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Accuracy of the Data of Biochemical Parameters in Blood Collected Above the Infusion Insertion Site

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ABSTRACT

The authors aimed to investigate the possibility of collecting blood samples from above patient intravenous infusion sites by temporarily stopping the infusions while collecting the blood. A hypotonic infusion solution was administered to 5 male patients through the cephalic veins in the forearms of their left upper limbs. The biochemical data of blood collected from the median cubital veins of both patients' arms were compared. The results showed that infusions could change some biochemical test parameters, such as potassium and glucose, to higher levels, even if the infusion was interrupted temporarily during the blood collection from above the insertion site. Blood counts remained unchanged under the same conditions. If the evaluation is performed solely to assess blood counts, using a blood collection site above the insertion site by temporarily interrupting the infusion is feasible.

Key words: biochemical test, blood collection, blood count, intravenous infusion

Blood sampling is a minimally invasive procedure frequently performed in clinical practice. Therefore, accurate test results are important, and nurses should use blood collection techniques that do not change blood test findings as per hospital protocol.

It is important to utilize appropriate blood collection techniques to obtain accurate blood results. Fist clenching and the use of tourniquets for intravenous (IV) distention have been reported to raise the potassium levels in blood, which can alter the resultant data.[1] In addition, hemolysis can be induced based on the gauge of catheter used or the amount of pressure applied. The induction of hemolysis is known to affect various types of hematologic data.[2]

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Because blood sampling data can substantially vary if the infusion solutions are mixed with the sample, selecting a blood collection site that is unaffected by the infusion is essential for accurate diagnoses in patients undergoing an infusion. In addition, existing blood collection guidelines do not recommend using the arm veins for blood sampling in circumstances where IV catheters are present in both arms.[3] According to the *Infusion Therapy Standards of Practice*,[4] venipuncture for phlebotomy should be performed on the opposite extremity of the infusion. If phlebotomies are performed on the extremity with infusing solutions, a vein below or distal to the infusion insertion site should be used.[4] A previous study that used hypotonic infusion solutions (Na^+, 35 mEq/L; K^+, 20 mEq/L; Cl^-, 35 mEq/L) on white male rabbits reported that when blood was collected from the region above the infusion insertion site during the infusion, the information on the biochemical parameters and blood counts was inaccurate.[5] This indicated that the infusion affects subsequent blood measurements.

To prevent such outcomes when patients are undergoing infusion therapy, it is common to collect blood from the contralateral upper limb of the infusion site. However, blood sampling is contraindicated in patients with shunts or in postmastectomy patients with lymph node dissections on the upper limbs contralateral to the infusion sites. Therefore, a previous study hypothesized that, because an infusion is administered intravenously and because the venous blood flows from the finger to the heart, blood collected from below the infusion insertion site would remain unaffected by the infusate; the findings of this study confirmed the hypothesis.[6]

The forearm is a common infusion insertion site; however, it is difficult to collect blood from below the insertion site during an infusion. Therefore, if blood can be drawn from above the insertion site during IV administration of the infusion without adversely affecting the results, the number of blood collection sites available for receiving infusion therapy would increase. The authors thus hypothesized that the biochemical data of the collected blood would not be affected by an infusate if the infusion was temporarily stopped, even if the nurse chose an area above the insertion site for blood collection. Accordingly, the authors conducted animal experiments to verify this hypothesis. The results suggested that by temporarily stopping the infusion during phlebotomy, the blood collected from above the insertion site was unaffected by the infusate.[7] The authors, therefore, aimed to investigate the possibility of collecting blood samples above the infusion insertion sites by temporarily stopping the infusion during blood collections in humans.

MATERIALS AND METHODS

Study Design

This study followed an experimental comparative design in which each participant was assigned to both the intervention and control procedures.

Participants

The participants were 5 healthy males nurses (licensed after clearing the National Nursing Examination in Japan) with no underlying comorbidities, who did not routinely use medication or supplements. The authors included only male participants in this study due to previous reports of gender-specific differences in the baseline values for many hematologic parameters.[8] Moreover, licensed nurses were selected because they were aware of risks associated with infusions and blood sampling and could sufficiently understand the explanation provided by the researchers. Furthermore, the authors considered that the participants should have an understanding of the invasiveness of blood collection before agreeing to participate. The mean age of the participants was 36.8 $\pm$ 4.4 years, and the mean body mass index was 22.8 $\pm$ 1.8 kg/m^2. The sample size was determined based on the sodium concentration in the administered infusate. The mean reference range for blood data was set at $\pm$2 standard deviations (SDs), corresponding to 140 $\pm$ 5 mEq/L, because the SD of sodium was $\pm$2.5. An effect size of 1.36 was calculated with G*Power software,[9,10] using a *t* test with an α error of 0.05, 1 - β error of 0.8, and a sample size of 5. The difference to be detected was 1.36 $\times$ SD (2.5), which was equal to 3.4. Because this study was intended for clinical application, it was required to detect a clinically significant difference, and a significant difference of 1 to 2 units between the mean sodium levels would not have been achieved because of the influence of the infusate but rather because of the blood variation caused by sampling from different sites. Therefore, a sample size of 5 (N = 5) was required to detect differences of approximately $\pm$3.4 in sodium levels with an SD of $\pm$1.

Ethical Considerations

The authors recruited participants using poster bulletins to prevent coercion. Those who applied were provided with both written and verbal explanations of the research purpose, as well as the intervention methods. They were also informed that even after consenting to participate, they could withdraw at any time. The authors processed the results of the data analyses on a private computer to ensure participant anonymity. The results of the data analyses were processed rapidly on the researcher's personal computer to ensure that participants were not identified.

Although the intervention was mildly invasive, the researcher was accompanied by a nurse; moreover, the experimental environment was prepared appropriately to ensure that any potential complications associated with the catheter use would be managed quickly. The nurses who participated in this study had >10 years of clinical experience. If medical consultations were required because of complications, all medical expenses were to be paid by the researchers and insurance held by the institution with which the authors were affiliated, and the Japanese Nursing Association's Nursing Liability Insurance System was used for prompt resolution of financial issues. The study protocol was approved by the Research Ethics Committee of the Aomori University of Health and Welfare (approval No. 1727).

TABLE 1

Composition of the Hypotonic Infusion Solution

Product name	Na^+	K^+	Ca^+	Mg^+	Cl^-	Glucose, mg/dL
Solita-T3G	35	20	0	0	35	7500

Data are in mEq/L unless otherwise specified. Abbreviations: Ca, calcium; Cl, chlorine; K, kalium; Mg, magnesium; Na, natrium.

Intervention Method

The participants were instructed to avoid eating and performing vigorous exercises for 2 hours before the intervention. Participants were subjected to bed rest for 10 minutes.

The peripheral IV catheters were inserted in the cephalic vein of the forearm of the left upper limb using a Surflo 24-gauge × three-quarter-inch venous indwelling catheter (catheter length, 19 mm; inner diameter, 0.47 mm; outer diameter, 0.7 mm; Terumo, Tokyo, Japan), and Solita-T3G (AY Pharmaceuticals, Tokyo, Japan) was administered at 100 mL/h with a Terufusion TE-261 infusion pump (Terumo). Solita-T3G is a hypotonic infusion solution often used in patients in Japan. It is also often administered long term. Because Solita-T3G contains a large amount of glucose, even if a small amount mixes with the blood collected, it can be identified as shown in Table 1.

After a 10-minute infusion, the flow was interrupted temporarily. Using a tourniquet with markers that enabled the application of appropriate pressure (developed by Mori et al,[11] Taiyo Corp, Tokyo, Japan) to the cubital fossa, which is above the infusion site on the right upper limb (ie, the experimental arm) and the contralateral cubital fossa (ie, the control arm), equal pressure was applied on both arms by 2 nurses. After disinfection, the blood was collected simultaneously from the median cubital vein of both arms using the vacuum blood collection method with Surshield Versatus blood collection sets and Venoject II vacuum collection tubes (Terumo). The contralateral median cubital vein of the cubital fossa of the right upper limb is a common site for collecting blood samples from patients undergoing infusions. This site was selected as the control arm because it could provide data regarding the collected blood samples that were unaffected by the infusate. Furthermore, if an infusion is interrupted for a long period of time, coagula may form in the indwelling catheter, and the infusion may not be administrable. Therefore, the procedures were performed by ensuring a minimum period of time after the infusion interruption, during which the tourniquet was applied, venipuncture site was disinfected, and the blood was collected; moreover, the authors measured the time from infusion interruption to the insertion of the blood collection catheter and the time from infusion interruption to the completion of blood collection.

The bleeding ceased at the collection site, and the catheter was removed. The experimental protocol is shown in Figure 1, and the experimental conditions are shown in Figure 2. The experiment was conducted only once for each participant.

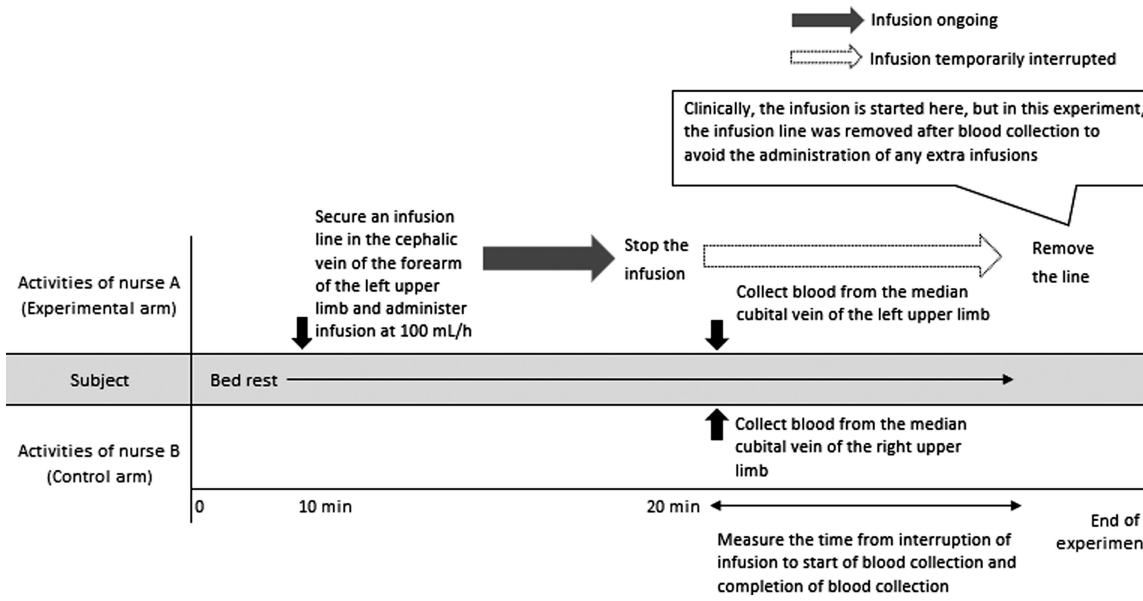

Figure 1 Schematic overview of the study protocol showing the timeline and summarizing the activities of 2 nurses (upper section: nurse A; lower section: nurse B) and the participant (middle section). Nurse A administers the infusion of the glucose-supplemented No. 3 solution through a venous line on the left upper limb (experimental arm) and interrupts it after 10 minutes. Both nurses collect cubital venous blood samples: Nurse A collects blood from the left cubital region (experimental arm), and Nurse B collects from the right cubital region (control arm).

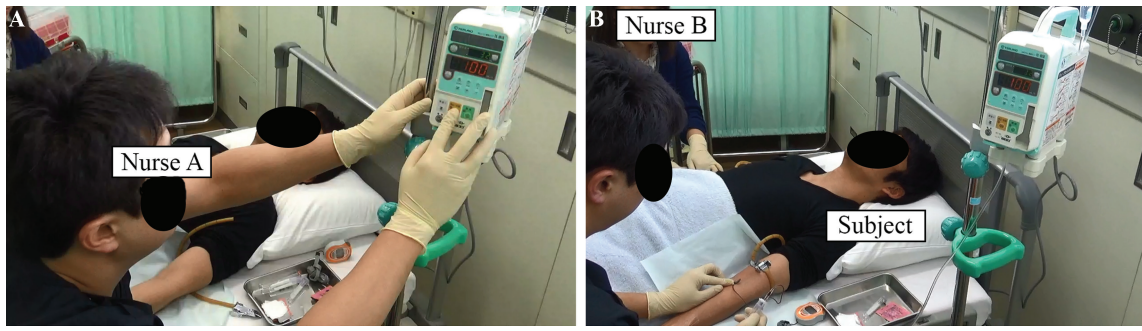

Figure 2 Representative photos of the procedure. (A) Nurse A stops the infusion pump before collecting the blood samples. (B) Nurses A and B collect venous blood samples from the participant simultaneously. Photos © the authors.

Data Parameters Collected

The biochemical analyses and blood cell counts, which are performed routinely in clinics, were conducted. The following 32 biochemical parameters were assessed: total protein, albumin, total bilirubin, direct bilirubin, thymol turbidity test, zinc sulfate turbidity test, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase, alkaline phosphates, lactate dehydrogenase, cholinesterase, leucine aminopeptidase, creatine phosphokinase, amylase, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, urea nitrogen, creatinine, uric acid, sodium, potassium, chloride, calcium, inorganic phosphorus, magnesium, serum iron, total iron-binding capacity, unsaturated iron-binding capacity, and glucose. The following 8 total blood count parameters were assessed: leukocytes, red blood cells, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and platelets. A total of 40 laboratory parameters were collected from both the experimental and control arms.

Data Analysis

Data (mean and SD) were calculated for the time between the infusion interruption to the start and end of the blood collection for the 40 test parameters investigated. Blood samples were sent to BML (Laboratory Service Corporation, Tokyo, Japan) for analysis. Subsequently, the data from both the experimental and control arms were compared using paired *t* tests, and differences between the mean values were calculated. The data were analyzed using SPSS 19.0 (IBM Corp, Armonk, NY), and the significance level was set at $<5\%$.

RESULTS

The participants did not experience any adverse events during the catheter insertion, administration of infusate, or blood collection. There were no complications, and the experiment was completed successfully.

The mean interval between the infusion interruption and the start of the blood sampling was 42.3 ± 5.4 seconds, and the mean interval from the infusion interruption to the end of the blood sampling was 60.0 ± 1.6 seconds.

Table 2 shows the means, SDs, and mean differences between the experimental and control arms, the upper and lower limits of the 95% confidence intervals (CIs), and the *P* values. The potassium levels in the experimental arm were significantly higher than those in the control arm (mean difference, 0.3 mEq/L; 95% CI, 0.11–0.39 mEq/L). In addition, the glucose levels in the experimental arm were significantly higher than those in the control arm (mean difference, 14.8 mg/dL; 95% CI, 4.80–24.86 mg/dL). There were no significant differences in the other test parameters.

DISCUSSION

Comparing the experimental and control arms, the potassium and glucose levels were significantly higher in the experimental arm than in the control arm, although there were no significant differences in any of the other parameters tested. The potassium values in a previous study were found to be higher than the physiological potassium concentration because of the use of a tourniquet or clenching[1]; however, it is unlikely that the tourniquet was tighter only on the experimental arm in this study. This is because tourniquets with markers were used to exert the same pressure on the experimental and control arms. Moreover, hemolysis may have caused the release of erythrocyte potassium into the blood, resulting in higher-than-average potassium values. However, hemolysis was not confirmed in any of the hematologic analyses. Therefore, it was unlikely that blood sampling techniques affected potassium levels in the experimental arm. In other words, these results suggested that the infusate, rather than the method of blood collection, affected the results obtained from the collected blood. The Solita-T3G solution used in this study contained 20 mEq/L of potassium and 7500 mg/dL of glucose; these values were higher than the normal potassium and glucose concentrations (4.0 mEq and 100 mg/dL, respectively) in humans. This suggested that the infusate affected the data obtained from the collected blood. These results differed from those reported in another animal study in which blood was collected from above the infusion insertion site by temporarily interrupting the infusion,[7] but the results were similar to those reported in a study in which blood was collected from

TABLE 2

Comparison of Data Between the Experimental and Control Arms (N = 5)

Test parameter	Unit	Experimental arm		Control arm		Difference in mean value	95% CI		*P* value
		Mean	SD	Mean	SD		Lower limit	Upper limit	
Total protein	g/dL	7.2	0.3	7.1	0.2	0.0	–0.14	0.20	.638
Albumin	g/dL	4.6	0.1	4.6	0.1	0.0	–0.09	0.09	1.000
Total bilirubin	mg/dL	0.6	0.4	0.6	0.4	–0.2	–0.60	0.03	.363
Direct bilirubin	mg/dL	0.3	0.1	0.2	0.1	–0.2	–0.03	0.06	.363
Thymol turbidity test	U	3.4	1.8	3.5	2.0	–0.2	–0.45	0.12	.195
Zinc sulfate turbidity test	U	4.7	0.5	4.9	0.6	–0.2	–0.48	0.01	.058
Aspartate aminotransferase	U/L	22.3	4.3	21.8	4.5	0.5	–0.95	1.95	.415
Alanine aminotransferase	U/L	40.7	16.7	40.5	16.9	0.2	–0.26	0.60	.363
γ-Glutamyl transpeptidase	U/L	41.2	23.7	43.5	23.9	–2.3	–6.46	1.79	.206
Alkaline phosphates	U/L	175.8	56.9	175.2	57.4	0.7	–3.87	5.20	.721
Lactate dehydrogenase	U/L	172.2	24.5	160.7	15.1	11.5	–3.70	26.70	.109
Cholinesterase	U/L	371.5	47.2	373.0	47.8	–1.5	–11.67	8.67	.720
Leucine aminopeptidase	U/L	50.0	5.9	50.7	6.9	–0.7	–2.10	0.77	.286
Creatine phosphokinase	U/L	101.0	24.8	101.0	23.4	0.0	–3.87	3.87	1.000
Amylase	U/L	69.2	13.3	68.7	12.5	0.5	–1.35	2.35	.518
Total cholesterol	mg/dL	207.0	31.1	206.8	33.4	0.2	–5.32	5.66	.941
Triglycerides	mg/dL	287.7	149.5	291.2	154.7	–3.5	–10.48	3.48	.254
HDL cholesterol	mg/dL	44.0	12.2	43.8	12.0	0.2	–1.06	1.39	.741
LDL cholesterol	mg/dL	124.8	23.4	127.0	24.4	–2.2	–5.64	1.31	.170
Urea nitrogen	mg/dL	14.9	3.3	14.7	3.4	0.1	–0.09	0.32	.201
Creatinine	mg/dL	0.8	0.1	0.8	0.1	0.0	–0.05	0.04	.786
Uric acid	mg/dL	5.8	1.1	5.9	1.2	–0.1	–0.11	0.01	.076
Sodium	mEq/L	138.3	1.2	138.5	0.8	–0.2	–0.96	0.62	.611
Potassium	mEq/L	4.6	0.6	4.3	0.5	0.3	0.11	0.39	.007
Chloride	mEq/L	102.3	1.4	102.7	1.2	–0.3	–1.19	0.52	.363
Calcium	mg/dL	9.1	0.2	9.1	0.1	0.0	–0.18	0.15	.809
Inorganic phosphorus	mg/dL	3.4	0.4	3.4	0.3	0.0	–0.06	0.10	.611
Magnesium	mg/dL	2.2	0.2	2.2	0.1	0.0	–0.13	0.13	1.000
Serum iron	μg/dL	109.8	17.6	108.8	17.3	1.0	–0.33	2.33	.111
Total iron-binding capacity	μg/dL	320.0	34.7	319.2	38.6	0.8	–4.78	6.44	.718
Unsaturated iron-binding capacity	μg/dL	210.2	41.9	210.3	44.7	–0.2	–4.74	4.40	.929
Glucose	mg/dL	110.5	12.6	95.7	15.1	14.8	4.80	24.86	.013
Leukocytes	/μL	5846	1398	5865	1384	–18.3	–244.1	207.5	.843
Red blood cells	$\times 10^4/\mu L$	5 12.8	22.3	509.7	25.0	3.2	–4.38	10.72	.330
Hemoglobin	g/dL	15.8	0.7	15.5	0.5	0.3	–0.09	0.59	.120
Hematocrit	%	45.9	1.6	46.2	1.6	–0.3	–1.03	0.33	.243
Mean corpuscular volume	fL	89.3	2.1	90.0	2.8	–0.7	–1.52	0.19	.102
Mean corpuscular hemoglobin	pg	30.5	0.3	30.5	0.4	0.0	–0.30	0.23	.758
Mean corpuscular hemoglobin concentration	%	34.1	0.6	33.8	0.4	0.3	–0.20	0.77	.194
Platelets	$\times 10^4/\mu L$	2 6.7	3.0	26.9	3.3	–0.3	–1.02	0.49	.404

Abbreviations: CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SD, standard deviation.

above the IV infusion insertion site, while the infusion was flowing.[5]

In contrast, the sodium and chloride levels in the experimental arm did not differ significantly. The sodium and chloride concentrations in Solita-T3G were 35 mEq/L, respectively, and were lower than the physiological values in humans (sodium, 140 mEq/L; chlorine, 100 mEq/L). If the infusion affected the sample, the sodium and chloride levels in the experimental arm should have been significantly lower than those in the control arm. Furthermore, no significant reductions in total protein, albumin, calcium, or magnesium levels were observed in the experimental arm, despite these components not being included in Solita-T3G. Therefore, the results of this study indicated that the higher-than-normal concentrations of infusion components in blood affected the data obtained from the blood samples, whereas infusions with lower concentrations of these components did not affect the blood sampling data.

In this study, no significant differences were observed in the values of leukocytes, red blood cells, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, or platelets between the experimental and control arms. Furthermore, there were no clinically relevant differences in the mean values or the lower and upper limits of the 95% CI. In particular, although hemoglobin is often assessed as an indicator of anemia, it has also been used to assess the hemoconcentration to determine the presence or absence of dehydration. This is because dehydration results in higher blood concentration and hemoglobin level, and vice versa. The presence of an infusate in the collected blood is expected to dilute hemoglobin, contrary to hemoconcentration; however, this phenomenon was not observed in this study.

To date, blood collection above the insertion site has not been considered feasible. The findings of this study suggest that the infusion affected some blood biochemical parameters, such as potassium and glucose, when the infusion was temporarily stopped for approximately 40 seconds and blood was collected from above the insertion site. However, the blood counts remained unaffected by the infusate. Follow-up research is necessary to validate these results with different IV solutions.

LIMITATIONS

IV infusion interruption can cause coagulation in the indwelling catheter or at its tip. If coagulation occurs, there is a risk that subsequent resumption of the infusion will be unsuccessful and that the catheter will need to be reinserted to avoid the entry of embolizing clots into the bloodstream. In this study, considering that the blood collection period lasted approximately 60 seconds from the infusion interruption and that the normal bleeding time before platelet aggregation was approximately ≤3 minutes, it was unlikely that stopping the infusion would have caused the blood to coagulate at the tip of the catheter. Therefore, additional research is necessary to estimate the duration for which an infusion can be interrupted before coagulation occurs at the catheter tip. Furthermore, the reason the infusate affected some of the blood biochemical data in the study remains unclear. For example, prolonging the duration of the infusion interruption could have eliminated the differential effects on blood biochemistry; however, additional evaluation may be required considering the time to coagulation. Another study with a larger number of participants and other infusates to conclusively validate the results of this study is warranted.

CONCLUSION

This study showed that IV infusions could cause some blood biochemical parameters such as potassium and glucose to be higher, despite the temporary interruption of the infusion when blood was collected above the insertion site. Nonetheless, even under the same conditions, the blood cell counts were not affected. This result confirmed our hypothesis for the blood cell counts but not for the biochemical parameters. Therefore, if blood collection from these sites is not feasible and if the evaluation is performed solely to assess blood counts, using a blood collection site above the insertion site by temporarily interrupting the infusion is feasible.

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