Does Calcium Balanced Heparin Affect Blood Gas and Electrolyte Analysis ?

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The effect of calcium-balanced heparin (471896, CIBA CORNING) on blood gas and electrolyte analysis was evaluated, by comparing with that of sodium heparin (Na heparin). One ml of whole blood was collected into a syringe, which contained calcium-balanced heparin (Ca balanced heparin) or Na heparin. 122 pairs of blood samples obtained from 15 patients were analyzed for Na, K, ionized calcium (Ca^{++}), total hemoglobin, pH, P_{CO_2}, and P_{O_2} by an automatic blood gas and electrolyte analyzer, CIBA CORNING model 288. There was a significant difference ($P < 0.05$) in pH, P_{CO_2}, Na, and Ca^{++} between the two different groups. Ca^{++} concentration was significantly less in Na heparin grouop than in Ca balanced heparin group, probably due to more chelation of Ca^{++} by Na heparin than Ca balanced heparin. The present study suggests that the Ca balanced heparin has minimal effect on the blood gas and electrolyte analysis, and is a suitable anticoagulant for the Ca^{++} measurement. (Key words: calcium balanced heparin, Na heparin, blood gas analysis, ionized calcium)

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In plasma, calcium is present in the form of free divalent calcium (Ca^{++}), in complexes with small inorganic and organic anions, and bound to proteins. The concentration of the total calcium can be measured accurately by atomic absorption spectrometry. It has been evident that the ionized calcium in plasma is the physiologically active fraction of calcium, which is mostly interesting for clinicans and physiologists. The concentration of plasma protein, blood pH, and anions such as lactate and bicarbonate are the possible factors that can affect the concentrations of three fractions of calcium.

Heparin has been widely used as an anticoagulant for the collection of specimens for the blood gas and electrolyte analysis in the operating room (OR) and intensive care unit (ICU). Heparin has the binding capacity for Ca^{++} in dose-dependent manner, which may result in the underestimation of Ca^{++} concentration. Thus, Ca balanced heparin has been introduced to minimize the error produced by Na heparin and Li heparin on the measurement of Ca^{++} concentration.

The present study was performed to evaluate the effect of Ca balanced heparin on the results of blood gas and electrolyte analysis comparing with that of Na heparin.

Subjects

Fifteen adult patients undergoing elective surgery under general anesthesia were involved in the present study. The demographic data of the patients are summarized in table 1. A 22 G catheter was inserted in radial artery to monitor blood pressure, and to obtain arterial blood sample for blood gas and electrolyte analysis.

Methods

1) Preparation of heparin containing syringes for sampling blood

We used Ca-balanced heparin (471896, Corning Diagnostics, 2000 IU·ml^{-1}) and Na

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Table 1. Demographic data of the patients

	age	number of patients
Open heart surgery	16–55	6
Esophageal cancer	63–71	3
Lung cancer	53–65	3
Hepatocellular cancer	58–61	2
Aortic aneurysm	62	1

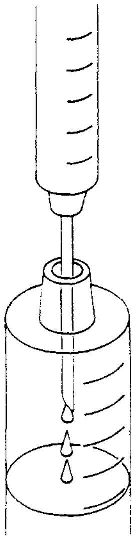

Fig. 1. The illustration of "needle-drop-count" method. The needle should be in the vertical position, and 1 ml syringe is recommended, since it is easier to push plunger than larger syringes. In this method, the amount of heparin can easily be varied by the number of drops and the size of needle.

heparin (Shimizu Co. Ltd., Japan, 1000 $IU \cdot ml^{-1}$). In the preliminary study, it was confirmed that the amount of heparin solution passing through a 23 G needle (23 G, 1 inch, Terumo Co., Japan), which was attached to heparin containing syringe in vertical position was 7.90 ± 0.44 microlitter (mean ± SD; 110 measurements with 11 different needles). It is stated that 10 IU heparin is sufficient to ensure anticoagulation of 1 ml blood. We prepared the syringes containing 3 drops of heparin solution with the needle-drop-count method shown in figure 1. This amount of heparin is more than twice the amount of heparin, that was considered to be sufficient for the anticoagulation, since the potency of heparin decreases as the time passes.

2) Blood gas and electrolyte analysis

1 ml of arterial blood was drown via the catheter into the syringes, one of which contained Ca-balanced heparin, and the other Na heparin. The measurement of pH, P_{CO_2}, P_{O_2}, total hemoglobin (tHgb), Na, K, and Ca^{++} were performed within 3 min after sample collection by Model 288 Analyzer (CIBA Corning Diagnostics, Mass., USA), at 37°C.

3) Statistical analysis

The difference of the paired data was evaluated by using paired Student's t-test, where $P < 0.05$ was considered as statistically significant. Mean difference of each sample was a % difference from the results which was obtained from specimens containing Ca balanced heparin. A linear regression was calculated by using a least squares method.

Results

122 pairs of blood samples obtained from 15 patients were analyzed. The mean value, the range and the difference of each variable are given in table 2. The statistical significance ($P < 0.05$) was found in pH, P_{CO_2}, Na, and Ca^{++} between the two different heparin groups. The difference of each variable between the groups was within 3%, except Ca^{++}. The concentration of Ca^{++} in Na heparin group was significantly less than that in Ca balanced heparin group, and its mean difference was 0.06 mM, which was 4.9% less than that of Ca balanced heparin. There were good correlation between the results of Ca-balanced heparin, and those of Na heparin (Na, K, and Ca^{++}; r = 0.949, 0.958, and 0.961, respectively, table 3). Ca^{++} showed good correlation between the two groups (fig. 2), and its slope and interception was 0.931 and 0.130, respectively. Blood gas analysis also showed good correlaltion between the two groups; pH, P_{CO_2}, and P_{O_2}: r = 0.991, 0.973, and 0.986, respectively.

Discussion

The dilution of blood sample, and the

Table 2. The effect of Ca-balanced heparin and Na heparin on blood gas and electrolyte analysis

	Ca-balanced heparin	Na heparin	mean and % difference
pH	7.448 ± 0.083 (7.234–7.595)	7.451 ± 0.082* (7.250–7.600)	0.003 (0.04%)
P_{CO_2} (mmHg)	35.0 ± 9.4 (20.1–62.5)	33.9 ± 8.9* (19.2–59.1)	-1.1 (-2.8%)
P_{O_2} (mmHg)	201.4 ± 96.1 (93.7–548.6)	205.4 ± 99.9* (90.1–572.9)	4.0 (1.7%)
Na ($mEq \cdot l^{-1}$)	138.0 ± 4.3 (124.2–151.6)	140.9 ± 4.6* (118.9–154.3)	2.8 (2.1%)
K ($mEq \cdot l^{-1}$)	3.76 ± 0.43 (2.65–4.99)	3.79 ± 0.43 (2.60–5.12)	0.02 (0.6%)
Ca^{++} ($mmol \cdot l^{-1}$)	1.17 ± 0.12 (0.97–1.99)	1.11 ± 0.09* (0.90–1.61)	-0.06 (-4.9%)
tHb ($g \cdot dl^{-1}$)	11.8 ± 2.0 (5.4–16.2)	12.0 ± 2.0 (6.3–16.1)	-0.12 (2.3%)

*$P < 0.05$ compared with control (n=122, mean ± SD)
Numbers in parenthesis represent range of each variable

Table 3. Correlation of variables between Ca-balanced heaprin and Na heparin groups

	A	B	r
pH	1.007	-0.054	0.991
P_{CO_2}	1.035	-0.060	0.973
P_{O_2}	0.949	6.279	0.986
Na	0.882	13.95	0.949
K	0.897	0.386	0.958
Ca^{++}	0.931	0.130	0.961
tHb	1.024	-0.386	0.918

$Y = A * X + B$
X; Na heparin group
Y; Ca-balanced heparin group

chelation of cations in plasma by the strong negative charge of heparin have been considered as the possible mechanisms of the effect of heparin on the blood gas and electrolyte analysis[2–8]. In the present study, the concentration of Ca^{++} was significantly less in Na heparin than that in Ca balanced heparin, indicating more chelation of Ca^{++} by Na heparin than Ca balanced heparin[5]. On the other hand, there were good correlation of Ca^{++} between the two groups, indicating that the degree of chelation by both heparin was constant within the analyzed range in the present study.

Although the composition of Ca balanced heparin is not available from the manufacturer, a small amount of Ca^{++} is most likely added to compensate the chelation of Ca^{++} by heparin. In a preliminary study with heparin free samples, Ca^{++} concentration was 0.01 mM/L less than that with Ca-balanced heparin ($n = 118$, $P < 0.05$), indicating that Ca balanced heparin has minimal effect on the Ca^{++} concentration.

After the introduction of Ca^{++} selective electrode by Ross in 1967[9], the concentration of Ca^{++} has been widely measured in the OR and ICU. However, there have been still considerable controversy concerning its normal value for human blood plasma (i.e., ranging from 1.08 to 1.28 $mmol \cdot \ell^{-1}$ for the normal mean)[10]. Furthermore, it is more important what is measured: activity, the concentration of substance, or the molality of the calcium ions[1]. In the present study, the Ca^{++} electrode was calibrated by the standard solution supplied by the manufacturer, and we did not attempt to answer

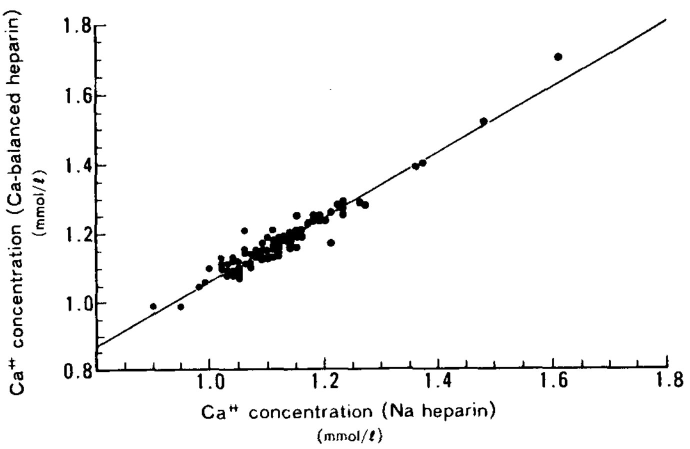

Fig. 2. The linear correlation of the Ca^{++} concentration between Ca-balanced heparin group (on Y axis), and Na heparin group (on X axis). (n = 122)

such questions. It is obvious that we need international consensus about the calibrating solution to be employed for "ionized calcium" analysis.

The blood gas and electrolyte analysis is one of the most popular laboratory tests in the OR and ICU for optimal patient care. There has been a great improvement in blood gas and electrolyte analyzer in last decade; a very small amount of blood sample is needed for such measurement nowadays, usually less than 0.5 ml. Indeed, in our ICU and OR, the amount of blood sample is less than 1 ml for such tests even in adult cases. Furthermore, in small infants and premature babies, the amount of blood samples for laboratory tests is sometimes clinically significant as blood loss, and the smaller the volume of sample is the better. On the other hand, commercially available heparinized syringes usually contain 100–150 IU of heparin, which is adequate for more than 10 ml of whole blood. Since the amount of blood sample needed for such tests is no more than 1 ml, the amount of heparin in those syringes is too excessive to obtain accurate laboratory results. As a result of the present study, small syringe with minimal heparin seems ideal for clinical tests.

The "needle-drop-count" method was introduced in the present study to prepare the syringes containing heparin solution in a sterile manner. Since the amount of single drop of heparin showed minimal variation, this method is easy, and practical. The amount of heparin solution can be changed by the number of drops, and the size of needle, thus this is a feasible method for small infants and premature babies, in whom the amount of blood sample, and heparin is strictly limited.

The present study demonstrates the minimal effect of Ca balanced heparin on the results of blood gas and electrolyte analysis, especially on Ca^{++}, compared with that of Na heparin. This heparin seems to be appropriate as an anticoagulant for laboratory test in the OR and ICU. And we introduced the easy and practical method, i.e., "needle-drop-count" method, to prepare the syringe with small amount of heparin solution in a sterile manner, which may be helpful in pediatric cases.

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