Laboratory Investigations

Methods for warming intravenous fluid in small volumes

Jan-Ake I. Schultz MD,
Craig Sims MBBS FANZCA,
Bruno Bissonnette MD FRCPC

Purpose: Laboratory experiments were performed to determine warming rates of albumin 5% at room temperature and human packed red blood cells (PRBCs) at 4°C in small volumes. Four methods used in clinical practice to warm volumes appropriate for neonates were studied.

Methods: The fluids were warmed either by infusion through a fluid warmer with temperature-controlled coaxial tubing (Group I), immersion in a water bath at 37°C (Group II), placing pre-filled syringes (10 and 20 ml) between a circulating water mattress and a forced-air warming blanket (Group III), or placing the same syringes between the water mattress and cotton towels (Group IV). The temperature of each fluid was recorded for the next 60 sec after the bolus injection in group I and every five minutes for a total of 30 min for the other groups. The time constant of warming for each group was calculated. The time constant and the temperature reached after the warming period were compared among groups.

Results: In group I 20 ml room temperature albumin 5% or 4°C blood reached temperatures of $36.9 \pm 1.5^\circ\text{C}$ and $34.5 \pm 2.3^\circ\text{C}$ within 60 sec, respectively. This was faster than all other techniques used ($P < 0.001$). The time constants measured for the albumin and the PRBCs were 0.23 ± 0.1 and 0.20 ± 0.05 minutes respectively. After 15 min albumin and PRBCs in group II reached $35.5 \pm 0.4^\circ\text{C}$ and $33.4 \pm 0.3^\circ\text{C}$, in group III reached $33.7 \pm 1.0^\circ\text{C}$ and $32.8 \pm 1.7^\circ\text{C}$, and in group IV reached $29.5 \pm 0.1^\circ\text{C}$ and $23.3 \pm 0.8^\circ\text{C}$ after 15 min respectively.

Conclusion: Warming of intravenous fluids in small volumes is accomplished most rapidly using a fluid warmer with temperature-controlled coaxial tubing and occurs more slowly in syringes, bottles, or bags exposed to various environmental conditions.

Objectif : Des expériences ont été réalisées en laboratoire afin de déterminer la vitesse de réchauffement de l'albumine 5 % à la température ambiante et de globules rouges humains concentrés (GRC) à 4 °C, en petits volumes. Quatre méthodes utilisées en pratique courante pour réchauffer des volumes appropriés à des nouveau-nés ont été étudiées.

Méthode : Les liquides ont été chauffés par perfusion au travers d'un réchauffe-liquide au moyen d'une tubulure coaxiale à température contrôlée (Groupe I), par immersion dans un bain d'eau à 37 °C (Groupe II), par insertion de seringues préremplies (10 et 20 ml) entre un matelas d'eau circulante et une couverture chauffante à air forcé (Groupe III) ou par insertion des mêmes seringues entre le matelas d'eau et des serviettes de coton (Groupe IV). La température de chaque liquide a été enregistrée pendant les 60 secondes qui ont suivi l'injection en bolus dans le groupe I et toutes les cinq minutes, pour un total de 30 min, dans les autres groupes. La constante de temps du réchauffement dans chaque groupe a été calculée. La constante de temps et la température atteinte après le réchauffement ont été comparés d'un groupe à l'autre.

Résultats : Dans le groupe I, 20 ml d'albumine 5 % à la température ambiante ou du sang à 4 °C ont atteint des températures de $36,9 \pm 1,5^\circ\text{C}$ et $34,5 \pm 2,3^\circ\text{C}$ en 60 s, respectivement. Cette méthode est plus rapide que toutes les autres techniques utilisées ($P < 0,001$). La constante de temps mesurée pour l'albumine et les GRC a été de $0,23 \pm 0,1$ et $0,20 \pm 0,05$ minutes respectivement. Après 15 min, l'albumine et les GRC ont atteint $35,5 \pm 0,4^\circ\text{C}$ et $33,4 \pm 0,3^\circ\text{C}$ dans le groupe II, $33,7 \pm 1,0^\circ\text{C}$ et $32,8 \pm 1,7^\circ\text{C}$ dans le groupe III, $29,5 \pm 0,1^\circ\text{C}$ et $23,3 \pm 0,8^\circ\text{C}$ dans le groupe IV, respectivement.

Conclusion : Le réchauffement de liquides intraveineux en petits volumes est réalisé plus rapidement en utilisant un liquide chauffant dans une tubulure coaxiale à température contrôlée et il se produit plus lentement dans des seringues, des bouteilles ou des sacs exposés à différentes conditions environnantes.

From the Department of Anaesthesia, The Hospital for Sick Children and University of Toronto, 555 University Avenue, Toronto, Ontario, Canada, M5G 1X8.

Address correspondence to: Dr. Bruno Bissonnette, Phone: 416-813-7455; Fax: 416-813-7543; E-mail: bruno@anacs.sickkids.on.ca
Accepted for publication August 13, 1998

WARM intravenous fluids are recommended to reduce hypothermia during neonatal surgery and anaesthesia.¹ Intraoperative fluid administration in neonates frequently consists of a slow maintenance infusion and intermittent boluses to replace blood loss and treat hypotension. There are inherent problems in warming these boluses with conventional fluid warmers. Most blood warmer designs incorporate large priming volumes which require either administration of large amounts of undesired fluid or disconnection to flush the extra volume when a change in infusate composition is required. Secondly, because the rate of infusion is usually slow in neonates, the warmed fluid tends to cool quickly to room temperature in the extension set before reaching the patient.^{2,3}

Paediatric anaesthetists attempt to overcome these problems by various methods including warming fluid in syringes, warming whole containers of fluid before drawing off the required volume, or using fluid warmers with special characteristics conducive for use in children. Different methods of warming small volumes of blood components have been compared with respect to their rate of warming in the neonatal ICU setting^{4,5} but not with emphasis on the rapid warming and administration often required intraoperatively.

This study was designed to determine if commonly used fluid warming methods in paediatric anaesthesia are capable of warming small volume of infusate to body temperature within 30 min of administration. The aim of the study was to measure the time required to warm either albumin or blood and to determine the differences in the warming curve between various methods and different bolus sizes. This study should help the anaesthetist to determine what fluid temperature can be achieved with each method if available time to warm up before administration is limited.

Methods

Four different methods used in paediatric anaesthesia to warm small volumes of infusate were studied in the laboratory. The fluids studied were room temperature human albumin 5% (Miles Inc., Elkhart IN) and time-expired 4°C human packed red blood cells.

The temperature of each fluid was measured using a thermocouple (Mon-a-Therm, St.-Louis, MO) inserted into the centre of the syringe, fluid container, or fluid path. Recording was achieved using a digital thermometer (model 6500, Mon-a-therm, St. Louis, MO). Each experiment was repeated three times and room temperature was maintained at 20°C. In group I, the fluid temperature was recorded every three seconds for the next 60 sec after the bolus reached the t-

piece connector. In groups II-IV, fluid temperature was recorded every five minutes for a total of 30 min.

In group I a fluid warmer (Hotline model HL90, Level 1 Technologies, Marshfield, MA)^{6,7} and its low volume (19 ml) coaxial tubing with temperature-controlled water (40°C) surrounding the infusion channel was used. A three-way stopcock and a T-piece extension (0.6 ml internal dead space) were added at the end of the delivery system. The temperature was monitored in the T-piece extension. The study bolus of 37 ml was given over 112 sec using a syringe pump. Data were collected for the first 20 ml of fluid going through the t-piece.

In group II, the albumin 5% bottle or PRBC bag was immersed in a laboratory water bath at 37°C. The containers of fluid were gently inverted three times after each temperature recording.

In group III, 10 and 20 ml syringes were placed between a circulating water mattress (Aquamatic-K-Thermia model RK600, American Hamilton Medical Systems, Cincinnati OH) set at 38°C and a paediatric warming blanket (model #536) designed for use with a forced-air warmer (Bair Hugger, model 500/OR; Augustine Medical, Eden Prairie MN) set to 38°C. Syringes remained untouched and continuously in contact with the heating surface throughout the study.

In group IV, the conditions were identical to those in group III except that four layers of cotton hospital towels replaced the forced air warming blanket of group III.

Using equations for heat balance and net heat flow^{8,9} the warming history of each experiment can be calculated from each measurement point if the time of measurement, the initial, and the final temperatures are known. These equations consist of:

$$Tr = \exp(-t/Ct)$$

where t is time, Tr is relative temperature and Ct is the time constant. Tr is defined:

$$Tr = (T - T_{\infty}) / (T_0 - T_{\infty})$$

where T is the temperature measured, T_0 is the initial temperature measured, and T_{∞} is the final equilibration temperature. The time constant for each method of warming at each measurement point was calculated.

Statistical analysis

All data are expressed as mean $\pm$ SD. Calculated time constants for each group were compared against all other groups with ANOVA and the Tukey HC test for multiple comparisons. Group I was specifically compared to groups II-IV using ANOVA and Dunnett's test for different time period of fluid warming. The temperatures for Groups II-IV were compared to each other using ANOVA and the Tukey HC test for mul-

multiple comparison. The calculated time constants for Albumin *vs* PRBCs within each group (I-IV) was achieved using the Student unpaired *t* test. Within groups III and IV the 10 ml and 20 ml subgroups were compared with each other using a Student unpaired *t* test. $P < 0.05$ was used to express statistical significance.

Results

Room temperature was maintained at $20 \pm 0.4^\circ\text{C}$. The time constant for warming each solution was different for each warming method studied ($P < 0.05$).

Group I showed the most rapid rate of warming ($P < 0.05$). The time constants measured for albumin and packed red blood cell warming were 0.23 ± 0.1 and 0.20 ± 0.1 min, respectively. Intergroup comparison was not different ($P = 0.23$). At 60 sec the temperature of albumin 5% and PRBCs averaged $36.9 \pm 1.5^\circ\text{C}$ and $34.5 \pm 2.3^\circ\text{C}$, respectively (Figure 1).

Group II demonstrated the second fastest warming time constant among the three remaining groups. The time constants for water bath warming were 6.4 ± 1.0 and 6.4 ± 0.8 min for albumin and PRBC, respectively. Intergroup comparison was not different ($P = 0.53$). The temperature of albumin and PRBC increased to 35.5 ± 0.4 and $33.4 \pm 0.3^\circ\text{C}$ after 15 min respectively. The temperature of albumin after an extra 15 min of warming increased to $36.7 \pm 0.2^\circ\text{C}$ ($P < 0.009$) whereas the gain in temperature for the blood after 30 min of warming was $36.6 \pm 0.1^\circ\text{C}$. ($P < 0.01$)

In group III, the 10 ml syringe of albumin reached a temperature of $33.7 \pm 1.0^\circ\text{C}$ at 15 min whereas it was $36.6 \pm 0.8^\circ\text{C}$ after 30 min of warming. ($P < 0.01$) The time constant of albumin warming in these conditions was 9.3 ± 1.5 min. This rewarming constant was different from those obtained in group II. ($P < 0.001$) The 10 ml of PRBCs reached a temperature of $32.7 \pm 1.7^\circ\text{C}$ at 15 min and $37.0 \pm 0.5^\circ\text{C}$ after 30 min ($P < 0.01$). This warming profile was associated to a time constant of 7.1 ± 1.2 min. The time constant for the PRBC was different from the albumin subgroup. ($P < 0.01$) The fluid contained within the 20 ml syringe showed a slower warming profile than what was observed with the 10 ml syringe. However, in the case of albumin 5%, the temperature reached within the 20 ml syringe after 15 min of warming ($32.9 \pm 0.8^\circ\text{C}$) was not different from the temperature reached with the 10 ml syringe ($33.7 \pm 1.0^\circ\text{C}$) after the same time. Adding 15 min of warming help increase the temperature for the 20 ml of albumin to $36.0 \pm 0.5^\circ\text{C}$ which was different from the temperature reached after 15 min ($P < 0.01$). The extra 15 min of warming for the 20 ml of PRBC increased the

FIGURE 1 Albumin 5% warming using four different methods.

FIGURE 2 Packed red blood cells warming using four different methods.

temperature to $35.8 \pm 0.8^\circ\text{C}$. ($P < 0.001$) The calculated time constant for the albumin was 10.1 ± 1.3 min whereas the PRBC showed a time constant of 11.3 ± 2.9 min. There was no difference between these two subgroups. ($P = 0.46$)

In group IV, all syringes warmed considerably slower than in group II and III (Table). The 10 ml syringe of albumin reached a temperature of only $33.8 \pm 0.4^\circ\text{C}$ after 30 min which was based on a time constant of 17.6 ± 0.9 min. The 10 ml syringe of PRBCs reached a temperature of only $30.7 \pm 0.5^\circ\text{C}$ after 30

TABLE

Group	I	II	III 10 ml	III 20 ml	IV 10 ml	IV 20 ml
albumin time constant (min)	0.23 ± .0	6.4 ± 1.0	9.3 ± 1.5	10.1 ± 1.3	17.6 ± 0.9	23.4 ± 2.7
blood time constant (min)	0.20 ± .1	6.4 ± 0.8	7.1 ± 1.2	11.3 ± 2.9	18.7 ± 1.1	26.1 ± 2.7
albumin temperature @ 15 min	N/A	35.5 ± 0.4	33.7 ± 1.0	32.9 ± 0.8	29.5 ± 0.1	27.8 ± 0.5
blood temperature @ 15 min	N/A	33.4 ± 0.3	32.7 ± 1.7	29.0 ± 0.6	23.3 ± 0.8	19.9 ± 1.4
albumin temperature @ 30 min	N/A	36.7 ± 0.2	36.6 ± 0.8	36.0 ± 0.5	33.8 ± 0.4	32.0 ± 0.4
blood temperature @ 30 min	N/A	36.6 ± 0.1	37.0 ± 0.5	35.8 ± 0.8	30.7 ± 0.5	27.1 ± 1.1

All data are expressed as Mean ± SD

Abbreviations: min = minutes; N/A = non applicable

min with a time constant of 18.7 ± 1.1 min. There was no difference between these groups ($P = 0.21$). The 20 ml syringe of albumin reached a temperature of $32.0 \pm 0.4^\circ\text{C}$ after 30 min with a time constant of 23.4 ± 2.7 min whereas the same volume of PRBCs warmed to a temperature of $19.9 \pm 1.1^\circ\text{C}$ after 30 min with a time constant of 26.1 ± 2.7 min. There was a difference between these groups ($P < 0.01$).

Discussion

This laboratory study reports very large efficacy differences in the warming of room temperature albumin 5% and 4°C packed red blood cells among the four methods evaluated. The utilization of a blood warmer using temperature-controlled coaxial tubing showed that a 20 ml bolus of 4°C PRBCs injected over 60 sec was heated to an average temperature of 34.6°C at the venous connection site. When the same volume of blood in a syringe was placed in contact with the surface of a circulating water mattress and covered with cotton blankets, 30 min were required to reach a temperature of 27.1°C . The efficacy of the other methods was intermediate between these two extremes.

It has been recommended that core temperature be maintained $>32^\circ\text{C}$ to avoid hypothermia related complications such as arrhythmia and coagulopathy.¹⁰ This temperature can be taken as a lowest acceptable core temperature during rapid transfusion. The 10 ml and 20 ml syringes of albumin 5% placed between a forced air warmer and a heating blanket required 15 min to exceed 32°C whereas the 10 ml and 20 ml PRBC syringes needed 15 and 20 min respectively to reach this threshold of 32°C .

The administration of a 20 ml bolus of fluid through the blood warmer over one minute corresponds to $1200 \text{ ml}\cdot\text{hr}^{-1}$, which should represent the most extreme simulation of a possible clinical scenario in neonatal anaesthesia. The blood warmer used in this study has been previously shown to be effective

for warming blood at continuous infusion rates between 50 and $3000 \text{ ml}\cdot\text{hr}^{-1}$.⁷ This study confirmed that it can be useful for warming small volumes of fluid administered in rapid bolus fashion. The small priming volume (19 ml) is an important advantage over other fluid warmers. Furthermore, in neonates and small infants, the priming fluid can be easily and effectively flushed if the fluid to be administered is different from the previous infusate. In addition, since the delivery tubing is actively heated there is little heat loss to the environment before the administered fluid reaches the intravenous insertion site. Finally, additional extension tubing is often unnecessary. Unfortunately, disadvantages of the fluid warmer studied include the additional equipment required and the subsequent additional cost. The Hotline® warmer has a list price of \$2,748.90 Can. and the disposable cost (tubing) is \$19.60 Can. This may prevent routine use and represents a major consideration.

The data derived from the water bath group agree closely with previous work by Linko *et al.*⁹ The time constant calculated in the present study is 6.4 min, which is similar to their reported value of 6.6 min.. Although water bath warming was the second fastest method studied, it cannot be used for emergency situations. Furthermore, it has been associated with nosocomial infections, needs to be used with proper technical precautions and may only be used with sealed containers.

The results obtained for warming PRBCs in syringes by various environmental methods also correlates with previous work. Strauss *et al.*⁴ exposed 15 ml PRBCs in 20 ml syringes to various environmental warming conditions for six hours. They found that syringes placed in an isolette at 37°C reached 30.5°C in 30 min. This result is intermediate to those reported in the present study for 20 ml syringes warmed between a forced air heater and a warming blanket which reached a temperature of 35.8°C in 30 min and

those warmed between cotton towels and the circulating water blanket which reached 27.1°C in 30 min. Strauss *et al.*⁴ evaluated the risk of bacterial contamination over the six hour period studied and failed to demonstrate bacterial growth. The syringes used in the present study were not cultured. In agreement with Luban *et al.*⁵ the present study also demonstrates that syringes with smaller volumes (10 ml) can be more rapidly warmed than larger (20 ml) syringes.

Intergroup comparison of albumin and PRBC warming profiles yielded conflicting results. While the respective time constants in each subgroup were similar in magnitude, in two of the six subgroups the difference was statistically significant. Physical laws¹¹ determine warming profiles for different fluids exposed under the same conditions. Subtle differences in the physio-chemical properties of albumin and PRBCs may confound the data yet our data demonstrate that albumin and PRBCs behave very similarly under equivalent heating conditions. Our observation of differences in only two of the six direct comparisons remains unexplained and may be related to subtle variations in experimental technique.

Three factors contributed to the slow fluid warming rate observed in syringes. According to the conductive heat transfer law, the temperature flux between two objects in contact with each other is expressed by:

$$T_c = k (T_1 - T_2)$$

The conductance coefficient (*k*) determines the rate of heat transfer. The factors contributing to *k* consist of the nature of the material and its surface area. The conductance coefficient of plastic is relatively low thereby imparting the qualities found in insulating items. Syringes made of plastic-PVC have a conductance coefficient of 0.25 kcal·m⁻¹·hr⁻¹·°C⁻¹. This low value hinders any efforts such as holding the syringe in one hand to change the temperature of the contents of the syringe. In comparison, the conductance coefficient for glass is 0.81 kcal·m⁻¹·hr⁻¹·°C⁻¹ and for aluminum is 237.0 kcal·m⁻¹·hr⁻¹·°C⁻¹.⁸ Syringes made from these materials would theoretically aid in the warming of their contents. However, this hypothesis was not tested in the present study.

Secondly, the surface area of a cylindrical syringe is small relative to the enclosed volume and the area of contact with the environmental conditions is small. This consideration is more pronounced with a 20 ml syringe which has a surface area/volume ratio 76% of that of the 10 ml syringe.

Thirdly, there is a relatively small temperature gradient between the heat source (38-40°C) and the syringe contents (4°C for PRBCs and 20°C for albumin). Blood bank guidelines prohibit the exposure of

blood components to temperatures capable of causing haemolysis.¹² In accordance with these observations more rapid warming by each method can be achieved by increasing the temperature gradient to which the fluid is subjected. Several authors have reported that PRBCs are undamaged by brief (less than one hour) exposure to temperature up to 47°C.¹³⁻¹⁷ However, warming PRBCs to temperatures > 38°C can cause acute red cell haemolysis^{4,14} and increased extracellular potassium concentration leading to major intraoperative complications, including death.¹⁵⁻¹⁷ Limitation of heat sources to 38°C provides a margin of safety by preventing overheating of the fluid even if inadvertently left in contact with the heat source for a period longer than intended. The second law of thermodynamics stipulates that it is impossible by any continuous self-sustaining process to transfer heat from a colder to a hotter milieu. Therefore, blood or fluid left in contact with the heat source or with the temperature-controlled coaxial tubing for long periods of time would never be warmer than the source itself.

In summary, this study has shown that warming small boluses of fluid is most rapidly achieved using a blood warmer with low volume dead-space and temperature-controlled coaxial tubing. Warming fluid in whole containers immersed in a warm water bath is significantly slower and associated with technical problems. Warming fluid in syringes, although more economical, is even slower and probably impractical if fluid administration is needed rapidly. If the syringe method is chosen then it should be kept in mind that smaller syringes warm more rapidly than large ones and that warmed air is more efficient than a warming mattress alone. If the other methods are considered in non-emergency situations, it is recommended that adequate time for warming is allowed before the fluid is needed. While these results provide some guidelines the ideal method for intraoperative administration of *iv* fluids in small amounts remains to be determined.

References

- 1 Bissonnette B, Davis PJ. Thermal regulation - physiology and perioperative management in infants and children. In: Motoyama EK, Davis PJ (Eds.). *Smith's Anesthesia for Infants and Children*. St-Louis: CV Mosby, 1995: 139-58.
- 2 Faries G, Johnston C, Pruitt KM, Plouff RT. Temperature relationship to distance and flow rate of warmed *iv* fluids. *Ann Emerg Med* 1991; 20: 1198-200.
- 3 Schultz J, Guest C, Bissonnette B. Fluid temperature in IV tubing with and without blood warming. Are conventional fluid warmers effective in pediatric anesthesia? *Anesthesiology* 1997; 87: A1045.

- 4 Strauss RG, Bell EF, Snyder EL, *et al.* Effects of environmental warming on blood components dispensed in syringes for neonatal transfusions. *J Pediatr* 1986; 109: 109–13.
- 5 Luban NLC, Mikesell G, Sacher RA. Techniques for warming red blood cells packaged in different containers for neonatal use. *Clin Pediatr* 1985; 24: 642–4.
- 6 Presson RG Jr, Bezruczko AP, Hillier SC, McNiece WL. Evaluation of a new fluid warmer effective at low to moderate flow rates. *Anesthesiology* 1993; 78: 974–80.
- 7 Smallman JMB, Morgan M. Evaluation of the Level 1 Hotline blood warmer. *Anaesthesia* 1992; 47: 869–71.
- 8 Kreith F, Bohn MS. Principles of Heat Transfer, 5th ed. New York: West Publishing Co, 1993.
- 9 Linko K, Palosaari S. Warming of blood units in water bath and cooling of blood at room temperature. *Acta Anaesthesiol Scand* 1979; 23: 97–102.
- 10 Russell WJ. A review of blood warmers for massive transfusion. *Anaesth Intensive Care* 1974; 2: 109–30.
- 11 Russell WJ. A discussion of the problems of heat exchange blood warming devices. *Br J Anaesth* 1969; 41: 345–51.
- 12 American Association of Blood Banks. Standards for blood banks and transfusion services. American Association of Blood Banks 1997; 1: 12.
- 13 Chalmers C, Russell WJ. When does blood haemolyse? A temperature study. *Br J Anaesth* 1974; 46: 742–6.
- 14 Gregory G. Anesthesia for premature infants. In: Gregory G. (Eds.). *Pediatric Anesthesia*, New York: Churchill Livingstone Inc, 1994: 351–73.
- 15 Rososhansky S, Szymanski I. Is blood warming before transfusion a safe procedure? (Letter) *Anesth Analg* 1994; 79: 197–8.
- 16 Sazama K. Reports of 355 transfusion-associated deaths: 1976 through 1985. *Transfusion* 1990; 30: 583–90.
- 17 Brown KA, Bissonnette B, McIntyre B. Hyperkalaemia during rapid blood transfusion and hypovolaemic cardiac arrest in children. *Can J Anaesth* 1990; 37: 747–54.