ORIGINAL RESEARCH

Khaya-warmer: blood warming in a resource-constrained setting

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Background: Blood warming poses a challenge for healthcare workers in a resource-constrained setting due to financial limitations. Various blood-warming methods have been studied, but to our knowledge, none have investigated inline gravitational blood warming using a preheated water bath. We aimed to test the efficiency of an improvised blood warmer (named the Khaya-warmer) to warm cold packed red blood cells (PRBC) to a mean temperature of 35℃, utilising consumables readily available in a resource-constrained setting. The primary outcome was the outflow temperature–time profile; secondary outcomes included flow rates and cost comparisons with standard methods.

Methods: This was a laboratory-based, experimental, proof-of-concept study. We ran 20 cold PRBC units through extended blood transfusion lines, each immersed in a 1 000 ml water bath preheated to 46℃. Using a 4-probe electronic thermometer, we measured the following temperatures: ambient, PRBC bag, water bath and outflow.

Results: Mean outflow temperature was 35.2°C (95% CI 35.1–35.4); mean emptying time 9.0 minutes (95% CI 8.7–10.2) with a mean flow rate of 25.4 ml.min^{-1} (95% CI 24.1–26.6).

Conclusion: The Khaya-warmer proved to be effective in safely warming cold PRBC units to a mean temperature of 35.2°C using a cost-effective method. Future studies include investigating various flow rates using a pressure bag or a flow regulating device, and to replace the preheated water bath with a thermally insulated flask.

Keywords: resource-constrained setting, blood warming, blood transfusion, inline gravitational flow blood transfusion, outflow temperature

Introduction

Blood warming in a resource-constrained setting poses a challenge for healthcare workers. Financial limitations, expensive devices and single-use consumables make fluid warmers a scarce commodity in these settings. The Western Cape Blood Service stores packed red blood cells (PRBC) and whole blood at 4–6℃. Transfusing 1 unit of PRBC at 4℃ or 1 L of a crystalloid solution at room temperature, causes a decrease in core temperature of 0.25℃.[1] This can contribute to the rapid development of hypothermia, which is defined as a core temperature below 35℃.[2] Preventing hypothermia is important not only for patient comfort, but also for preventing morbidity and mortality. Important issues in the perioperative setting include impaired wound healing, coagulopathy with an increase in allogeneic transfusion requirements, arrhythmias and death.[3-7]

Approved, commercially available fluid warming systems are the gold standard for fluid warming prior to transfusion. Examples include the HOTLINE® Level 1 Fluid Warmer (SIMS Level 1, Inc., Rockland, MA, USA), the Level 1 Rapid Infuser (Level 1 Technologies Inc., Rockland, MA, USA), the Ranger™ Blood/Fluid Warming Unit (Arizant Healthcare, Eden Prairie, MN, USA) and the enFlow™ IV Fluid/Blood Warmer (GE Healthcare, Munich, Germany). These fluid warmers can deliver fluids at acceptably rapid rates while maintaining outflow temperatures above 32℃. However, their cost has rendered them unavailable in resource-constraint settings where hypothermia is a frequent risk.

Out of necessity, improvised methods of fluid warming are often used at resource-constrained healthcare facilities. Examples include running warm water over a cold unit of PRBC, exposing PRBC units to sunlight, flushing warm saline into PRBC units and most commonly submerging PRBC units in a warm water bath.[8,9] These techniques are associated with numerous issues, including being time consuming and ineffective during emergencies requiring rapid transfusions. Furthermore, these techniques waste water, do not warm PRBC homogeneously and most importantly, pose a high risk of haemolysis. Warming PRBC to temperatures above 47℃ causes significant haemolysis.[10-13]

The ideal solution would be a safe, cost-effective method that is available in all healthcare settings. We decided to investigate the efficacy and cost-effectiveness of an inline gravitational warming device using consumables readily available in a resource-constrained setting.

Methods

We conducted a laboratory-based, experimental, proof-of-concept study to determine whether PRBC units can be warmed safely to a mean temperature of 35℃ using a warm water bath, that we named the Khaya-warmer. The primary outcome was the mean temperature of the warmed PRBC. Secondary outcomes included the rates of transfusion through the Khaya-warmer as well as cost-effectiveness. The Health Research Ethics Committee of the Stellenbosch University granted approval for the study (HREC reference number: S20/11/342).

A unit of cold PRBC was suspended, on a mobile drip stand, 100 cm above the working surface, measured from the top of the blood bag to the working surface. A graphical representation of the system is given in Figure 1. The warm water bath consisted of an empty 1 000 ml, plastic, 0.9% sodium chloride solution bottle (B Braun medical, Autosterile 0.9% Sodium Chloride for Irrigation 1 000 ml), from which the neck had been cut off. The bottle was secured to a drip stand using cable ties, with the shoulder of the bottle at the level of the working surface. The outflow receptacle was a similar plastic bottle with a polyvinyl chloride funnel placed in the inlet. The receptacle was placed on a bench with the height of the neck of the bottle in line with the working surface (outflow bottle).

Two extension lines, each 100 cm long, and each with a priming volume of 7.79 ml and a 3-way tap (Becton Dickinson L303/100), were attached to a blood transfusion line, 180 cm long, with a priming volume of 12.7 ml, incorporating a 200-micron blood filter (B Braun Medical, BBMZA20210, 10 drops/ml needle free filtered dropper, male Luer lock). The roller clamp was closed shut and the extended transfusion line was inserted into the unit of PRBC. The first 60 cm ran from the PRBC unit to the inlet of the empty warm water bath. The subsequent 303 cm was carefully coiled within the empty warm water bath, taking care not to kink the tubing. The distal 30 cm was outside the bottle with the distal end placed in the PVC funnel of the outflow bottle.

We used an electronic 4-probe thermometer (Sloth Electronics (Pty) Ltd.). A temperature probe, labelled 'ambient', was suspended above the working surface and recorded the room temperature. A 1 cm cut was made in the top corner of the PRBC bag and a temperature probe labelled 'blood' was placed inside the unit. A temperature probe labelled 'water bath' was placed in the water bath. The distal outflow end of the transfusion set was secured to the temperature probe labelled 'outflow' to measure the outflow temperature. A combination of boiled water and cold tap water to a total of 1 000 ml at a starting temperature of 46°C was placed in the water bath. In our laboratory, this was
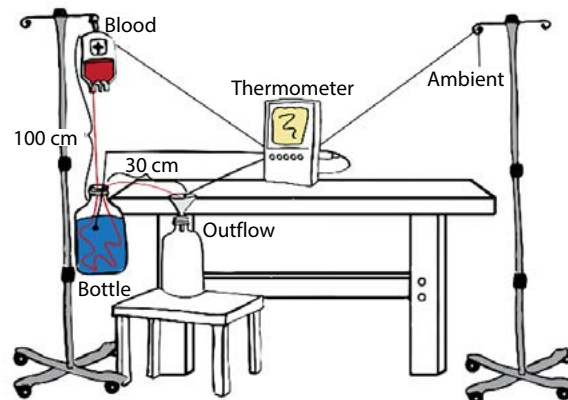

Figure 1: Diagram illustrating the Khaya-warmer system

a combination of ± 420 ml boiled water and ± 580 ml cold tap water. A timer was started as soon as the roller clamp was fully opened, allowing the cold blood to drain through the transfusion line within the warm water bath and into the outflow bottle. The timer was stopped as soon as the PRBC unit was empty. The volume drained into the outflow bottle was measured in millilitres. We conducted 20 experiments at a room temperature of 21°C.

Data were downloaded from the electronic thermometer into a Microsoft Excel® spreadsheet (Microsoft Corp., Redmond, Washington, USA) for graphing and checked for errors. Descriptive statistics were performed using MedCalc® Statistical Software v20.110 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2022). Sample size calculation was done using the following equation:[14]

$$N = \frac{4*(Z_{1-\alpha/2})^2*s^2}{\omega^2}$$

Where N = sample size; $Z_{1-\alpha/2}$ = 1.96; s = standard deviation; ω = width of the desired 95% confidence interval (CI). For a desired

Table I: Results of the 20 experiments

		Mean (95% CI)	Range
Outflow temperature	Initial	22.0 (21.7–22.3)	21.3–24.3
	Maximum	38.9 (38.7–39.0)	38.2–39.6
	End	34.3 (34.0–34.6)	32.9–35.6
	Mean	35.2 (35.1–35.4)	34.8–35.6
Blood bag temperature	Initial	3.9 (3.1–4.8)	-0.5–6
	Mean	6.2 (5.6–6.8)	3.3–8.2
Water bath temperature	Initial	46.0	46.0–46
	End	36.5 (36.1–37.0)	34.3–37.9
	Mean	40.9 (40.6–41.2)	39.2–41.8
Mean ambient temperature		21.1 (21.1–21.2)	20.9–21.4
Duration (minutes)		9.0 (8.7–10.2)	7.6–13.4
Volume delivered (ml)		241 (230–252)	200–300
Flow rate (ml.min⁻¹)		25.4 (24.1–26.6)	19.4–29.8

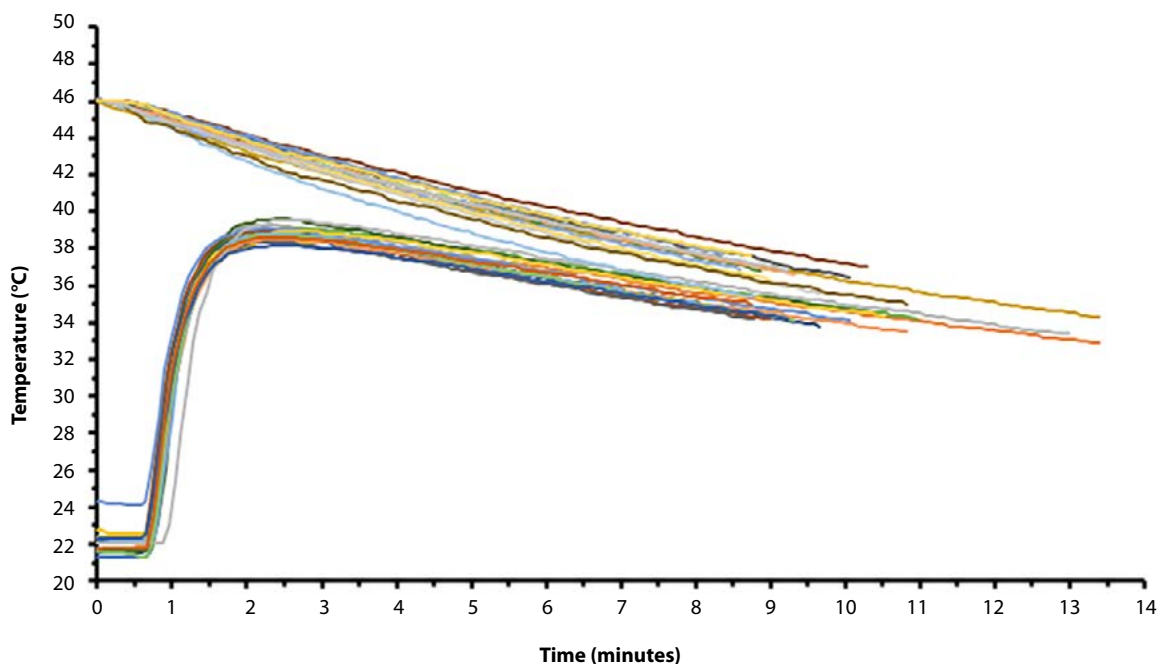Temperatures are in degrees Celsius; 95% CI – 95% confidence interval

Figure 2: Water bath and outflow temperatures over time
Upper plots – water bath temperatures; lower plots – outflow temperatures
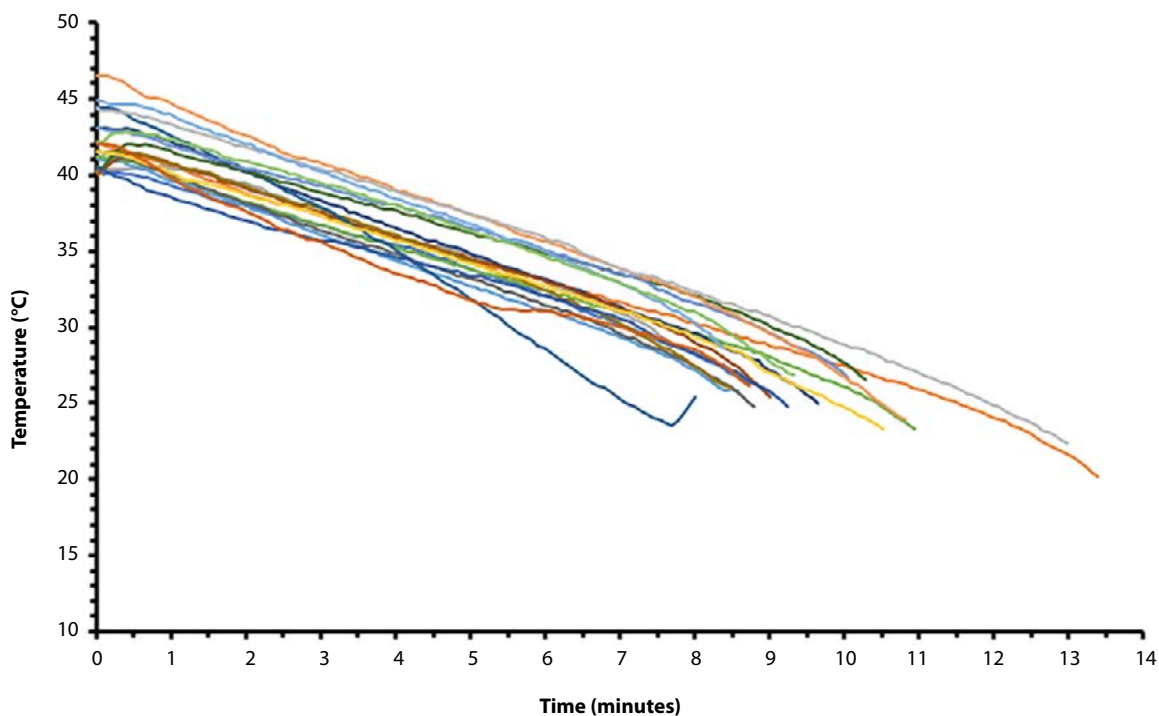Lag times in outflow temperatures were due to transfusion lines not being preprimed with blood.

Figure 3: Temperature gradients between blood bag and water bath over time

95% CI of 1.0°C and standard deviation 1.0°C, the minimum required sample size is 15 experiments. We planned 20 experiments to allow for incomplete experiments resulting from technical difficulties. We purchased 20 units of expired PRBC units from the Western Cape Blood Service.

Results

Results are presented in Table I and Figures 2 and 3. After an approximate one-minute lag, output temperature increased steeply to a mean maximum of 38.9°C at 2.5 minutes, decreasing linearly to a mean end-temperature of 34.3°C. Mean delivered volume was 241 ml, transfused during a mean of 9 minutes. All experiments started with a warm water bath temperature of 46°C, which decreased linearly during the study. The temperature gradient between the water bath and the blood bag also decreased linearly.

Regarding the cost-effectiveness of the Khaya-warmer: given the current cost of the commercially available fluid warming

devices, the HOTLINE® Level 1 Fluid Warmer (SIMS Level 1, Inc., Rockland, MA) is approximately 73 times more expensive than the Khaya-warmer and the Ranger™ Blood/Fluid Warming Unit (Arizant Healthcare, Eden Prairie, MN, USA) is 103 times more expensive. The single-use administration sets are 5–6.2 times more expensive than those of the Khaya-warmer.

Discussion

Hypothermia is a major contributor to perioperative mortality.[15] Transfusing warm intravenous fluids and blood products can help to avoid this complication. However, the preferred commercially available fluid warmers are expensive. In this study we designed and tested a simple, inexpensive device using resources available at most public healthcare facilities. It consistently warmed PRBC units to a mean temperature of 35.2℃ at a mean flow rate of 25.4 ml.min⁻¹.

To our knowledge there are no studies that have evaluated blood warming, using inline, gravitational flow through a warm water bath. Proving the efficacy and safety of this method can be beneficial for preventing hypothermia, especially in settings that have previously relied on improvised methods either not considered safe or even shown to be harmful. We did not compare our technique with other improvised methods. However, considering the disadvantages of the latter, our device appears effective and safe. For example, methods such as running warm water over a cold PRBC unit, exposing PRBC units to sunlight, flushing warm saline into a PRBC bag and, most commonly, submerging a PRBC unit in a warm water bath,[8,9] are associated with a myriad of issues. These include being time consuming and thus not feasible in an emergency, wasting water, inability to warm the PRBC homogeneously and most importantly, haemolysis within the PRBC.[12,13] A meta-analysis published in 2015 concluded that heating blood to 46℃ does not produce significant haemolysis.[13] Studies done by Chalmers[10] and Van der Walt[11] supported this finding. In our study, the Khaya-warmer water temperature never exceeded 46℃ and the mean blood outflow temperature was 35.2℃, with a maximum of 38.9℃. The risk of haemolysis was therefore well controlled. The 1 000 ml water used in the warm water bottle can be replaced for subsequent transfusions. There is also no transfusion time delay, a disadvantage of prewarming methods.

The decrease of the warm water bath temperature over time to a mean nadir of 36.5℃ resulted in a corresponding decrease in temperature gradient between the blood bag and water bath. This necessitates replacing the warm water with each subsequent transfusion. To ameliorate this, the size of the warm water bath can be increased. However, this could pose a safety concern, should the bath tip over. Another option would be to replace the warm water bath with a thermally insulated flask to prevent loss of heat to the environment. This possibility can be explored in a future study. We noted that the temperature within the PRBC units increased by as much as 10℃ during its exposure to the environment, but the temperature increases were insufficient to prevent the decline in temperature gradients between blood bag and water bath.

Infusion times ranged widely (7.6–13.4 minutes) due to various influences. Firstly, the coiling of the transfusion set inside the warm water bath did not follow the same pattern with each experiment. It is well known that flow through a straight tube is more rapid than the flow through a curved tube. This phenomenon is caused by secondary flow in the curved tube. Dean's number is used to quantify this phenomenon and is affected by the inside tube diameter and the coil radius.[16,17] A future study can possibly look at different ways of coiling to achieve an optimal flow speed. Secondly, the volume of the PRBC units varied. The average transfused volume, excluding the volume remaining in the transfusion line, was 241 ml (95% CI: 230–252). Lastly, according to the Hagen–Poiseuille equation a greater viscosity due to an increased haematocrit will also decrease flow rate.[18] This was not measured in our study, but it is known that the haematocrit differs between various PRBC units. The PRBC unit volumes and their haematocrits are factors that cannot be controlled.

The flow rates achieved in this study were maximal for this arrangement, as a gravitational feed and an open roller clamp approach was used. Our main purpose was to create a system that consistently warms blood to a mean temperature above 35℃ at a moderately rapid infusion rate. Thus, we did not investigate faster flow rates by, for example, increasing the height of the suspended PRBC bag, or applying a pneumatic pressure bag or a flow regulator. The disadvantage of these manoeuvres would be the reduced contact time of the PRBC with the heat source, which would perhaps reduce outflow temperatures. These are also options for future studies.

The preferred method for blood warming is the use of the more expensive, commercially available devices. When comparing the Khaya-warmer with the HOTLINE® Level 1 Fluid Warmer (SIMS Level 1, Inc., Rockland, MA) and the Ranger™ Blood/Fluid Warming Unit (Arizant Healthcare, Eden Prairie, MN, USA), the mean flow rates of 25.4 ml.min⁻¹ achieved by the Khaya-warmer is 6 times less than that of the Ranger™ (153 ml.min⁻¹) and the HOTLINE® (152 ml.min⁻¹) warming devices.[19] It should be noted that in the quoted study, 0.9% sodium chloride was used, which has a lower viscosity and thus an increased flow rate compared to PRBC. During simulated transfusions using gravitational flow of 0.9% sodium chloride, outflow temperatures were 35.2℃ for the Ranger™ and 31.1℃ *for the* HOTLINE®.[19] Ideally blood and IV fluids should be warmed to 37℃ prior to infusion to reduce the risk of hypothermia. Russell[20] stated that a minimum blood warmer outflow temperature of 32℃ can be acceptable, which is less than the mean temperature (35.2℃) of our study. The HOTLINE® is approximately 73 times more expensive than the Khaya-warmer, while the Ranger™ is 103 times more expensive. The single use administration sets are 5–6.2 times more expensive than that of the Khaya-warmer. Thus, the Khaya-warmer is a viable alternative in a resource-constrained setting.

PRBC units are said to be stored at 4–6°C, but we received several units at lower temperatures; even as low as -0.5°C. This wide temperature range could be regarded as a possible limitation. However, all of our outflow temperatures were satisfactory.

Conclusion

We constructed an inline gravitational flow blood warming system using materials that are readily available in a resource-constrained setting. We could successfully and safely warm PRBC units to our targeted 35°C mean outflow temperature, at a mean flow rate of 25.4 ml.min^{-1}. The heat source temperature never exceeded 46°C, with subsequent low risk for haemolysis. While commercial devices are preferred, our system could provide a safe and effective solution for warming PRBC in a financially-constrained setting. Potential for future studies include investigating the effects of various flow rates using a pressure bag or a flow regulating device, and also replacing the preheated water bath with a thermally insulated flask.

Ethical approval
This study is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

Prior to commencement of the study, ethical approval was obtained from the Stellenbosch University Health Research Ethics Committee (Project ID: 19282; HREC Reference No: S20/11/342).

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

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References

1. Sessler D. Mild perioperative hypothermia. N Engl J Med. 1997;336(24):1730-7. https://doi.org/10.1056/NEJM199706123362407.
2. Tveita T, Sieck GC. Physiological impact of hypothermia: the good, the bad, and the ugly. Physiology. 2022;37(2):69-87. https://doi.org/10.1152/physiol.00025.2021.
3. Jurkovich GJ, Greiser WB, Luterman A, Curreri WP. Hypothermia in trauma victims: an ominous predictor of survival. J Trauma. 1987;27(9):1019-24. https://doi.org/10.1097/00005373-198709000-00011.
4. Rajagopalan S, Mascha E, Na J, Sessler DI. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. Anesthesiology. 2008;108(1):71-7. https://doi.org/10.1097/01.anes.0000296719.73450.52.
5. Staikou C, Paraskeva A, Drakos E, et al. Impact of graded hypothermia on coagulation and fibrinolysis. J Surg Res. 2011;167(1):125-30. https://doi.org/10.1016/j.jss.2009.07.037.
6. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. N Engl J Med. 1996;334(19):1209-15. https://doi.org/10.1056/NEJM199605093341901.
7. Sun Z, Honar H, Sessler DI, et al. Intraoperative core temperature patterns, transfusion requirement, and hospital duration in patients warmed with forced air. Anesthesiology. 2015;122(2):276-85. https://doi.org/10.1097/ALN.0000000000000551.
8. Milligan J, Lee A, Gill M, et al. Performance comparison of improvised prehospital blood warming techniques and a commercial blood warmer. Injury. 2016;47(8):1824-7. https://doi.org/10.1016/j.injury.2016.05.038.
9. Chirawurah J, Agbekoh PE, Kaufmann EE. Design of a blood-warming device for resource-limited settings. Eur J Sci Res. 2013;103(1):7-15.
10. Chalmers C, Russell WJ. When does blood haemolyse? a temperature study. Br J Anaesth. 1974;46(10):742-6. https://doi.org/10.1093/bja/46.10.742.
11. Van der Walt JH, Russell WJ. Effect of heating on the osmotic fragility of stored blood. Br J Anaesth. 1978;50(8):815-20. https://doi.org/10.1093/bja/50.8.815.
12. Nienaber L. Evaluation of red blood cell stability during immersion blood warming. S Afr J Anaesth Analg. 2003;9(4):11-5. https://doi.org/10.1080/22201173.2003.10873013.
13. Poder TG, Nonkani WG, Tsakeu Leponkouo É. Blood warming and hemolysis: a systematic review with meta-analysis. Transfus Med Rev. 2015;29(3):172-80. https://doi.org/10.1016/j.tmrv.2015.03.002.
14. Machin D, Campbell MJ, Tan SB, Tan SH. Sample size tables for clinical studies. 3rd ed. Chichester: Wiley-Blackwell; 2009, p. 128, equation 10.22. https://doi.org/10.1002/9781444300710.
15. Hart SR, Bordes B, Hart J, Corsino D, Harmon D. Unintended perioperative hypothermia. Ochsner J. 2011;11(3):259-70.
16. Sobti A, Sehgal R, Kumar Wanchoo R. Flow of viscoelastic fluid through a helical coil. Chem Biochem Eng Quart. 2017;31(1):11-20. https://doi.org/10.15255/CABEQ.2015.2314.
17. Garber A, Hernandez L, Mullin C, Simon M. Pressure flow through a coiled tube group M5 BE 310 Spring; 2004. Available at: http://www.Seas.Upenn.Edu/Courses/Belab/LabProjects/2004/ Be310s04m5.Doc.
18. Jayanthi NVG, Dabke HV. The effect of IV cannula length on the rate of infusion. Injury. 2006;37(1):41-5. https://doi.org/10.1016/j.injury.2005.09.001.
19. Turner M, Hodzovic I, Mapleson WW. Simulated clinical evaluation of four fluid warming devices. Anaesthesia. 2006;61(6):571-5. https://doi.org/10.1111/j.1365-2044.2006.04589.x.
20. Russell WJ. A review of blood warmers for massive transfusion. Anaesth Intens Care. 1974;2(2):109-30. https://doi.org/10.1177/0310057X7400200202.