Original Article doi: https://doi.org/10.1590/1983-1447.2022.20210071.en

Start-up delay in syringe infusion pumps with different rates and priming techniques of intravenoust sets

Atraso na inicialização em bombas de infusão por seringa com diferentes velocidades de infusão e técnicas de preenchimento do sistema de infusão

Retardo en la puesta en marcha en bombas de infusión de jeringa con diferentes velocidades de infusión y purga del sistema de infusión

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How to cite this article:

Vieira NM, Pires MPO, Crespo GB, Nascimento LPP, Peterlini MAS, Pedreira MLG. Start-up delay in syringe infusion pumps with different rates and priming techniques of intravenoust sets. Rev Gaúcha Enferm. 2022;43:e20210071. doi: https://doi.org/10.1590/1983-1447.2022.20210071.en

Revista Gaúcha de Enfermagem

ABSTRACT

Objective: To investigate infusion pumps start-up delay according to different brands of infusion pumps, flow rates and intravenous sets priming techniques.

Method: The experimental study simulated clinical practice under controlled conditions, using a 50 mL syringe with NaCl 0.9% solution, two syringe infusion pumps (A and B), six rates (0.3, 0.5, 1.0,5, 10 and 20 mL/h), two purging techniques (manually or infusion pump's electronic bolus). Data were analyzed according to mean, standard deviation, Student's t and ANOVA tests (p<0.05). Results: The start-up delay was greater in low rates regardless the priming technique. The electronic bolus increased the infusion pump A accuracy at 0.3mL/h (p=0.010), 0.5 mL/h (p=0.002) and 1.0mL/h (p=0.004). Pump's accuracy in all studied rates and manual IV sets filling was similar.

Conclusion: In low infusion rates the start-up delay was greater despite the infusion pump brand and electronic bolus improved pumps accuracy.

Keywords: Critical care. Infusion pumps. Nursing. Patient safety. Syringes.

RESUMO

Objetivo: Verificar o atraso de inicialização de bomba de infusão, segundo diferentes marcas de bombas de infusão, velocidades e técnicas de preenchimento do sistema de infusão intravenosa.

Método: Estudo experimental que simulou a prática clínica, utilizando seringas de 50 mL com solução de NaCl 0,9%, duas marcas de bombas de infusão por seringa (A e B), seis velocidades (0,3;0,5;1,0; 5; 10 e 20 mL/h), dois modos de preenchimento do sistema (manual ou eletrônico pelo modo bolus do equipamento). Os dados foram analisados segundo média, desvio padrão e testes t de Student e ANOVA (p<0,05).

Resultados: O atraso na inicialização foi maior em velocidades baixas, independentemente da marca e modo de preenchimento. O preenchimento eletrônico aumentou a acurácia na bomba A em 0.3 mL/h (p=0,010), 0.5 mL/h (p=0,002) e 1.0 mL/h (p=0,004). A acurácia em preenchimento manual foi semelhante.

Conclusão: Em baixas velocidades de infusão o atraso de inicialização foi maior e o preenchimento do sistema de infusão pelo modo eletrônico melhorou a acurácia dos equipamentos.

Palavras-chave: Cuidados críticos. Bombas de infusão. Enfermagem. Segurança do paciente. Seringas.

RESUMEN

Objetivo: El objetivo fue investigar el retraso en la operación de bombas de infusión de acuerdo con diferentes marcas de bombas de infusión, velocidades de infusión y técnicas de purga de lo sistema de infusión.

Método: Estudio experimental que simuló la práctica clínica en condiciones controladas con jeringas de 50 mL y solución de NaCl 0,9%, dos bombas de infusión de jeringa (A y B), seis velocidades (0,3;0,5;1,0; 5; 10 y 20 mL/h), dos modos de purga (manual o electrónico por la bomba de infusión - bolo). Los datos se analizaron según media, desviación estándar, Test-T y ANOVA (p<0,05).

Resultados: El retraso de la operación de las bombas ocurrió en tasas bajas independientemente de la técnica de purga. El modo electrónico aumentó la precisión de la bomba de infusión A en 0,3 mL/h (p=0,010), 0,5 mL/h (p=0,002) y 1,0 mL/h (p=0,004). Con la técnica manual la precisión fue similar.

Conclusión: Los retrasos de operación fueran significantes en bajas velocidades de infusión y el modo electrónico optimizó la precisión

Palabras clave: Cuidados críticos. Bombas de infusión. Enfermería. Seguridad del paciente. Jeringas.

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INTRODUCTION

Infusion pumps are electromechanical devices designed to control the delivery of fluids, drugs, nutrients, and blood components under positive pressure to the patients. They might have several methods for infusion, such as peristaltic, from a cassette, piston-driven, and using a syringe⁽¹⁻³⁾ The choice of equipment for intravenous (IV) therapy includes factors associated with safety, such as patient age, the severity of illness, type of therapy, infusion rate, and potential for adverse events.^(4,5)

Syringe infusion pumps (SIPs) are used to deliver low volumes of fluids and drugs, in neonates and children, and during anesthesia and critical care. Factors such as the size of the syringe, complacency and resistance, the height between the patient's vascular access site and the pump, type and size of IV sets, type of vascular access, use of in-line filters, and priming techniques used for the IV sets can influence the performance of the equipment⁽⁶⁻⁸⁾.

However, these parameters are not consistently applied in daily clinical practice, mainly in critical care units. Devices are often placed much above the height of the patient's bed, the same syringe size, essentially 20 to 50 mL, is used regardless of the programmed infusion rate, and long IV lines between the pump and the patient are used. These demonstrate the non-application of specific science-based protocols for the desired performance and use of SIP. For example, during the COVID-19 pandemic, infusion pumps are often placed outside the patients' rooms to avoid dissemination of the virus and contamination of the pumps; however, the use of long IV lines with loops between the equipment and the patient's vascular access site can increase the risk of flow inaccuracy.

Start-up delay is a documented concern related to the use of SIP, which can compromise patient safety during drug infusion in critically ill patients. The start-up delay can be a consequence of using the same syringe size for infusion at different rates programmed in the SIP, in addition to the mechanism of infusion and system complacency, possibly resulting in medication errors⁽⁶⁻¹¹⁾.

Infusion pumps are used to deliver most IV fluids and drugs and medication errors during the administration process are known to be a frequent cause of adverse events in hospitals⁽¹¹⁾. During the administration of critical drugs in severely ill patients, the delay in continuous fluid delivery after starting the infusion pump can lead to severe adverse events that compromise patient safety^(4,12).

The aim of this study was to investigate the delay in initiation of the infusion with two different brands of infusion pumps according to different infusion rates and purging techniques for IV sets, namely, bolus administration and manual filling of the syringe and IV set.

METHODS

Study design

An experimental study was conducted in the city of Sao Paulo under controlled conditions of temperature (22 ± 2 °C) and humidity ($62\pm6\%$).

Sample

Two different commercially available brands of SIP named A and B comprising six pieces of equipment (three pieces of equipment of each SIP brand were used to control a possible variation within the same brand), were randomly set at infusion rates of 0.3 mL/h, 0.5 mL/h, 1.0 mL/h,5,10, and 20 mL/h, and two IV tube purging techniques were used to verify the occurrence of start-up delay.

The infusion pumps were obtained directly from the manufacturers with quality control inspection approval and certification. The manufacturers had no influence on the study design and development. SIP A could be programmed to be used with 10 mL, 20 mL, and 50 mL syringes, and the SIP B was compatible with 5 mL, 10 mL, 20 mL, and 50 mL syringes. The infusion rates could range from 0.1 mL/h to 999.9 mL/h in both devices. According to the manufacturer's instructions, the pumps were programmed to pressure alarm limits of 40 kPa.

Data Collection

Syringes of 50 mL (14.2 x 3 x 3 cm) of the same batch of production (Terumo^{*}, Japan) were prefilled with normal saline solution (NaCL 0.9% in water), and the IV tubing was purged manually or by pushing the bolus button of the SIP.

For manual purging, the IV tubing was manually filled by the researcher with positive pressure applied using the hands, without the use of any device. The bolus filling of the IV tubing was performed by pressing the bolus button of the SIP. Both techniques are followed by the nurses in clinical practice when using the SIP. The use of an electronic bolus of the SIP followed the manufacturer's recommendations.

A low-compliance IV tubing made of polyvinyl chloride, 150 cm long and 10 mL of fluid for priming was used. A three-way stopcock was installed between the syringe and the tubing to maintain the solution and pressure inside the IV system after purging it manually or using the bolus option of the pumps. At the end of the IV tubing a 24-gauge polyurethane catheter was installed.

The infusion pump was placed on a saline support 90 cm from the floor, simulating the height of the patient's bed. The distal tip of the catheter remained in the same line as the equipment and, at the beginning of the experiment, the syringe was placed in the infusion pump and connected to the catheter, simulating clinical practice, and the catheter was inserted into a graduated beaker Becker. The IV system was checked twice for creases, loops and the presence of air.

To study the start-up delay, an analytical balance Shimadzu^{*} (AUY220, Japan) was used, and the time of the first drop identified by the balance after the start of the infusion was registered by the equipment and by a precision chronometer (Lineup^{*}, Brazil), in minutes. The analytical balance has lateral and superior doors to allow the placement of the substances to be measured over the balance plate in the interior, and once the lateral doors are closed, a reduction in external influences is obtained, enhancing the precision of the measurements. The Becker with the final tip of the IV system was placed inside the balance, and the doors of the analytical balance were closed, just maintaining a minor portion of the superior door opened to the IV system entrance. The study was conducted between March and December 2016.

Data Analyses

Data were registered in the software Microsoft Excel^{*}, and analyzed according to mean and standard deviation. For the analysis of variance, Student's t-test and ANOVA tests were used ($p \le 0.05$).

Ethical considerations

Since this was a laboratory study with no involvement of human beings, it did not require approval from the ethics committee or subject consent forms. The names and brands of the SIP are not revealed; thus, there is demonstrate no commercial purpose or conflicts of interest.

A total of 72 measures of the time spent in the first infusion were analyzed. The dependent variable was analyzed for each SIP brand (Table 1), and the purging technique (Table 2) was considered as an independent variable.

			Star-up delay	1		
Infusion Rate	SIP A			SIP B		
	Manually Mean (SD)	e-Bolus* Mean (SD)	р†	Manually Mean (SD)	e-Bolus* Mean (SD)	p†
0.3 mL/h	74.2 (25.8)	6.7 (2.5)	0.010	97.7 (10.7)	19.3 (10.6)	<0.001
0.5 mL/h	70.9 (17.7)	3.0 (1.5)	0.002	44.2 (13.4)	7.7 (2.5)	0.009
1 mL/h	25.5 (7.7)	0.2 (0.2)	0.004	34.7 (19.9)	3.0 (1.6)	0.051
5 mL/h	4.3 (3.8)	0.6 (0.3)	0.273	5.0 (1.2)	0.1 (0.7)	0.003
10 mL/h	1.8 (0.8)	0.7 (0.4)	0.495	2.3 (0.6)	0.4 (0.1)	0.006
20 mL/h	0.9 (0.8)	0.3 (0.2)	0.230	0.9 (0.3)	0.1 (0.1)	0.016
p‡	<0.001	<0.001		<0.001	<0.001	

Table 1 – Start-up delay in the SIP A and the SIP B, in minutes, according to infusion rate and priming technique. São Paulo, 2016

Legend: SIP A: syringe infusion pump of the brand A; SIP B: syringe infusion pump of the brand B; *electronic bolus; † t Test; ‡ ANOVA.

Star-up delay in minutes									
Infusion	Manually			e-Bolus					
Rate	SIP A	SIP B	р*	SIP A	SIP B Mean (SD)	р*			
	Mean (SD)	Mean (SD)		Mean (SD)					
0.3 mL/h	74.2 (25.8)	97.7 (10.7)	0.219	6.7 (2.5)	19.3 (10.6)	0.116			
0.5 mL/h	70.9 (17.7)	44.2 (13.4)	0.104	3.1 (1.5)	7.7 (2.5)	0.049			
1 mL/h	25.5 (7.7)	34.7 (19.9)	0.495	0.2 (0.2)	3.0 (1.6)	0.039			
5 mL/h	4.3 (3.8)	5.0 (1.2)	0.755	0.6 (0.3)	0.1 (0.7)	0.282			
10 mL/h	1.8 (0.8)	2.3 (0.6)	0.393	0.7 (0.4)	0.4 (0.1)	0.310			
20 mL/h	0.9 (0.8)	0.9 (0.3)	0.854	0.3 (0.2)	0.1 (0.1)	0.268			

Table 2 – Start-up delay according to the priming technique, in minutes, and infusion rate with SIP A and SIP B. São Paulo, 2016

Legend: SIP A: syringe infusion pump of the brand A; SIP B: syringe infusion pump of the brand B; * t Test.

The results presented in Table 1 demonstrate that there was a significant variance in the start-up delay, and the delay was higher with lower infusion rates in both devices (p<0.001).

The highest delay observed in infusion pump B was 97.7 minutes (\pm 10.7) at 0.3 mL/h, and the shortest delay was 0.1 minutes (\pm 0.1) at 20 mL/h. As the infusion rate increased and the equipment's electronic bolus option was used to purge the IV tubing, all devices demonstrated better performance. It was found that the electronic bolus filling technique led to less start-up delay at all infusion rates with infusion pump B, and with pump A at 0.3 mL/h, 0.5 mL/h, and 1.0 mL/h.

The delay in both SIP A and B at all flow rates studied was statistically similar when the IV tubes were purged manually; however, there was a shorter delay in SIP A at 0.5 mL/h and 1.0 mL/h when the electronic bolus mode was used (Table 2).

DISCUSSION

The results of this study showed that the technique of purging IV tubes prior to infusion influenced the performance of the SIP. This influence was seen more in SIP B and at flow rates below 1 mL/h. At a rate of 20 mL/h, the devices were more accurate, demonstrating a start-up delay of approximately one minute.

Another study that analyzed the performance of SIP at a rate of 1.0 mL/h found that passing an initial bolus of 2 mL through the tube before connecting the infusion system to

the patient reduced the start-up delay. The time to start the infusion ranged from six to 50 min, showing shorter boot times when bolus was performed⁽¹³⁾. In the present study, at a rate of 1.0 mL/h, the use of bolus function decreased the delay by approximately 25 min in SIP A and 31 min in B. The delays with low infusion rates identified in this study and mainly when the IV system was filled manually can lead to severe adverse events related to delays in medication delivery in clinical practice.

The electronic bolus function of the equipment probably enhanced the SIP accuracy and reduced the start-up delay due to a balance of pressures achieved within the infusion system. To initiate the administration, the equipment's infusion pressure must overcome the hydrostatic pressure, the resistance of the syringe plunger, and complacency of the IV set. At low infusion rates, the time spent to overcome these pressures resulted in longer start-up delays. However, if the electronic bolus is activated and the pressure required to overcome the other influencing pressures is maintained in the IV set, the programmed rate can be achieved more accurately at low infusion rates. At higher rates, these pressures are overcome more quickly, demonstrating less effect of electronic bolus on SIP accuracy.

It is important to highlight the variations in the deviation values in SIP A and SIP B (notably in SIP A), and with both purging techniques, mainly at low infusion rates. The results indicate that there were variations within the same equipment brand. This hypothesis was based on our clinical experience of performance variations with the equipment of the same brand; hence, we decided to study three pieces of equipment from each manufacturer.

In this experiment, we used 50 mL syringes, which can influence the clinically relevant delay identified at low infusion rates. These findings corroborate those of other studies, which showed the effect of using 50 mL syringes at low rates, compared to that with 10 mL syringes^(9,14). One study demonstrated that the equipment required almost one hour to achieve 50% of the programmed flow rates with 50 mL syringes, while with 10 mL the time was approximately 20 min. This phenomenon occurs because of the pressure exerted by the equipment to override the system complacency, and applying the bolus reduces the system resistence⁽⁹⁾. In critical care units, 20 or 50 mL syringes are usually used with infusion pumps, regardless of the infusion rate, for drugs or solutions that require 24 h of continuous infusion. The results of our study and those of previous studies reinforce the need for considering using smaller syringe sizes at low flow rates.

In addition, the findings related to the significant impact of the purging technique on SIP performance have relevant implications for clinical practice, demonstrating that filling the infusion system using the bolus mode instead of manually enhances the device performance during drug administration at low rates.

These data are especially important for anesthesiology and critical, neonatal, and pediatric care to prevent or reduce the impact of adverse events, mainly related to infusion of catecholamines and other vasoactive drugs⁽¹⁰⁾. In 2020, an *in vitro* study demonstrated the performance variations in modern equipment at low infusion rates, impacting the efficacy of short-acting cardiovascular drugs⁽⁶⁾.

The features of the SIP, position of the equipment, syringe size, multidrug infusion, and infusion rate compromise the quality of the infusion^(11,12,15). Another experimental study showed that a SIP has flow delays and irregularities and that only flow controllers can resolve most of the performance concerns associated with pumps.⁽⁷⁾ One study reported that start-up delay is critical to analyze the SIP performance and safety, especially in critical care patients receiving drugs at low flow rates⁽¹²⁾.

Therefore, additional caution is necessary when using SIP at the lowest flow rates, mainly during the use of vasoactive drugs in severely ill patients. The lowest flow rates can lead to the highest start-up delays; hence, clinicians should use flow rates under 1 mL/h only in specific situations due to the increased risk of dosing errors and related adverse events.

This study has limitations regarding the possible influence of the size or brand of the syringe on the accuracy of the analyzed equipment. Studies with other sizes and brands of syringes should be conducted to understand the influence of different types of accessories used in intravenous therapy on dosing errors. Moreover, only two brands of SIP were investigated, compromising the generalization of the results to other similar equipment.

Start-up delay has a high potential to compromise patient safety during the use of vasoactive drugs in patients in intensive care, as the delay in the infusion can lead to a deleteriously long time to start drug therapy. A simple strategy of using electronic purging can significantly increase the equipment performance at low infusion rates. Nurses can use this option especially during the infusion of vasoactive drugs at low infusion rates.

The start-up delay was higher at lower rates, mainly at the infusion rate of 0.3 mL/h.

The purging technique influenced the performance of the SIP, especially causing a start-up delay with low infusion rates. Purging the IV system through the bolus option of the pump, thereby maintaining the pressure within the IV system, led to shorter delays, improving the SIP performance.

REFERENCES

- 1. U.S. Food and Drugs Administration (FDA) [Internet]. Silver Spring: FDA; 2018 [cited 2018 Aug 22]. Infusion Pumps; [about 3 screens]. Available from: https://www. fda.gov/medical-devices/general-hospital-devices-and-supplies/infusion-pumps
- Mandel JE. Understanding infusion pumps. Anesth Analg. 2018;126(4):1186–9. doi: https://doi.org/10.1213/ANE.00000000002396
- Wilson AMMM, Peterlini MAS, Pedreira MLG. Hemolysis risk after packed red blood cells transfusion with infusion pumps. Rev Lat-Am Enfermagem. 2018;26:e3053. doi: https://doi.org/10.1590/1518-8345.2625.3053
- Giuliano KK. Intravenous smart pumps: usability issues, intravenous medication, administration error, and patient safety. Crit Care Nurs Clin North Am. 2018;30(2):215-24. doi: https://doi.org/10.1016/j.cnc.2018.02.004
- Moreira APA, Escudeiro CL, Christovam BP, Silvino ZR, Carvalho MF, Silva RCL. Use of technlogies in intravenous therapy: contributions to a safer practice. Rev Bras Enferm. 2017;70(3):595–601. doi: https://doi.org/10.1590/0034-7167-2016-0216
- Baeckert M, Batliner M, Grass B, Buehler PK, Daners MS, Meboldt M, et al. Performance of modern syringe infusion pump assemblies at low infusion rates in the perioperative setting. Br J Anaesth. 2020;124(2):173–82. doi: https://doi. org/10.1016/j.bja.2019.10.007
- Batliner M, Weiss M, Dual SA, Grass B, Meboldt M, Daners MS. Evaluation of a novel flow-controlled syringe infusion pump for precise and continuous drug delivery at low flow rates: a laboratory study. Anaesthesia. 2019;74(11):1425-31. doi: https://doi.org/10.1111/anae.14784

- Kim UR, Peterfreund RA, Lovich MA. Drug infusion systems: technologies, performance, and pitfalls. Anesth Analg. 2017;124(5):1493–505. doi: https:// doi.org/10.1213/ANE.00000000001707
- Madson ZC, Vangala S, Sund GT, Lin JA. Does carrier fluid reduce low flow drug infusion error from syringe size? World J Clin Pediatr. 2020;9(2):17–28. doi: https:// doi.org/10.5409/wjcp.v9.i2.17
- Genay S, Décaudin B, Scoccia S, Barthélémy C, Debaene B, Lebuffe G, et al. An in vitro evaluation of infusion methods using a syringe pump to improve noradrenaline administration. Acta Anaesthesiol Scand. 2015;59(2):197–204. doi: https://doi. org/10.1111/aas.12439
- Neal D, Lin JA. The effect of syringe size on reliability and safety of low-flow infusions. Pediatr Crit Care Med. 2009;10(5):592–6. doi: https://doi.org/10.1097/ PCC.0b013e3181a0e2e9
- Felipe MAA, Latour JM, Peterlini MAS, Pedreira MLG. Placement of syringe infusion pumps and solution density can impact infusion performance: an experimental study. J Neonatal Nurs. 2020;26(3):149–51. doi: https://doi.org/10.1016/j. jnn.2019.09.010
- 13. Van der Eijk AC, Van Rens RMFPT, Dankelman J, Smit BJ. A literature review on flow-rate variability in neonatal IV therapy. Paediatr Anaesth. 2013;23(1):9-21. doi: https://doi.org/10.1111/pan.12039
- 14. Kannan S. Potential hazard with syringe infusion pump. Anaesthesia. 2001;56(9):906-24. doi: https://doi.org/10.1046/j.1365-2044.2001.02230-13.x
- Snijder RA, Egberts TCG, Lucas P, Lemmers PMA, van Bel F, Timmerman AMDE. Dosing errors in preterm neonates due flow rate variability in multi-infusion syringe pumps setups: An in vitro spectrophotometry study. Eur J Pharm Sci. 2016;93:56-63. doi: https://doi.org/10.1016/j.ejps.2016.07.019

Acknowledgment:

Financial support – National Council for Scientific and Technological Development – CNPq, Brazil. Grants n. 474906 and 308281/2015-2.

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The authors declare that there is no conflict of interest.

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Editor-in-chief: Maria da Graça Oliveira Crossetti

Received: 03.29.2021 Approved: 09.13.2021