ORIGINAL ARTICLE

Tanaffos (2011) 10(2), 20-24

Effect of Fluid Balance on Alveolar-Arterial Oxygen Gradient in Mechanically Ventilated Patients

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ABSTRACT

Background: *Fluid balance affects outcome in critically ill patients. We studied the effect of fluid balance on oxygen exchange by assessing alveolar-arterial oxygen gradient (PA-a O_2) in mechanically ventilated patients. Our primary objective was to evaluate the difference in PA-aO_2 and the secondary goal was to evaluate the differences in age and mortality rate.*

Materials and Methods: *This retrospective observational study was performed on patients who were admitted to medical and surgical ICUs of Sari Imam Hospital, Mazandaran University of Medical Sciences, from 2003 to 2009. Daily fluid balance was calculated by input minus output. Thirty patients with continuous positive fluid balance (PFB) and 30 subjects with continuous negative fluid balance (NFB) during 4 consecutive days were enrolled in this study. PA-a O_2 was calculated in these two groups.*

Results: *The mean (±SD) age was 48.9±21.2 yrs. in PFB group (19 males and 11 females) and 37.1±15.7 yrs. in NFB group (25 males and 5 females) which showed a statistically significant difference in age between the two groups (p=0.017). The 24h, 48h, and 96h fluid balances were 1226^{cc}±881, 1311^{cc}±751, and 957^{cc}±661 in PFB group and -1122^{cc}±692, -920^{cc}±394, and -1164^{cc}±695 in NFB group, respectively. The mean differences (±SD) of PA-a O_2 in 24h, 48h, and 96h versus the same value in the admission day were 11.3±39.2, 1.69±51.1, and -1.50±64 in PFB subjects and -21.8±60.8, -27.8±84.9, and -19.3±68.7 in NFB patients. The difference was statistically significant only in the first day of admission (p=0.015). However, no difference was detected in overall mean oxygen gradient during 96h among the two groups. Mortality rate was significantly higher in PFB patients (P<0.0001).*

Conclusion: *Positive fluid balance had no significant effect on PA-a O_2 but can be used as a predictor of mortality.* ***(Tanaffos 2011; 10(2): 20-24)***

Key words: *Fluid balance, Alveolar-arterial oxygen gradient, PA-a O_2, Mechanical ventilation*

INTRODUCTION

Many studies have shown that daily fluid balance is a predictor of outcome in critically ill patients. A positive fluid balance contributes to increased mortality both in medical and surgical patients (1-7). On the other hand, increased rate of successful weaning and decreased rate of hospital mortality were associated with negative daily fluid balance (8, 9). Therefore, fluid balance management is an important step in overall management of critically ill patients (10). We hypothesized that positive fluid balance might be associated with increased

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Received: 17 October 2010
Accepted: 25 December 2010

extravascular lung water and consequently interfere with gas exchange and oxygenation, and consequently increasing the alveolar-arterial oxygen gradient (11-13). Higher amount of extravascular lung water is associated with greater hypoxia and therefore greater alveolar-arterial oxygen gradient (14) and probably wider range of adverse effects.

The main objective in the majority of these studies was to evaluate the clinical effect of fluid balance and effect of fluid balance on oxygenation was not addressed appropriately in a clinical setting.

MATERIALS AND METHODS

This retrospective observational study was conducted from 2003 to 2009 on 1000 adult mechanically ventilated patients admitted to medical surgical ICUs of Sari Imam Hospital for whom fluid intake and output data existed.

Intake and output documentations were extracted to find patients with 4 consecutive days of continuous positive or negative fluid balance as our inclusion criteria.

Exclusion criteria were as follows: COPD, pneumonia, VAP during hospitalization, heart failure or use of inotropic agents, acute or chronic renal failure with hemodialysis, homodynamic instability or shock with systolic blood pressure less than 90 mmHg, and need of vasopressor agents to maintain blood pressure, recent thoracic or upper abdominal surgery, and significant hemorrhage or diarrhea.

Accordingly, 30 patients with continuous positive fluid balance (PFB) and 30 subjects with continuous negative fluid balance (NFB) were included in this study.

In selected patients, data regarding demographic characteristics, admission diagnosis, arterial blood gases (ABG), fractional concentration of inspired oxygen (FIO_2), applied PEEP, renal function and outcome were collected. Daily fluid balance was calculated as input minus output. Alveolar PO_2(PAO_2) was calculated according to simplified form of the alveolar gas equation: $PAO_2=FIO_2(P_B-P_{H2O})-Pa_{CO2}/R$ where FIO_2 is fractional concentration of inspired O_2, P_B is barometric pressure, P_{H2O} is water vapor pressure and R is respiratory quotient. The Alveolar-arterial O_2 gradient (PAO_2-PaO_2) was calculated by subtracting measured arterial PO_2 (PaO_2) from calculated PAO_2.

First day admission PAO_2-PaO_2 gradient was calculated as baseline and also in 24, 48, and 96 hours after establishing a continuous positive or negative fluid balance.

The primary purpose was to assess the difference in alveolar-arterial O_2 gradient (PA-aO_2) and the secondary purpose was to compare the differences in age and mortality rate between the two groups.

This study was approved by the Institutional Review Board of Mazandaran medical faculty.

Statistical analysis:

Statistical analysis was performed using SPSS version 17 software. The data were presented as the mean ± SDs unless otherwise indicated. A value of $p<0.05$ was considered to be statistically significant. The unpaired t-test and ANOVA test were used to compare PA-aO_2, differences of oxygen gradient Vs. baseline, age, and creatinine between the two groups. Statistical comparisons of admission diagnosis, gender, and mortality between groups were made using Chi-Square test. Friedman's test was used to compare the differences in overall mean values of PA-aO_2 in each group during 96 hours.

RESULTS

The characteristics of 60 subjects who met the inclusion criteria are presented in Table 1.

The mean age was 48.9±21.2 yrs. in PFB group (19 males, 11 females) and 37.1±15.7 yrs. in NFB group (25 males, 5 females). There was a significant statistical difference in age among the two groups ($p=0.017$) but no gender difference was found. The mean values for admission PA-aO_2, inspired FIO_2, and creatinine showed no statistical differences. Based on considered criteria, most patients had admission diagnosis of trauma, especially head trauma, and central nervous system problems. Of course, there was no significant difference in admission diagnosis between the two groups (p=0.47). The interval between initiation of mechanical ventilation and establishing fluid balance was 5.2±6.1 days in PFB patients and 3.9±4.1 days in NFB subjects with no statistical difference (p=0.32). All patients received isotonic crystalloid solution.

Mean values for fluid balance in 24, 48, and 96 hours in PFB group were 1226±881, 1311±751 and 957±661; whereas, in NFB group these values were -1122±692, -920±394 and -1164±695, respectively (Table 2).

As shown in Table 2, there was no significant difference in inspired FIO_2 and also applied PEEP among the two groups. Mean values for $PA\text{-}aO_2$ during 24, 48, and 96 hours were 134±67.5, 124.7±55.8, and 121.5±56.9 in PFB group and 101.9±54.5, 95.9±53.7, and 104.4±38.8 in NFB group, respectively (Fig. 1). Overall mean oxygen gradient was 125.9±52.9 in PFB group and 106.5±34.9 in NFB group with no significant statistical difference. Difference in mean oxygen gradient in 24h Vs. baseline was 11.3±39.2 in PFB group and -21.8±60.8 in NFB group and this difference was statistically significant (p=0.015). There was no difference in this value in 48 and 96 hours among the two groups. As shown in Figure 2, NFB group had a significantly higher survival rate ($p<0.0001$).

Table 1. Group characteristics *

Characteristics	Positive fluid balance (n=30)	Negative fluid balance (n=30)	P-value
Age (years)	48.9 ± 21.2	37.1 ± 15.7	0.017
Gender (No.%)			
Male	19 (63.3%)	25 (83.3%)	
Female	11 (36.7%)	5 (16.7%)	0.072
Admission day $PA\text{-}aO_2$	123.1 ± 64.7	123.7 ± 65.2	0.55
Admission day Creatinine (mg/dl)	0.99 ± 0.55	0.87 ± 0.31	0.32
Admission day FIO_2	39.8 ± 8.03	38.3 ± 6.2	0.42
Admission diagnosis, No.			
Multiple trauma	2	5	
ICH	7	2	
SAH	3	4	
Head trauma	10	11	
CVA	5	4	
Miscellaneous	3	4	
Days before establishing continuous fluid balance	5.2 ± 6.1	3.9 ± 4.1	0.32

*Values are given as mean ±SD or No. (%), unless otherwise indicated. P<0.05 was considered to be statistically significant. $PA\text{-}aO_2$ = Alveolar-arterial oxygen gradient; ICH = Intracranial hemorrhage; SAH = Subarachnoidal hemorrhage; CVA = Cerebrovascular accident.

Table 2. Mean values for fluid balance, FIo_2, oxygen gradient, and differences in oxygen gradient vs. baseline.

Variables	Positive fluid balance			Negative fluid balance		
	24h	48h	96h	24h	48h	96h
Intake – Output (ml)	1226±881	1311±751	957±661	-1122±692	-920±394	-1164±695
FIO_2	39.3±7.7	39±6.9	37.5±6.4	37.8±6.1	36.3±5.1	34.5±5.3
$PA\text{-}aO_2$	134.7±67.5	124.7±55.8	121.5±56.9	101.9±54.5	95.9±5.7	104.4±38.8
Differences in O_2 gradient vs. baseline	11.3±39.2*	1.69±51.1	-1.50±64	-21.8±60.8	-27.8±84.9	-19.3±68.7

*Statistically significant

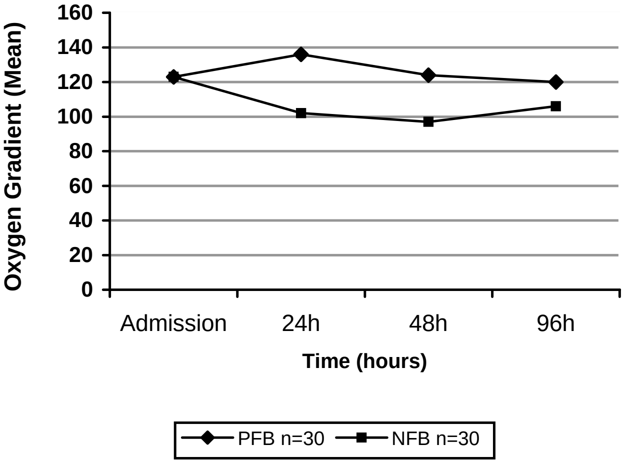

Figure 1. Mean oxygen gradient in admission day, 24, 48, and 96h showed an increasing trend in PFB subjects and a decrease in NFB group but the difference was not statistically significant.

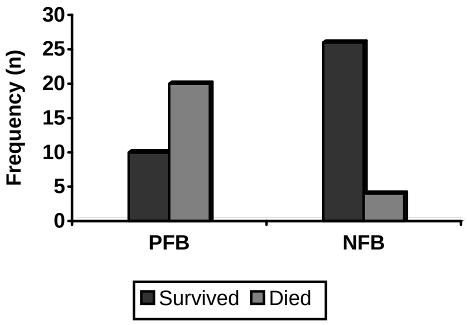

Figure 2. Mortality rate in the two groups. PFB group had a higher mortality rate ($p<0.0001$). Columns represent the number of patients in each group. The numbers on top of the columns show prevalence of those who survived or died.

DISCUSSION

This study had two main findings. First was that variations of fluid balance had no significant effect on oxygen gradient in mechanically ventilated patients. Although, there was a significant difference in mean oxygen gradient in 24h Vs. baseline, we did not find significant impairment in gas exchange and oxygenation in patients with positive fluid balance. Despite several studies showing that fluid balance may influence lung mechanics and oxygenation (15,16), the reason that we did not find such result is probably because extravascular lung water might not increase to the level that impair gas exchange and oxygenation in patients with positive fluid balance. As shown, changes in extravascular lung water of less than 100-200% may not be detected by clinical methods like assessment of oxygenation (17).

The second major finding is that patients with negative fluid balance were younger and had lower hospital mortality rate. Of course, lower rate of morbidity and mortality were shown in patients with negative fluid balance in various clinical settings. In a study in patients with septic shock, negative fluid balance assumed to be an independent predictor of survival (18). In addition, in one investigation in patients with "acute lung injury/acute respiratory distress syndrome" (ALI/ARDS), cumulative fluid balance was lower in survived patients compared to those who died (6). Furthermore, negative cumulative fluid balance was associated with weaning outcome in medical and surgical patients (9,19). Better outcome in patients with negative fluid balance in our study may be related to younger age, good cardiovascular reserves and less organ failure. Therefore, they were able to maintain a negative fluid balance. Similar results have been suggested by other authors (20). Hence, according to theses studies, we think positive fluid balance is probably a predictor of the severity of the underlying disease and failure of cardiovascular and renal system to eliminate excess fluid, especially in older ages.

Of course, there are several limitations to this study. To met exclusion criteria and eliminate other etiologies of increased alveolar-arterial oxygen gradient, the majority of subjects in our study were patients with central nervous system problems. In addition, because only intake and output were recorded in our ICUs, other routes of fluid loss (i.e. insensible loss) were not considered in estimating the fluid balance. Furthermore, we did not evaluate extravascular lung water during the study.

In conclusion, positive fluid balance has no significant effect on PA-a O_2 but could be used as a predictor of mortality.

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