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Knowledge among clinical personnel on the impact of hemolysis using blood gas analyzers

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Abstract

Objectives: In the light of a rapidly increasing use of POCT blood gas testing, where tests and interpretation are performed by non-laboratory personnel, the objective was to investigate the knowledge among personnel in the Nordic countries using blood gas analyzers with focus on the interference from hemolysis.

Methods: Information was obtained from a self-developed, pre-tested online questionnaire. The questions covered demographic information about the respondents and specific questions on handling of and knowledge about blood gas analyses and the impact of hemolysis. The questionnaire was distributed by e-mail to relevant colleagues on behalf of the Nordic preanalytical scientific working group under the Nordic Federation of Clinical Chemistry.

Results: A total of 117 respondents completed the questionnaire. 62.7 % respondents both used the analyzer and interpreted the results. 59.6 % respondents did not know to which degree the blood gas analyzer can identify hemolysis. 4.4 % answered that all levels or high levels of hemolysis can be detected. 3.9 % considered the result valid despite hemolysis if it is released from the instrument. 73.7 % of all respondents knew that hemolysis alters potassium measurements, while knowledge about the effect on PaO_2 and bicarbonate measurements were more divergent.

Conclusions: The knowledge about blood gas analyzers with focus on the interference from hemolysis is sparse among non-laboratory personnel using the blood gas analyzers. This emphasizes the need for better education and competence management, which perhaps is even more important for these analyses than for other point-of-care tests.

Keywords: preanalytical; hemolysis; blood gas analyzers; blood sample integrity; POCT

Introduction

The preanalytical phase is important in laboratory diagnostics as several issues can affect the test results and their reliability. Previous studies have shown that *in vitro* hemolysis is the most prevalent preanalytical error [1]. Hemolysis is defined as rupture of erythrocytes and release of intracellular components into serum or plasma [1, 2]. It is well known that *in vitro* hemolysis can alter the measurement of potassium and other primarily intracellular substances to either false high or false normal results (in case of hypokalemia) [2, 3]. Conversely, extracellular substances will primarily be false decreased due to dilution [2, 3]. Furthermore, the released intracellular components can interfere with the chemical reaction used in the requested analysis, which can results in spectrophotometric interference as released hemoglobin absorbs light strongly at 415 nm, 540 nm, and 570 nm [3].

In many laboratories, sample integrity is checked by automated chemistry and immunochemistry equipment to assure that hemolysis, icterus and lipemia, respectively, does not interfere with the measurement of the requested analyses (HIL check) [4]. This is in accordance with ISO 15189:2022 stating that specified requirements of an examination method may include interfering substances [5]. However, interference from hemolysis in arterial blood samples for blood gas analyses may be just as common as in blood samples sent to core laboratories, and studies have indeed found hemolysis in up to 4–13 % of blood gas samples [6–10]. It is known that hemolysis in blood gas samples alter potassium measurements, whereas results on e.g. pH, HCO_3, and pO_2 are divergent [10, 11]. Sodium, Ca^{2+} and pCO_2 has also been stated as prone to hemolysis [10]. Unfortunately, blood gas analyzers are unable to identify hemolysis, icterus and lipemia [10], and undetected hemolysis in blood samples for blood gas analysis can therefore lead to erroneous clinical interpretation and treatment.

Originally, blood gas analyzers only measured pO_2, pCO_2, pH, and SaO_2 [12]. Today, the number of analyses

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included in “blood gas testing” have expanded considerably, and modern blood gas analyzers also perform rapid measurements of e.g. electrolytes, glucose, lactate, creatinine, and hemoglobin and are a key element in the swift clinical management of critically ill patients [13]. This underlines the need for valid test results, especially when the personnel responsible for the preanalytical and analytical phase are working outside the core laboratories. However, it is not well established what clinical and laboratory personnel know about the impact of hemolysis on blood gas analyses. Moreover, do they know what to be aware of and when? The aim of this study was to investigate the knowledge among clinical personnel on blood gas analyzers with focus on the interference from hemolysis.

Materials and methods

This questionnaire study was carried out from October 2022 to May 2024. The questionnaire consists of 13 questions covering demographic information about the respondents as well as specific questions on handling of and knowledge about blood gas analyses and hemolysis (see Table 1). Questions were adjusted in collaboration with the Nordic preanalytical scientific working group under the Nordic Federation of Clinical Chemistry (NFKK) and also tested by local anesthesiologists. The questionnaire was distributed to personnel handling the blood gas analyzers through the NFKK on behalf of the Nordic preanalytical scientific working group under NFKK.

Table 1: All the questions in the survey.

1. Please type your title	**% (%)**
Medical doctor	37 (31.6)
Chemist or medical doctor at laboratory department	17 (14.5)
Other	56 (47.9)
Not specified	7 (6.0)
2. Please type your place of employment	**% (%)**
Intensive care unit	38 (32.5)
Clinical department including emergency department	33 (28.2)
Pediatric department	5 (4.3)
Other	15 (12.8)
Not specified	26 (22.2)
3. Please type your country	**% (%)**
Denmark	52 (44.4)
Sweden	22 (18.8)
Finland	13 (11.1)
Norway	2 (1.7)
Not specified	28 (23.9)
4. Your knowledge about the blood gas analyzer	**% (%)**
I “just” use the instrument	7 (6.0)
I use the analyzer, and I interpret the results	74 (63.2)
I use the analyzer, I interpret the results, and I have a deeper knowledge about the analyzer	36 (30.8)
5. Type of blood gas analyzer you use?[a]	**% (%)**
Radiometer, ABL	79 (67.5)
Siemens epoc	2 (1.7)
Siemens (other)	6 (5.1)
I do not know	27 (23.1)
Other	6 (5.1)
Not specified	1 (0.9)
6. Do you assess the quality of a blood sample before you analyze it?	**% (%)**
Yes	84 (71.2)
No	30 (25.4)
I do not know	4 (3.4)
7. If yes to question 6, how do you assess the quality?	**% (%)**
Air bubbles	36 (42.9)
Volume	28 (33.3)
Clots	25 (29,8)
Other	59 (70.2)

Table 1: (continued)

8. To which degree can your blood gas analyzer identify hemolysis?	**% (%)**
All levels of hemolysis can be detected	4 (3.5)
Only high levels of hemolysis can be detected	1 (0.9)
The instrument does not mark for hemolysis	41 (36.0)
I do not know	68 (59.6)
9. Does your blood gas analyzer indicate for hemolysis on any test results? If yes, how is it marked?	**% (%)**
There is no indication of hemolysis	48 (43.6)
It is indicated in the laboratory information system	1 (0.9)
It is indicated in the patient's medical record	0 (0.0)
It is indicated on a print from the blood gas analyzer	7 (6.4)
I do not know	54 (49.1)
10. Action taking in the presence of hemolysis on any test results from your blood gas analyzer?	**% (%)**
If the result is released from the analyzer, it is considered valid despite of hemolysis	4 (3.9)
The result might be biased but can be used as an indicator of the clinical condition of the patient	5 (4.9)
The result is not valid and another arterial blood sample must be collected	35 (34.0)
Because of hemolysis, venipuncture is performed instead	0 (0.0)
The clinical biochemistry department is contacted for consultation	3 (2.9)
There is no indication of hemolysis from the analyzer	44 (42.7)
Another option than those mentioned	12 (11.7)
11. Do you believe that hemolysis has any clinical impact on any PaO_2 measurement on the analyzer?	**% (%)**
Not at all	9 (7.9)
To some degree	29 (25.4)
Very much	18 (15.8)
It depends on the sample material (arterial, venous etc.)	6 (5.3)
I do not know	52 (45.6)
12. Do you believe that hemolysis has any clinical impact on any bicarbonate measurement on the analyzer?	**% (%)**
Not at all	6 (5.2)
To some degree	32 (27.6)
Very much	13 (11.2)
It depends on the sample material (arterial, venous etc.)	2 (1.7)
I do not know	63 (54.3)
13. Do you believe that hemolysis has any clinical impact on any potassium measurement on the analyzer?	**% (%)**
Not at all	0 (0.0)
To some degree	20 (16.5)
Very much	70 (57.8)
It depends on the sample material (arterial, venous etc.)	2 (1.7)
I do not know	29 (24.0)

[a]Percentages more than 100 % as multiple answers are possible.

To elucidate the knowledge about interference of hemolysis in blood gas specimens among personnel responsible for interpretation of the results, a subgroup analysis on medical doctors working outside the core laboratories was performed.

No formal ethical approval was necessary as respondents were anonymous and no patient data was used.

Results

In total, 117 respondents completed the questionnaire. See Table 1 for background characteristics. Of all respondents, 37 (31.6 %) were medical doctors working outside the core laboratory. Most respondents (63.2 %) both used the analyzer and interpreted the result. In the subgroup of medical doctors working outside the core laboratories, 97.3 % interpreted the results (data not shown). A minority of 36 (30.8 %) of all respondents declared also to have a deeper understanding about the blood gas analyzer (Table 1).

The majority, 84 (71.8 %) of the respondents, assessed the quality of a blood sample before they analyzed it, whereas 30 (25.6 %) did not (Table 1). Among medical doctors working outside the core laboratories, 23 (62.2 %) assessed the quality of the blood sample before they analyzed it (Figure 1), while 12 (32.4 %) did not. The remainder did not answer the question (data not shown). Results on how the yes-respondents assessed the quality of the blood samples are presented in Figure 1.

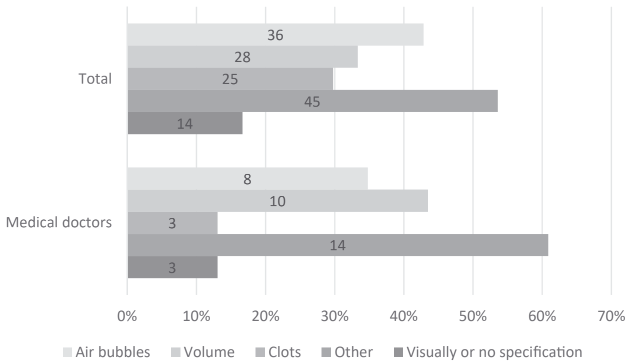

Figure 1: How do you assess the quality? (Yes-responders, question 6)*. Total: n=84 medical doctors: n=23. Number of respondents are indicated as small numbers. *Percentages sum to more than 100 % as multiple answers are possible.

When focusing on the ability of the blood gas analyzer to identify hemolysis (question 7, 8 and 9), 68 (59.6 %) did not know to which degree the blood gas analyzer can identify hemolysis, whereas four respondents (3.5 %) answered that all levels or high levels of hemolysis can be detected (Table 1). Four respondents (3.9 %) considered the result valid despite hemolysis if it is released from the instrument. Many respondents did know that there is no indication of hemolysis from the analyzer (n=44), but a comparable number did not know whether the analyzer do flag for hemolysis or not (n=54) (Table 1).

Knowledge about how hemolysis affects the measurements on the blood gas analyzer; 84 (73.7 %) of all respondents and 35 (97.2 %) of the medical doctors knew that hemolysis alters potassium measurements very much or to some degree (Figure 2). Knowledge about the effect on PaO_2 and bicarbonate measurements were more divergent as shown in Figure 2.

Discussion

In this survey among 117 clinical and laboratory personnel in four Nordic countries, we found that less than a third of respondents declared to have a deeper understanding about the blood gas analyzer. This is in line with the finding that most of the respondents do not know to which degree the blood gas analyzer can identify hemolysis. Likewise, almost half of all respondents and more than 80 % of the medical doctors did not know if the blood gas analyzer indicates for hemolysis. Furthermore, assessment of the blood sample quality prior to analysis was very heterogeneous and in general insufficient.

To our knowledge, this is the first survey with focus on clinical personnel and their knowledge about hemolysis in blood gas analyses, and it rises several issues to address.

Clinical impact

Most medical doctors participating in this survey, of whom almost all interpret the analysis results, knew that hemolysis alter the measured potassium concentration. However, only 25.7 % of the medical doctors knew that the blood gas analyzers do not flag for hemolysis. Although most of the respondents (71.8 %) declared to assess the sample quality, this still leaves over 25 % that does not. Furthermore, most of the respondents assessing the sample quality did not look for air bubbles, sample volume or clots before analyzing the sample. Clotting and insufficient volume are well-described preanalytical errors, and bubbles can significantly alter analyte concentrations in blood gas measurements [12]. Thus, even though the respondents

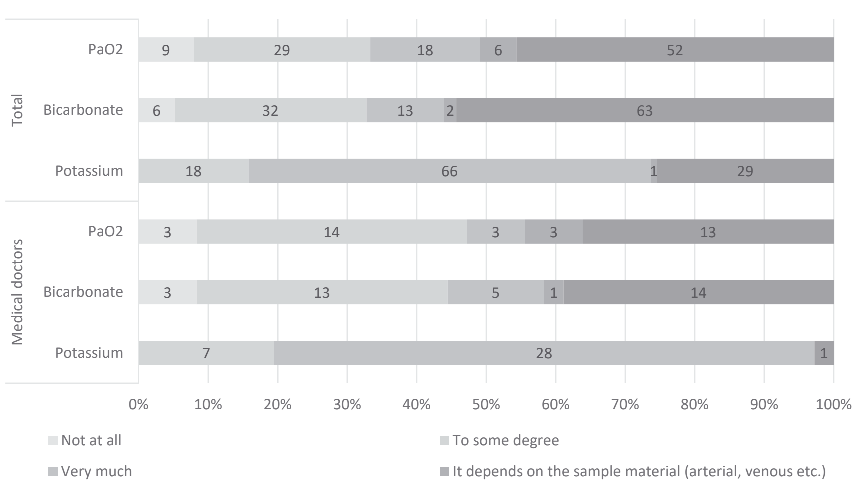

Figure 2: Do you believe that hemolysis has any clinical impact on PaO_2/bicarbonate/potassium measurement on the analyzer? (Question 11–13). Total: n=114 for PaO_2 and potassium, n=116 for bicarbonate. Medical doctors: n=36.

declare to assess the quality of the blood samples, this evaluation seems inadequate to reveal all preanalytical errors. Consequently, if the medical doctors responsible for patient's care are not aware of potential hemolysis and other preanalytical errors, they risk relying on the results released from the instrument, which could lead to erroneous conclusions. Of particular note is the finding that four respondents considered the result valid despite hemolysis if it was released from the instrument. This could be critical and ultimately lead to wrong treatment of the patients. Supporting this, ±8 % of all paired potassium results analyzed on blood gas analyzer and core laboratories in a recent multicenter study were outside the reference change value, indicating a risk of incorrect diagnosis and subsequently incorrect clinical care of the patients in emergency departments [14]. The importance of all these aspects is emphasized by the fact that POCT are used incrementally due to a wish for faster patient flow and a swifter handling of alarming situations – a necessity that increases the importance of a robust and reliable test result: The faster the action, the more important the reliability of the test result upon which the action is based. The increasing use and organizational reliability on POCT result therefore stresses the need for better knowledge about the different caveats and pitfalls in POCT measurements in general.

How to improve

Our study identified a limited knowledge on blood gas analyzers among personnel responsible for blood gas testing and interpretation. This indicates a need for improved education of the personnel handling the blood gas analyzers. The ISO 15189:2022 states that 'The laboratory shall specify the competence requirements for each function influencing the results of laboratory activities, including requirements for education, qualification, training, re-training, technical knowledge, skills and experience' and 'The laboratory shall have a process for managing competence of its personnel, that includes requirements for frequency of competence assessment' [5]. Furthermore, it is stated that an appropriate theoretical and practical training program for all POCT personnel should be developed and implemented [5]. Managing competences of the personnel handling the blood gas analyzers is however complex as the instruments and the staff performing the POCT measurements primarily are located outside the core laboratories. A well-organized POCT organization and the implementation of user management is a necessity to solve this problem. User management implies education and competence assessment of the relevant staff, which is a huge, but very important task for the laboratories to fulfil. It is crucial that this is supported by the hospital administration and adheres to relevant international guidelines and as of lately the updated ISO 15189:2022, which now has included the POCT area on behalf of the former ISO 22870. In addition, the updated ISO 15189:2022 requires performance of risk assessment. The laboratory is required to identify potential risks to patient care in the pre-examination, examination and post-examination processes. This includes risk assessment of the use of POCT. For this purpose, a risk analysis model to diminish negative impact on patient care by preanalytical errors in blood gas analysis has been proposed [15]. This model is based on identification of errors that may occur while performing blood gas analysis, possible consequences and preventive actions [15].

Another possible improvement area is e-learning and audit as known from the blood sampling area: Willman et al. evaluated a large-scale online e-learning program on venous blood specimen collection with promising results [16]. An e-learning program on blood gas analysis may also improve the whole testing process of blood gasses, including the preanalytical phase and the external staff responsible for these analyses [16]. Another option is the use of an observation scheme or checklist for quality control as suggested for phlebotomy by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for the Preanalytical Phase [17]. Introduction of an observation scheme in blood gas testing may also improve the preanalytical phase in this area. Within the context of improvement, it would be interesting to provide a follow-up survey focusing on the effect of education of POCT users outside of core laboratories.

Today, sample integrity check generally is performed by automated chemistry and immunochemistry equipment in many laboratories. As shown in this survey, some clinicians responsible for interpreting the analysis results are used to lab results without preanalytical flaws (unless clearly stated along with the results), and despite differences in skills of the performing staff, the expectation for flawless results are clearly the same. It is therefore mandatory to consider, how it is technically possible to qualify POCT results besides optimizing the education as mentioned. Casati et al. [10] proposed to introduce automated processing of serum indices in blood gas analyzers, and Buno et al. also stated that technological improvements are desirable [18], as they will ensure that hemolysis, icterus and lipemia does not interfere with the measurements. As an alternative, a photometric hemolysis detection system intended for use with POCT has shown promising results [19]. These are all options that the laboratories need to take into consideration to minimize the risk of decision-making based on erroneous test results.

Strengths and limitations

A limitation of the study is the use of a non-validated questionnaire. However, to our knowledge no validated questionnaire exists in this area. Furthermore, the questionnaire was adjusted and improved in collaboration with members of the Nordic preanalytical scientific working group under NFKK, and finally, the questionnaire was tested on local anesthesiologists to ensure a user-friendly design and appropriate questioning.

As the questionnaire was distributed widely, we have no knowledge about the non-responders. Consequently, we do not know if respondents are representative of the targeted population. However, we have respondents from four Nordic countries indicating the problem to be general and not limited to one hospital or country. The laboratory departments in the Nordic countries are generally well-organized with well-functioning POCT organizations. Furthermore, the hospitals are very similar. Thus, we assume our results to be representative of the hospitals in the Nordic countries. We can only speculate if the results can be extrapolated to other countries, but as stated, many of the observations and challenges are compatible with previous European studies within this area, so our qualified guess is that it can be extrapolated at least to other European countries.

Conclusions

The knowledge about blood gas analyzers with focus on the interference from hemolysis is sparse among extra-laboratory personnel using the blood gas analyzers. This emphasizes the need for better education and competence management when personnel working outside the core laboratories are responsible for the preanalytical and analytical phase of laboratory testing. Also, technical solutions that can ensure the preanalytical handling and sample integrity are warranted. The literature in this area is generally sparse, and more research with focus on the knowledge of blood gas analysis among end-users is warranted. As many blood samples for blood gas analyses are handled outside the core laboratories by clinical personnel, our study enlightens an area with great potential for improvement.

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Data availability: The raw data can be obtained on request from the corresponding author.

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