry, too high concentrations of methylene blue (MB) would result in absorption readings that do not reliably allow detection of concentration differences due to saturation of the measuring cell. Therefore, we chose concentrations that resulted in calibration curves for both dyes in the linear part of the calibration curve. For MB and eosin yellow (EY) this resulted in maximum concentrations of 40 and 75 mg/L, respectively.

MB solutions were prepared in a concentration of 40 mg/L, using NS as solvent in one solution and G5 in the other. The SF was either NS or G5. This resulted in $3 \times 2 \times 2$ (administration rate × solvent × SF) combinations.

A 2-mL (2-m, 6-French) IV tube was completely filled with MB solution. Subsequently an infusion pump containing a syringe with SF was started at one of three administration rates. Samples of 0.67 mL were collected in tubes using a fraction collector. Administration of SF was stopped after 10 mL of SF was administered. Collected samples were transferred from the tubes onto a 96-well plate. This process was performed 3 times for each unique combination of administration rate, solvent, and SF.

For the determination of MB concentrations a calibration curve was made using different dilutions of MB, samples at each concentration were transferred in duplicate onto a 96-well plate. Absorption of MB was measured at 668 nm.

Part 2: influence of system volume in different administration profiles. The experimental setup is shown in Figure 1(b). G5 was selected as solvent and NS was selected as SF for the second part of the study to comply with clinical practice in our intensive care unit (ICU). The goal of this part of the study was to investigate how the IV tubing volume affected the required volume of SF in different administration profiles. The administration rate was kept constant at 50 mL/h. EY was used as a secondary dye, and was dissolved in G5 to a concentration of 75 mg/L. The EY concentration was determined using the same procedure as with MB. Either a 2-mL (2-m, 6-French) IV tube was used, or two 2-mL IV tubes were connected to create a combined IV tubing volume of 4 mL.

An important concept is the shared infusion tubing, which consists of the tubing and connectors that are shared by all fluids. The three-way stopcocks and the IV tubing that runs between the stopcocks and the fraction collector are all considered part of the shared infusion tubing. The volume of the shared infusion tubing is called the shared infusion volume (SIV).

The administration profiles were coded as shown in Figure 2. The coding consists of three parts: IV tubing volume, a start condition that describes the content of the IV tubing before the start of the administration profile, and the order in which MB, SF, and EY are administered with the corresponding volumes.

For example, in Figure 2, 2-mL tubing is used which is filled with 2 mL of MB (MB_2) before the start of the experiment. At the start of the experiment, first 5 mL of SF (SF_5) is administered, followed by 2 mL of EY (EY_2), and 9 mL of SF (SF_9). It must be noted that in profiles where the tubing is filled with MB at the start, the total volume of MB is equal to the SIV, including the three-way stopcocks that are part of the SIV. In profiles with 2 or 4 mL tubing, the SIV is 2.52 or 4.52 mL, respectively.

Three types of administration profiles were created for the two tubing volumes. One profile type started with the

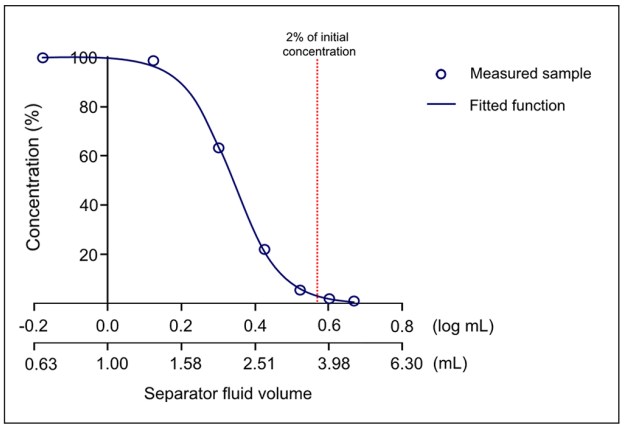

Figure 3. Determination of the SFV at 2% of the initial dye concentration (dashed line). Sample data (circles) were transformed to a logarithmic scale to enable curve fitting (continuous line). The resulting equation was used to obtain the log mL SFV at the 2% concentration, which in turn was transformed back to mL.

tubing completely filled with MB, followed by NS, EY, and NS (2-MB_2-NS_5EY_2 and 4-MB_4-$NS_5EY_4NS_9$). The two other types started with the tubing filled with NS, after which MB, NS, EY, and NS were administered. In these two profiles the administered volumes of MB and EY were both 25% (2-NS_2-$MB_{0.5}NS_5EY_{0.5}NS_9$ and 4-NS_4-$MB_1NS_5EY_1NS_9$), or both 50% of the tubing volume (2-NS_2-$MB_1NS_5EY_1NS_9$ and 4-NS_4-$MB_2NS_5EY_2NS_9$). In two profiles (2-NS_2-$MB_1NS_5EY_1NS_9$ and 4-NS_4-$MB_1NS_5EY_1NS_9$) the administration sequences were identical, only the tubing volume differed.

Each profile was administered three times. Infusion pumps were controlled from a laptop using custom software that allowed predefining administration sequences for automatic execution. The collection of samples and calibration procedures were identical to the first part of the study, with the addition of a calibration curve for EY. EY's absorption was measured at 524 nm.

Determination of SFV. We arbitrarily chose a concentration of 2% relative to the original MB and EY solutions as the cut-off point to determine the minimal required SFV. We assumed that in clinical practice no meaningful chemical interaction would occur at this cut-off point.

GraphPad Prism[14] was used to determine the SFV by curve fitting starting from the data point with the highest measured concentration (Figure 3). For part 1 of the study, nonlinear regression was applied in GraphPad Prism using the "log (inhibitor) vs normalized response–variable slope" setting. In part 2, nonlinear regression was applied using the "plateau followed by one phase decay" setting. The cut-off concentration was entered into the resulting equation to obtain the corresponding SFV.

Materials

Fluids used in the experiments were NS, a 0.9% sodium chloride solution in water, and G5, a 5% glucose solution in water. Both were obtained from Baxter (The Netherlands). MB and EY were obtained from Merck (Germany).

The experimental setup consisted of three Alaris Asena GH syringe pumps (Carefusion, UK), a Pharmacia LKB FRAC-200 fraction collector (Pharmacia, Sweden), a Hewlett-Packard Probook 6560b laptop (Hewlett-Packard, USA), a StarTech ICUSB2324X USB to serial adapter (StarTech, UK), three generic RS232 cables, 50-mL BD Plastipak syringes (Becton-Dickinson, USA), Steritex 3W three-way stopcocks (Codan, Denmark), Vygon V-Green IV (2-m length, 2-mL volume, 6-French outer diameter) IV tubes (Vygon, France), and generic round-bottom polystyrene tubes. Custom software was written in Java (Oracle Corporation, USA) for external coordinated control of the infusion pumps using their serial communication protocol.[15]

UV-Vis measurements were performed using a SYNERGY-HT multiwell plate reader (BioTek Instruments Incorporated, USA), which used Corning Costar 3596 96-well plates (Corning Incorporated, USA).

Statistical analysis

IBM SPSS Statistics was used for the statistical analysis.[16] Statistical significance was determined at a two-sided p-value <0.05.

In the first part of the study, we investigated the influence of administration rate, dye solvent, and SF on the SFV. Group differences for administration rate were assessed using a one-way analysis of variance (ANOVA). If the ANOVA result was statistically significant, post hoc pairwise comparisons with Bonferroni correction were performed. For the variables dye solvent and SF, a Student's t test was performed.

In the second part of the study, SFV required to flush MB and EY from the IV tubing are abbreviated as SFV_{MB} and SFV_{EY}, repectively. The ratio of SFV_{MB} and the SIV ($Ratio_{MB/SIV}$) was calculated by dividing SFV_{MB} by the SIV. A $Ratio_{MB/SIV}$ of 2 indicates the SFV required to flush MB from the IV tubing is twice the SIV. In a similar fashion, $Ratio_{EY/SIV}$ was calculated. Statistically significant differences between groups were assessed using the Student's t test.

Results

SFVs for each combination of administration rate, solvent, and SF in part 1 of the experiment are listed in Table 1. There was no statistically significant relation between administration rate and SFV as determined by a one-way ANOVA ($F(2.33)=1.50$, $p=0.24$). The choice of solvent

Table 1. Separator fluid volume for each combination of solvent, separator fluid, and administration rate.

Solvent	Separator fluid	Rate (mL/h)	Separator fluid volume Mean ± SD (mL)
NS	NS	50	3.80 ± 0.00
		100	3.93 ± 0.06
		200	3.93 ± 0.12
	G5	50	3.60 ± 0.00
		100	3.63 ± 0.06
		200	3.73 ± 0.29
G5	NS	50	3.73 ± 0.06
		100	3.77 ± 0.06
		200	3.77 ± 0.12
	G5	50	3.57 ± 0.06
		100	3.70 ± 0.10
		200	3.63 ± 0.06

SD: standard deviation; NS: normal saline (0.9% NaCl); G5: glucose 5% solution in water.

Table 2. Overall differences in profiles using 2 and 4 mL tubing volume.

IV tubing/shared infusion volume	2 mL/2.52 mL ($n = 9$)	4 mL/4.52 mL ($n = 9$)	p[a]
SFV_{MB} mean ± SD	3.89 ± 0.57	4.91 ± 0.88	0.01
SFV_{EY} mean ± SD	4.41 ± 0.56	5.63 ± 0.15	<0.001
$Ratio_{MB/SIV}$ mean ± SD	1.54 ± 0.22	1.09 ± 0.19	<0.001
$Ratio_{EY/SIV}$ mean ± SD	1.75 ± 0.22	1.25 ± 0.03	<0.001

SD: standard deviation; SFV_X: separator fluid volume required to clear the IV tubing of solution X; $Ratio_{X/SIV}$: ratio of SFV_X and the shared infusion volume; EY: eosin yellow; MB: methylene blue.
[a]Student's *t* test.

Table 3. SFV_{MB}, SFV_{EY}, $Ratio_{MB/SIV}$, and $Ratio_{EY/SIV}$ values in various administration profiles.

Profile	SFV_{MB} Mean ± SD	SFV_{EY} Mean ± SD	$Ratio_{MB/SIV}$ Mean ± SD	$Ratio_{EY/SIV}$ Mean ± SD
2-MB_2-$NS_5EY_2NS_9$	4.52 ± 0.16	5.06 ± 0.16	1.79 ± 0.06	2.01 ± 0.06
2-NS_2-$MB_{0.5}NS_5EY_{0.5}NS_9$	3.27 ± 0.06	3.90 ± 0.36	1.30 ± 0.02	1.55 ± 0.14
2-NS_2-$MB_1NS_5EY_1NS_9$	3.89 ± 0.27	4.29 ± 0.19	1.54 ± 0.11	1.70 ± 0.07
4-MB_4-$NS_5EY_4NS_9$	6.04 ± 0.27	5.70 ± 0.16	1.34 ± 0.06	1.26 ± 0.04
4-NS_4-$MB_1NS_5EY_1NS_9$	4.19 ± 0.13	5.67 ± 0.06	0.93 ± 0.03	1.25 ± 0.01
4-NS_4-$MB_2NS_5EY_2NS_9$	4.51 ± 0.17	5.54 ± 0.21	1.00 ± 0.04	1.22 ± 0.05

Note that normal saline was used as separator fluid in all profiles. SFV_X: separator fluid volume required to clear the IV tubing of solution X; $Ratio_{X/SIV}$: ratio of SFV_X and the shared infusion volume; EY: eosin yellow; MB: methylene blue; NS: normal saline.

had no statistically significant relation with SFV (G5 vs NS mean ± standard deviation (SD), 3.69 ± 0.10 mL vs 3.77 ± 0.17 mL, $p = 0.12$). Using G5 as SF required less SFV than NS (G5 vs NS mean ± SD, 3.64 ± 0.13 mL vs 3.82 ± 0.11 mL, $p < 0.001$). The 95% confidence intervals (CI) for SFs G5 and NS were [3.58−3.71] and [3.77−3.88], respectively.

For experimental part 2, the time courses of concentrations of the six administration profiles can be found in Supplemental Figures S1−S6. Overall differences between profiles using 2 and 4 mL IV tubes are displayed in Table 2. SFV_{MB} was smaller than SFV_{EY} overall (SFV_{MB} vs SFV_{EY}: mean ± SD, 4.40 ± 0.89 mL vs 5.02 ± 0.74 mL, $p < 0.001$). $Ratio_{MB/SIV}$ was smaller than $Ratio_{EY/SIV}$ overall ($Ratio_{MB/SIV}$ vs $Ratio_{EY/SIV}$: mean ± SD, 1.31 ± 0.31 vs 1.50 ± 0.30, $p < 0.001$). Table 3 lists the SFV_{MB}, SFV_{EY}, $Ratio_{MB/SIV}$, and $Ratio_{EY/SIV}$ values of the individual administration profiles.

Discussion

In our first experiment, we investigated the impact of administration rate, solvent, and SF on the SFV. We found a marginal difference between using G5 and NS as SF, but

found no advantage in the choice of solvent or administration rate. In our second experiment, we administered several simulated sequential drug profiles where drug solutions were separated by a SF. We found that extending the IV tubing using an additional IV tube, required a larger SFV. In this case, with the inner and outer diameter of the tubing remaining the same, both the tubing's length and volume were doubled. Per mL of tubing volume we found that the required SFV was smaller when longer tubing was used. To our knowledge, this study is the first to investigate the factors contributing to the requirements of the SFV.

The Royal College of Nursing[1] recommends using at least twice the priming volume of the device for flushing, but does not provide any empirical data to support their recommendation. Another publication recommends a flushing volume of 3−5 mL with no further explanation.[17] One study provided empirical evidence suggesting that flushing twice the priming volume of a Soluset IV system (Abbott Laboratories, USA) is sufficient to deliver >95% of the preceding medication.[18] However, in this study only volumetric infusions were taken into account, whereas syringe pumps that commonly administer more concentrated drug solutions through narrower tubing systems may require different volumes. In our study, we found that for an IV tubing system with a SIV of 2.52 mL, the mean SFV_{MB} was 3.89 mL and the mean SFV_{EY} was 4.91 mL, rendering a $Ratio_{MB/SIV}$ of 1.5 and a $Ratio_{EY/SIV}$ of 2.0. Hence, flushing the system with a SFV that is at least twice the priming volume as a rule of thumb seems reasonable to have sufficient separation between incompatible drugs delivered one after the other.

In part 1 of this study we found that when G5 is used as a SF, a marginally smaller SFV is required than using NS. One explanation might be that G5 is more viscous than NS and therefore slightly more effective as a SF. An alternative explanation may attribute this finding to artifacts in the study. At the start of each experiment, priming of the tubing and starting both the pump and the fraction collector had to be performed manually. Therefore, the difference between G5 and NS may also be caused by human variability. Although statistically significant, a difference between means of only 0.2 mL has little to no impact in clinical practice.

Overall, profiles with longer tubing also required a larger SFV (Table 2). For example, in profile 4-MB_4-$NS_5EY_4NS_9$ both the IV tubing lengths (and volumes) and the administered volumes of MB and EY are twice that of profile 2-MB_2-$NS_5EY_2NS_9$ (Table 3). As there is more MB and EY present in the IV tubing in 4-MB_4-$NS_5EY_4NS_9$, it is not surprising that a larger SFV_{MB} and SFV_{EY} are required compared to 2-MB_2-$NS_5EY_2NS_9$. When comparing 2-NS_2-$MB_1NS_5EY_1NS_9$ to 4-NS_4-$MB_1NS_5EY_1NS_9$, the IV tubing length differs, but the administration sequence is the same. Again, the SFVs are larger with longer tubing. This finding may also be explained by Poiseuille flow, which describes the flow through a cylindrical tube where the cross-section of the tube can be divided into laminae (circular layers of fluid).[19,20] Each lamina has its own velocity. The outer lamina will have a lower velocity than the middle lamina due to friction with the tubing wall. Assuming Poiseuille flow takes place within the IV tubing, there will be a difference when the middle and outer lamina reach the end of the tube. In longer tubing, the contact time with the tubing wall is longer, hence a greater difference in velocities of the lamina and therefore more dispersion will occur. In that case it can be expected that the dye can be measured for a longer period of time, which is illustrated in Supplemental Figure S7. Supplemental Table S8 lists the timespans in which MB and EY were measured at the end of the tubing at a concentration >2%. When the same dye volume is administered at the same rate, but through longer tubing (e.g. when comparing 2-NS_2-$MB_1NS_5EY_1NS_9$ to 4-NS_4-$MB_1NS_5EY_1NS_9$), the dye is measured for a longer period of time. This observation is compatible with more dispersion and that diffusion has taken place, however a larger sample size is required before any conclusions can be drawn. Overall, $Ratio_{MB/SIV}$ and $Ratio_{EY/SIV}$ decrease as the IV tubing's length increases. Future studies must reveal whether shorter tubing also requires a larger SFV proportional to its volume.

Remarkably, SFV_{EY} overall was larger than $SFV_{MB.}$ One explanation may be the higher initial concentration of EY (75 mg/L) compared to MB (40 mg/L). Another explanation may be that EY may adhere more to the IV tubing wall than MB, so that its dispersion is not only caused by laminar flow but also by interaction of the solute with the tubing wall. However, this theory requires further study. It is also possible that this difference was (in part) caused by the layout of the experimental setup (Figure 1b). EY was connected to a three-way stopcock that is more distal from the fraction collector than the three-way stopcock to which MB is connected. The distance from the stopcock to the fraction collector was slightly larger for EY than for MB. The mean difference between SFV_{EY} and SFV_{MB} was 0.6 mL, which is a little over twice the internal volume of a three-way stopcock (0.26 mL). Possibly SFV_{MB} may have been larger than SFV_{EY} if MB was connected to the stopcock distal from the fraction collector instead.

Guiffant et al.[21] found that pulsed (turbulent) flow induced by repeated boluses was more effective in clearing proteins from a catheter than continuous (laminar) flow. Ferroni et al.[22] found similar results when the goal was to reduce bacterial colonization of IV catheters. Although we did not focus on flushing catheters in this study, it is possible that administering SF in a pulsed manner is also more effective in clearing IV tubing of drugs compared to the continuous flow as was studied. The volumes used in the studies performed by Guiffant et al.[21] and Ferroni et al.[22] (10 mL in both studies) were high compared to our study,

especially considering the flushing volume relative to the internal volume of the catheter (0.14 mL) at a ratio of 71 to 1. Considering a patient's fluid restrictions, administering a relative equivalent of 142 mL of SF in 2 mL of tubing would be highly undesirable.[9,10]

In this study, a concentration of 2% of the original concentration was considered sufficiently low to prevent a chemical reaction between the drug solutions in the IV tubing. It must be noted that sampling took place at the end of the IV tube, hence a negligible concentration can be expected in IV tubing segments distal from the patient. We therefore believe that in clinical practice no meaningful chemical interaction will occur at this cut-off point. In some cases a lower cut-off point may be desired, however this would require a larger SFV. This could be relevant to patients with a limited fluid intake regimen. Samples collected using the fraction collector were relatively large (0.67 mL). If it was possible to use a smaller sample volume, this would yield more data points and therefore a more accurate representation of the concentration courses and calculation of the corresponding flushing volumes. A possible concern is whether the dyes used in this study properly reflected the behavior of IV solutions that are used in clinical practice, while also providing sufficient discrimination when measured analytically. MB and EY are soluble in both NS and G5, and can be measured using UV-Vis spectrophotometry. The UV spectra of MB and EY do not interfere with each other, allowing for good discrimination. Hence, we believe that MB and EY serve as suitable models for IV drugs in this experimental setting.

For drugs such as insulin that are known to interact and even adhere to the tubing wall, larger SFVs may be required. The same may hold for highly viscous drug solutions.[3,4,23] For future studies we recommend comparing SFVs for such drugs or drug solutions. We did not study the adsorption of MB or EY on the tubing, however some degree of adsorption is likely as it is known MB can adsorb onto polymer material.[24] The impact of adsorption on our results will require further study. In clinical practice the venous pressure in the patient provides a counter pressure to the administered IV solutions. This counter pressure may be different at the site of a central venous catheter compared with the site of a peripheral venous catheter. In our experimental setup there was no resistance at the end of the tubing, hence it is unknown to which extent such counter pressures would have affected our results. In this study the collected fractions were relatively large and there was a limited number of fractions that could be collected in one experimental run. This limited the number of data points we could acquire and also the number of different drug solutions that could fit in a single administration profile. A future follow up on this study could use continuous diode-array detection (DAD), which would allow sampling at a frequency of 1 Hz.[25] This would also allow for longer and more complex administration profiles.

Conclusion

A larger volume of the IV tubing that is used by multiple drugs, requires a larger volume of SFV. Existing recommendations to flush using a SFV that is at least twice the tubing's priming volume were confirmed in profiles where 2-m (2-mL) tubing was used. The ratio of SFV to the tubing's priming volume, decreases when the tubing is longer. Shorter tubing may require a larger SFV relative to its internal volume. The SFV was not affected by the choice of administration rate or solvent. G5 required a marginally smaller SFV than NS, however its clinical impact is debatable.

Author contributions

F.D. designed the study, performed the statistical analysis, and wrote the paper. D.M. performed the experiments and wrote the paper. W.D. took part in the interpretation of data, critically revised the manuscript for important intellectual content. W.B., D.J.T., and M.W.N. designed the study, took part in the interpretation of data, and critically revised the manuscript for important intellectual content. All authors approved the final version submitted for publication.

Declaration of conflicting interests

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Ethical approval

As this study did not involve any human or animal subjects and did not use any patient data, ethical approval from our institutional review board was therefore considered to be unnecessary for this study.

Data accessibility statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Supplemental material

Supplemental material for this article is available online.

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Appendix 1

Flushing	The administration of a fluid to clear the dead space of IV tubing and catheters of its content.
Flushing volume	The volume of fluid required to successfully perform flushing.
Locking procedure	The practice of filling a catheter with a fluid for a period of time when the catheter is not used. Locking is performed to prevent catheter occlusion and thrombus formation, or to reduce bacterial colonization.
Priming volume	The volume of fluid required to fill the IV tubing ensuring all air is removed from the tubing.
Shared infusion tubing	The part of the tubing that is shared by, and accessible to all IV fluids.
Shared infusion volume	Volume of the shared infusion tubing.
Separator fluid	ntravenous (IV) solution that is used to separate two incompatible solutions within the IV tubing.
Separator fluid volume	The volume of separator fluid required to safely separate two incompatible solutions.
Tubing	The collection of IV tubes and extension sets that connect an IV bag or syringe(s) to the patient's IV access.