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Short Communication

Electrolyte-balanced heparin in blood gas syringes can introduce a significant bias in the measurement of positively charged electrolytes

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Abstract

Background: Heparin binds positively charged electrolytes. In blood gas syringes, electrolyte-balanced heparin is used to prevent a negative bias in electrolyte concentrations. The potential pre-analytical errors introduced by blood gas syringes are largely unknown. Here, we evaluate electrolyte concentrations in non-anticoagulated blood compared with concentrations in electrolyte-balanced blood gas syringes.

Methods: Venous blood was collected into plain tubes. Ionized calcium, potassium, sodium and hydrogen ions were analyzed directly using a blood gas analyzer and the remaining blood was collected into different blood gas syringes in random order: Preset (Becton Dickinson), Monovette (Sarstedt) and Pico 50-2 (Radiometer).

Results: Ionized calcium and sodium concentrations were significantly lower in blood collected in Becton Dickinson and Sarstedt syringes compared to non-heparinized (NH) blood. The mean bias exceeded biological variation-based total allowable error, which in most cases leads to clinically misleading individual results. In contrast, ionized calcium concentrations in blood collected in Pico 50-2 syringes were identical to values obtained from NH blood. Sodium showed a minor, yet statistically significant, bias.

Conclusions: Despite the fact that blood gas syringes now contain electrolyte-balanced heparin, one should be aware of the fact that these syringes can introduce pre-analytical bias in electrolyte concentrations. The extent of the bias differs between syringes.

Keywords: blood gas syringes; electrolyte-balanced heparin; ionized calcium; potassium; pre-analytical errors; sodium.
### Table A

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### Diagrams B

**B**

- **BD**
  - ![Graph](image)

- **RM**
  - ![Graph](image)

- **SS**
  - ![Graph](image)

**Calcium ($\text{Ca}^{2+}$)**

**Potassium ($K^+$)**

**Sodium ($\text{Na}^+$)**

**pH**

**Difference in concentration from non-harmonized blood, mmol/L**

**Concentration in NH blood, mmol/L**

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*Note: Diagrams B show the difference in concentration from non-harmonized blood for each parameter (Calcium, Potassium, Sodium, and pH) across different conditions (BD, RM, SS). The graphs illustrate the distribution of data points and the zero bias line.*
Syringes (personal communication with H. Froklage, Radiometer) for a potential heparin bias caused by heparin in RM blood collected into syringes manufactured by RM were assessed using Bland-Altman analysis (6). BD syringes introduced the most pronounced bias in concentrations of all electrolytes, while the biases introduced by RM syringes were minimal (Figure 1B). Similarly, the 95% limits of agreement were the narrowest and always encompassed zero bias with RM syringes.

Taken together, two out of the three syringes tested here introduced a clinically significant negative bias for many subjects in both ionized calcium concentrations and sodium concentrations, despite the fact that all syringes contain electrolyte-balanced heparin. These findings were not caused by inadequate filling volumes since the negative bias persisted after filling the syringes to more than the minimally necessary volume (according to manufacturers instruction, data not shown). The mean bias exceeded the TE for ionized calcium and sodium, which are based on intra-individual biological variation. Therefore, a clinically significant difference in results can be introduced by using the syringes from BD or SS for analysis of these electrolytes. Electrolyte values in blood collected into syringes manufactured by RM were more comparable to values measured in NH blood.

ABL blood gas analyzers do not use an algorithm to correct for a potential heparin bias caused by heparin in RM syringes (personal communication with H. Froklage, Radiometer). Therefore, the extent of interference found for the ABL blood gas analyzer used in this study is expected to be reproduced on an analyzer from a different manufacturer. Differences in the process of balancing heparin with electrolytes between manufacturers most likely explain the findings described here.

In conclusion, one should be aware of the bias that can be introduced in electrolyte concentrations by the use of different blood gas syringes, despite the fact that blood gas syringes now contain electrolyte-balanced heparin. These results emphasize the need for improving the manufacturing process of balanced heparin. Furthermore, a single type of electrolyte-balanced heparin should be used in one laboratory only in order to minimize the pre-analytical effects on variation of sodium, potassium and ionized calcium concentrations.

The experimental procedures were in accordance with the Declaration of Helsinki, Dutch law and the standards of the medical Ethical Commission of our institution. Informed consent was obtained from each subject before blood sampling.

Conflict of interest statement

Authors’ conflict of interest disclosure: The authors stated that there are no conflicts of interest regarding the publication of this article.

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