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Original article

Comparison of the Effects of Heparin 1000 and 5000 Units on Arterial Blood Gases

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SUMMARY

Analysis of arterial blood gases is necessary for managing the respiratory and metabolic parameters of patients in the intensive care unit. The aim of this study was to compare the effects of heparin 1000 and heparin 5000 units on arterial blood gases in patients admitted to the intensive care unit. This study was a triple-blinded clinical trial. A total of 78 patients with head injury were randomly selected from the emergency department of a hospital in an urban area of Iran in 2017. Data was collected using a questionnaire and a checklist of laboratory parameters. Data was analyzed using descriptive and inferential statistical methods via the R software.

Statistically significant differences in Na, SaO2, Ca, BEecf ($p < 0.001$), and HCO3, BEe and K were observed between the two groups ($p < 0.01$). No statistically significant difference between the values of PaCO2, PH and PaO2 in the two groups were reported ($p > 0.05$).

The results of this study confirmed that heparin 1000 and heparin 5000 units had no effects on respiratory parameters in analyzing arterial blood gases. However, the concentration of heparin had a significant effect on metabolic parameters for the analysis of arterial blood gases and electrolytes.

Key words: **heparin concentration, arterial blood gas, electrolyte**

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INTRODUCTION

Analysis of arterial blood gases is recognized as a golden standard in the intensive care unit for the assessment of the respiratory system and the acid and base condition in patients with electrolyte and respiratory disorders (1). Acid and base disorders can lead to life-threatening complications in the disease process. The process of analyzing and monitoring arterial blood gases is an essential part of the diagnosis and treatment processes, oxygenation and the acid-base balance, especially in patients admitted to the intensive care unit. It is required for the diagnosis of acid and base disorders by the physician in patients with respiratory and metabolic problems (2 - 4). Besides the measurement of gases and electrolytes, arterial blood gas tests can measure methemoglobin, carboxy hemoglobin and hemoglobin levels. This information is essential for the treatment of patients suffering from acid and base disorders and respiratory or metabolic diseases (5). Heparin in the form of liquid is used as anticoagulant in the blood gases test, which may influence the results of these parameters (6, 7). The minimum amount of blood needed for analyzing arterial blood gases is 0.3 ml. A high proportion of heparin to the blood volume can lead to an increase in the final concentration of heparin and blood dilution, which may be a major contributor to medical errors in patients admitted to the intensive care unit. This is very important in neonates as collecting blood samples is difficult (8). Sampling from the arterial line, which is continuously heparinized by the catheter route is one of the most common laboratory errors in sampling arterial blood gases (9). Hamilton et al. illustrated that the effect of heparin on blood parameters was 35-50%. The results of this study emphasized that the level of heparin affected PaO2 and PaCO2 pH with the highest effect on PaCO2. Sachs et al. also showed that in the presence of dif-ferent concentrations of heparin and calcium levels also decreased by 5% (4). This evidence suggests that heparin affects not only blood gases but also influ-ences electrolytes including calcium, potassium, sodi-um, chlorine, etc.

In a study by Chhapola et al. the effect of different heparin volumes on arterial blood gases and electrolyte parameters, increased heparin levels reduced PaCO2, Na and HCO3 was investigated, but it had no statistically significant effect on PaO2 levels (10).

Sampling for appropriate examinations is one of the tasks of a medical team. Most laboratory errors are related to the pre-analysis steps and the wrong technique performed by healthcare staff. Also, the collection of a sample with a heparin-impregnated syringe with different concentrations is one of the sources of errors before analysis. The attention of the healthcare staff to the details of the patient's readiness for sampling, sampling process, and sending it to the laboratory influence the accuracy of results (11). An incorrect use of heparin to impregnate the syringe may increase the acidity level in arterial blood gases, which may disturb the diagnosis and treatment of patients (1). Despite its importance, the correct amount of heparin concentration and the amount of blood sample required to prevent the negative effect of heparin concentration on arterial blood gases have not been reported. Therefore, there are various hospital policies for blood sampling (1). Different sampling by nurses in various nursing wards for impregnating the syringe in terms of the amount of heparin can lead to a lack of unity for performing the procedure and policy in treatment centers. Therefore, the aim of this study was to compare the difference between heparin 1000 and heparin 5000 units on arterial blood gases, which could lead to the recommendation of a united procedure for performing this test.

METHODS

This randomized, triple-blinded clinical trial was performed in a hospital in an urban area of Iran in 2017. In this study, the sample collector, laboratory expert, and data analyst were blinded to the study. It was performed on 78 patients with a traumatic head injury with GCS = 5 - 8 who underwent mechanical ventilation support and were hospitalized in the intensive care unit in an urban area of Iran. Blood sampling was conducted after obtaining the required permissions, providing explanations about the method and aim of the study and signing the informed consent form by the legal guardian of the patients.

Inclusion criteria were: the patients' willingness to participate in the study, appropriate arterial blood flow to the limb for blood sampling, aged 18 - 70 years, traumatic head injury and receiving mechanical ventilation support for one week, mechanical ventilation support for at least 15 minutes before blood sampling, level of consciousness of 5 - 8 based on the Glasgow Coma Scale, and the hemoglobin level > 10.

Exclusion criteria were: the presence of a lesion or fistula on the limb, evidence of peripheral vascular diseases around the site of blood sampling, any coagulopathy or moderate to high doses of anticoagulant therapy, the presence of active infection in the arterial line and any damage to the limb including fractures, dislocation, burns, acute chest traumas and underlying diseases such as heart, kidney and lung diseases, and diabetes that could affect the results of arterial blood gases.

Therefore, 156 sample were selected of which 78 eligible patients were recruited in this study. A randomized sampling method was used, so that heparinized syringes were randomly selected using flipping the coin. Codes A and B were given to the syringes and were defined as A1, A2, A3...A78 and B1, B2, B3...B78. The samples were assigned into the heparin groups of 1000 units (syringes with heparin 1000 units) and heparin group 5000 units (the common method of heparin administration using syringes with heparin 5000 units). To maintain the same conditions in the groups, two specimens of the same patient in terms of all possible confounding factors and homogeneity were taken. Therefore, 1 ml blood was taken using insulin syringes of heparin 1000 units and heparin 5000 units from the radial artery of each patient, coded as A and B (for controlling time as a confounding factor), placed in an ice cube and sent to the laboratory within 10 minutes. Laboratory staff who had no information of the sampling process analyzed them using the Medica Easy Stat analyzer® made by the USA in 2016. Before the study, this device was calibrated and tested using three standard solutions of alkalosis, acidosis and normal acidity every 24 hours automatically (in 8 minutes) in the first morning shift and manually at the end of the morning shift. In case of any problem, the company's representative was requested to resolve the problem. The accuracy (reliability) of insulin syringes was assessed using 10 syringes as they were filled and emptied, and different volumes and amounts of the remaining heparin in the dead space of the needle and syringe were assessed. It should be noted that the analysis time from each sample to the next sample was two minutes. Data were recorded in the checklist of arterial blood gases for each patient and a checklist of the results of laboratory parameters. For the validity of the questionnaire and checklist, 10 faculty members of the school of nursing assessed qualitative content validity, which led to some modifications.

Ethical considerations

Each questionnaire was coded to ensure the anonymity of the patients. The ethics code (IR.MEDSAB.REC.1396.62) for this research was granted by the ethics committee affiliated with Sabzevar University of Medical Sciences. This study was registered on the Iranian clinical trials registration website with the following decree code: IRCT2017091836266N1.

The collected data was entered into the software R and descriptive and inferential statistics were used for data analysis. The mean and frequency were used to determine the distribution of variables. Also, paired t-test and Wilcoxon test were used for the analysis of data with normal and non-normal distributions, respectively. The significant level was considered $p < 0.05$.

RESULTS

The participants included 51 male (65%) and 27 female (33.8%) patients aged 18-65 years, with a mean age 37.76 ± 13.42 years. The patients were diagnosed with intracranial hemorrhage (17%), subdural hemor-

Table 1. *Arterial blood gases and electrolytes in the groups*

Variables	Groups		P-value
	Heparin 5000 units Mean ± SD	Heparin 1000 units Mean ± SD***	
pH	7.43 ± 0.06	7.44 ± 0.07	0.464
HCO3	25.94 ± 0.43	26.12 ± 0.45	0.003*
PaCO2	37.73 ± 0.75	37.91 ± 0.82	0.597
PaO2	92.85 ± 0.83	92.57 ± 0.81	0.766
Bee	1.99 ± 0.45	1.86 ± 0.46	0.002*
BEecf	2.02 ± 0.40	1.89 ± 0.41	< 0.001**
SaO2	97.85 ± 0.19	97.79 ± 0.18	< 0.001**
Ca	1.13 ± 0.04	1.03 ± 0.05	< 0.001**
Na	135.65 ± 0.070	137.49 ± 0.61	< 0.001**
K	3.97 ± 0.08	3.93 ± 0.010	0.001**

*P < 0.01; **P < 0.001; ***Standard Deviation rhage (34%), sub arachnoid hemorrhage (25.5%), epidural hemorrhage (13.5%) and diffused axonal injury (10%). The mean values of pH, PaO2, and Na in the group of heparin 1000 units were higher than those of heparin 5000 units. The mean variables of HCO3, PaCO2, BEe, BEecf, SaO2, Ca, K in the heparin group 5000 units were higher than those of heparin 1000 units. No statistically significant differences between the values of PaCO2, pH and PaO2 in the groups were reported ($p > 0.05$). There were statistically significant differences between Na, SaO2, Ca, BEecf, HCO3 BEe and K values ($p < 0.01$). The mean and standard deviation of variables in the groups of heparin 1000 units and heparin 5,000 units were reported in Table 1.

DISCUSSION

In this study, the difference between heparin 1000 and heparin 5000 units on arterial blood gases were studied, which showed some changes in arterial blood gases and other variables.

There were no significant differences between the results of pH, PaO2 and PaCO2 in the groups ($p > 0.05$). Therefore, the results of this study were consis-tent in the PaO2 parameter with the result of the study by Malekzadeh et al., whereas in PaCO2 and pH parameters were converse with the results of studies of Malekzadeh et al., Copula et al., Hooper et al., Zokaei et al (1, 10, 12, 13). It seems that the non-significant results of PaCO2 and pH parameters in this study could be attributed to the concentration of heparin, because in some studies with significant statistical results, the heparin concentration was 15 - 30% (1). However, in this study according to the suggestion by Hutchison for the prevention of fatal effects of heparin on the results of arterial blood parameters, 20 units per milliliter were used (1). Chhopola considers that the effect of heparin on pH and PaO2, with the concentrations of heparin more than 40% and 35%, has a false effect (10). Hajin and Zokaei believe that the effect of heparin in the concentration of more than 10% causes a statistically significant change in PaCO2 (7, 13). On the other hand, other factors affecting arterial blood gases and electrolytes are the size of the syringe and needle size (14). Since the size of the syringe used in some studies was 2-5 milliliters (10, 12, 13), it seems that this factor could also lead to differences in results (15).

Also, the comparison of the mean of pH in the groups indicated a decrease in pH in the group of heparin 5000 units than in the group of heparin 1000 units. This reduction was not statistically significant ($p > 0.05$), but the same amount of difference could be clinically important, possibly causing misdiagnosis and treatment described by other studies (1).

The results of this study on HCO3-, BEe, BEecf and SaO2 showed significant differences between the groups ($p < 0.05$), which were similar to the results of the studies performed by Malekzadeh et al., Chhopola et al., Hooper et al., and Zokaee et al. (1, 8, 12, 13). In this study, HCO3 in the group of heparin 5000 units compared to the group of heparin 1000 units had lower values in arterial blood, which could indicate the effect of this parameter on the concentra-tion of heparin. A probable reason could be that the increased heparin concentration leads to acid and base disorders including metabolic acidosis due to the reduction of HCO3. In this study, additional hep-arin levels reduced the HCO3-, BEe, BEecf parame-ters, especially in the group of heparin 5000 units compared to the group of heparin 1000 units. There-fore, with increasing the concentration of heparin in syringes, metabolic acidosis occurs, which according to the results of this study has no association with the disease, and additional heparin leads to meta-bolic acidosis, and misinterpretation of the results.

In the present study, a significant difference between the two groups of heparin 1000 units and 5000 units ($p < 0.001$) was reported in terms of electrolytes (Na, K and Ca). According to the results, potassium and calcium in the heparin 5000 group compared to the heparin 1000 group had higher levels in arterial blood gases indicating an increased effect of heparin concentration on calcium and potassium levels. The results of this study were similar to those of studies by Chhopola et al., Hooper et al., Zokaee et al. (10, 12, 13) and were converse to the results of studies by Hijin et al. and Hooper et al. in terms of calcium levels (7, 12).

Researchers believe that heparin concentrations should not exceed 10 IU/mL of ionized calcium, which results in disturbances and mistakes in the parameters of arterial blood gases, especially calcium that is more sensitive to heparin concentrations (7).

The results of this study showed a difference in sodium levels in two groups with heparin concentrations of 1000 units and heparin 5,000 units, the sodium levels of which were decreased through increasing the concentration of heparin. This finding can be substantiated by the fact that sodium ion is a heparin-soluble salt that is combined with blood. Therefore, increasing the concentration of heparin and sodium increases errors in arterial blood parameters especially electrolytes. The increase in the combined effect of liquid heparin on electrolytes such as Ca, Mg, K in the presence of sodium has been described (14, 16). Therefore, with the presence of higher concentrations of heparin, it is expected that sodium levels are reduced and the amounts of other electrolytes such as potassium and calcium are increased, which is also well-documented in terms of clinical significance.

Limitations

It was impossible to assess arterial blood gases in patients admitted to intensive care units with more health problems. One of the strengths of this study was the large number of samples and similarities of the groups as each patient was considered its own control.

CONCLUSION

The results of this study indicated that there were no statistically significant differences in pH, PaO2, PaCO2 in the groups of heparin 1000 units and 5000 units indicating that heparin had no effects on respiratory parameters. However, it had significant effects on metabolic parameters such as HCO3, BE, Becf and electrolytes. Therefore, it can be said that heparin used in syringes does not have much effects on respiratory parameters and mainly influence metabolic parameters.

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Upoređivanje efekata heparina od 1000 jedinica i 5000 jedinica na gasove arterijske krvi

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SAŽETAK

Analiza gasova arterijske krvi neophodna je za praćenje respiratornih i metaboličkih parametara kod bolesnika na intenzivnoj nezi. Cilj ove studije bilo je upoređivanje efekata heparina od 1000 jedinica i 5000 jedinica na gasove arterijske krvi kod bolesnika u jedinici intenzivne nege.

Ova studija sprovedena je kao trostruko slepa klinička studija. Izabrano je ukupno 78 bolesnika sa povredama glave metodom slučajnog uzorka, na departmanu urgentne medicine u jednoj od bolnica u urbanom delu Irana, 2017. godine. Podaci su prikupljeni pomoću upitnika i liste laboratorijskih parametara i analizirani su primenom deskriptivnih i inferencijalnih statističkih metoda u okviru R softvera.

Uočene su statistički značajne razlike u vrednostima Na, SaO2, Ca, BEecf ($p < 0,001$), HCO3, BEe i K između dveju grupa ($p < 0,01$). Nije utvrđena statistički značajna razlika među vrednostima PaCO2, PH i PaO2 u krvi ispitanika ovim grupama ($p > 0,05$).

Rezultati ove studije potvrdili su da heparin od 1000 jedinica i 5000 jedinica nisu imali efekte na respiratorne parametre u analiziranim gasovima arterijske krvi. Međutim, koncentracija heparina imala je značajan uticaj na metaboličke parametre u analizi gasova arterijske krvi i elektrolita.

Ključne reči: **koncentracija heparina, gasovi arterijske krvi, elektrolit**