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Letters to the Editor

Letters to the editor raising points of current interest or commenting on articles previously published in the journal are welcome. Letters should be 400 words or less with no more than 5 references and are subject to editing for length and clarity. Address letters to aacnacc@aacn.org.

SARS-CoV-2 has caused 117 799 584 cases of COVID-19 across the world,[1] and to date it has caused 529 301 deaths in the United States.[2] The care of critically ill patients with COVID-19 infection has rapidly evolved, and health care workers have adapted to the complex care these patients require.[3] One of the various challenges has been the delivery of medications by infusion pumps placed outside of patients' rooms, and we read with interest the manuscript by Blake et al.[4] By placing infusion pumps outside of patients' rooms, the distance between the pumps and the patient has significantly increased. Unstable critically ill patients with COVID-19 infection are receiving medications (eg, sedatives, vasopressors, fluid boluses) administered by infusion pumps through very long intravenous (IV) tubing. The time it takes for the medications to travel the additional distance imposed by the long IV tubing may vary. Adverse clinical effects may develop, especially during titration of doses to their desired effect. Anecdotally, while using infusion pumps outside of patients' rooms, we have noted that patients may remain critically hypotensive despite increases in the dose of the selected vasopressors at the pump level. At the same time, some patients become dangerously hypertensive after several attempts of up-titration of vasopressors. Similar situations have been noted with continuous infusions to control heart rate and sedation. Here we explore the different variables that may play a role in the time it takes for medications to be delivered from their infusion pump to the patient.

The Hagen-Poiseuille equation describes the variables involved in the flow of liquids through IV tubing.

$$Q = \frac{\Delta P \pi r^4}{8 \eta L}$$

Where Q = flow of liquid through tubing, Δ = difference in pressure, π = pi, r^4 = radius of tubing to the fourth power, η = viscocity of liquid, and L = length of tubing.

Infusion pumps typically move fluid forward by different mechanisms. The flow rates and patterns of flow produced by the mechanism of pump operation can be of clinical importance. For example, when highly concentrated solutions of short-acting vasoactive drugs are given by continuous infusion at low flow rates, there may be unexpected clinically significant hemodynamic fluctuations.[5,6]

The radius of the IV tubing can be rather standard. However, accidental compression of the tubing can cause a significant decrease in flow.

The flow rate at which medications travel is inversely related to the length of the IV tubing. With an increase in the length of the tubing, a proportional decrease in the flow rate might occur and therefore an increase in the time that it takes for medications to travel from the infusion pump to the patient.

Conclusion

Several factors are implicated in the delivery of drugs from the infusion pump to patients. The length of IV tubing may be an important factor involved in the delivery of medications. There may be clinically significant adverse effects because of very low flow rates of concentrated vasoactive drugs. This is based on anecdotal observations at the bedside. Animal studies and gravimetric computer models may be necessary to confirm these findings.

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FINANCIAL DISCLOSURES
None reported.

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Authors' Response

Thank you very much for your response to our article, "Flow Accuracy of IV Smart Pumps Outside of Patient Rooms During COVID-19."[1] The issues you have observed in the clinical setting with the use of extended intravenous (IV) tubing when IV smart pumps (IVSPs) are relocated outside of patient rooms are consistent with what we know about fluid dynamics. As practicing intensive care unit (ICU) nurses, we have experienced firsthand the frustration that comes with a delayed pharmacotherapeutic effect in a critically ill patient. We have also seen the consequences of up-titrating a medication too aggressively because of a delayed response, only to find that we had inadvertently exceeded the intended target. In both of these clinical scenarios, our current IV infusion practices can unknowingly put the patient's safety at risk, which is one of the reasons we are so passionate about this work and appreciate your interest.

As researchers, our goal is to improve IV medication administration safety and accuracy at the point of care, with our current efforts focused on clinical issues that impact flow rate accuracy. We are in the process of setting up testing to measure the impact of common clinical variables in our University of Massachusetts Amherst IV infusion laboratory such as:

- How does the addition of IV extension tubing impact IV medication delivery?
- To what extent does the type and size of venous access device impact IVSP flow rate accuracy?
- How much does varied head-height differential affect flow rate accuracy during secondary medication administration?

Mathematical and computer modeling, along with some excellent descriptive presentations, have been disseminated describing the relevant phenomena,[2-11] but clinically relevant studies have yet to be widely published.

Important Points to Address

Hagen-Poiseuille Equation

The Hagen-Poiseuille (H-P) equation is a fluid dynamic law for laminar flows relating flow (Q) and pressure loss (ΔP); it can be used to predict the pressure differences over the length of the tubing caused by a *constant flow* or the flow caused by a *constant pressure difference*. In the form you have described in your letter, the H-P equation is very applicable to IV fluid flow through gravity infusion in which pressure between the medication bag and the patient are constant and flow is determined by the roller clamp. Once we add the use of IVSP for IV fluid delivery, we must address the situation using a different form of the H-P equation. In the case of an already running, titratable medication, the equation is useful for estimating the outlet pressure encountered by the IVSP,[8] which can then be used to estimate the reduced flow rate. In many current IVSP designs, flow may slow between 5% and 20% when very high outlet pressures exist, whereas some newer designs, as well as syringe pumps, exhibit very little if any slowing against pressure. From a clinical perspective, the H-P equation provides minimal explanation for the observed time delays because outlet pressure remains relatively constant once an infusion is established outside of a patient room.

Tubing Length Versus Flow Decrease

A "proportional relationship" between flow and tube length would imply a decrease in flow rate of 50% if tubing length were doubled; in fact, the impact is not this significant. For some designs of IVSPs there may be a decrease in flow with doubled tubing length, but flow does not have a simple proportional relationship with length; rather, actual flow rate depends additionally on the programmed flow rate as well as tubing inner diameter and fluid viscosity. When using a 30-foot extension of standard IV tubing with 8 mL primed volume, the rate would decrease in some IVSPs up to 14% at 1000 mL/h, but there will be minimal

impact for rates less than 100 mL/h. There are other factors at play in the all-too-common scenario described in your letter. We will go into more detail regarding outlet pressure and dead volume, which are important considerations for nurses to understand when using IVSP.

Outlet Pressure

Pump outlet pressure is caused by the IVSP infusing at a constant flow rate through the tubing. This pressure is produced by friction in the fluid present in the entire tubing between pump and patient and is predictable by solving the H-P equation for pressure difference (ΔP). Flow rate accuracy testing reported by manufacturers is done using an outlet pressure of zero. In the clinical setting, we know many factors can increase outlet pressure and therefore reduce flow rate accuracy to a greater degree than the +/- 5% reported by manufacturers. Partial tubing obstruction, high flow rates, increased fluid viscosity, small-bore tubing and catheters, long catheters, needle-free connectors, the use of manifolds, dependent loops, and the use of extension tubing can all lead to increased pump outlet pressure.

Outlet Pressure Related to Extended Tubing

As previously stated, increased tubing length will have minimal impact on pump flow rates less than 100 mL/h. For low–flow rate titratable medications as described in the letter, the most significant clinical effect related to outlet pressure will be seen when adding length to an already running, continuous infusion. Outlet pressure may also be increased if there is restriction of the tubing as it passes under or through a closed door. Any kinking in the tubing as it travels from the IVSP to the patient may also increase outlet pressure, thus slowing the flow.

Dead or "Common" Volume

Dead volume is the volume of fluid already in the tubing when a rate change occurs, or the distance a newly added medication must traverse before reaching the patient's blood stream. This is often referred to as *common volume* when the tubing contains more than 1 medication or fluid.

New Medication "Y'ed" Into an Already Running Infusion

If a nurse must add a vasopressin drip to an existing norepinephrine drip for increased blood pressure support, both medications will be passing together through some length of common or dead volume of the IV tubing. The time delay before the vasopressin reaches the patient's blood stream is dependent on how much space is between its tubing connection point and the blood stream, as well as the total flow rate of both medications. This effect is seen to some degree when IVSPs are placed at the bedside; the Luer lock closest to the venous access device is typically less than 6 inches. If the norepinephrine is infusing at 10 mL/h, it will take a vasopressin drip programmed at 6 mL/h about 2 minutes to traverse the 6 inches of dead volume and reach the patient. Now let us consider an IVSP placed outside the room with a new vasopressin drip connected to a Luer lock also outside the room. In this case, the distance of dead volume and subsequent time delay is significantly increased. The time delay for a newly added 6 mL/h vasopressin drip connected 15 ft from the patient running through standard sized tubing is increased to about 85 minutes by our calculations. Any additional factors slowing the flow because of outlet pressure as previously discussed will slow this time down even farther.

Titratable Medication That Is Already Running

In the case of a titratable norepinephrine infusion that is already running continuously, the observed effect will depend heavily on whether the norepinephrine is being infused alone or together in the same line with other fluids. If the norepinephrine drip is being infused by itself and not joining other fluids along its path to the patient, the delay will be significantly decreased, maybe even imperceivable because of the incompressibility of fluids. Considering a typical scenario in which a low-flow-rate, titratable medication is running with other fluids through a common volume, the delay before therapeutic effect could be dramatic. Unfortunately, this is a more challenging situation to calculate and is going to depend heavily on the rates of all fluids involved in addition to the length of tubing that makes up the common volume. If the goal of titration is exceeded and the medication must be titrated back down, similar delays can be expected.

Suggested Clinical Practice Strategies

Some practice adjustments may need to be applied during critical medication titrations

to prevent dangerous consequences of extended tubing setups for critical titratable medications. Ideally these medications would be infused through dedicated lines in which there is no common volume, thus physiological effects will be observable almost immediately. The next best option would be to attach the titratable medication as close to the patient as possible using a low-volume manifold or "Y" it into a fluid whose rate is going to stay constant. If that fluid rate is expected to change, the nurse must take into account that this will cause a dramatic and potentially dangerous change in the delivery rate of the titratable medication. If none of these strategies are an option for the patient, another strategy might be to anticipate delayed physiologic effects, especially when we know that the infusion conditions make quick response to titration unrealistic. For example, if the mean arterial pressure (MAP) goal is 65 to 85 mm Hg and the patient is on norepinephrine to keep the MAP above 65 mm Hg, consider a "soft" goal of 70 mm Hg to make it easier to avoid more serious hypotension that would lead to more rapid up-titration and medication-induced MAP fluctuations that could be harmful to the patient.

Conclusion

Although the use of significantly lengthened IV extension tubing can help reduce clinician exposure to coronavirus disease 2019 (COVID-19), it also presents significant clinical challenges that can have a negative impact on patient outcomes. In the short term, an improved understanding of the relevant principles can help improve safety. In the long term, innovation in IVSP remote control is currently being studied in response to the COVID-19 pandemic; this innovation would eliminate the issues discussed here while also helping to protect health care workers. Additionally, IVSPs that are minimally impacted by outlet pressure already exist and would be safer for patients in these situations but are not used by most hospitals. Overall, when nurses understand the implications of extended IV tubing and ways to mitigate the effects, IV medication delivery will be safer for patients.

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FINANCIAL DISCLOSURES
None reported by Jeannine W.C. Blake. Robert Butterfield has been employed by an infusion pump manufacturer and is currently a paid consultant for several infusion pump manufacturers. He serves on national and international infusion pump standards committees and provides pro bono consulting and technical support to major hospitals and advocacy organizations in the domain of infusion therapy research, education, and planning. As a medical device development consultant and clinical outcomes researcher, Karen Giuliano has performed consulting services for numerous medical device companies, including Ivenix and ICU Medical.

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