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ORIGINAL LABORATORY RESEARCH REPORT

Simulation Analysis of Flow Rate Variability During Microinfusions: The Effect of Vertical Displacement and Multidrug Infusion in Conventional Infusion Pumps Versus New Cylinder-Type Infusion Pumps

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BACKGROUND: Medication dosing errors can occur during microinfusions when there is vertical pump displacement or multidrug infusion through a single intravenous path. We compared flow rate variability between new-generation cylinder-type infusion pumps and conventional infusion pumps under simulated conditions.

METHODS: We evaluated the flow rates during microinfusions using different infusion pumps (syringe pump with 10/30/50-mL syringes, peristaltic pump, and cylinder pump). Two visible dyes were used as model drugs. The study samples were quantified using spectrophotometry. For vertical displacement, the infusion pumps were moved up and down by 60 cm during microinfusions at 0.5 mL·h^{-1} and 2 mL·h^{-1}. In the multi-infusion study, the second drug flow was added through 4 linearly connected stopcocks either upstream or downstream of the first drug. We compared the total error dose between the cylinder pump and the syringe pump with a Mann-Whitney *U* test and additionally estimated the effects of the infusion pumps on total error doses by linear regression analysis.

RESULTS: There were repetitive patterns of temporary flow increases when the pump was displaced upward and flow decreases when the pump was displaced downward in all settings. However, the amount of flow irregularities was more pronounced at the lower infusion rate and in the syringe-type pump using larger volume syringes. The total error dose increased in the syringe pump loaded with a 50-mL syringe compared to that of the new cylinder pump (regression coefficient [β] = 4.66 [95% confidence interval {CI}, 1.60–7.72]; *P* = .008). The initiation and cessation of a new drug during multidrug microinfusion in the same intravenous path affected the lower rate first drug leading to a transient flow rate increase and decrease, respectively. The change in flow rate was observed regardless of the port selected for addition of the second drug, and the total error dose of the first drug did not significantly vary when an upstream or a downstream port was selected.

CONCLUSIONS: In the microinfusion settings, attention must be paid to the use of the syringe pump loaded with large-volume syringes. The novel cylinder pump could be considered as a practical alternative to syringe pumps with small syringes given its flow stability without the need for frequent drug replacement. (Anesth Analg XXX;XXX:00–00)

KEY POINTS

- **Question:** Is there a specific type of infusion pump that can reduce flow rate variability in various microinfusion settings, such as vertical pump displacement or multidrug coinfusion?
- **Findings:** Regardless of the infusion pump type, vertical pump displacement or multidrug coinfusion transiently affected the flow accuracy during microinfusion; however, the flow irregularities were minimized in the syringe-type pump using a small syringe or in the cylinder-type pump.
- **Meaning:** The novel cylinder-type infusion pump could be considered a practical alternative to the syringe pump with a small syringe without frequent drug replacement.

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GLOSSARY

CI = confidence interval; **COVID-19** = coronavirus disease 2019; **EDs** = error doses; **IC** = indigo carmine; **IR** = infusion rate; **TT** = tartrazine

In critically ill patients, infusion pumps are frequently used for continuous infusion of various medications or fluids. Therefore, precise administration at the set flow rate is essential. Maintaining a constant flow rate is especially important in pediatric patients, who use highly concentrated drug solutions that are delivered at low flow rates.[1]

The currently used infusion pumps have good performance and a low error rate of approximately 3% to 10% under normal conditions.[2–5] However, flow interruptions or flow irregularities still occur during vertical displacement or coinfusion of multiple medications through a single path, particularly at low infusion rates (IRs).[6–13] Despite continued improvements in infusion pump hardware, these limitations cannot be fully resolved because of the inherent flaws of the hardware design or the driving mechanism of the infusion pumps.[14–16]

A cylinder-type infusion pump with a new driving mechanism was recently developed to integrate the advantages and compensate for the disadvantages of existing infusion pumps.[17,18] We compared the flow rate variabilities caused by vertical displacements of the pump body between the new cylinder-type pump and representative, conventional infusion pumps with different driving mechanisms. In addition, we also evaluated flow rate variability during multidrug infusions.

METHODS

Study Design

This is an in vitro experimental study observing the flow rate variability of 3 infusion pumps under various settings including vertical displacement and multidrug infusion. In specific, we compared the total error doses (EDs) during low flow infusion among the different infusion pumps by the vertical displacement of the pump body (experiment 1) and during multidrug infusion (experiment 2) to evaluate the effect of the infusion device on the flow rate variability during microinfusion. As the performance of a syringe pump can vary by the volume of the loaded syringe, we initially explored the effect of syringe size on syringe pump flow rate variability in experiment 1. Ethics approval was not required. The experimental design was based on the intravenous drug infusion doses that are possibly used in pediatric critical care settings.

Infusion Pumps

The following 3 infusion pumps with different driving mechanisms were used: a conventional syringe-type infusion pump (Injectomat MC Agilia; Fresenius Kabi) loaded with different volume syringes (10-, 30-, and 50-mL syringes for experiment 1); a conventional peristaltic-type pump (TE-112, Terumo) with a 100-mL normal saline bag; and a new-generation cylinder-type pump (Anyfusion H-100; Meinntech) with a 100-mL normal saline bag.

The flow accuracy and stability of the cylinder-type pump were attributed to the novel operating principle using a high-precision motor control and a dedicated cylinder cartridge that is tightly fixed to the pump body by an autolocking system.[18] Continuous fluid infusion by the cylinder-type pump is based on the rotation of 2 pistons inside a donut-shaped dedicated cylinder cartridge with an independent driver control for each piston. The 2 implanted pistons were programmed to maintain a certain distance during rotation. When a certain amount of fluid is aspirated through the cylinder inlet, the piston in front is pushed forward by the aspirated fluid volume and simultaneously extrudes the same amount of fluid through the cylinder outlet. This unique driving mechanism keeps the amount of fluid constant inside the cylinder cartridge and reduces the accidental bolus injection during piston rotation.

The following will briefly review the working principles of the 2 representative conventional infusion pumps. In the syringe-type pump, the plunger was pushed forward by a linear motion of 1 piston with 1 driver, which continuously extrudes the fluid from the syringe.[19] In the peristaltic-type pump, the peristaltic force waves compress and release the infusion line to administer fluid in a set flow rate.[20]

Reagents as Model Drugs and Study Sample Preparation

Two visible dyes, including tartrazine yellow (TT) and indigo carmine blue (IC), were used as the model drugs. The dyes were freshly prepared with 0.9% normal saline (TT: 0.5 mg/mL, IC: 1 mg/mL) and infused at a rate of 0.5 or 2 $mL \cdot h^{-1}$ as appropriate for the experiment. For the study sample preparation, we collected 3 consecutive fluid drops from the catheter into the 1.5-mL clear microtube every minute.

A 200 µL serial dilution of TT or IC in 0.9% normal saline was prepared to generate the standard curves. These samples and the study samples were distributed into 96-well microplates. The absorbances at 425 nm for TT and 610 nm for IC were read using a microplate ELISA photometer (Mithras2 LB 943, Multimode multiplate reader; The Berthold Technologies) to analyze the concentrations of TT and IC. Standard curves were generated using the linear regression model.

There was no absorbance interference between the 2 dyes. We repeated all experiments 3 times at each setting and averaged the results.

Experiment 1: Flow Irregularities by Vertical Displacement of the Pump Body

Two infusion pumps of each type were used as follows: (1) carrier fluid infusion (0.9% normal saline) at 15 mL·h^{-1}; and (2) infusion of the experimental drug (TT) at 0.5 and 2 mL·h^{-1}. The syringe pump was loaded with a syringe (10/30/or 50-mL) while the peristaltic and cylinder-type pumps were loaded with 100-mL fluid bags, and they were connected to the catheter via 750-mm long tubes 1.0 mm in inner diameter (polyvinyl chloride extension tubes, JMS Hankook Medical) with 3-way stopcocks. All the fluid line extensions were previously filled with 0.9% normal saline, and air bubbles were carefully removed from the infusion system.

Before any vertical movement, each infusion system was placed on a table 90 cm high (the original vertical level) and maintained at set IR for 10 minutes to confirm a steady flow. To evaluate the effect of vertical displacement of the pump body on the flow rate variability, the pump body loaded with the experimental drug was elevated by 60 cm after steady flow had been attained. The pump was maintained at this height for 10 minutes to reestablish a steady-state infusion flow. Then the infusion pump was lowered by 60 cm back to its original vertical level and was observed for an additional 10 minutes before terminating the experiment. This experiment was repeated using IRs of 0.5 and 2 mL·h^{-1} to observe the effects on the low flow rate infusion.

We measured the total ED (the area above or below the set IR from vertical pump displacement until reestablishing steady infusion flow) and maximum change (%) in the IR (the maximum increase or decrease of IR by vertical displacement compared to the set IR) by upward and downward vertical displacement.

Finally, the compliances of syringe pumps loaded with syringes of different sizes were measured using a previously described method.[6] When the infusion line was occluded at an IR of 2 mL·h^{-1}, the time required to attain an occlusion pressure of 100 mm Hg was monitored using an FloTrac pressure transducer, and the volume released to the balancing system after occlusion cessation was measured using an electronic balance (FX-200i; A&D Company). We then estimated compliance (μL·mm Hg^{-1}). All experiments were repeated 5 times for each syringe size, and we averaged the data.

Experiment 2: Flow Irregularities of a Lower Speed Drug by Adding a Higher Speed Drug in the Multidrug Infusion Setting

We observed the effect of initiation or cessation of a faster second drug to the same fluid path on the flow irregularities of the first drug, which was infused at a lower flow rate in 2 types of infusion pumps (syringe- and cylinder-type). Figure 1 and Supplemental Digital F1

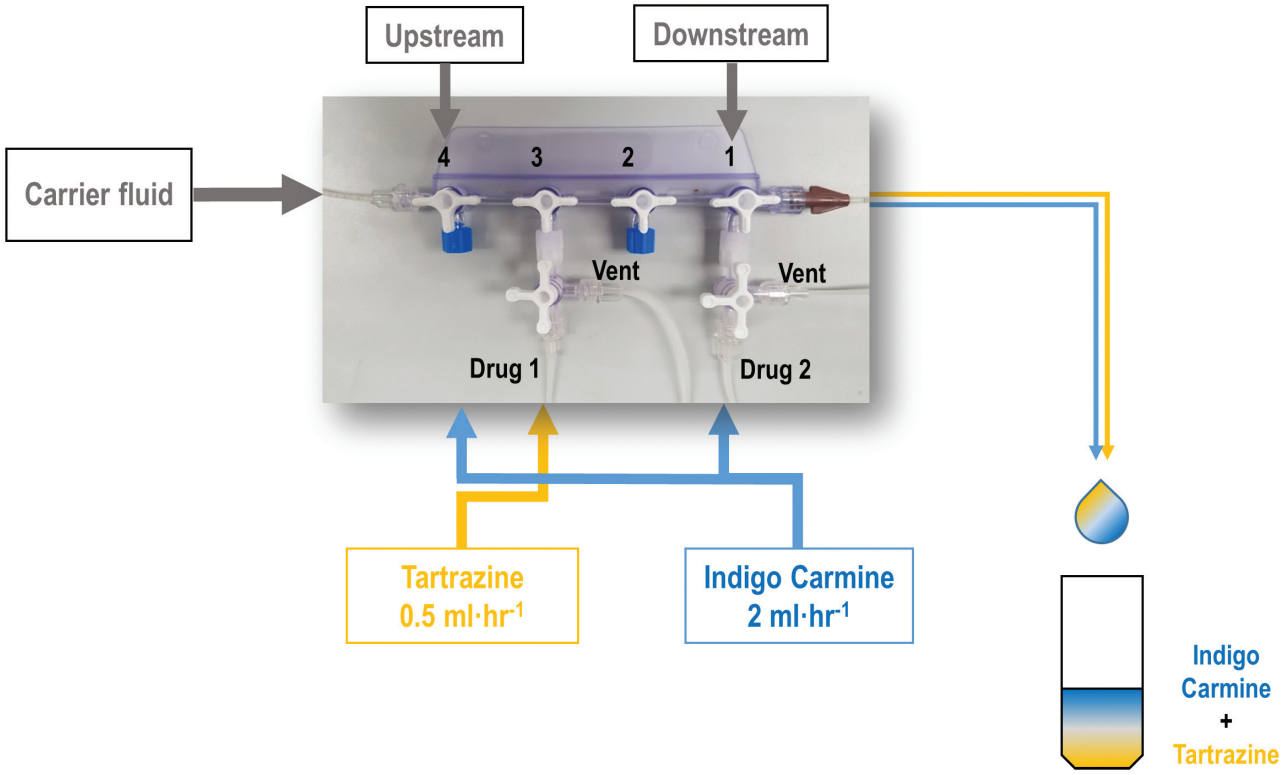

Figure 1. Experimental setup of multidrug infusion.

Content 1, Figure 1, http://links.lww.com/AA/D671, show the experimental setting of multidrug infusions. Four 3-way stopcocks were linearly connected. A 7Fr central venous catheter (3-lumen Arrow guard Blue, Teleflex Medical) and an infusion line extension were connected to either side of the 4 stopcocks. The venting method was used to run the infusion pump continuously, which minimized the start-up delay or impact from intrinsic compliance factors.[14] When it was time to add the experimental drug to the infusion system, the vent stopcock was closed and the experimental drug port was opened. The syringe pump was loaded with a 10-mL syringe while the cylinder-type pump was loaded with a 100-mL fluid bag. A total of 3 infusion pumps of each type were required for the experiment, as follows: (1) carrier fluid infusion (0.9% normal saline) at 15 mL·h^{-1}; (2) the first drug (TT) at 0.5 mL·h^{-1}; and the second drug (IC) at 2 mL·h^{-1}.

After 5 minutes of carrier fluid infusion, delivery of the first drug (TT at 0.5 mL·h^{-1}) was initiated at the third upstream port in the stopcock (port 3) into the infusion system. This infusion was maintained for 20 minutes using a carrier fluid to reach the steady-state flow. Next, the second drug was added to the infusion system either at the first downstream position of the stopcock (port 1) or at the fourth upstream position of the stopcock (port 4). The second drug infusion was maintained for 45 minutes, and the whole experiment ended after 60 minutes. We compared the total ED and the IR fluctuation (%) between the 2 different infusion pumps. The IR fluctuation (mL) is the difference between peak IR and least IR of the first drug during the second drug infusion period. The fluctuation amount was expressed in percentage (%) by comparing the IR fluctuation (mL·h^{-1}) to set IR.

The IR of the first drug was calculated to simulate the administration of dopamine (concentration of 2000 μg·mL^{-1}) at approximately 5 μg·kg^{-1}·min^{-1} to a 3.4-kg newborn child. The IR of the second drug was calculated to represent the administration of dobutamine (concentration of 1 mg·mL^{-1}) at approximately 10 μg·kg^{-1}·min^{-1} or electrolyte replacement for a 3.4-kg newborn child. In addition, the carrier fluid IR (15 mL·h^{-1}) was set to satisfy the hourly maintenance fluid requirement for a 3.4-kg newborn child.

Statistical Analysis

We used descriptive statistics to present quantitative data (in graphs) and used inferential statistics for limited variables. Total EDs were calculated using ORIGINPRO software (OriginLab Corp). The total EDs of the cylinder-type infusion pump were compared with that of the syringe pump using a Mann-Whitney *U* test. In experiment 1, the relationship between the syringe size and the total ED of the syringe-type infusion pump was analyzed using the Jonckheere-Terpstra test and linear regression was used to estimate the effect size. In addition, in experiment 1, we used a linear regression to identify the relationship between the type of infusion device and the total ED after adjustment of experimental covariates (the direction of pump movement and the IR). All *P* values are 2-sided. A *P* value <.05 was considered statistically significant. All analyses were performed with the aid of SPSS software version 25.0 (IBM Corp) and GraphPad Prism 8 (GraphPad Software Inc).

A conditional power calculation method revealed that a sample size of 24 afforded a 90% power in terms of detecting an R^2 value (a coefficient of determination) of 0.326 attributable to the variable of interest (the type of infusion pump) after adjustment of 2 covariates (the vertical displacement direction and the IR) with a significance level (α) of .05. Our primary aim was to compare the total EDs during microinfusion by 3 infusion pumps with different driving mechanisms. Each infusion pump was subjected to a total of 12 measurements (2 IRs × 2 vertical directions × 3 experimental repeats). However, the results of the peristaltic pump were excluded from the analysis because stable steady-state flow was not achieved before vertical pump movement (Figure 2). Consequently, a total of 24 measurements (12 derived using the syringe pump and 12 for the cylinder pump) were included in the comparison. This analysis was performed using PASS 2020 version 20.0.3 (NCSS Statistical Software, LLC).[21] F2

RESULTS

Experiment 1

There were consistent, repetitive patterns of temporary flow increases (inadvertent bolus drug injection) with pump upward displacement and flow decreases with downward displacement in all settings. The flow irregularities were greater when the IR was lower (Figure 2A). Table 1 shows the total ED and the maximal flow rate change (%) caused by vertical pump displacement in each setting. T1

In the syringe pump, there was minimal flow rate variability with vertical pump displacement when a 10-mL sized syringe was used. The total ED and maximal change in flow rate became larger as the syringe size increased (P = .042 in 0.5 mL·h^{-1} vs P = .001 in 2 mL·h^{-1}; Table 1). Linear regression revealed that the effect of syringe size on total ED was a 0.13-mL increase per 1-mL of increased syringe size after adjusting for the effects of the displacement direction and the IR (regression coefficient [β] = 0.13 [95% confidence interval {CI}, 0.07–0.19]; P < .001; Table 2). The compliances of the syringe pump infusion systems differed significantly by the 3 syringe sizes (P < .001) (Supplemental Digital Content 2, Table 1, http://links.lww.com/AA/D672, and Supplemental Digital Content 3, Figure 2, http://links.lww.com/AA/D673). The 10-mL syringe T2

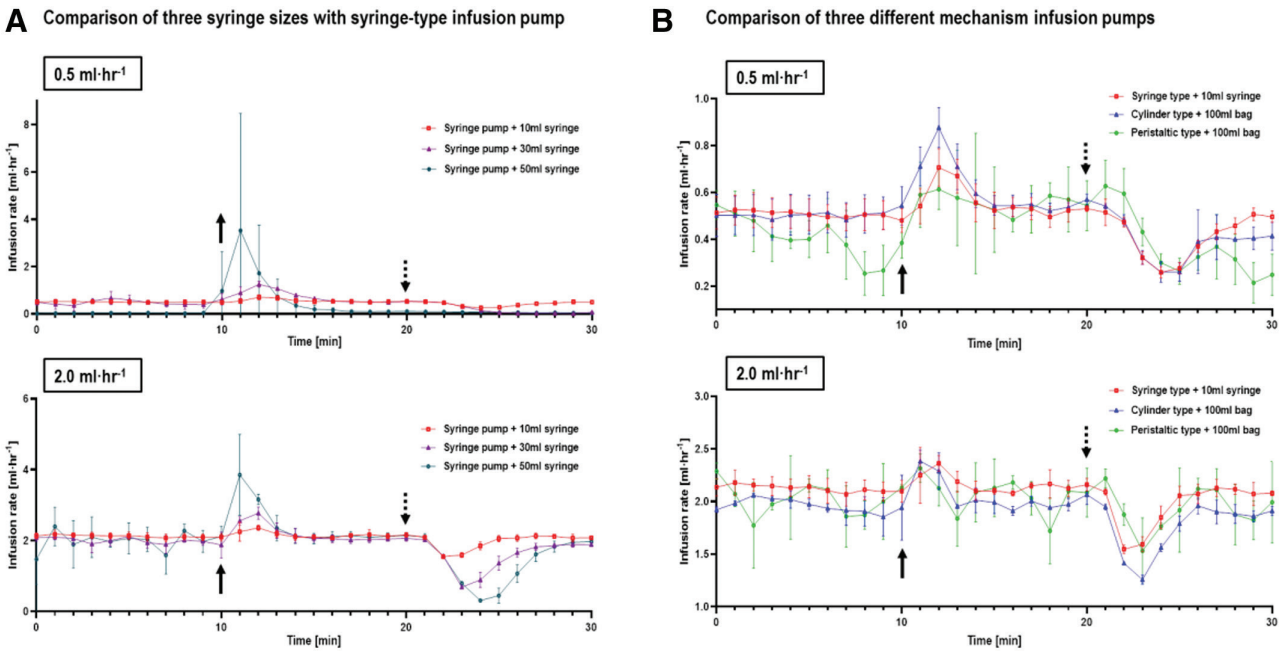

Figure 2. Measured flow rate during vertical displacement. A, Comparison of 3 syringe sizes (10-/30-/50-mL) in the syringe-type infusion pump at 2 infusion rate of 0.5 and 2 mL·h^{-1}. B, Comparison of 3 different driving mechanism infusion pumps (syringe type with 10-mL syringe/peristaltic type with 100-mL infusion bag/cylinder type with 100-mL infusion bag) at 2 infusion rates of 0.5 and 2 mL·h^{-1}. The straight arrows indicate the start of a 60 cm upward movement. The dotted arrows indicate the start of a 60 cm downward movement. The experimental data are plotted according to mean values with error bars.

Table 1. The Flow Rate Variability During Vertical Movement Across Different Infusion Pumps, Syringe Sizes, and Infusion Rates

			0.5 mL·h^{-1}			2 mL·h^{-1}		
Infusion pump	Direction of movement	Syringe size (mL)	Total error dose (mL)	Maximum infusion rate change (%)	*P* value	Total error dose (mL)	Maximum infusion rate change (%)	*P* value
Syringe type	Upward	10	0.43 ± 0.06¶	41.3 ± 16.1		0.49 ± 0.1¶	19.1 ± 5.1	
		30	2.53 ± 1.14†	149.5 ± 25.5	.042	1.87 ± 0.41†	38.8 ± 8.6	.001
		50	6.97 ± 9.41‡	610.4 ± 984.3		3.82 ± 1.06‡	95.7 ± 54.2	
	Downward	10	0.98 ± 0.13¶	(−) 46.4 ± 1.7		1.38 ± 0.24¶	(−) 22.7 ± 2.0	
		30	3.11 ± 0.25†	(−) 99.3 ± 4.6		3.86 ± 0.31†	(−) 65.8 ± 1.7	.001
		50		(−) 92.4 ± 0.5		6.74 ± 0.07‡	(−) 85.2 ± 1.3	
Cylinder type	Upward		1.09 ± 0.55¶, †, ‡	75.3 ± 17.1		0.58 ± 0.24¶, †, ‡	20.4 ± 3.2	
	Downward		1.05 ± 0.06¶, †, ‡	(−) 48.2 ± 8.4		0.58 ± 0.24¶, †, ‡	(−) 37.2 ± 2.2	

Data are presented as the mean ± standard deviation. The total error dose of the cylinder-type infusion pump was compared with that of each syringe size using a Mann-Whitney *U* test. The total error dose, indicated by the same symbol for in upward or downward vertical movement, indicates a combination compared to each other (¶, †, ‡). The results of comparing the total error dose between the cylinder-type infusion pump and the syringe-type infusion pump with each of the 3 different syringe sizes were statistically nonsignificant. The *P* values are results of the Jonckheere-Terpstra test used to test the difference between the 3 syringe sizes for total error dose in syringe-type infusion pump.

showed the lowest compliance and the 50-mL syringe the highest (0.29 ± 0.04 µL·mm Hg^{-1} vs 1.26 ± 0.03 µL·mm Hg^{-1}, $P < .001$, respectively).

Regarding the effect of infusion device type on the flow rate variability, the syringe pump loaded with a 10-mL syringe showed the least flow irregularities (Tables 1 Table 2). However, when a large syringe (50-mL) was used, the total ED using the syringe pump increased by 4.66 mL compared to that of the new cylinder pump after adjusting for the vertical displacement direction and the IR (regression coefficient [β] = 4.66 [95% CI, 1.60–7.72], $P = .008$; Table 2). The results of the peristaltic pump were excluded in the final analysis because a stable steady-state flow was not achieved before performing any vertical pump movement (Figure 2B).

Experiment 2

Table 3 presents the IR fluctuation of the lower speed first drug when a higher speed second drug was added to the single infusion system. The addition of the second drug to the single infusion path either upstream (port 4) or downstream (port 1) transiently increased the flow rate of the first drug. The cessation of the second drug transiently reduced the flow of the first drug. Downstream addition of the higher speed

Table 2. Relationship Between Syringe Sizes in Syringe Pump and Total Error Dose and Between Type of Infusion Pump and Total Error Dose Controlling for the Vertical Displacement Direction and Infusion Rate

Comparison parameters	Regression coefficient (β) (95% CI)	*P* value
1. Syringe sizes in syringe pump (1 mL size as reference)		
10-mL vs 30-mL vs 50-mL	0.13 (0.07–0.19)	<.001
2. Syringe pump versus cylinder pump (reference)		
10-mL syringe versus cylinder pump	−0.56 (−0.28 to −0.84)	<.001
30-mL syringe versus cylinder pump	1.46 (0.95–1.97)	<.001
50-mL syringe versus cylinder pump	4.66 (1.60–7.72)	.008

Data are presented as β coefficient (95% CI). The *P* values are the results of the multiple linear regression models adjusting the impact of vertical displacement direction and infusion rate. (1) In the relationship of syringe pump with 3 different syringe sizes and total error dose, controlling for the impact of vertical displacement direction and infusion rate, the total error dose increased 0.13 (mL) per 1 mL increase in syringe size (β = 0.13 [0.07–0.19]; *P* < .001). (2) In the relationship of type of infusion pump and total error dose, controlling for the impact of vertical displacement direction and infusion rate, the total error dose increased 4.66 mL in syringe pump loaded with 50-mL syringe compared to the new cylinder pump (β = 4.66 [1.60–7.72]; *P* = 0.008).

Abbreviation: CI, confidence interval.

Table 3. The Flow Rate Variability During Multidrug Coinfusion With 2 Different Types of Infusion Pumps: Syringe- and Cylinder-Type Infusion Pump

	Upstream infusion		Downstream infusion	
Variables	**Syringe type**	**Cylinder type**	**Syringe type**	**Cylinder type**
Total error dose (mL)	42.8 ± 0.67	38.18 ± 3.03	43.60 ± 0.79	38.54 ± 1.45
Infusion rate fluctuation (mL·h^{-1})	0.14 ± 0.11	0.05 ± 0.03	0.18 ± 0.03	0.15 ± 0.06
Infusion rate fluctuation (%)	28.8 ± 21.16	10.63 ± 6.85	35.32 ± 6.65	30.85 ± 11.63

Data are presented as the mean ± standard deviation. The infusion rate fluctuation (mL·h^{-1}) is defined as the difference between peak infusion rate and least infusion rate of the first drug during the second drug infusion period. The fluctuation amount was expressed in percentage (%) by comparing the infusion rate fluctuation (mL·h^{-1}) to set infusion rate.

second drug led to slightly faster and larger changes to the first drug infusion compared to that when the second drug was added upstream (Figure 3). However, these results were not clinically significant. In addition, the total EDs and the IR fluctuations during this period were not significantly different between the types of infusion pumps.

DISCUSSION

In this experimental study, we observed the influence of external factors on the flow rate accuracy using different types of infusion pumps in the pediatric intensive care setting. Vertical pump displacement caused similar patterns of flow rate variability in all settings. However, the amount of flow irregularities was more pronounced at lower IRs and in the syringe-type pump loaded with larger volume syringes. The new cylinder-type infusion pump showed relatively stable performance to that of the syringe-type pump using a 10-mL syringe. Moreover, in multidrug microinfusion circumstance, addition of a faster second drug through the same intravenous path affects the flow rate of the lower rate first drug by a transient flow increase regardless of the upstream or downstream port selection.

During microinfusion of potent drugs, it is important to maintain an accurate flow rate. This is particularly true in critically ill pediatric patients.[22] The infusion pump manufacturers have worked to eliminate their design flaws and improve their accuracy since their introduction in the 1950s.[23] The reported error range of the currently commercialized infusion pumps is 5% to 20%. However, this error range further increases in certain conditions such as pump vertical displacement, external vibration, and concurrent multidrug infusion.[10,11,18]

The syringe-type infusion pump is indispensable in current clinical practice with the lowest known error rate of 3%.[24] However, one unresolved problem of syringe pumps is the possibility of unintended bolus injection caused by external environmental factors.[23] This drawback may be caused by a mechanical gap between the loaded syringe and the syringe holding area. This gap causes an "internal motion" of the plunger endplate and leads to an unintended bolus injection during pump body displacement.[25] Consistent with previous studies, an inadvertent flow increase was found during upward pump displacement and demonstrated a siphoning phenomenon.[6,8,10] The siphon phenomenon is related to an increase in hydrostatic pressure, which exacerbates the effect of the mechanical gap during vertical displacement.[25] In addition, downward vertical displacement leads to a decrease in the hydrostatic pressure, which reduces the infusion system pressure and causes aspiration into the system.[6,8,26] In this study, we did not measure the retrograde aspiration volume directly. However, we observed a reduction of the IR after the pump downward displacement, which may indirectly show the risk of decrease in the infusion system pressure and thus delayed drug delivery.

This phenomenon with the syringe pump was minimized when the smallest 10-mL syringe was

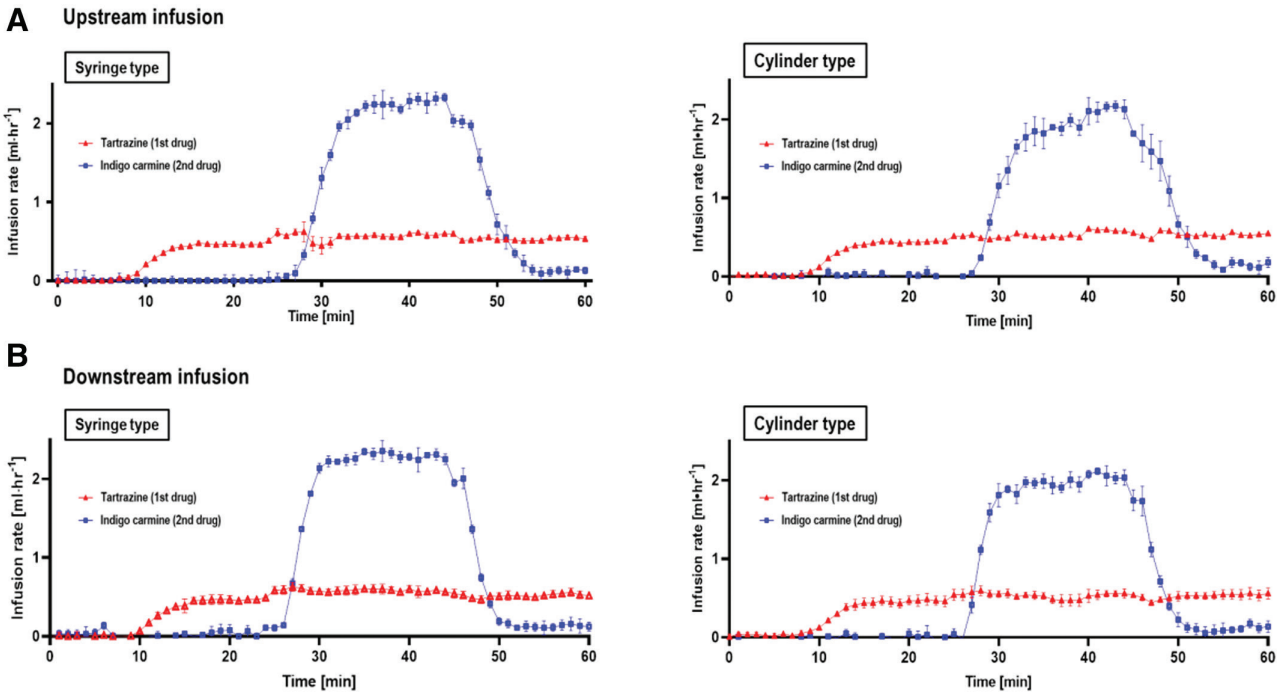

Figure 3. Measured infusion rates during multidrug coinfusion. A, Upstream infusion of the second drug and (B) downstream infusion of the second drug into the same intravenous path with syringe- and cylinder-type infusion pump. The first drug infusion (tartrazine yellow, red line) was affected by the second drug (indigo carmine blue, blue line) initiation and cessation. All experimental data are plotted according to mean values with error bars.

used. It became more pronounced as the syringe volume increased. The low IR is closely related to a very slow linear motion of the plunger, which is activated by the driver in the syringe pump. When considering the syringe plunger movement speed with a low IR (0.5 mL·h^{-1}), it would be approximately 1.5 mm·h^{-1} with a 50-mL syringe and 2.8 mm·h^{-1} with a 10-mL syringe. It is technically challenging to maintain the extremely small plunger movement for the driver. This would be closely related to the inaccuracy of the syringe pump with a larger syringe size.[7,14,27,28]

After conversion of the total ED during upward displacement observed in this study into an epinephrine bolus (at a concentration of 0.02 mg·mL^{-1}), the advertent bolus dose was approximately 0.14 mg epinephrine using a 50-mL syringe and approximately 0.01 mg with a 10-mL syringe. In previous in vivo studies, variations in vasoactive drug infusions at low IRs caused blood pressure fluctuations.[29,30] Therefore, AQ4 to administer a low flow rate drug using a syringe pump, it is safer to choose a smaller syringe for flow stability. However, using a small volume syringe requires frequent syringe changes. These changes may be dangerous for inotropic-dependent patients because of the possible fluctuation of drug delivery after each stop and restart of infusion (start-up delay).[14] Also, frequent syringe replacement is accompanied by increased clinical workload, infection risk, and increased syringe consumption.

In our study, the peristaltic-type infusion pump operated at low IR failed to reach a steady-state infusion, even without pump vertical movement. In addition, this pump had error ranges of (–)24.8% to 9.3% at 0.5 mL·h^{-1} and (–)11.4% to 14.4% at 2 mL·h$^{-1,}$ which are higher than the reported error range of 10%.[31] The higher error ranges at low flow rate infusion may be explained by the inherent mechanism of the peristaltic pump, in which a row of horizontally placed fingers sequentially compresses the infusion line developing a waveform.[32] This waveform leads to a periodic change in the IR, which causes intermittent EDs. These errors are problematic, especially in vulnerable patients with potent drug administration.

Interestingly, the novel cylinder pump used with an infusion bag had comparably stable performance to that of the syringe pump loaded with a 10-mL volume syringe. Therefore, the novel cylinder pump could be considered an alternative to maintain flow accuracy at the low flow rate infusion. The cylinder pump with the novel driving mechanism integrates the advantages and compensates for the disadvantages of conventional infusion pumps. For example, the cylinder pump produces precise infusion that is comparable to that of a syringe pump loaded with a small syringe, and it can be connected to a large infusion bag as is a peristatic infusion pump. Extending the drug replacement cycle has the clinical advantage of reducing the chance of hemodynamic instability in

inotropic-dependent patients and the clinical workload of the medical staff.

We also tested the flow rate accuracy of the low flow rate drug during concurrent multidrug infusion. Several previous studies explored the interaction in a laboratory model using syringe pumps with large syringes at various IRs.[11–13] These studies demonstrated the possibility of an inadvertent bolus injection of the first drug after the initiation of the second drug, and aspiration of the first drug into the infusion system after cessation of the second drug. We also found that steady-state infusion of the first drug was affected by the second drug infusion through the same path. However, unlike the results of Tsao et al[11] and Décaudin et al,[12] we did not find a significant difference in infusion error according to the entry point of the second drug. This discrepancy may be explained by the different compliances of the infusion system due to different sizes in the syringes between the studies.[33] We used a small-volume syringe with low compliance, and a low-compliance system will substantially reduce the volume of the bolus injection or aspiration that follows the initiation or cessation of a second drug.[27] These findings reinforce the importance of using a small syringe in the syringe pump, even during multidrug coinfusion. In the cylinder pump, the first drug IR seemed to be less influenced by the second drug infusion than it was in the syringe pump. Overall, the compliance of the entire system may be more important than the choice of infusion pump type, because the infusion system consists of several components, including the fluid bag/syringe and fluid tubing line.

Moreover, in the current coronavirus disease 2019 (COVID-19) era, some hospitals may place their infusion devices outside patient rooms and run infusion lines that are longer than usual. A long infusion tubing system may increase overall compliance and result in greater dosing errors (over- or underdoses) of several potent drugs infused to the patients critically ill with COVID-19 infections. Previously, long infusion lines with large dead spaces increased infusion dose errors.[34,35] Therefore, the use of a long infusion line requires special attention, as it may lead to detrimental hemodynamic changes in the vulnerable patients. Further studies are needed for details.

This study has several limitations. First, in our experimental setup, the IR measurement was not automated. Although 3 consecutive drops of the experimental drug were manually collected every minute by the same experienced researcher, it might have been insufficient to demonstrate the IR in a continuous manner compared to an automated analysis. Second, we included a single model device for each infusion pump mechanism. Therefore, the results of this study may be limited to the device models included in our experiment.

CONCLUSIONS

Regardless of the driving mechanism of the infusion pump, vertical displacement of the pump or adding a new drug for multidrug microinfusion in the same intravenous path transiently affects the flow accuracy and results in dosing errors. Moreover, in the microinfusion settings, attention must be paid to the use of the syringe-type pump loaded with large-volume syringes. The novel cylinder-type infusion pump could be considered a practical alternative to the syringe pump with small syringe given its comparable flow stability without the need for frequent drug replacement. ■

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DISCLOSURES

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