ORIGINAL ARTICLE

Comparison of adaptive support ventilation and synchronized intermittent mandatory ventilation in patients with acute respiratory distress syndrome: A randomized clinical trial

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Background: Suitable mechanical ventilation strategies can reduce the incidence and severity of ventilator-associated lung injury in patients with acute respiratory distress syndrome (ARDS). In this study, the effects of adaptive support ventilation (ASV) and synchronized intermittent mandatory ventilation (SIMV) on respiratory parameters and arterial blood gases (ABGs) parameters were compared in ARDS patients. **Materials and Methods:** Twenty-four patients were randomly divided into two groups of ASV and SIMV. Patients were followed up for 3 days, and respiratory parameters including rapid shallow breathing index (RSBI), spontaneous breathing rate (SBR), minute volume, and peak inspiratory pressure (PIP) as the primary outcomes and ABG parameters including PaO_2, FiO_2, $PaCO_2$, HCO_3, and PaO_2/FiO_2 ratio as the secondary outcomes were measured. **Results:** PIP in patients in the SIMV group on the 1st day ($P = 0.013$), 2nd day ($P = 0.001$), and 3rd day ($P = 0.004$) was statistically significantly more compared to those in patients in the ASV group. RSBI, SBR, and minute volume between the ASV and SIMV groups during the 3 days were not statistically significantly different ($P > 0.05$). The mean arterial blood pressure, heart rate, PaO_2, and PH between both groups were similar ($P > 0.05$). At the end of the 2nd and 3rd days, the level of FiO_2 and $PaCO_2$ in ASV was significantly lower than those in ASV group. HCO_3 in each of the 3 days in the ASV group was statistically significantly lower than that in the SIMV group ($P < 0.050$). PaO_2/FiO_2 ratio in patients in the ASV group in the 3 days was statistically significantly higher than that in the SIMV group ($P < 0.050$). **Conclusion:** By reducing PIP and improving oxygenation and ABG parameters, ASV mode may be a safe and feasible mode during mechanical ventilation in patients with ARDS.

Key words: Adaptive support ventilation, intensive care units, respiratory distress syndrome, synchronized intermittent mandatory ventilation, ventilation strategies

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INTRODUCTION

In the absence of left atrial hypertension, acute respiratory distress syndrome (ARDS) is an acute, diffuse, inflammatory form of lung injury that is associated with a variety of etiologies.[1] ARDS in one of the frequent problems in intensive care units (ICUs) that can have unwanted effects on a wide range of diseases. Its rate has been estimated between 7 and 85 cases/100,000 persons. During the last decades, the mortality rate of ARDS was reported between 30% and 40%.[2,3] There is no specific pharmacological treatment of ARDS, but mechanical ventilation of the injured lung is important and is reported that gas exchange parameters and clinical status would improve in the majority of these patients after mechanical ventilation.[4-6] Ventilator-associated lung injury in patients with ARDS as an important cause of poor clinical outcomes can lead to alveolar rupture in air dissection (pulmonary interstitial emphysema, pneumothorax, or pneumomediastinum).[7,8] Hence,

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strategies of mechanical ventilation are required to reduce the incidence and severity of ventilator-associated lung injury in these patients.

Synchronized intermittent mandatory ventilation (SIMV) and adaptive support ventilation (ASV) are two modes of mechanical ventilation in the ICU with different strategies that allow the patient to have spontaneous breathing along with mandatory breathes by ventilator in a coordinated process. In SIMV, breaths are patient triggered or time triggered, flow limited, and volume cycled, and patients can breathe spontaneously between mandatory ventilator-cycled breaths.[9] On the other hand, ASV uses the most sophisticated close-loop techniques that could provide full, assisted, or spontaneous types of breath and alternate support according to the patient condition.[10] In passive patients is a volume-targeted pressure controlled and in spontaneously breathing patients,ASV is a volum-targeted pressure support.[11,12]

The employment of SIMV and ASV in patients with ARDS has been assessed previously, but most of the studies focused on weaning, duration of ventilation, and the time of extubation, whereas respiratory parameters are evaluated in limited studies.[13-18] One study reported that compared with the SIMV mode, the use of ASV mode made a significant difference in some respiratory parameters in patients with neurosurgical disorders in the ICU.[19] Other studies show that on comparing between ASV and volume-controlled ventilation (VCV) in patients with ARDS, ASV provided better respiratory mechanics in terms of peak airway pressure and tidal volume with no significant differences in the arterial blood gas analysis.[17]

The objectives of this study were to assess the respiratory, arterial blood gas (ABG), and hemodynamic effects of the ASV mode compared to the SIMV mode in patients with ARDS in the ICU.

MATERIALS AND METHODS

The protocol of this prospective randomized controlled trial is approved by the Institutional Review Board and Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1397.047) and registered in the Iranian Registry of Clinical Trials with the ID: IRCT20190908044730N1. Between June 2017 and March 2018, 24 eligible patients diagnosed with ARDS who were hospitalized in the ICU of AL-Zahra Hospital, in Isfahan, Iran, were enrolled. Confirmed patients with ARDS using Berlin definition were included if they met the inclusion criteria and none of the exclusion criteria. Inclusion criteria were patients with age between 18 and 70 years and those with expected duration of ventilation > 72 h, no acute renal failure, stable hemodynamic without using vasopressor drugs, body mass index <30 kg/m^2, acute hypoxemia (P/F ratio <300 mmHg), and bilateral established infiltration based on chest radiograph. Exclusion criteria were patients with chronic lung disease; pregnant women; and those with smoking, heart failure (<45%), existence of any brainstem lesions, clinical evidence of left atrial hypertension, and apnea. In addition, dead patients and those who were withdrawn from the ICU before 72 h were excluded from the study. The legal substitute decision makers for each patient were informed about the objectives of the study, and written informed consent was obtained before intervention.

Using block randomization based on P/F ratio (mild, moderate, and severe), eligible patients were randomly allocated to two groups of intervention to receive mechanical ventilation with either SIMV or ASV mode. All patients were ventilated with Hamilton C2 ventilator (made by Hamilton Medical company, Switzerland) and were monitored by Saadat monitor (made by ASAMTEB, Iran) after scoring using Acute Physiology and Chronic Health Evaluation II (APACHE II) score. The strategy of SIMV mode was as follows: a low flow-volume of 6 cc/kg was set which reduces to 4 cc/kg to keep plateau pressure below 30 cmH_2O and positive end-expiratory (PEEP) was adjusted by fraction of inspired oxygen (FiO_2) based on ARDS-specific protocol to meet the oxygen saturation of pulse oximetry (SpO_2) between 88 and 95% at minimum possible FiO_2. Ventilation rate was set to maintain the patients' respiratory rate not exceeding 35 breaths per minute to keep the pH lower than 7.30. In the ASV group, the minute ventilation was set at 120% and PEEP was adjusted by FiO_2 according to the ARDS protocol to maintain SpO_2 of 88%–92% at the minimum possible FiO_2. The peak pressure alarm was set at 45 cmH_2O to keep plateau pressure below 35 cmH_2O. Inspiratory trigger sensitivity was set to 2 L/min. To prevent patient confrontation with ventilator and prevention and treatment of restlessness of the patient, they received intravenous midazolam and/or morphine infusion according to the Richmond Agitation Sedation Scale score.[18]

Lung protection strategies were continued for 3 days and along with collecting patients characteristics and paraclinical data at baseline, rapid shallow breathing index (RSBI), spontaneous breathing rate (SBR), minute volume, peak inspiratory pressure (PIP), ABG parameters (PaO_2, FiO_2, $PaCO_2$, HCO_3, and PaO_2/FiO_2 ratio), mean arterial blood pressure (MABP), heart rate (HR), and pH level were measured daily during this period. APACHE II was used to assess the severity of the underlying illness.

The sample size calculation was based on the respiratory outcome as reported by Ghodrati *et al.*[19] using a two-sided

t-test, 80% power to detect a difference, with a two-sided 5% level of significance. A sample size of 12 patients in each group was required. Statistical analyses were done using SPSS version 23 (SPSS Inc., Chicago, IL, USA). Descriptive data were presented as mean ± standard deviation for continuous and number (%) for categorical data. Because of a low number of patients in the studied groups, the continuous variables were compared between the two groups using Mann–Whitney test and the categorical variables were compared by Chi-square test. The trend of the studied variables during the 3 days of follow-up was assessed by repeated measurements of ANOVA with controlling baseline hematocrit (HCT) value as a covariate. The level of statistical significance was considered to be <0.05.

RESULTS

Figure 1 shows the study flowchart. Twenty-eight patients were reviewed to select eligible patients. Four patients were not eligible and were not enrolled in the study. The eligible patients were randomly assigned to two study groups. During follow-up, three patients were excluded (sepsis in one patient in the SIMV group and in the ASV group, one patient with sepsis and one withdrawal from the ICU). Finally, 11 patients in the SIMV group and 10 patients in the ASV group were included in the analysis.

The demographic and paraclinical characteristics of the studied patients are presented in Table 1. Patients in the ASV group were older than patients in the SIMV group but was not statistically significant (P = 0.244). Gender combination between groups was not statistically significantly different (P = 0.387).

The mean of APACHE II, Glasgow Coma Scale, white blood cell, creatinine, potassium, and sodium between the groups was not statistically significantly different (P > 0.05). The mean of HCT in the SIMV group was statistically significantly more than that of patients in the ASV group (P = 0.011). Other variables included severity of ARDS, causes of ARDS, sedation score, and duration of ventilation, which were not statistically significant between the two groups.

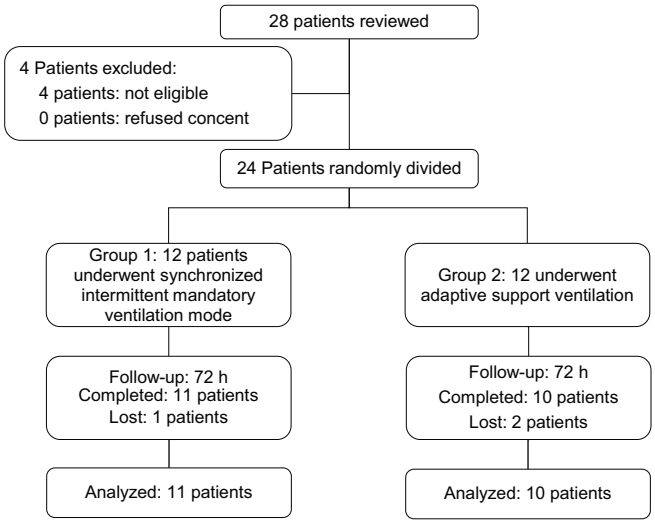

Figure 1: The flowchart of the study

The comparison of respiratory mechanics between the SIMV and ASV groups is reported in Table 2. RSBI, SBR, and minute volume during the 3 days within groups and between groups were not significantly different. SBR in patients in the SIMV group (P = 0.001) and patients in the ASV group (P = 0.009) had statistically significantly increased during the three studied days. However, the trend between both groups was not statistically significantly different (P = 0.243). The mean of PIP in patients in the SIMV group on the 1st day (P = 0.013), 2nd day (P = 0.001), and 3rd day (P = 0.004) was statistically significantly more when compared to that in patients in the ASV group, and the trend of PIP between the groups was statistically significant (P = 0.005).

Table 3 shows the comparison of ABG parameters and hemodynamics between SIMV and ASV groups. MABP,

Table 1: Baseline demographic and paraclinical characteristics of the studied patients by groups

	SIMV group (*n*=11)	ASV group (*n*=10)	*P*[a]
Age (year)	47.8±20.6	59.7±16.9	0.244*
Sex			
Male	8 (73)	5 (50)	0.387[t]
Female	3 (27)	5 (50)	
Severity of ARDS			
Moderate	6 (54.5)	7 (70)	0.466
Sever	5 (45.5)	3 (30)	
Causes of ARDS			
Pneumonia	3 (27.3)	5 (50)	0.484
Pancreatitis	1 (9.1)	0 (0)	
Multiple trauma	2 (18.2)	20 (2)	
Sepsis	3 (27.3)	3 (30)	
Over blood infusion	2 (18.2)	0 (0)	
Sedation score	0.001±0.89	0.4±0.84	0.306
Ventilation time (day)	6.45±1.69	7.5±1.84	0.205
APACHE II	15.8±5.7	17.8±4.6	0.305
GSC	4.3±1.3	4.7±1.3	0.541*
WBC	11627.3±3925.6	12690±4799.9	0.597*
HCT	36.6±5.4	29.6±5.1	0.011*
Cr	1.1±0.4	1.5±0.9	0.303*
K	4.2±0.4	4.3±0.5	0.646*
Na	141.5±3.2	141.1±5.9	1.000*

Data are mean±SD and *n* (%). *P* values calculated by *Mann–Whitney test or [t]Chi-square test. ARDS=Acute respiratory distress syndrome; SD=Standard deviation; APACHE II=Acute Physiology and Chronic Health Evaluation II; GCS=Glasgow Coma Scale; HCT=Hematocrit; WBC=White blood cells; Cr=Creatinine

Table 2: Comparison of respiratory mechanics between the studied groups

	SIMV group (*n*=11)	ASV group (*n*=10)	P^a
Rapid Shallow Breathing Index			
Day 1	57.2±32.2	55.9±29.9	0.568
Day 2	61.7±28.4	42.6±14.9	0.245
Day 3	64.0±33.2	58.2±37.9	0.778
P^b	0.761	0.264	
P^c	0.531		
Peak inspiratory pressure (cmH_2O)			
Day 1	26.1±9.5	17.8±6.6	0.013
Day 2	29.2±10.1	16.3±7.2	0.001
Day 3	28.2±10.1	16.1±6.9	0.004
P^b	0.358	0.479	
P^c	0.018		
Spontaneous breathing rate (breaths/min)			
Day 1	60.3±37.5	75.7±36.3	0.359
Day 2	88.3±15.4	94.5±8.9	0.375
Day 3	94.0±7.6	97.0±6.5	0.275
P^b	0.001	0.009	
P^c	0.376		
Minute volume (L/min)			
Day 1	11.1±2.1	9.3±3.9	0.130
Day 2	10.4±2.6	9.5±4.5	0.378
Day 3	10.5±3.7	8.9±3.2	0.751
P^b	0.195	0.500	
P^c	0.313		

Data are mean±SD. P^a: Comparison between two groups in each day and calculated by Mann–Whitney test. P^b: Comparison of the trend of variables in each group during 3 days and calculated by Friedman test, P^c: Comparison of the trend of variables between the two groups during 3 days and calculated by repeated measurements of ANOVA with controlling baseline HCT value as a covariate. HCT=Hematocrit; SD=Standard deviation; ASV=Adaptive support ventilation; SIMV=Synchronized intermittent mandatory ventilation

HR, and pH within and between both the studied groups were similar ($P > 0.05$). PaO_2 in each day between the groups was not significantly different, and its trend between the groups was not statistically significantly different ($P = 0.260$). FiO_2 and $PaCO_2$ in patients in the SIMV group in day 2 and day 3 were significantly more when compared to that in patients in the ASV group. The trend of changes in FiO_2 and $PaCO_2$ during the 3 days was not statistically significantly different ($P > 0.05$). HCO_3 in each of the 3 days in the SIMV group was statistically significantly more when compared to that in patients in the ASV group ($P < 0.050$). In addition, the trend of changes in HCO_3 during the 3 days was statistically significantly different ($P = 0.002$). The PaO_2/FiO_2 ratio in patients in the SIMV group in the 3 days was statistically significantly lower when compared to that in patients in the ASV group ($P < 0.050$). The trend of changes in the PaO_2/FiO_2 ratio during the 3 days was statistically significantly different ($P = 0.048$), and also the trend of changes in the PaO2/FiO_2 ratio during the 3 days in patients in the SIMV group was statistically significant ($P = 0.035$).

Table 3: Comparison of arterial blood gas parameters and hemodynamics between the studied groups

	SIMV group (*n*=11)	ASV group (*n*=10)	P^a
Mean arterial blood pressure			
Day 1	96.2±7.6	93.2±12.0	0.621
Day 2	92.4±6.5	97.4±12.3	0.180
Day 3	92.0±7.8	96.5±10.2	0.217
P^b	0.211	0.717	
P^c	0.382		
Heart rate (beats/min)			
Day 1	101.7±17.1	99.3±15.9	0.647
Day 2	91.5±29.6	92.6±9.0	0.167
Day 3	92.2±16.4	91.3±17.2	0.480
P^b	0.513	0.905	
P^c	0.942		
PH (mol/L)			
Day 1	7.4±0.06	7.3±0.06	0.138
Day 2	7.4±0.05	7.4±0.05	0.776
Day 3	7.4±0.08	7.4±0.07	0.289
P^b	0.168	0.105	
P^c	0.213		
PaO_2 (mmHg)			
Day 1	73.1±20.6	81.9±15.1	0.181
Day 2	72.8±17.9	79.2±14.0	0.260
Day 3	69.2±16.6	82.6±14.9	0.091
P^b	1.000	0.497	
P^c	0.260		
FiO_2 (%)			
Day 1	73.3±42.2	44.4±20.3	0.051
Day 2	70.1±28.2	49.5±17.1	0.032
Day 3	60.8±21.0	44.0±15.0	0.046
P^b	0.215	0.273	
P^c	0.055		
$PaCO_2$ (mmHg)			
Day 1	46.7±13.4	40.0±7.5	0.260
Day 2	50.7±13.1	34.7±9.8	0.015
Day 3	51.3±9.2	37.8±10.1	0.005
P^b	0.178	0.202	
P^c	0.166		
HCO_3			
Day 1	27.8±6.8	18.7±5.9	0.015
Day 2	32.3±7.0	20.4±5.1	0.001
Day 3	33.0±4.7	22.2±4.3	0.002
P^b	0.067	0.179	
P^c	0.002		
PaO_2/FiO_2 ratio			
Day 1	102.9±54.2	158.8±42.1	0.014
Day 2	104.2±47.3	177.8±55.2	0.003
Day 3	121.6±48.7	198.1±66.0	0.008
P^b	0.035	0.497	
P^c	0.048		

Data are mean±SD. P^a: Comparison of variables between the two groups in each day and calculated by Mann–Whitney test, P^b: Comparison of the trend of variables in each group during 3 days and calculated by Friedman test, P^c: Comparison of the trend of variables between the two groups during 3 days and calculated by repeated measurements of ANOVA with controlling baseline HCT value as a covariate. ASV=Adaptive support ventilation; SIMV=Synchronized intermittent mandatory ventilation; HCT=Hematocrit; SD=Standard deviation

DISCUSSION

The present study has compared ASV with SIMV in the respiratory effects in patients with ARDS. Our results demonstrate that the use of ASV in patients with ARDS is associated with lower PIP compared with the use of SIMV, where RSBI, SBR, and minute volume are similar between both modes. This significant difference in PIP can be explained by the different algorithms used in the two studied modes, whereas unlike the SIMV mode, in the ASV mode, the inspiratory pressure and rate are adjusted to maintain the preset minute ventilation while minimizing the work of breathing. Although this shows that the ASV mode can effectively reduce PIP under the same condition of RSBI, SBR, and minute volume, were significant differences between the two modes for FiO_2, $PaCO_2$, and HCO_3.

There is no similar study to assess the differences between respiratory and ABG parameters in two ASV and SIMV modes in patients with ARDS. In a randomized controlled trial, Gruber *et al*. showed a significant difference in peak airway pressures and tidal volumes and nonsignificant differences in minute ventilation and $PaCO_2$ between the ASV and pressure-regulated volume-controlled ventilation (PCV) with automode during two phases of controlled and assisted ventilation in patients after cardiac surgery.[15] In another study, Gruber *et al*. compared the ASV and SIMV modes in hospitalized patients in the neurosurgical ICU and reported that peak airway pressure and expiratory tidal volume in ASV mode were significantly lower than that in the SIMV mode, although ABG findings were not significantly different between these modes.[19] The results of Han *et al*.'s study show that respiratory rate, tidal volume, and PIP in patients with chronic obstructive pulmonary disease under ASV mode were significantly lower than those in the SIMV group. Some of other studies showed that PIP in ASV was lower than SIMV mode,[11,19-21] though in our study, in contrast to these studies, ABG findings were significantly different. The differences between these findings can be explained by the differences between studies with regard to studied patients, different ventilation strategy, duration of ventilation, and study design. Despite these differences, all the three studies show that the ASV mode can lead to improved ventilation conditions in patients with different disorders.

Choi *et al*.[22] assessed the ASV mode when compared with VCV in patients with ARDS and showed that PIP in ASV mode was significantly less than that in the VCV mode and ABG findings were not significantly different between these modes. They reported that the mean of PIP after 30 min of ventilation in patients with ARDS was 25.6 ± 6 cmH_2O, which was higher than that of our findings. PIP on the 1st day of ventilation in our study was 17.8 ± 6.6. Furthermore, ABG findings were significantly different between the studied groups in the present study. However, both these studies show lower mean of PIP in the studied patients in the ASV mode, but the differences between studies can be due to different in ventilation strategies and the duration of study. We studied two groups that employed different strategies which were followed for 3 days, whereas in Choi *et al*.'s study, patients with ARDS were followed in short period (for first 30 min ventilated in VCV mode, in second 30 min in ASV mode, and in third 30 min ventilated in VCV mode again).

To evaluate the efficacy of mechanical ventilation in patients with ARDS, oxygenation improvement can be used as an important factor. Our findings show that the PaO_2/FiO_2 ratio in the ASV group during the 3 studied days was significantly greater than that in the SIMV group; the PaO_2/FiO_2 ratio was persistently improving with subsequent days of ventilation in the ASV mode. This was similar to the results of Doneria *et al*.[23] that show higher PaO_2/FiO_2 ratio in the ASV group as compared to the SIMV group during spontaneous breathing trial and weaning in ICU. In addition, in a case report, Kath *et al*.[24] showed improvement in oxygenation and PaO_2/FiO_2 ratio and successful management of ventilator-associated pneumonia by using ASV. These findings implied that ASV could improve oxygenation earlier more effectively than SIMV in patients with ARDS.

The small study sample, single-center design, and the unblinded nature of the study (as with most studies on mechanical ventilation) were among the main limitations of the present study. Hence, multicentric studies with larger sample size are warranted to compare ASV and SIMV modes of ventilation in patients with ARDS for selecting the best mode.

CONCLUSION

Our results suggest that ASV mode may be a safe and feasible mode during mechanical ventilation in patients with ARDS with respect to reducing PIP and improving oxygenation and ABG parameters, which show improvement in the recovery of the respiratory function and ventilation volume and decrease in the work of respiratory muscles.

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Conflicts of interest

There are no conflicts of interest.

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