Comparing the Effects of Pulsatile and Continuous Flushing on Time and Type of Peripheral Intravenous Catheters Patency: A Randomized Clinical Trial

Seyed Javad Hosseini\(^a\), Fereshteh Eidy\(^b\), Majid Kianmehr\(^c\), Ali Asghar Firouzian\(^d\), Fatemeh Hajiabadi\(^e\), Mahmoud Marhamati\(^f\), Mahbobeh Firooz\(^g\)

\(^a\)Department of Nursing, Esfarayen Faculty of Medical Sciences, Esfarayen, Iran
\(^b\)Department of Biostatistics, Esfarayen Faculty of Medical Sciences, Esfarayen, Iran
\(^c\)Department of Basic Sciences, Esfarayen Faculty of Medical Sciences, Esfarayen, Iran
\(^d\)Department of Medical Surgical, Faculty of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

**Introduction:** Peripheral intravenous catheters (PICs) patency techniques such as flushing are widely used in the hospitals to facilitate infusion of drugs and blood to patients.\(^1\) It is expected that the PICs remain in situ for 72-96 hours (h).\(^2\) Phlebitis and occlusions are common causes of PICs failure.\(^3\) The frequent PICs replacing can cause pain and anxiety in patients; hence, the medical team tries to keep PICs for as long as possible.\(^4\) The effective factors in maintaining a functional catheter include the use of appropriate disinfection solutions before inserting, choosing the right PIC size, injecting the drugs based on the protocol, adequate fixation of PIC in situ, and ultimately using different catheter patency techniques.\(^5\) These techniques are either an infusion of normal saline (N/S) during 24 h (keep vein open, KVO) or an intermittent solution injection known as flushing. In the flushing technique, a small amount of solution such as N/S is injected into the catheter for a short time. Nowadays, it is recommended in both pulsatile and continuous approaches.\(^6\) The continuous flushing (CF) produces a laminar flow with a greater velocity in the middle part than the lateral intraluminal surface of the PIC and venous. However, a turbulent flow is created in the pulsatile flushing (PF) due to varying speed in lateral and central of duct.\(^7-9\) Drugs can deposit on the intraluminal surface, while it is presumed that turbulent flow is more effective than laminar flow in cleaning the duct. An in vitro study showed a greater effect of PF on reducing the bacterial colonization in the central venous catheter (CVS) than the CF technique.\(^10\) As far as the researchers investigated, there was no comparative research evaluating the effects of these techniques on PICs patency in the clinical studies. CF technique was performed in a few research studies on hospitalized patients and the results showed that neither changing in volume nor frequency can significantly affect patency time. Unfortunately, there is no standard protocol or sufficient clinical evidence related to flushing and there is no consensus among the researchers regarding the instructions used to maintain catheter patency.\(^11,12\)

**Methods:** In this double-blind randomized clinical trial, 71 patients were randomly assigned into two groups of PF (n = 35) and CF (n = 36). The PF protocol was performed as successive injections of 1 mL normal saline (N/S) per second (sec) with a delay of less than 1 sec until the completion of 5 mL of solution. However, CF protocol was performed by injecting 5 mL N/S within 5 sec without any delay before and after each medicine administration. Data related to the time and type of PICs patency were collected using a patency checklist every 12 hours (h) up to 96 h. The statistical analysis was done by R statistical software (Version 3.5.1).

**Results:** The results showed that the number of PICs remaining open was not significantly different between PF and CF groups during 96 h. The highest number of PICs excluded from the study was related to the time of 96 h as a result of partial patency in the two groups.

**Conclusion:** There was no difference between CF and PF regarding the time and type of PICs patency. Thus, both techniques can be used to maintain the catheter patency.
facilitated decision making for selecting the best technique, and subsequently increased PICs longevity. Nursing knowledge has always sought to improve patient care quality, and flushing techniques may reduce catheter insertion frequency and result in less pain and anxiety in patients. Therefore, this study aimed to compare the effects of PF and CF on time and type of PICs patency in patients admitted to medical and surgical wards of Imam Khomeini Hospital in Esfarayen, Iran.

Materials and Methods
In this double-blinded randomized clinical trial (IRCT20141222020394N4), 71 patients were selected by convenience sampling and then randomly assigned into two groups of CF and PF. All the patients signed an informed consent to participate in the study.

The inclusion criteria were: age range of 18-60 years; receiving medication through PICs for a minimum of 6 h and a maximum of 12 h; not receiving continuous infusion over 12 h; normal hematocrit, PT, and PTT tests; absence or having only one major risk factor (hypertension, diabetes, hyperlipidemia); and the lack of vascular diseases. The exclusion criteria were: receiving hyperosmolar solution through the PIC; receiving more than two simultaneous drug injections; receiving heparin and warfarin; leakage and catheter removal from its place; being under cardiopulmonary resuscitation; and patient discharge from the hospital before the replacement of the PIC due to occlusion.

Randomization was performed by applying a random number table (numbers 0–4 correspond to PF group and 5–9 to CF group) and the patients were randomly assigned into two groups. For allocation concealment, the intervention type was determined on a piece of paper and put inside envelopes that were numbered sequentially. The envelopes were opened based on the entry of the participants to the study, and then the type of group was determined. The patient and catheter evaluator were blinded to the group in which the patient was assigned.

Upon the patient's hospitalization in the ward, demographic information questionnaire was filled for them in the pre-intervention phase. Then, the nurse inserted a PIC No. 20 (Mais India) in the forearm area. The insertion site was disinfected with 70% alcohol before the insertion; then, it was fixed by two anti-allergic adhesives in situ. The date and time of PIC insertion were recorded. The study process from recruitment to analysis is shown in Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Figure 1).

Following a pilot study (10 patients in the each group), using mean (SD) time of 80.04 (16.18) and 91.05 (15.81) between CF and PF groups, respectively, statistical power of 0.8, and a 95% confidence interval, the sample size was determined to be 33 in each group based on the mean comparison formula. Considering the possible subject loss, 36 patients were included in each group. One patient was excluded due to discharge against medical advice in the PF group (Figure 1). In the PF group, 5 mL N/S was

![Figure 1. Flow chart of the study](chart.png)
injected by successive boluses of 1 mL per second (sec) with a delay less than 1 sec until it was completed. In the CF group, 5 mL N/S was injected into PICs within 5 sec without any delay. All techniques were performed through injection port (top of PIC) before and after each medicine administration.

In order to evaluate PIC patency, the researcher inserted syringe (2 mL) in PIC entry (after removing the luer lock plug) and syringe plunger was pulled by hand motion; blood reversing in the syringe barrel was considered the PIC patency. Two criteria were applied to differentiate partial patency and occluded PICs. In case the blood reversing was not shown, but N/S can be injected into the PICs that were considered partial patency. Also, PICs blood reversing was not shown and N/S cannot be injected into the PICs were considered as occlusion. Patency was evaluated every 12 h. The time of the PICs with partial open and occluded were recorded in the checklist and excluded from the study. The study was continued for 96 h (to be considered as the catheter longevity as routine) in the absence of occlusion. We also recorded the type and number of injection drugs every 12 h.

The validity of the PIC patency checklist was confirmed through content validity by 10 faculty members, and the reliability was approved based on the inter-evaluator agreement (kappa statistic: 0.87). Finally, the data were analyzed by the R Statistical software (Version 3.5.1). The Kolmogorov-Smirnov test was used to evaluate the normality of data, and Mann-Whitney U test and Chi-square were used to examine the homogeneity of demographic variables in the two groups. The type of patency (full and partial) and PIC occlusion were reported using the descriptive statistical indices (frequency and mean). The Fisher’s exact test was also applied to compare the patency of catheters in the two groups. A P-value less than 0.05 was considered as significant.

**Results**

The mean (SD) age in the PF and CF groups was 45.52 (14.03) and 47.97 (12.77) years, respectively. The results of Mann–Whitney U-test showed that the mean age was not significantly different between the two groups (P = 0.44). Moreover, the results of Chi-square (for gender, BMI, history of chronic disease and type of the ward variables) and Fisher’s exact (type of antibiotic) tests indicated no significant differences between the two groups (Table 1).

Based on the results, 19 and 12 PICs remained open in the PF and CF groups after 96 h, respectively. The largest number of PICs in the PF (n = 13) and CF (n = 20) groups excluded from the study were related to the partial patency at hour 96. Moreover, occlusion occurred in 3 and 4 PICs during the 96-h interval in the PF and CF groups, respectively. The results of Fisher’s exact test revealed no statistically significant difference between the PF and CF groups regarding the type of catheter patency (P = 0.22) (Table 2).

### Table 1. Baseline demographic and clinical data

| Variables                  | Pulsatile flushing (PF) N (%) | Continuous flushing (CF) N (%) | P value |
|----------------------------|--------------------------------|--------------------------------|---------|
| Gender                     | 16 (45.7)                      | 13 (36.1)                      | 0.41    |
| Male                       | 19 (54.3)                      | 23 (63.9)                      |         |
| Ward                       | Medical                        | 29 (82.9)                      | 29 (80.6) | 0.21 |
|                           | Surgical                       | 6 (17.1)                       | 7 (19.4)  |     |
| History of chronic disease | Yes                            | 11 (31.4)                      | 16 (44.4) | 0.49 |
|                           | No                             | 24 (68.8)                      | 20 (55.6) |      |
| BMI                        | Underweight                    | 1 (2.9)                        | 1 (2.8)   |     |
|                           | Normal                         | 22 (62.9)                      | 26 (72.2) | 0.25 |
|                           | Pre-obesity and obesity        | 12 (34.3)                      | 9 (25)    |      |
| Antibiotic type            | Ceftriaxone                    | 27 (77.2)                      | 28 (77.7) | 0.39 |
|                           | Cefazoline                     | 4 (11.4)                       | 3 (8.3)   |     |
|                           | Gentamycin                     | 2 (5.7)                        | 3 (8.3)   |     |
|                           | Ciprofloxacin                  | 2 (5.7)                        | 2 (5.7)   |     |

*Chi square test, †Fisher exact test*

The results of Mann–Whitney U-test revealed no statistically significant difference between the PF and CF groups regarding the time (h) of using PICs for injection drugs based on complete open (P = 0.49) (Table 3).

**Discussion**

According to the results, no statistically significant difference was found between the PF and CF groups regarding the time and type of PICs patency. Since the flushing techniques have not been thoroughly assessed in previous clinical studies, we had limitations in comparing the results of this study with similar cases.

Keogh et al., examined the effect of four different CF regimes (3 mL and 10 mL N/S executed every 6 and 24 h before and after each drug injection) and reported that none of them were superior to another. The occlusion occurred in 14% of the PICs, which was more than CF group in our research (11.11%). The difference seems to be due to different size of the PICs used in the two studies. While we used merely the No. 20 PICs, Keogh et al., used No. 20 and 22 PICs. According to a previous study, the PICs larger and smaller than No. 20 can decrease the catheters’ longevity. Furthermore, the mentioned study did not determine the N/S injection time in the CF protocol.

The results of an in vitro study by Ferroni et al., revealed that PF technique is at least twice as effective as CF in reducing the catheters’ bacterial colonization rate. CF technique consisted of injecting 10 mL N/S in one hand movement into catheters. Moreover, PF was done through injecting 1 mL N/S in one-tenth of a sec with 0.9 sec pause until the injection of 10 mL was completed. The flushing time lasted 10 sec and was less than that in our study. Increasing injection time leads to decreasing the flow velocity, which subsequently decreases clearing rate. To create a turbulent flow, the Reynolds number
Comparing pulsatile & continuous flushing on PICs patency

Comparing the frequency of time and type of PICs patency in the two groups

| Groups                  | N    | Time (h) | P value |
|-------------------------|------|----------|---------|
|                         | 12   | 24       | 36      | 48      | 60      | 72      | 84      | 96      |
| **Continuous flushing (CF)** |      |          |         |         |         |         |         |         |
| Open                    | 36(100) | 36(100) | 36(100) | 32(88.9) | 32(88.9) | 28(77.78) | 28(77.78) | 12(33.33) |
| Partial open            | 0 (0)  | 0 (0)    | 0 (0)   | 1 (2.8)  | 1 (2.8)  | 4(11.11)  | 4(11.11)  | 20(55.56) |
| Occlusion               | 0 (0)  | 0 (0)    | 0 (0)   | 3 (8.3)  | 3 (8.3)  | 4(11.11)  | 4(11.11)  | 3(8.57)   |
| **Pulsatile flushing (PF)** |      |          |         |         |         |         |         |         |
| Open                    | 35(100) | 35(100) | 35(100) | 31(88.58) | 31(88.58) | 29(82.87) | 29(82.87) | 19(54.28) |
| Partial open            | 0 (0)  | 0 (0)    | 0 (0)   | 3 (8.57) | 3 (8.57) | 5(14.28)  | 5(14.28)  | 13(37.15) |
| Occlusion               | 0 (0)  | 0 (0)    | 0 (0)   | 1 (2.85) | 1 (2.85) | 1(2.85)   | 1(2.85)   | 3 (8.57)  |

*Fisher’s exact test

| Table 2. Comparing the time (h) of PICs patency (completely open) between the two groups |
|-----------------------------------------------|---------------|
| Pulsatile flushing med* (IQR) x | Continuous flushing med* (IQR) x | P       |
| 96 (96-96)                        | 96 (87-96)    | 0.49   |

| Table 3. Comparing the time (h) of PICs patency (completely open) between the two groups |
|-----------------------------------------------|---------------|
| 96 (96-96)                        | 96 (87-96)    | 0.49   |

*Median, *Interquartile range (Q1-Q3). *Mann–Whitney U- test

N/S before and after medicine administration, which can act as a locking. In general, 1-3 mL N/S is recommended for injecting into PICs in this technique.11

Xu et al., suggested no differences on the catheter patency between the two groups in the injection of N/S (3 mL) and heparinized saline (3 mL plus 150 heparin units) after drug injection. Occlusion occurred in 18.16% with 3 mL N/S, while in current study 11.11% of the PICs were closed for a total of 96 h in the CF group. The higher volume of N/S used for flushing technique may be the reason for the difference, which allows for better purification of the PICs duct.

The main limitation of current study was the implementation of protocols on patients receiving injectable medications less than three injections simultaneously. It is recommended that similar studies be performed with more medications. Also, future studies can compare the effects of flushing and saline lock separately on PICs patency.

Conclusion

There are different methods for the patency of PICs such as the continuous infusion of N/S in 24 h, locking method with N/S or the heparinized saline, as well as the PF and CF approaches. The flushing technique is done before and after every injection of the drug into the catheter. Their time and solution volume are important in purifying the PICs and venous ducts. Current study results revealed no difference between the CF and PF techniques at the patency time of PICs. Thus, both techniques can be used for this aim.

Acknowledgments

We would like to thank the clinical research development unit Imam Khomeini Hospital in Esfarayen, Iran and the patients admitted to the medical and surgical wards that perfectly cooperated in this study. We thank the vice-chancellor of research at Esfarayen Faculty of Medical Sciences for the financial support of the study.

Ethical Issues

The ethics committee of Sabzevar University of Medical Sciences, Iran approved the study protocol (ethics code: 1395.112). Informed oral and written consent was obtained from all participants after a brief explanation about the aims of the study.
Research Highlights

What is the current knowledge?
One of the techniques used to keep the peripheral venous catheter patency is flushing, which can be applied in the clinical setting in two continuous and pulsatile modes. Limited studies have compared the effects of these two techniques.

What is new here?
Continuous flushing (CF) and pulsatile flushing (PF) have similar effects on the peripheral venous catheters patency, and both can be used in clinical settings.

Conflict of Interest
The authors declared no conflict of interests.

Author’s Contributions
SJH, MF: Conception and design; AAF, MM: acquisition of data; FE: Analysis and interpretation of data; FH, MK, MF, SJH: Drafting the article; MF; SJH: Review of article and find approval.

References
1. Xu L, Hu Y, Huang X, Fu J, Zhang J. Heparinized saline versus normal saline for maintaining peripheral venous catheter patency in China: an open-label, randomized controlled study. J Int Med Res 2017; 45(2): 471-80. doi: 10.1177/0300060516685203
2. Heng SY, Yap RT, McGrouther DA. Innovative Solutions and Insights to Phlebitis Prevention. Am Med J 2020; 133(3): 261-264. doi: 10.1016/j.ammed.2019.07.047
3. Milani K, Taravella R, Thillard D, Chauvin V, Martin E, Edouard S, et al. Peripheral venous catheter-related adverse events: evaluation from a multicentre epidemiological study in france (the CATHEVAL Project). PloS one 2017; 12(1): e0168637. doi: 10.1371/journal.pone.0168637
4. Van Loon FH, Puijn LA, Van Aarle WH, Dierick-Van Dael AT, Bouwman AR. Pain upon inserting a peripheral intravenous catheter: size does not matter. J Vasc Access 2018; 19(3): 258-65. doi: 10.1177/1129729817747531
5. Lee S, Kim K, Kim JS. A Model of phlebitis associated with peripheral intravenous catheters in orthopedic inpatients. Int J Environ Res Public Health 2019; 16(18):3412. doi: 10.3390/ijerph16183412
6. Chou PL, Fu JY, Cheng CH, Chu Y, Wu CF, Ko PJ, et al. Current port maintenance strategies are insufficient: view based on actual presentations of implanted ports. Medicine (Baltimore) 2019; 98(44): e17757. doi: 10.1097/MD.0000000000017757
7. Moureau NL. Vessel health and preservation: the right approach for vascular access. 1st ed. Berlin: Springer; 2019.
8. Boord C. Pulsatile flushing: a review of the literature. J Infus Nurs 2019; 42(1): 37-43. doi: 10.1097/NAN.0000000000000311
9. Koeppen BM, Stanton BA. Berne and Levy physiology e-book: elsevier health sciences. 6th ed. United States: Mosby; 2017.
10. Tong C, Peng X, Hu H, Wang Z, Zhou H. The effect of different flushing methods in a short peripheral catheter. Acta Cir Bras 2019; 34(8): e201900804. doi: 10.1590/s0102-86502019008000004
11. Okamura N, Yamato T, Yamaoka I. Evaluation of the amount of residual lipid emulsion in chambers of flushed totally implantable venous access devices using fluorescence imaging. Eur J Clin Nutr 2019; 73(7): 1084-7. doi: 10.1038/s41430-019-0443-8
12. Keogh S, Flynn J, Marsh N, Mihala G, Davies K, Rickard C. Varied flushing frequency and volume to prevent peripheral intravenous catheter failure: a pilot, factorial randomised controlled trial in adult medical-surgical hospital patients. Trials 2016; 17(1): 348. doi: 10.1186/s13063-016-1470-6
13. Wallis MC, McGrail M, Webster J, Marsh N, Gowdward J, Playford EG, et al. Risk factors for peripheral intravenous catheter failure: a multivariate analysis of data from a randomized controlled trial. Infect Control Hosp Epidemiol 2014; 35(1): 63-8. doi: 10.1086/674398
14. Ferroni A, Gaudin F, Guiffant G, Flaud P, Durussel JJ, Descamps P, et al. Pulsatile flushing as a strategy to prevent bacterial colonization of vascular access devices. Med Devices (Auckl) 2014; 7: 379-83. doi: 10.2147/MEDER. S71217
15. Parreira P, Sousa LB, Marques IA, Santos-Costa P, Braga LM, Cruz A, et al. Double-chamber syringe versus classic syringes for peripheral intravenous drug administration and catheter flushing: a study protocol for a randomised controlled trial. Trials 2020; 21(1): 78. doi: 10.1186/s13063-019-3887-1
16. Guiffant G, Durussel JJ, Merckx J, Flaud P, Vigier JP, Mousett P. Flushing of intravascular access devices (IVADs) - efficacy of pulsed and continuous infusions. J Vasc Access 2012; 13(1): 75-8. doi: 10.1530/JVA.2011.4847
17. House AA, Wanner C, Sarnak MJ, Piña IL, McIntyre CW, Komenda P, et al. Heart failure in chronic kidney disease: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. Kidney Int 2019; 95(6): 1304-7. doi: 10.1016/j.kint.2019.02.022
18. Zhong L, Wang HL, Xu B, Yuan Y, Wang X, Zhang YY, et al. Normal saline versus heparin for patency of central venous catheters in adult patients - a systematic review and meta-analysis. Critical Care 2017; 21(1): 5. doi: 10.1186/s13054-016-1585-x
19. Lópe-Briz E, Ruiz García V, Cabello JB, Bort-Martí S, Carbonell Sanchis R, Burls A. Heparin versus 0.9% sodium chloride locking for prevention of occlusion in central venous catheters in adults. Cochrane Database Syst Rev 2018; 7(7): CD008462. doi: 10.1002/14651858.CD008462. pub3
20. Klein J, Jepsen A, Patterson A, Reich RR, Mason TM. Heparin versus normal saline: flushing effectiveness in managing central venous catheters in patients undergoing blood and marrow transplantation. Clin J Oncol Nurs 2018; 22(2): 199-202. doi: 10.1188/18.CJON.199-202
21. Heidari Gorji MA, Rezaei F, Jafari H, Yazdani Cherati J. Comparison of the effects of heparin and 0.9% sodium chloride solutions in maintenance of patency of central venous catheters. Anesth Pain Med 2015; 5(2): e22595. doi: 10.5812/aapm.22595