Effect of intravenous infusion dead space on time to drug delivery in infants

Bryce G. Gregerson, MD^a, Alexa L. Larsen^b, Seth M. Kelly, MD^c, Joshua D. Sonnier, MD^a, and Andrew L. Juergens, MD^a

^aDepartment of Emergency Medicine, Scott & White Medical Center, Temple, Texas; ^bBaylor University, Waco, Texas; ^cDepartment of Emergency Medicine, University of Maryland Medical Center, Baltimore, Maryland

ABSTRACT

Infusion dead space is the internal volume of a catheter and tubing through which a fluid must pass before reaching a patient's intravenous space. It is a factor in time to delivery for intravenous administration and can be significant, depending on the volume and rate of infusion. A 10-kg infant was simulated, receiving an epinephrine infusion with a concentration of 20 mcg/mL at a rate of 0.1 mcg/kg/min, which equals 3 mL/h. Commonly used pediatric intravenous equipment was selected. The tubing was flushed with a dyed solution. The setup was connected to 24- and 22-gauge catheters, with and without extension tubing. Each configuration was tested by allowing the intravenous solution to drip onto chromatography paper until color could be seen. The time from the start of the infusion to the visualization of dye was recorded 10 times for each configuration. The average time was 88 seconds for a 24-gauge catheter and 439 seconds with extension tubing added. For the 22-gauge catheter, the average time was 98 seconds and 431 seconds with extension tubing. Though often considered inconsequential, infusion dead space can cause significant delays in drug administration, especially in small patients and with slow, concentrated infusions. When appropriate, clinicians should consider bolus administration of critical medication before starting an infusion.

KEYWORDS Infusions; intensive care units; intravenous; pediatric emergency medicine; pediatrics; vascular access devices

The internal volume of an intravenous catheter and tubing constitutes a dead space that a fluid or medication must pass through before it can reach a patient. The transit time of a fluid through this space can be significant, depending on the volume and rate of infusion.¹ This delay is especially pronounced for pediatric patients, for whom infusion rates and total volume of fluid administered must be low due to their smaller bodies and lower weights.^{2–5} For some medications administered intravenously, a delay of just a few minutes can significantly increase mortality in adults and children.^{6,7} Much of the published data on this topic is either outdated or focused on adults. This study used a patient model in an attempt to quantify the time to onset of drug delivery in a typical 1-year-old pediatric patient in an emergency department setting and to compare measured values with predicted values based on the published dead volumes of infusion equipment.

METHODS

The protocol was reviewed by the institutional review board and exempted as nonhuman research. A 10-kg infant

was simulated, receiving an epinephrine infusion with a concentration of 20 mcg/mL at a rate of 0.1 mcg/kg/min, which yielded a flow rate of 0.05 mL/min or 3 mL/h. Commonly used pediatric intravenous equipment available in the emergency department was selected, including 22-gauge and 24-gauge Insyte Autoguard shielded intravenous catheters (Becton, Dickinson, and Company, Franklin Lakes, NJ) and extension tubing made by ICU Medical Inc. (San Clemente, CA). The 24-gauge catheters were 0.75 inches long, with an inner diameter of 0.521 mm and an inner volume of approximately 4.06 mm³ or 0.004 mL.⁸ The 22-gauge catheters were 1.00 inch long with an inner diameter of 0.648 mm and an inner volume of 8.38 mm³ or 0.008 mL. The extension tubing was 18 cm long and had a published volume of approximately 0.31 mL.

Green dye was added to saline and placed in a 20-mL syringe pump. The tubing that led from the pump was primed with the colored saline solution. The setup was then connected to the 22- and 24-gauge catheters and the pump was started. In the first part of the trials, a 22- or 24-gauge intravenous catheter alone was used. In the

Corresponding author: Andrew Juergens, MD, Department of Emergency Medicine, Scott & White Medical Center, 2401 S. 31st St., Temple TX, 76508 (e-mail: Andrew.Juergens@BSWHealth.org)

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second half of the trials, extension tubing was added. When the extension tubing was added, it was flushed with normal saline and a 0.05-cc air bubble was introduced into the proximal portion of the extension tubing to separate the normal saline with dye from the normal saline without dye. This technique avoided the mixing of dye from one volume of saline to the other, so diffusion should not have factored into the time to dye visualization.

The intravenous solution was allowed to drip onto individual strips of chromatography paper until color could be seen. The time from the start of infusion to the visualization of dye was recorded 10 times for each configuration. The tubing was flushed dry with air between tests.

The predicted values of time-to-dye visualization were calculated using the published volumes of the catheters and extension tubing and the flow rate of 3 mL/h. The average measured time for each setup was compared with the predicted value using a one-sample *t* test. Outliers were not included in the calculation of the average or standard deviation.

RESULTS

The average time to first visualization of dye for the 22-gauge catheter was 98 ± 6 seconds, and it was 431 ± 19 seconds for the 22-gauge catheter with 18 cm of extension tubing. Based on the published internal volumes for the 22-gauge catheter alone, the predicted time to visualization is 10 seconds. For a 22-gauge catheter with 18-cm extension tubing, the predicted time to visualization is 382 seconds, which represents a difference of 88 seconds between measured and predicted times for the 22-gauge catheter by itself and a difference of 49 seconds for the catheter and the extension tubing together (Table 1).

For the 24-gauge catheter, the average time to visualization of dye was 88 ± 7 seconds without the tubing, but the predicted time was just 5 seconds, a difference of 83 seconds. With the extension tubing added, the average time was measured to be 439 ± 13 seconds after one data point was removed as an outlier that was greater than 3 standard deviations away from the mean. The predicted time for the catheter and tubing together was 377 seconds, which is a difference of 62 seconds between observed and expected values (Table 1).

A statistically significant difference existed between the average observed times for the 22-gauge and the 24-gauge catheters alone. The difference between the observed times for the 22-gauge versus the 24-gauge catheter with the extension tubing added was not statistically significant.

DISCUSSION

The results support the hypothesis in that the measured times to visualization are longer than the predicted times. Although this article did not seek to determine the cause of such a delay, the relative consistency in the differences between observed and expected times (83 and 89 seconds for the

Table 1. Time to dye visualization: Delay of onset of drug delivery due to dead volume

Variable	Size of catheter	
	22-Gauge	24-Gauge
Predicted without extension, s	10 ^a	5 ^b
Measured without extension, s + SD (no. of trials)	98 ± 6 (10) ^a	88 ± 7 (10) ^b
Predicted with extension, s	382	377
Measured with extension, s + SD (no. of trials)	431 ± 19 (9) ^c	439 ± 13 (9) ^c

^a Predicted vs measured time for the 22-gauge catheter without extension was significantly different, $P < 0.005$.

^b Predicted vs measured time for the 24-gauge catheter without extension was significantly different, $P < 0.005$.

^c The first trial was removed as an outlier. It indicates a likely systematic error due to initiation of drip in tubing for first time.

catheters alone and 67 and 62 seconds for the catheters and extension tubing) suggests that the delay is caused by a factor intrinsic to the equipment or the procedure employed in this study.

Regardless of causation, in this patient model the medication took 1.5 minutes to reach the simulated infant through a catheter alone at a flow rate of 3 mL/h. When extension tubing was used, the medication did not reach the infant for more than 7 minutes. Extension tubing can be useful in providing clinicians with more space in which to work. However, clinicians should be aware of the potential delay in drug administration.

Though often considered inconsequential, these results show that infusion dead space can cause significant delays in drug administration, especially in small patients and with slow, concentrated infusions. We recommend that clinicians consider bolus administration of critical medication before starting an infusion.

This study only considered the common practice of priming the line to the catheter. It did not take into account other practices, such as priming to the patient or administration of medications through a Y connection or piggyback. One limitation of this study is that this model assumed no diffusion between the volume of drug and the volume of normal saline in flushed extension tubing. This study also measured only the onset of drug administration; it did not examine the time to reach a steady state of infusion. Further studies are necessary to quantify this delay and its clinical implications.

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In memoriam

PERCY EDGAR LUECKE JR., MD

Department of Pediatrics, Baylor University Medical Center at Dallas

Dr. Percy Luecke Jr. died on October 29, 2017, at the age of 91. He had served as a pediatrician at Baylor University Medical Center for many decades, following in the footsteps of his father, pediatrician Percy Luecke Sr. He was born in 1926 at Baylor Hospital in Dallas and graduated from Woodrow Wilson High School, Southern Methodist University, and Washington University School of Medicine. He completed his pediatrics residency at St. Louis Children's Hospital. Once he came to practice in Dallas, he led several

important campaigns for public health, including a polio immunization campaign and a campaign for water fluoridation, both through the Dallas County Medical Society. He participated in local, state, and national medical associations and served as president for the Dallas County Medical Society and the Dallas Pediatric Society. From 1969 to 1986, Dr. Luecke was chief of pediatrics at Baylor University Medical Center. He also served two terms on the board of the Dallas Independent School District during the period when schools were desegregated. As a pediatrician, Dr. Luecke proved to be a great diagnostician with keen insight into the minds of children and their anxious parents.