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Research Article

A RANDOMIZED CONTROLLED TRIAL TO COMPARE APRV AND SIMV MODE IN PATIENTS WITH ARDS

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A B S T R A C T

Background: Acute respiratory distress syndrome (ARDS) is the most common organ failure leading to intensive care. Airway pressure release ventilation (APRV) mode produces tidal ventilation using an inverse ratio method,it releases airway pressure from an elevated baseline to simulate expiration which facilitates oxygenation and the timed releases aid in carbon dioxide removal. We compared this relatively newer mode withSynchronized intermittent mandatory Ventilation (SIMV) mode in managing ARDS patients

Aims: Patients oxygenation, sedation requirement, hemodynamics, vasopressor use were compared and also the impactof twoventilatory modes on patient outcome and duration of hospital stay were studied

Methods: We randomized 40 patients to receive either APRV or SIMV using random number table during August 2013 to August 2014.With 95% confidence and 80% power, the calculated sample size was 3.The data was analyzed using Statistical Package for Social Sciences version 15.0. Comparison was done using independent samples "t"-test or Mann-Whitney U test, depending on the normality of distribution.Mechanically ventilated patients between age group of 16 -60 years with a preformed diagnosis of ARDS were included. Patients who required deeper levels of sedation or Obstructive lung diseases were excluded.

Results: APRV group had higher P/F ratio (238.00. +/- 59.40) as compared to SIMV group (200.30+/- 35.99), NMBD and sedation use was lower in APRV group (p= 0.008), Mean reduction in lung injury score was greater in APRV (p= 0.004)

Conclusion: Primary use of APRV as compared to SIMV showed better clinical improvement in terms of P/F ratio, chest X-ray and lung compliance, lower sedation and NMBD requirement in ARDS patients, but no improvement in hemodynamic variables or the outcome of the patients.

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INTRODUCTION

Acute lung injury in response to various insults leads to inflammatory reaction of the lung leading to alveolar edema and lung collapse primarily of the dependent lung regions and development of acute respiratory distress syndrome (ARDS), the leading cause of arterial hypoxemia and respiratory failure. Mechanical ventilation is the mainstay of treatment modality.[1] which has been questioned over time and again owing to its potential to cause ventilator induced lung injury (VALI).[2]

Despite its recognition since over 30 years mortality rate is 30-50% which has prompted the researchers to develop lung protective ventilation strategy.

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Traditionally ARDS patients were being ventilated with Synchronized intermittent mandatory ventilation mode (SIMV). The newer APRV mode which was first introduced in 1987 for ARDS patients is a mode of ventilation which produces tidal ventilation using inverse ratio method by time cycled switching between the two airway pressures.[3] In SIMV mode spontaneous breaths are coupled with pressure support from ventilator which in clinical trials has been shown to have similar effects on cardiac output and gas exchange as totally controlled ventilation.[4,5] In APRV there is uncoupling of mechanical breaths and ventilator cycle which may offerpotential benefits like lower airway pressures, better gas exchange, improved hemodynamics,increased patient comfort, decreased sedation requirement,[4] lower minute ventilation and shorter duration of ventilatory support.[5,6,7] APRV mode may improve clinical outcome measures in ARDS patients by limiting iatrogenic lung injury and reducing ICU stay. To test

this hypothesis we designed a randomized controlled trial comparing APRV with SIMV in adult patients with ARDSbased onHemodynamic Variables, Sedation andNeuromuscular blockers requirement, Ventilatoryfunction &Final Outcome in terms of ICU stay and mortality.

MATERIALS AND METHODS

Our study entitled "a randomized controlled trial to compare aprv and simvmode in patients with ards" was undertaken after taking permission from the Institutional Ethics Committee. 40 patients after obtaining informed consentfrom the relative were randomized to receive ventilation with either APRV or SIMV mode using random number table during August 2013 to August 2014.

With 95% confidence and 80% power, the calculated sample size was 3.The data was analyzed using Statistical Package for Social Sciences version 15.0 &Comparison was done using independent samples "t"-test or Mann-Whitney U test, depending on the normality of distribution.

Patients were divided into two groups:-

- Group I – Patients on SIMV mode (N=20)
- Group II– Patients on APRV mode(N=20)

Mechanically ventilated patientsbetween age group of 16 -60 years with a preformed diagnosis of ARDS were included in the study.

Patients<16 and >60 years, who required deeper levels of sedation for management of the underlying disease –(cerebral edema, status epilepticus), neurological cause of respiratory failure, Obstructive lung diseases-asthma/COPD were excluded from the study.

The severity of illness was evaluated by APACHE II &GCS score at the time of admission. Both APRV and SIMV were provided with Hamilton C1 ventilator.

In the APRV group, in addition to FiO_2 we controlled 4 variables (P_{high}, P_{low}, T_{high}, T_{low}). P_{high} was set at no more than 30cms H_2O, P_{low} was set at 0 -5cms H_2O. Starting T_{high} was set at 3.2 seconds and T_{low} at 0.8 seconds to achieve a ratio of 4:1. FiO_2 was adjusted to maintain PaO_2> 60 mmHg. We focused on adequate tidal volume (>6ml/ kg) as a target to titrate P_{high} As the patients started improving we progressively reduced P_{high} by 2cms H_2O and increased T_{high} by 0.5 seconds.

In the SIMV group ventilator settings were adjusted so that tidal volume was between 5 – 6 ml/ kg and respiratory rate 15-20 breaths / min, adjusted according to blood gases, titrating sedation and pressure support level. Pressure support was kept between 10-15cms H20.

PEEP and FiO_2 were set according to PEEP / FiO_2 titration table.

We assessed the following variables

MAP, average pulse rate, vasopressor use to quantify hemodynamics.NMBDs use, Sedation requirement (Patients were sedated using Midazolam/fentanyl according to patients hemodynamics and patients response was monitored using Ramsay sedation score (RSS).

As measures of pulmonary function, P/F ratio at baseline and for 6 days thereafter werenoted. We also assessed no of quadrants involved on chest x-ray, PEEP used for each patient, static compliance and used them to calculate lung injury score on day 2 and compared it with lung injury score at day 1.

Based on the above mentioned variables the two groups were compared. To study the impact of two modes on outcome, number of ventilator days and final outcome of the patients in two groups were compared.

RESULTS

Demographic data did not reveal statistically significant difference (p>0.05) between the two groups and groups were comparable with respect to age, gender, mean age (± standard deviation) was 43.00±11.97yrs and 39.05±13.19yrs respectively The severity of illness was assessed on the basis of GCS score and APACHE II score at the time of admission which were comparable and did not show any statistical significant differencebetween the two groups (p>0.05). Therefore the twogroups were matched for the baseline characterstics. (table 1) At baseline mean PF ratio was 173.45±52.45 in Group I and 173.05±51.84 in Group II, thus showing mean value to be slightly higher in Group I as compared to Group II but did not show a significant difference between two groups (p=0.478).

Table 1 Comparison of demographic data

PARAMETER	TOTAL (MEAN)	GROUP I (SIMV)	GROUP II (APRV)	P VALUE (FOR INTERGROUP DIFFERENCE)
AGE	41.30+12.59	43.00+ 11.97	39.05+13.19	0.200
GENDER MALE		50%	60%	
GCS AT ADMISSION	9.15+2.10	9.05+2.04	9.25+2.04	1.00
APACHE SCORE	22.08	23.90	20.25	0.087

At all the subsequent time interval the mean value in Group II was slightly higher as compared to that in Group I but the difference between two groups was significant statistically only when Group I had a mean value of 200.30±35.99 as compared to Group II that had a mean value of 238.00±59.40 (p=0.014).(figure 1) Median values also showed a similar trend throughout in both the groups.(figure 2) In both the groups, mean value was higher than baseline at all the time intervals and the difference from baseline was also significant statistically at all the time intervals (p<0.05) .Mean Average MAP ranged from 68.30±9.90 in Group I as compared to 67.60±10.78 mm Hg in Group II, thus showing the difference between two groups was not significant (p=0.832).

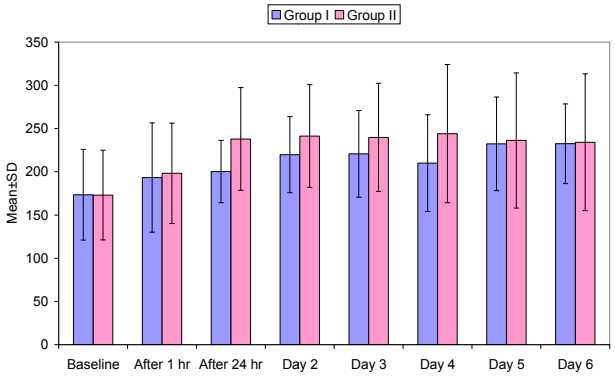

Figure 1 Comparison of two groups for PF ratio at baseline and at different time intervals

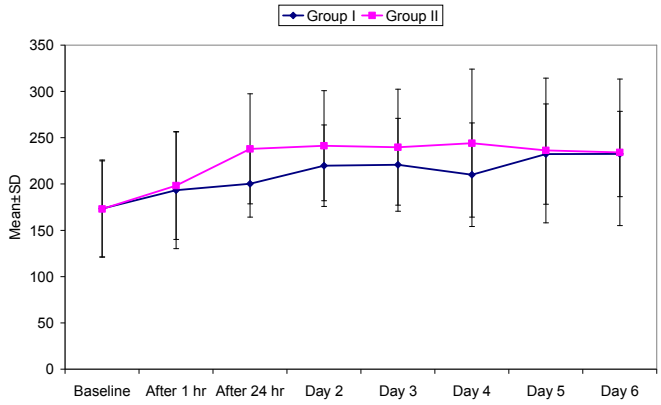

Figure 2 Evaluation of Change in P/F ratio throughout the period of study

Mean heart rate ranged from 56 to 150 bpm. It was 119.20±17.33 in Group I as compared to 103.75±20.71 bpm in Group II, the difference between two groups was significant (p=0.015). No significant difference in vasopressor use between two groups was observed, however, NMBD use was significantly lower in Group II as compared to Group I (p=0.008) (figure 3).

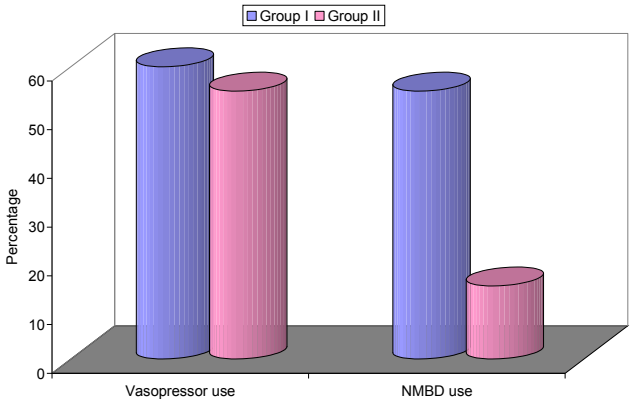

Figure 3 Comparison of Vasopressor and NMBD use

Lung injury scores were significantly higher in Group I as compared to Group II on both days 1 and 2 observations (p<0.05). In both the groups a significant reduction in Lung Injury scores was observed between day 1 and day 2 (p<0.05) (figure 4).

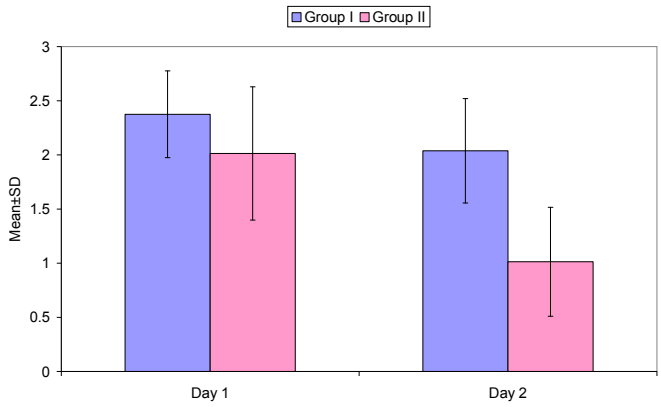

Figure 4 Lung Injury Score

Mean reduction in LIS was higher in Group II as compared to Group I and this difference between two groups was statistically significant too (p=0.004) (figure5)

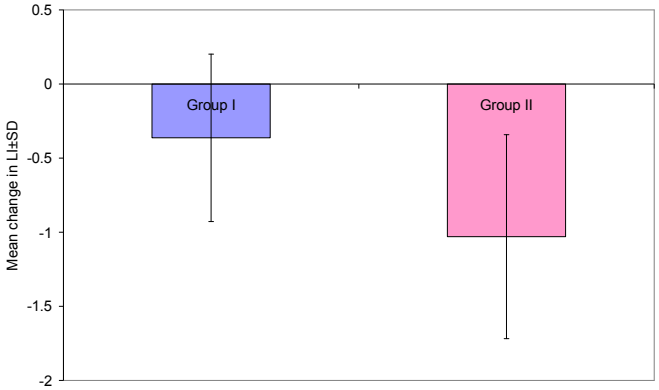

Figure 5 Change in Lung Injury Score (Day 2~Day 1) between two groups

DISCUSSION

We conducted a prospective study and our goal was to compare the two partial ventilatory modes of ventilation i.e. APRV and SIMV in patients with ARDS.

The mean HR revealed statistically significant difference between the two groups **(p<0.05)** and it was higher in SIMV group than the APRV group probably because of better patient comfort on APRV mode.Average MAP did not reveal any significant difference between the two groups (p>0.05).Vasopressor usage was noted in both the groups with 12 patients in group I and 11 patients in group II requiring it. The difference was not significant (p>0.05). T.Varpula *etal*. also reported similar physiological changes in both the groups.[7] However Putensen *etal* . and Lianji LIU *etal*.found increased cardiac performance of APRV group and less vasopressor requirement than the control group.[5,9]

In our studypressure support was quite less (10-15cms of water) thus, spontaneous breathing with a relatively low level of PS may have been associated with the same physiological benefits as with the unsupported spontaneous breathing.

Sedation scores were of lower order in APRV group (RSS = 3) as compared to SIMV group where the sedation scores were of higher order (RSS = 5).Statistically, this difference was significant (p<0.001), probably because of better patient ventilator synchrony in APRV.Similar facts regarding sedation requirement were also observed by Sydow M *etal*. and Kaplan *etal*. [4,9]

Putensen*etal*.reported that patients on APRV group were maintained at (RSS = 3) as compared to PCV group which had to be maintained with NMBDs at (RSS= 5).[5] However, some studies like T.Varpula *etal*. and R. Maxwell *etal*. found no difference in sedation requirements in APRV and SIMV group.[7,11]

Eleven patients in group I and three patients in group II had to be paralyzed during the course of their mechanical ventilation. Thus NMBDs use was lower in APRVgroup and the difference was statistically significant (p = 0.008). APRV promotes near elimination of neuromuscular blockade as shown by Sydow M *etal*. and Kaplan *etal*. [4,10]

Ventilatory parameters were studied using P/F ratio and Lung injury score (LIS). In present study, we found P/F ratios to be slightly higher in APRV group as compared to SIMV group at all time intervals but the difference was not found to be statistically significant (p>0.05) except at 24 hours where the

P/F ratios in groups II was higher than group I and the difference was statistically significant. (p=0.014).Valentine DD *etal*. concluded that all three modes SIMV, APRV & PSV provided acceptable oxygenation in patients after cardiac surgery.[12]Yoshida *etal*in a retrospective study found better P/F ratios in ARDS patients ventilated with APRV as compared to PSV[13].T.Varpula *etal* found significant improvement in P/F ratios in the APRV group after 24 hours and concluded that both APRV and SIMV were comparable with respect to P/F ratios during the first seven days[7]. LianjiLIU *etal*. conducted a retrospective analysis and found that APRV offered better oxygenation and better P/F ratio than SIMV during first 7 days of mechanical ventilation in ARDS patients.[9] Maxwell *etal* found no difference in P/F ratios during the 5 day observation period in trauma patients ventilated with APRV or PCV mode.[11] APRV mode potentially benefits ARDS patients because it allows spontaneous breathing with relatively low level of pressure support and this has been proved by many experimental and clinical studies. Downs and Stock, Putensen *etal* and Lianji LIU *etal* have shown in their studies that APRV mode of ventilation results in improved ventilation perfusion matching, and better arterial oxygenation.[3,5,9] Improved oxygenation and increased venous return due to spontaneous breathing results in increased cardiac output and hence enhanced oxygen delivery as shown by Putensenetal[5,6] Our observation has been consistent with the findings of the previous studies.

Lung injury scores (LIS) were found to be 2.375 ± 0.4 and 2.013 ± 0.6 on day 1 and 2.038 ± 0.482 and 1.013 ± 0.503 on day 2 in groups I and II respectively. In both the groups a significant reduction in LIS was observed between day 1 and day 2 ($p<0.05$). Mean reduction in LIS was higher in Group II as compared to Group I and this difference between two groups was statistically significant too (p=0.004). No study has compared LIS in both the groups. In our study, we found less number of quadrants involved on chest x-ray after ventilating patients with either mode or improvement in compliance and P/F ratios. By incorporating PEEP, we calculated LIS score at day 2 which showed improvement as compared to day 1, improvement being greater in APRV group as compared to SIMV. Most of the studies have assessed improvement in imaging with the help of CT scan and have found that persistent spontaneous breathing improves lung aeration.[5,8] Yoshida *etal*.with the help of helical CT scan concluded that APRV is a better mode of ventilation than PSV in improving atelectasis in ARDS patients.[13]Putensen*etal*.also found APRV use to be associated with increase in respiratory system compliance.[5,6]

Outcome of ARDS patients was studied using duration of mechanical ventilation and mortality rate. Duration of ventilator use was 8.90 ± 5.87 days in Group I and 8.85 ± 4.37 days in Group II which was found to be statistically insignificant between the two groups ($p>0.05$). T.Varpula *etal*. and LianjiLIU *etal*. were also unable to demonstrate any difference between APRV and SIMV regarding number of ventilator-free days.[7,9] In contrast Putensen *etal*. found shorter duration of ventilator stay as opposed to the PCV group.[5]

Less than half of the total patients (17/40) in our study survived and were discharged. Mortality rate was slightly higher in the APRV group as compared to the SIMV group, but the difference is statistically insignificant (p=0.749). However, Lianji LIU *etal* demonstrated lower mortality in the APRV group.[9] There may be several reasons of mortality in a critically ill patient which cannot be explained by difference in ventilator mode alone.

There were certain limitations in our study. Since patients on ventilator had ever changing peak pressure, mean airway pressures, tidal volume and minute ventilation, it was not feasible for us to note and compare these parameters between the two groups and hence these parameters are not presented here. This is one of the drawbacks of our study and we relied upon P/F ratios and various other clinical parameters like static compliance, CXR for assessing the ventilatory function.

More dynamic comparisons could have been done with variables noted at multiple intervals of time and average values obtained, could have provided additional support to results that we have obtained from our study. Multicentertrials, more manpower and extended duration of study period would have helped us in conducting a better study.

Still with these limiting factors, the results obtained from this study will provide valuable insight into the management of critically ill patients, which could be explored more in near future.

CONCLUSION

In ARDS, primary use of APRV with maintained unsupported spontaneous ventilation as compared to SIMV is feasible and potentially beneficial, Shows better clinical improvement in terms of P/F ratio, chest X-ray and lung compliance, lowers sedation and NMBD requirement, Shows no improvement in hemodynamic variables & proved no change in outcome of the patients in terms of number of ventilator days or mortality.

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