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The impact of heparin on Hb levels during blood gas analysis in critical patients

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Abstract

Laboratory anticoagulants are acidic, resulting in a fall in blood hydrogen potential (pH), increased plasma oxygen (PO2) levels, and reduced hemoglobin levels. This study intends to assess the difference in hemoglobin levels between blood gas analysis (BGA) examinations performed with sodium heparin and lithium heparin anticoagulants utilizing Ethylene Diamine Tetraacetic Acid (EDTA) anticoagulants. Analytical observational research was performed on sixty samples of hemoglobin concentration test findings on BGA examination of arterial patients who were not receiving anticoagulant medication. Statistical analysis obtained the differences in hemoglobin concentrations examined using anticoagulants sodium heparin with EDTA (p-value = 0.000). Hemoglobin concentrations were examined using anticoagulants lithium heparin with EDTA (p-value 0.002). There was a substantial difference in the assessment of hemoglobin concentration with sodium and lithium heparin anticoagulants and with EDTA anticoagulants. The final concentration of heparin blood and dilution in the blood is the result of selecting anticoagulant kinds and quantities. Thus, it must be taken into account when collecting blood samples because it affects laboratory test findings.

Keywords

Hb level, Heparin, Blood gas

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Introduction

Hemoglobin is a complex compound consisting of heme (iron compound) and globin (simple protein) [1]. Hemoglobin is the largest constituent component of erythrocytes that carries oxygen to tissues and regulates the body's alkaline acid balance [2]. Average hemoglobin values in men are above 13.6 g/dL and above 12 g/dL in women. Hemoglobin levels that are less than average are called anemia [3].

Anemia is a deficiency of red blood cells, hemoglobin, or blood circulation. This condition results in decreased oxygen capacity to the tissue, causing weakness and

shortness of breath [4]. Previous studies have found that almost 80% of Intensive Care Unit (ICU) patients have anemia during treatment, with hemoglobin levels of approximately 10.8 g /dL [5]. Anemia increased from 60% to 66% when entering the ICU treatment room; after three days of treatment, the incidence rate rose to 90% and raised on the eighth day of treatment by 97% [6]. Regular laboratory examinations are required to enforce medical diagnosis, monitoring, and administration of therapy, especially in the ICU [7].

Hemoglobin examination was conducted using a complete blood specimen taken from the veins and mixed with ethylenediaminetetraacetic acid (EDTA) anticoagulants [8]. Hemoglobin can also be known as concentration from the results of blood gas analysis examination (BGA) [9]. This total hemoglobin concentration (tHb) parameter can be checked in conjunction with other BGA parameters pH, PO_2, PCO_2, SaO_2, and HCO_3 [10]. BGA examination uses heparin as an anticoagulant mixed with arterial blood samples to prevent blood clotting [11]. There are two types of heparin, namely liquid heparin (sodium heparin) and powder (lithium heparin) [12]. Excessive addition of heparin can affect pH, PO_2, PCO_2, and HCO_3 parameters, thus affecting the accuracy of results [13].

Previous research has found that pre-analytical errors averaged 46-77.1%, which included hemolysis events, less sample volume than provisions, illegible handwriting, specimen errors, clotting, container vacuum errors, anticoagulant usage errors, and comparison of sample volume with inappropriate anticoagulants [14]. Potential results inaccuracies may occur due to improper sampling techniques, transport procedures, and inappropriate sample storage conditions [15]. This study aims to determine the difference in hemoglobin concentration by using sodium heparin and lithium heparin anticoagulants with EDTA anticoagulants.

Methods

Placeholder study design and sample

This observational analytical research involves 60 samples conducted at the Installation of Anesthesiology and Intensive Therapy of Gadjah Mada University Academic Hospital from September to October 2019.

Inclusion and exclusion criteria

According to the doctor's advice, the inclusion criteria are patients in the treatment period, getting a BGA examination order, and taking repeated specimens with a period of 1x24 hours from the first specimen retrieval. The exclusion criteria in this study were patients who received anticoagulant therapy and specimens taken from different types of blood vessels, time of retrieval, and location of insertion.

Data collection

Respondents are selected according to the criteria, given an explanation, and informed consent. The nurse took a 3 ml specimen of arterial blood using a three ml syringe. The

collected blood specimens are divided into two parts. 1.5 ml of blood is inspired into a syringe containing sodium heparin 450 IU, and the remaining 1.5 ml is mixed into an EDTA tube. According to orders from the doctor, for the next 1x24 hours are taken arterial blood specimens as much as 3 ml then divided into two parts. 1.5 ml of blood is inspired into the Preza-Pak II syringe containing lithium heparin, and the remaining 1.5 ml is mixed into the EDTA tube. Hemoglobin concentration in specimens with heparin anticoagulants was measured using Opti CCA-TS_2 and EDTA anticoagulants using Sysmex XP 100. The test results are analyzed using computer software.

Statistical analysis

The collected data was conducted a normality test using One-Sample Kolmogorov-Smirnov. Furthermore, the different tests applied are paired T-Tests to compare the averages of two groups paired with each other. Different measuring instruments between Sysmex XP 100 and Opti CCA-TS_2 in determining hemoglobin concentration tested consistency levels between two raters using Cohen's Kappa test.

Ethics

The study has met the declaration of Helsinki 1975, the Council for International Organizations of Medical Sciences (CIOMS), and the World Health Organization (WHO) 2016. Proof of ethical feasibility received from the Health Research Ethics Committee Faculty of Medicine of Universitas Muhammadiyah Surakarta, number 2413/B.1/KEPK-FKUMS/X/2019.

Results and Discussion

Respondent characteristics

This study observed 60 patient hemoglobin test results by established criteria. Respondents to this study were divided into two: patients who used sodium heparin anticoagulants and patients who used lithium heparin anticoagulants. Respondents who received sodium heparin consisted of 17 men and 13 women, while respondents who obtained lithium heparin anticoagulants consisted of 15 men and 15 women. The characteristics of respondents are shown in Table 1.

Table 1. Respondent characteristics

Category	Sodium Heparin (n=30), n (%)	Lithium Heparin (n=30), n (%)
Age		
Median (min-max)	57 (26-83)	33 (50-83)
Gender		
Male	17 (56.67)	15 (50)
Female	13 (43.3)	15 (50)
Medical Diagnosis		
Acute	6 (20)	11 (36.67)
Chronic	24 (80)	19 (63.3)

Most hemoglobin concentration measurements in this study showed low levels of anemia. Anemia in intensive care patients with inflammation and infection tends to be

faster, followed by the length of the treatment period [16, 17]. Anemia in the ICU is found in the first week, around the 3rd to the 7th day [18]. The prevalence of anemia in critically ill patients is influenced by pre-existing disease severity and comorbidity factors [13].

Hemoglobin concentration measurement results

Hemoglobin concentrations measured using heparin anticoagulants (sodium and lithium) are observed and compared to hemoglobin concentrations of EDTA anticoagulants, shown in Table 2.

Table 2. Hemoglobin concentration measurement

Anticoagulants	Hemoglobin Concentration			Category		Anemia (%)
	Average	Min	Max	Low	Normal	
Sodium heparin	10.02 ± 1.39	7.2	13	29	1	96.7
Lithium heparin	10.43 ± 1.54	6.7	12.8	27	3	90

Statistical analysis shows a significant difference between hemoglobin concentrations in each anticoagulant. This difference is due to factors that affect hemoglobin concentrations that researchers do not control. Besides, acidic heparin can decrease blood pH and increase PO_2, decreasing hemoglobin in the arterial blood [19]. Heparin is recommended for electrolyte measurement because of the minimal impact on dielectric measurements compared to EDTA anticoagulants. The dielectric examination results revealed that heparin has no significant difference with pure blood [14]. This dielectric examination is necessary to determine the condition of anemia [20]. The use of heparin needs to be considered because it affects the results of the examination.

Differences in hemoglobin concentration using heparin anticoagulants with EDTA

Data on hemoglobin concentration in normally distributed heparin anticoagulants were analyzed using Paired T-Test to determine the significance of the difference with EDTA shown in Table 3. Anticoagulant sodium heparin with EDTA indicates p-value = 0.000, and lithium heparin with EDTA shows p-value = 0.002, which means there is a significant difference between the concentration of hemoglobin using heparin anticoagulants with hemoglobin concentrations using EDTA anticoagulants because p-value <0.05.

Table 3. Hemoglobin concentration measurement

Anticoagulants	Mean	t	df	Sig. (2-tailed)
Sodium Heparin_EDTA	-1.3267 ± 1.19	-6.101	29	.000
Lithium Heparin_EDTA	-.8600 ± 1.38	-3.409	29	.002

The final concentration of heparin blood and dilution in the blood are two things to be aware of when sampling because it can affect BGA results. The greater the volume of liquid heparin used, the greater the level of bias and difference in measurement results due to the dilution effect [21]. The effect of blood dilution results in a decrease in hemoglobin levels and the count rate of blood components, especially if the blood sample volume is less than the provision [1]. The use of liquid sodium heparin has a significant effect on examining electrolytes, hemoglobin, and lactate [22]. The use of

liquid sodium heparin was found lower electrolyte concentration levels [23]. Lithium heparin shows more stable electrolyte test results. CLSI recommends lithium heparin as an anticoagulant for BGA over sodium heparin for such reasons [15].

Analysis of the deal level of Sysmex XP 100 hemoglobin gauge with Opti CCA-TS2

Two different measuring instruments tested their consistency levels to determine the agreement of Sysmex XP 100 measurement results with Opti CCA-TS_2 using Cohen's Kappa test shown in Table 4. Kappa test results on sodium heparin and EDTA anticoagulants showed p-value = 0.690, so it can be concluded that there is no significant agreement in classifying hemoglobin in quality (low, normal, and high) between Sysmex XP 100 and Opti CCA-TS_2 because the p-value > 0.05. Kappa's coefficient value indicates -0.056, which means the deal's strength between the two gauges is poor. Kappa test results on lithium heparin anticoagulants showed a p-value = 0.014, so it can be concluded there is a significant agreement in the classification of hemoglobin quality between Sysmex XP 100 and Opti CCA-TS_2 because of the p-value < 0.05. Kappa's coefficient value indicates 0.429, which means the deal's strength between the two measuring instruments is moderate.

Table 4. Cohen's Kappa Test

Anticoagulants	Value	Asymp. Std. Error[a]	Approx. Tb	Approx. Sig.
Sodium Heparin_EDTA	-.056	.047	-.399	.690
Lithium Heparin_EDTA	.429	.233	2.449	.014

Measurement results on sodium heparin anticoagulants showed no agreement between Opti CCA-TS-2 and Sysmex XP 100, while lithium heparin showed significant agreement between the two devices with moderate deal strength quality. In addition to the dilutive effect factors of the heparin type described earlier, BGA analyzers have different hemoglobin sensitivity, causing less valid results [24]. AGD analyzer showed valid results in a brief examination of hemoglobin concentrations in the ICU [6]. Sysmex XP 100 has more precise precision and accuracy than other invasive methods [25].

From the results and discussion above, there are factors that affect hemoglobin concentrations such as age, dehydration conditions, diet, drugs consumed, gender, and smoking habits that were not controlled by the researchers, with the result that can be used as a basis for further research.

Conclusion

There were significant differences in hemoglobin concentration results using heparin anticoagulants (sodium and lithium) on BGA examinations with EDTA anticoagulants on routine blood tests. BGA analyzer (Opti CCA TS-2) has a moderate level of agreement and consistency compared to the automated hematology analyzer (Sysmex XP 100) in hemoglobin concentration check.

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