ORIGINAL ARTICLES

Changes in the Acid-Base Equilibrium of Pleural Fluid During the First 2 Hours After Thoracentesis

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OBJECTIVE: The aim of this study was to assess changes in the acid-base equilibrium of pleural fluid during the first 2 hours after thoracentesis and to determine whether, as with arterial blood, it is important to keep the fluid on ice.

PATIENTS AND METHODS: A prospective, descriptive, comparative study was performed in 53 consecutive patients with pleural effusion. Thoracentesis was performed and pleural fluid was collected in 5 heparinized syringes to determine the pH, PO_2, and PCO_2 at baseline and at 30, 60, 90, and 120 minutes. In the first 26 patients, pleural fluid was collected in a further 4 syringes that were kept on ice prior to performing the same measurements at 30, 60, 90, and 120 minutes.

RESULTS: The patients had a mean (SD) age of 70 (14) years, 66% were smokers, 72% were men, 63% had right-sided pleural effusion, 85% had unilateral effusion, and 15% had massive effusion. In 10 patients the effusion was a transudate, in 35 it was lymphocytic, and in 8 it was neutrophilic. The etiology was benign in 34 cases and neoplastic in 19 cases. The baseline pH was 7.35 (0.1) and baseline values of PO_2 and PCO_2 were 57.8 (20) mm Hg and 53.7 (15) mm Hg, respectively. No significant changes were observed in the first 2 hours for either pH or PCO_2, whereas PO_2 did undergo a significant change over this period. The difference between the baseline value and the value obtained at 120 minutes was 0.005 (0.02) for pH, 12.5 (19) mm Hg for PO_2, and 0.8 (3) mm Hg for PCO_2, with correlation coefficients of 0.97, 0.49, and 0.98, respectively. Comparison of values by simple regression analysis did not reveal a significant difference in the changes in pH, PO_2, or PCO_2 associated with keeping samples on ice. Multivariate analysis revealed that neoplastic effusion and a higher red blood cell count in pleural fluid had a significant influence on pH changes.

CONCLUSIONS: The pH and PCO_2 of pleural fluid did not change significantly during the first 2 hours following thoracentesis, whereas PO_2 did undergo a significant change. Keeping samples on ice during this period is unnecessary. Only a higher red blood cell count in pleural fluid and neoplastic effusion had a limited effect on changes in the pH of samples from our patients during the first 2 hours following thoracentesis.

Key words: *Pleural fluid. pH. PO_2. PCO_2. Effect of time.*

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Evolución del equilibrio ácido-base del líquido pleural durante las 2 primeras horas de la toracocentesis

OBJETIVO: Valorar los cambios en el equilibrio ácido-base del líquido pleural durante las primeras 2 h de la toracocentesis y la importancia de su conservación en hielo como ocurre en la sangre arterial.

PACIENTES Y MÉTODOS: Estudio prospectivo, descriptivo y comparativo de 53 pacientes consecutivos con un derrame pleural. Se realizó toracocentesis con extracción del líquido pleural en 5 jeringas heparinizadas para determinar el pH, presión arterial de oxígeno (PO_2) y de anhídrido carbónico (PCO_2) basales, a los 30, 60, 90 y 120 min. En los primeros 26 pacientes se obtuvieron 4 jeringas que se conservaron en hielo y se realizaron las mismas determinaciones en el tiempo.

RESULTADOS: Los pacientes tenían una edad media (± desviación estándar) de 70 ± 14 años, el 66% eran fumadores, el 72% varones, un 63% tenía un derrame derecho, un 85% unilateral y el 15% masivo. En 10 casos era un trasudado, en 35 exudado linfocitario y en 8 neutrofílico. La etiología fue benigna en 34 casos y neoplásica en 19. El valor basal del pH fue de 7,35 ± 0,1, y los de PO_2 y PCO_2 de 57,8 ± 20 y 53,7 ± 15 mmHg, respectivamente, y no presentaron cambios significativos durante las primeras 2 h, a excepción de la PO_2. El pH presentó una diferencia entre su valor basal y a los 120 min de 0,005 ± 0,02, la PO_2 de 12,5 ± 19 mmHg y la PCO_2 de 0,8 ± 3 mmHg, con unos coeficientes de correlación de 0,97, 0,49 y 0,98, respectivamente. El estudio comparativo y la regresión simple no demostraron una influencia significativa de la conservación en hielo en los cambios de pH, PO_2 o PCO_2. Una etiología neoplásica y un mayor número de hematíes influyeron de forma significativa en los cambios de pH en el análisis multivariante.

CONCLUSIONES: El pH y la PCO_2 pleurales no presentaron cambios significativos durante las primeras 2 h de la toracocentesis, a diferencia de la PO_2. La conservación en hielo no estaría indicada durante este período. Sólo un número más elevado de hematíes o una etiología neoplásica tuvieron una influencia limitada en los cambios de los valores del pH de nuestros pacientes en las primeras 2 h.

Palabras clave: *Líquido pleural. pH. PO_2. PCO_2. Efecto del tiempo.*

Introduction

Analysis and classification of pleural effusion requires various different determinations to be performed on the liquid obtained by thoracentesis.[1,2] In the assessment of the acid-base equilibrium of this fluid, the normal pH is alkaline, with higher pH values in transudates and lower values in the majority of pleural exudates. A reduced pH represents an accumulation of hydrogen ions in the pleural space and an increase in metabolic activity (inflammatory or infiltrative), and it is usually accompanied by a decrease in the concentration of glucose or an increase in that of CO_2.[1-3] Although the PCO_2 of pleural fluid can affect the pH value, the usefulness of this measurement, and of the PO_2 of pleural fluid, is more controversial and it is currently in less widespread use. Unlike PO_2 and PCO_2, the pH of pleural fluid has diagnostic, prognostic, and therapeutic implications.[4] The most frequent causes of pleural fluid acidosis are parapneumonic pleural effusion or empyema, esophageal rupture, tuberculous or lupus pleuritis, and malignant effusion.[4-8] Determination of pH is also essential for the management of parapneumonic effusion and a reduction in the pH indicates increased infiltration or reduced effectiveness of pleurodesis in patients with malignant effusion.[4-8]

Standard practice for analysis of acid-base equilibrium in pleural fluid involves obtaining samples anaerobically with a heparinized syringe and performing measurements immediately after thoracentesis or storing samples at low temperature.[9-11] In the absence of such measures there is a possibility of spontaneous acidosis, environmental contamination, and erroneous values being obtained for pleural fluid parameters. However, there is no clear evidence in the literature to support those hypothetical possibilities, nor is accurate data available with which to establish temporal changes in acid-base equilibrium or the period of time within which analyses should be performed, especially in terms of the complete set of relevant values or the pH more than an hour after thoracentesis.[11,12]

The aim of this study was to assess the importance of changes in the acid-base equilibrium of pleural fluid stored at room temperature during the first 2 hours after thoracentesis and to evaluate the point at which those changes become significant or clinically relevant. In addition, we assessed the influence of keeping samples on ice, as with arterial blood. Particular attention was paid to the concentration of lactate dehydrogenase (LDH), the cytologic profile, and the etiology of the pleural effusion.

Patients and Methods

A prospective, descriptive study was undertaken between June 2003 and May 2004 in 53 consecutive patients admitted to a tertiary care hospital with pleural effusion and an indication for thoracentesis without having undergone analysis or intervention in the previous 30 days. Thoracentesis was performed under sedation and local anesthetic (2% mepivacaine chlorohydrate without vasoconstrictor; Scandinibsa, Laboratorios Inibsa, Barcelona, Spain) was introduced using a 10-mL syringe. Local anesthesia was performed with 3 to 4 mL of local anesthetic injected into the skin and intercostal space up to the level of the parietal pleura, without crossing the pleura or injecting anesthetic into the pleural cavity at any point during the procedure. The syringe was then discarded to prevent the anesthetic interfering with the pH values of the pleural fluid.[13] Three fresh 20-mL syringes were used to obtain 60 mL of pleural fluid for biochemical analysis (proteins, LDH, cholesterol, amylase, and adenosine deaminase), microbiological analysis (acid-fast bacillus smear and culture), and cytology. Patients were excluded from the study in the following situations: lack of signed informed consent; contraindications for thoracentesis[14]; suspected traumatic thoracentesis or the presence of blood clots in the extracted liquid; purulent or hematic pleural fluid (more than 200 000 red blood cells/μL); insufficient pleural fluid to perform all determinations; and inability to analyze baseline acid-base equilibrium within the first 10 minutes of extraction or within a window of 5 minutes either side of the stipulated time in subsequent measurements. In the first 24 hours after thoracentesis the same measurements were made in plasma in order to differentiate between transudates and exudates and proceed with assessment of the etiology.

Analysis of Acid-Base Equilibrium in Pleural Fluid

Samples of 2 to 3 mL of pleural fluid were immediately transferred from the syringe used for thoracentesis to heparinized syringes (3 mL syringe for arterial blood samples containing 200 units of heparin and a 22-guage needle; Quick ABG, Marquest Medical Products, Englewood, Colorado, USA). Samples were transferred slowly and the presence of residual air bubbles was avoided by removing a portion of the transferred liquid prior to sealing the syringe.[15,16] The syringes were only opened once at the time of sample processing. Within 10 minutes of thoracentesis the first syringe was taken to the laboratory to obtain baseline values for acid-base equilibrium at room temperature. Analysis of acid-base equilibrium was performed using the same apparatus throughout the study (blood gas analyzer 248, Ciba Corning Diagnostics, Medfield, Massachusetts, USA) with hourly calibration of the system. Measurements were performed at 37±0.15°C in less than 60 seconds with samples of 60 to 85 μL and washes were performed every 30 minutes to prevent blockage of the system. Measurements were made of pH, PO_2, and PCO_2; base excess, actual or plasma bicarbonate, standard bicarbonate, estimated oxygen saturation, and total CO_2 were estimated using the same system.

In the first 26 patients, 9 separate syringes of pleural fluid were collected. The first syringe was used to obtain the baseline values and the remaining 8 syringes were separated into 2 sets: 4 syringes were kept at room temperature and 4 were kept on ice. Every 30 minutes for the first 2 hours after thoracentesis (at 30, 60, 90, and 120 minutes) 1 syringe from each set was processed within a margin of 5 minutes to allow for washing of the analyzer and the values obtained were recorded along with the ambient temperature to confirm its stability over the course of the measurements. These measurements corresponded to measurement group 1. In the remaining 27 patients only 5 syringes were collected. The first syringe was processed immediately and the remaining 4 were kept at room temperature to perform the same measurements over the following 2 hours. Measurement group 2 was made up of these latter measurements along with those performed similarly over the same time period at room temperature in the first 26 patients, who also provided the samples for measurement group 1.

TABLE 1
Main Characteristics of the Patients Providing Samples for the 2 Measurement Groups*

	Group 1	Group 2
Number of patients	26	53
Age, years	70 (13)	70 (14)
Men	17 (65.4)	38 (72)
Smokers, n (%)	15 (57.7)	35 (66)
Right-sided effusion, n (%)	19 (73)	33 (63)
Unilateral effusion, n (%)	24 (92)	45 (85)
Massive effusion, n (%)	3 (11)	8 (15)
Effusion 1/3 of hemithorax, n (%)	6 (23)	19 (36)
Transudate, n (%)	3 (12)	10 (19)
Lymphocytic exudate, n (%)	18 (69)	35 (66)
Neutrophilic exudate, n (%)	5 (19)	8 (15)
Benign etiology, n (%)	18 (69)	34 (64)
Malignant etiology, n (%)	8 (31)	19 (36)
Pleural glucose, mg/dL	66 (38)	85 (41)
Pleural proteins, g/dL	3.5 (1)	3.7 (1.2)
Pleural LDH, U/L	899 (987)	754 (956)
Pleural amylase, U/L	49 (31)	61 (64)
Pleural cholesterol, mg/dL	91 (94)	77 (71)
Number of red blood cells per µL pleural fluid	31321 (59142)	20430 (43513)
Number of leukocytes per µL pleural fluid	1554 (1855)	1255 (1476)
Percentage neutrophils in pleural fluid	25.4 (30)	26 (27)
Percentage lymphocytes in pleural fluid	74.6 (30)	74 (28)

*Data are shown as the mean (SD) or number (%) if so specified. Group 1 refers to patients providing samples of pleural fluid kept at room temperature and samples kept at low temperature; group 2 refers to patients with pleural fluid kept at room temperature and includes the patients contained within group 1; LDH, lactate dehydrogenase.

Statistical Analysis

A descriptive analysis of the main characteristics of the patients and the pleural effusion was performed independently for each of the 2 measurement groups. Comparisons were made between the mean values for acid-base equilibrium at 30, 60, 90, and 120 minutes and the baseline values or between the values at the beginning and the end of the experiment using the nonparametric Wilcoxon test in group 1 and the Student-Fisher test (paired *t* test) in group 2. Correlations between the values obtained at the beginning and the end of the analysis period were assessed using the Pearson correlation coefficient. Simple linear regression analysis was used to assess the impact of keeping samples at low temperature on changes in pH, PO_2, and PCO_2; the difference between the baseline value and the value at 120 minutes was considered as the dependent variable. Simple linear regression analysis was also performed in group 2 along with multiple regression analysis using only 6 of the variables analyzed in order to maintain a positive number of degrees of freedom. The variables were selected based on univariate analysis and their relationship with inflammation or pleural metabolic activity. The difference between the initial pH and the pH at 120 minutes was the dependent variable. All statistical calculations were performed using SPSS version 11.0. Statistical significance was established at $P \leq .05$.

Results

Table 1 shows the main characteristics of the patients and pleural effusions. The etiologies of the pleural effusions were as follows: 8 of the patients corresponding to measurement group 1 had malignant pleural effusion (6 derived from the lungs and 2 from the breast), 8 had nonspecific effusions, 4 had parapneumonic effusions, 3 had tuberculous effusions, 2 had cardiogenic effusions, and 1 had effusion as a result of liver disease; of the patients corresponding to measurement group 2, which represents the entire study population, 19 had malignant pleural effusion (14 from the lungs, 4 from the breast, and 1 esophageal), 10 had nonspecific effusions, 6 had parapneumonic effusion, 6 had tuberculous effusion, 7 had cardiogenic effusion, and the remainder were isolated cases of nephropathy, liver disease, pulmonary embolism, hypothyroidism, and effusion attributable to major abdominal surgery.

Table 2 shows the values for acid-base equilibrium of pleural fluid in measurement group 1. The measured or calculated parameters did not show significant differences from baseline values, with the exception of PO_2 and oxygen saturation. The mean (SD) differences between the baseline value and the value obtained at 120 minutes at room temperature for pH, PO_2, and PCO_2 were 0.011 (0.033), 5.4 (21) mm Hg, and 0.4 (2) mm Hg, respectively; the differences between the baseline values and the values at 120 minutes in samples kept on ice were 0.001 (0.26), 6.3 (16) mm Hg, and 0.9 (5) mm Hg, respectively; and the differences between the values at 120 minutes at room temperature

TABLE 2
Acid-Base Equilibrium of the First 26 Patients Studied—Group 1* *(Continued on Next Page)*

	Baseline	Room Temperature					
		30 min	60 min	90 min	120 min	30 min	
pH	7.337 (0.129)	7.336 (0.129)	7.337 (0.129)	7.337 (0.128)	7.336 (0.128)	7.340 (0.115)	
PCO_2, mm Hg	57 (17)	56.9 (16)	57 (16)	56.5 (15)	57.3 (16)	55.2 (13.6)	
PO_2, mm Hg	58 (22)	62 (17)†	64 (14)†	67.6 (15)†	63.4 (22)†	60.6 (21)†	
HCO_3a, mmol/L	28.8 (3.7)	28.6 (3.8)	28.8 (4.1)	29.1 (4.2)	28.4 (4.3)	27.8 (6.5)	
HCO_3s, mmol/L	26 (4.3)	26.1 (4.1)	26.1 (4.5)	26.1 (4.5)	26.1 (4.5)	26 (4)	
BE, mmol/L	4.4 (3.17)	4.8 (3.3)	4.5 (3.3)	4.6 (3.2)	4.6 (3.7)	4.4 (3.3)	
$SatO_2$, %	80 (16)	86 (10)†	88 (7)†	89.7 (6)†	88 (9)†	84 (13)†	
tCO_2, mmol/L	30.6 (3.8)	30.6 (4)	30.6 (4)	30.9 (4.5)	30.5 (4.4)	30.5 (4.1)	

*Data are expressed as mean (SD).
HCO_3a indicates actual or plasma bicarbonate; HCO_3s, standard bicarbonate; BE, base excess; $SatO_2$, estimated oxygen saturation; tCO_2, total carbon dioxide.
†$P \leq .05$ compared with baseline value.

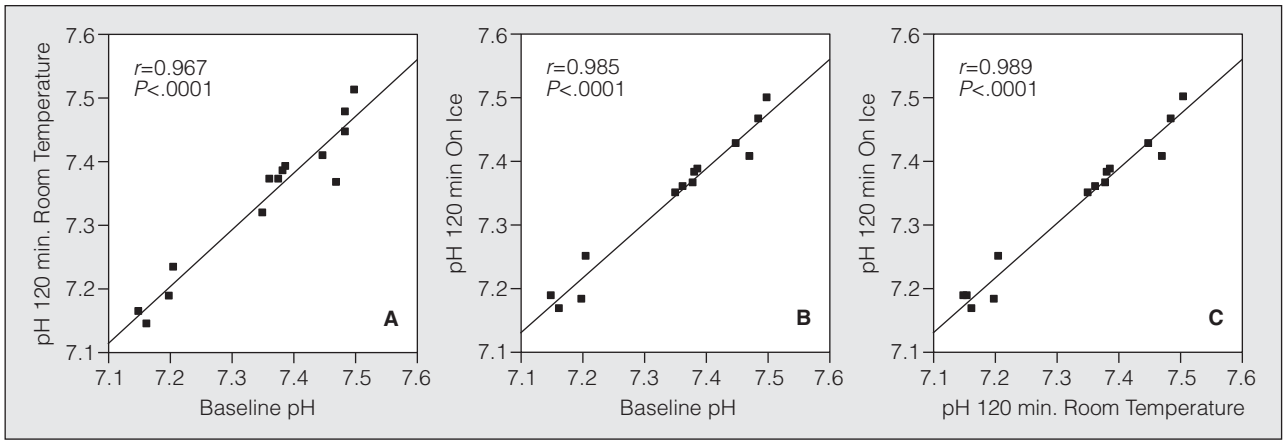

Figure 1. Correlations for pH in group 1 measurements: baseline versus 120 minutes at room temperature (A); baseline versus 120 minutes on ice (B); 120 minutes at room temperature versus 120 minutes on ice (C).

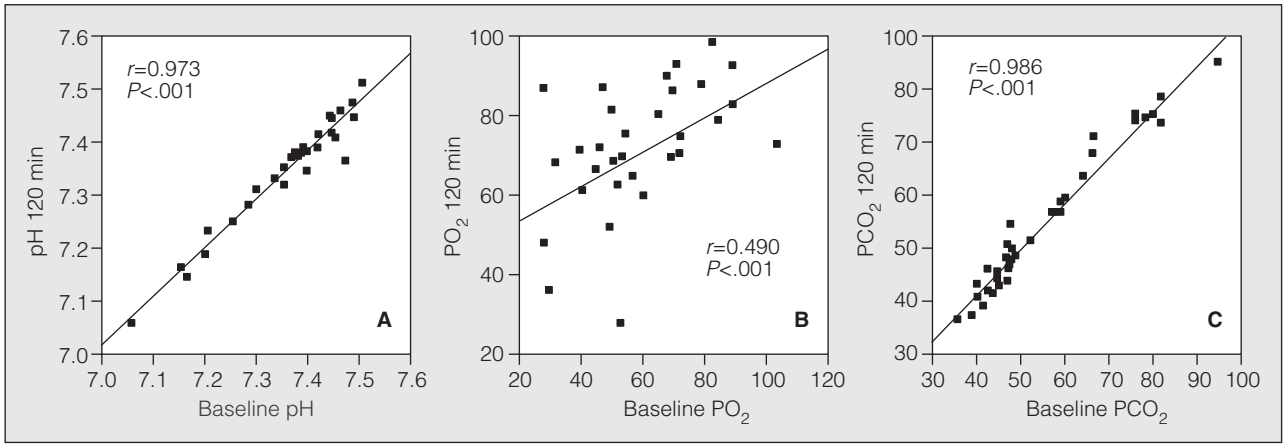

Figure 2. Main correlations in group 2 measurements: baseline pH versus pH after 120 minutes at room temperature (A); baseline PO_2 versus PO_2 after 120 minutes at room temperature (B); baseline PCO_2 versus PCO_2 after 120 minutes at room temperature (C).

and in samples kept on ice were 0.001 (0.02), 0.9 (17) mm Hg, and 1.3 (4.7) mm Hg, respectively. Figure 1 shows the correlations observed for the pH value. The correlation coefficients for the values of PCO_2 between baseline and 120 minutes at room temperature, baseline and 120 minutes on ice, and between 120 minutes at room temperature and 120 minutes on ice were 0.996, 0.960, and 0.964, respectively. The same correlations for the PO_2 of pleural fluid were 0.557, 0.702, and 0.607, respectively. Simple regression analysis did not reveal a significant effect on pH, PO_2, or PCO_2 as a result of keeping pleural fluid on ice for the first 2 hours after thoracentesis.

TABLE 2
(Continued From Previous Page)

	On Ice		
	60 min	**90 min**	**120 min**
	7.341 (0.119)	7.342 (0.114)	7.336 (0.113)
	56.2 (14)	55.7 (13.6)	56 (13.4)
	63.4 (20.4)†	62.8 (15.4)†	64.4 (15)†
	29 (4.3)	29 (4.2)	29 (4.5)
	26 (4.4)	26 (4.2)	26 (4.3)
	4.7 (3.5)	4.7 (3.4)	4.5 (3.6)
	84 (18)†	85.6 (13)†	86 (13)†
	30.8 (4.3)	30.8 (4.3)	30.7 (4.6)

Table 3 shows the values for acid-base equilibrium of pleural fluid in measurement group 2. The measured or calculated parameters did not show significant differences from baseline values, with the exception of PO_2 and oxygen saturation. The difference between the mean value at baseline and 120 minutes was 0.005 (0.025) for the pH, 12.5 (19) mm Hg for PO_2, and 0.8 (3) mm Hg for PCO_2. Figure 2 shows the correlations between these values at baseline and 120 minutes. Simple linear regression analysis did not reveal a significant influence on pleural fluid pH for any of the following variables: pleural levels of LDH, glucose, amylase, or cholesterol, pleural leukocyte count, percentage of lymphocytes or neutrophils in pleural fluid, or infectious etiology of the effusion. Baseline pH, malignant etiology, and red blood cell count had a limited but significant influence in the univariate

TABLE 3
Acid-Base Equilibrium in the Group 2 Measurements (n=53)*

	Baseline	30 min	60 min	90 min	120 min
pH	7.352 (0.109)	7.350 (0.108)	7.353 (0.108)	7.352 (0.108)	7.350 (0.104)
PCO_2, mm Hg	53.7 (14.6)	52.8 (14)	53 (14)	52.8 (13.5)	52.9 (13)
PO_2, mm Hg	57.8 (20.2)	63.2 (14.2)†	67.1 (11.7)†	71.3 (13)†	70.3 (18)†
HCO_3a, mmol/L	28.4 (4.1)	28.2 (4.1)	28.3 (4.4)	28.5 (4.6)	28.1 (4.3)
HCO_3s, mmol/L	26 (4.1)	26.3 (4)	26.1 (4.2)	26 (4.3)	26 (4.3)
BE, mmol/L	4.1 (3.1)	4.3 (3.1)	4.1 (3.1)	4.2 (3.1)	4.2 (3.4)
$SatO_2$, %	82 (14)	88 (8.5)†	89.7 (6.7)†	91.7 (5)†	92 (6)†
tCO_2, mmol/L	30.1 (4.3)	29.9 (4.6)	29.9 (4.6)	30.1 (4.7)	29.8 (4.7)

*Data are expressed as mean (SD).
HCO_3a indicates actual or plasma bicarbonate; HCO_3s, standard bicarbonate; BE, base excess; $SatO_2$, estimated oxygen saturation; tCO_2, total carbon dioxide.
†$P \leq .05$ compared with baseline value.

TABLE 4
Results of Multivariate Analysis Following Introduction of All the Variables Into the Model and a Process of Sequential Exclusion*

Variable	Coefficient b	Standard Error	Standardized Beta	*P*
All Analyzed Variables				
Constant	0.572	0.222		.014
Pleural LDH	1.1×10^{7}	<0.0001	–0.004	.978
Initial pH	–0.076	0.030	–0.331	.016
Number of red blood cells in pleural fluid	-1.4×10^{7}	<0.0001	–0.241	.044
Number of leukocytes in pleural fluid	-3.5×10^{6}	<0.0001	–1.54	.141
Percentage neutrophils	-1.9×10^{4}	<0.0001	–0.203	.197
Malignant etiology	0.021	0.007	–3.137	.003
Sequential Exclusion of Variables				
Constant	0.0045	0.004		.247
Malignant etiology	–0.0245	0.007	–0.453	<.0001
Number of red blood cells in pleural fluid	-1.67×10^{7}	<0.0001	–0.284	.019

*LDH indicates lactate dehydrogenase.

analysis. The multiple regression model highlighted the importance of the 6 variables analyzed (corrected R^2=0.377; F=5.943; P<.001) and the process of elimination of the variables by sequential exclusion gave a final model in which only the red blood cell count in pleural fluid and malignant pleural effusion remained (corrected R^2=0.295; F=15.03; P=.001) (Table 4).

Discussion

The results of this study demonstrate that there are no significant changes in the pH or PCO_2 of pleural fluid from various types of pleural effusion kept at room temperature or on ice during the first 2 hours after thoracentesis. Analysis of the data, the good correlation of the results, and the minimal differences between the mean initial and final values for pH and PCO_2 rule out a requirement for storage of samples on ice. The presence of statistically significant spontaneous acidosis with clinical implications was not found to occur during the first 2 hours after thoracentesis in our patients.

Only 4 previous studies have assessed temporal changes in pH along with sample storage conditions for pleural fluid (MEDLINE 1966-2004).[9,12,17,18] One study reported a mean reduction in the pH of pleural fluid of 0.54 following storage at 37°C for 24 hours.[9] In that study, no intermediate measurements were made and a tendency towards a greater reduction was observed in samples from patients with empyema or malignant pleural effusion. In 2 other studies it was initially established that it was necessary to store pleural liquid at low temperature following successful maintenance of pH values for between 8 and 24 hours (changes of less than 0.02 with storage at a temperature of 0°C to 5°C).[17,18] Only a single recent study has cast doubt on those earlier suggestions [12]; in that study, analysis of temporal changes in pH at room temperature over a period of 1 hour revealed no significant changes. However, analysis of samples kept on ice was not performed and the same syringe was used for all 4 measurements, implying a greater risk of environmental contamination. Ours is the only study to simultaneously analyze changes in all components of acid-base equilibrium in samples kept at room temperature and on ice over an extended period of time; the study obtained pH and PCO_2 values that did not show significant changes within the first 2 hours following extraction of the pleural fluid, using the same fluid in separate heparinized syringes without contact with local anesthetic.

The usefulness of analyzing PCO_2 or PO_2 in pleural fluid is less clear and is not in such widespread use in studies of pleural effusion.[10,17] Variations in PCO_2 are attributed to changes in intrapleural production of CO_2 or its diffusion from the blood. The importance of

analyzing this parameter centers on its influence on pH values and the increase seen in patients with increased metabolic activity due to inflammation and pleural infiltration. The absence of changes in PCO_2 during the first 2 hours has not been assessed previously and its stability, along with that of the pH, confirms the absence of significant spontaneous acidosis during this period. The pleural fluid itself was not found to produce acidosis and was ruled out as an independent determinant of pH in pleural effusions containing a limited number of cells; in these effusions, the majority of cells were malignant and had low metabolic activity, and empyemas were excluded.[19,20] Nevertheless, the importance of empyemas would diminish given that determination of pH is not recommended in the presence of pus in the pleural space, since pH does not alter the treatment plan and leads to obstruction of the measurement apparatus in the majority of cases.[6,21-23]

PO_2 is the least commonly analyzed variable in pleural fluid and the results are the most susceptible to variation during sample processing.[14,15,23,24] In patients with malignant pleural effusion, the PO_2 usually decreases as the consumption of oxygen by the malignant cells present in the fluid and pleural tissue increases or as the diffusion of oxygen from peripheral blood is blocked.[23] The PO_2 of pleural fluid was the only variable that showed a significant increase over the study period; however, the stability of the other values for acid-base equilibrium suggested that this change cannot be attributed to altered metabolic activity. Even though we followed current recommendations for the processing of pleural fluid and the use of a blood gas analyzer,[15,25,26] we believe that the measures taken during external manipulation did not prevent the entry of oxygen in the form of smaller, or microscopic, bubbles. Thus, the PO_2 increased over time as a result of the increased opportunity for diffusion of oxygen.[15-17] However, the clinical significance of these changes in PO_2 is currently unclear compared with the better known consequences of a change in pH or PCO_2; the implications would, nevertheless, be sufficient to recommend that PO_2 of pleural fluid be determined within 30 minutes of thoracentesis, even when the liquid is kept on ice.

Univariate analysis ruled out a requirement to keep samples on ice in an attempt to prevent significant changes in the acid-base equilibrium of pleural fluid in the first 2 hours after thoracentesis. In the multivariate analysis, only red blood cell count and malignant etiology had a significant impact on changes in pH. In reality, the influence of these factors was minimal when the coefficients obtained are taken into account along with the fact that overall there were no substantial changes in pH. However, the findings of other studies do not rule out the possibility that the influence could be greater in a larger subgroup of fluid samples from patients with malignant pleural effusion, a greater number of red blood cells, or the presence of pus. In empyemas or pleural infections they would be particularly notable due to their greater capacity to generate acidosis.[9,19,20] This capacity would diminish in patients with malignant pleural effusion and it would be minimal in effusions attributable to rheumatoid arthritis, where it is likely that the increased presence of hydrogen ions is secondary to diffusion problems caused by pleural inflammation.[9,19,20]

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