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Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

Kazi Iftikhar Qureshi, Tariq Mahmood, Ali Aftab, Ahmed Mujadid Burki, Hatim Saifee*, Reema Iftikhar**

Department of Anesthesia, Pakistan Navy Station Shifa Hospital, Karachi Pakistan, *Department of Anesthesia, Aga Khan University Hospital, Karachi Pakistan, **Department of Anesthesia, National Institute of Cardiovascular Diseases, Karachi Pakistan

ABSTRACT

Objective: To assess the role of early neuromuscular blockade in the acute respiratory distress syndrome among patients managed in Critical Care Unit.

Study Design: Comparative Cross-sectional Study.

Setting and Duration of Study: Critical Care Unit, Pakistan Navy Station Shifa Hospital, Karachi Pakistan, from Oct 2019 to Oct 2021.

Methodology: Patients diagnosed with moderate or severe acute respiratory distress syndrome by consultant critical care physician and admitted in critical care unit were included in the study. They were randomly divided in to two groups. Group A received cisatracurium infusion for 48 hours in addition to treatment as usual while group B just received treatment as usual. Ninety days' mortality was assessed in all the patients and use of early neuromuscular blockade along with other factors were associated with mortality among the study participants.

Results: A total of 280 patients were admitted in the intensive care unit with moderate to severe Acute respiratory distress syndrome during the study period. Out of them 200(71.4%) were male while 80(28.6%) were female. 159(56.8%) patients survived within 90 days of admission while 121(43.2%) died within those 90 days. Use of early neuromuscular blockage had no statistically significant relationship (*p*-value-0.848) with 90 days' mortality in our study participants.

Conclusion: Mortality rate was more than 40% in patients suffering from moderate to severe acute respiratory distress syndrome in our data set. Use of early neuromuscular blockage did not provide any added benefit in reduction of mortality in patients studied for two years in our critical care unit.

Keywords: Acute Respiratory Distress Syndrome, Cisatracurium, Mortality.

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INTRODUCTION

Critical care is an emerging specialty in our part of the world. Anesthesia and medical experts look after most of the critical care units where trained intensivist have not been available.[1] Organ support is the main indication for which patients are admitted in critical care units.[2] High mortality has always been a problem for critical care units and treating teams focus on patient specific interventions to reduce the morality in intensive care units.[3]

ARDS is a fairly common emergency condition managed by critical care physicians in routine in all parts of the world.[4] Moderate or severe patients of ARDS are managed in critical care unit and their prognosis depends on number of factors during the course of management. Multiple guidelines have been available to manage such patients and reduce the mortality.[5] Use of neuromuscular blockage is one of the strategies which have been discussed widely across the globe regarding its long and short term benefits for these patients.[6]

Number of original research articles, review articles and opinions have been published regarding use of early neuromuscular blockage in patients of ARDS. A study published in 2019 in New England Journal of Medicine concluded that among patients with moderate-to-severe respiratory distress syndrome, no added benefit of early neuromuscular blockage was found as compared to treatment as usual. They compared short term morbidity and mortality and both were not statistically different in patients who were given early neuromuscular blockage as compared to those who were not give.[7] De Souza *et al.,* in 2019 published an interesting paper highlighting that use of early neuromuscular blockage in patients of ARDS should be discouraged as it provides no added benefit in terms of long term or short term mortality. Treating team may tailor the plan and use this option in special circumstances instead of routine.[8] Papazian *et al.,* published similar data in 2010 from France and revealed that role of neuromuscular blockage is important in patients suffering from acute

Correspondence: Dr Kazi Iftikhar Qureshi, Department of Anesthesia, Pakistan Navy Station Shifa Hospital, Karachi Pakistan

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respiratory distress syndrome. It improves long term survival even after discharge from critical care unit at cost of limited adverse effects.[9]

Critical care is evolving in our country and local guidelines are lacking at this point of time. A local study published by Hussain *et al.,* came up with the findings that ARDS was commonly seen in our critical care units and carried high mortality.[10] Limited local data has been available regarding various therapeutic options which could decrease the mortality in critically ill patients of ARDS. We therefore planned this study with the rationale to assess the role of early neuromuscular blockade in the acute respiratory distress syndrome among patients managed in critical care unit.

METHODLOGY

This study was conducted at the intensive care unit of PNS Shifa hospital from October 2019 to October 2021. Sample size was calculated by WHO Sample Size Calculator by using population prevalence proportion of morality with ARDS as 16.5%.[11] Non probability Consecutive sampling technique was used to gather the sample.

Inclusion Criteria: All patients between the age of 18 and 60 years admitted in intensive care unit with diagnosis of moderate to severe ARDS were included in this study.

Exclusion Criteria: Exclusion criteria were the patients with documented allergy to cisatracurium or contraindication to use of neuromuscular blockage were excluded from the study. Patients who themselves or their care-givers did not give written informed consent were also excluded from the study.

Patients admitted after the diagnosis of moderate or severe ARDS in the critical care unit of PNS Shifa hospital Karachi were recruited in the study once ethical considerations were complete and approval for study was obtained for IREB committee. The diagnosis of ARDS was made by consultant critical care physician on the basis of criteria set by European Society of Intensive Care Medicine.[12] Severity of ARDS was determined on the basis of PaO2/FiO2. Moderate ARDS was defined as PaO2/FiO2 of 101–200 mmHg while severe was defined as PaO2/FiO2 of <100 mmHg.[13] Patients were randomly divided into two groups via lottery method. Group A received cisatracurium along with treatment as usual while Group B received only routine treatment. Cisatracurium was used for neuromuscular blockage and given intravenously as 3-ml rapid intravenous infusion of 15mg followed by a continuous infusion of 37.5mg per hour for 48 hours.[14] Patients were followed up for 90-days to look for 90-day mortality in both groups.

Statistical Package for the social sciences (SPSS 24.0) was the software used or the data analysis of this study. Frequency and percentages were calculated for the qualitative variables while mean and standard deviation was calculated for quantitative variables. Pearson chi-square test was used to see the relationship of use of early neuromuscular blockage and other variables with 90-days mortality among the study participants by keeping *p*-value less than or equal to 0.05 as significant.

RESULTS

A total of 280 patients were admitted in the intensive care unit with moderate to severe Acute respiratory distress syndrome during the study period. Out of them 200(71.4%) were male while 80(28.6%) were female. Mean age of the study participants was 39.97±8.966 years. Table-I summarized the baseline characteristics of patients suffering from acute respiratory distress syndrome included in the study. One hundred and forty-three patients (51.1%) had early neuromuscular blockade while 137(48.9%) did not have early neuromuscular blockage. 159(56.8%) patients survived within 90 days of admission while 121(43.2%) died within those 90 days.

Table-I: Characteristics of Patients Admitted in Critical Care Unit with Acute Respiratory Distress Syndrome (n=280)

Study Parameters	n(%)
Age (years)	
Mean+SD	39.97±8.966 years
Range (min-max)	21 - 65 years
Gender	
Male	200(71.4%)
Female	80(28.6%)
Severity of acute respiratory distress syndrome	
Moderate	182(65%)
Severe	98(35%)
90 days' mortality	
Patients alive	159(56.8%)
Not alive	121(43.2%)
Use of early neuromuscular blockage	
No	137(48.9%)
Yes	143(51.1%)

Table-II summarized the findings of statistical test applied on data collected for this study. Use of

early neuromuscular blockage had no statistically significant relationship (*p*-value-0.848) with 90 days' mortality in our study participants while age more than 40 years (*p*-value<0.001) and presence of severe acute respiratory distress syndrome (*p*-value-0.001) had statistically significant relationship with presence of 90 days in our study participants.

Table-II: Association of Various Factors Including use of Early Neuromuscular Blockage with the 90 days' Mortality in Target Population (n=280)

	No 90-day mortality	90-day mortality	*p*-value
Age			
40 year or less	115(72.3%)	52(42.9%)	<0.001
40-60	44(37.7%)	69(57.1%)	
Gender			
Male	116(72.9%)	84(69.4%)	0.517
Female	43(27.1%)	37(30.6%)	
Use of early neuromuscular blockage			
No	77(48.4%)	60(49.6%)	0.848
Yes	82(51.6%)	61(50.4%)	
Severity of acute respiratory distress syndrome			
Moderate	116(72.9%)	66(54.5%)	0.001
Severe	43(27.1%)	55(45.5%)	

DISCUSSION

Critical care settings have been designed to perform the function of organ support in patients who had been severely affected by any medical or surgical illness. Critical care medicine is an evolving specialty in Pakistan with very limited number of experts who are especially trained in this field. It demands an overlap of knowledge of organ support and all other medical or surgical parameters which can affect the patients and his prognosis during the time of organ support at this specialized setting. ARDS is a potentially fatal condition with high mortality and critical care experts across the globe have been trying to introduce various strategies to reduce the mortality related to this condition. Therefore, this study was conducted with an aim to assess the role of early neuromuscular blockade in the acute respiratory distress syndrome among patients managed in critical care unit.

An interesting paper was published in 2020 in Journal of intensive care regarding use of neuromuscular blockade in acute respiratory distress syndrome. It was concluded that neuromuscular blockage improves oxygenation only after 48 hours but does not reduce morbidity parameters and mortality risk in patients admitted with acute respiratory distress syndrome in intensive care unit.[15] We studied use of early neuromuscular blockage and focused only on 90-day mortality and found out there is no added benefit of this intervention in patients of ARDS.

Wongtangman *et al.,*[16] in 2021 studied this subject from another angle and performed a study with an objective to look for optimal sedation in patients who received neuromuscular blockage for treatment of ARDS. They revealed that use of deeper sedation increases mortality rate therefore, neuromuscular blockage and sedation should not be used in routine but only on needful basis.[16] Our study was slightly different from study conducted by Wongtangman *et al.,* and we studied the role of early neuromuscular blockage in reducing mortality among ARDS patients but our results were not significant.

Needham *et al.,* published similar study in 2012 and compared 48-hr infusion of the cisatracurium with placebo for survival in patients suffering from respiratory distress syndrome. They concluded ninety days' mortality was seen less in the patients who were early on administered with cisatracurium. All the morbidity parameters including need for mechanical ventilation and stay in critical care unit were also found statistically significantly decreased in patients who received 48 hours' infusion of cisatracurium.[17] Our results were different from the results generated by Needham *et al.,* and use of early neuromuscular blockage had no relationship with 90-day mortality.

Alhazzani *et al.,* in 2013 published a systematic review and meta-analysis of randomized controlled trials regarding use of neuromuscular blocking agents in acute respiratory distress syndrome. They revealed that short-term infusion of cisatracurium besylate reduces hospital mortality in patients admitted with ARDS in critical care unit.[18] Our results did not support the results generated by Alhazzani *et al.,* More research is required in this regard to ascertain role of neuromuscular blockage in patients suffering from ARDS.

Our study is really important and adds to local statistics regarding use of neuromuscular blockage in patients managed for ARDS. If mores studies produce similar results then local guidelines could be made to discourage use of this agent.

LIMITATION OF STUDY

Study design was not appropriate to evaluate the intervention. Placebo controlled randomized trial would have been a better design to assess efficacy or efficiency of a medication. Control of confounding factors and effect modifiers is also of utmost importance in these type of trials.

CONCLUSION

Mortality rate was more than 40% in patients suffering from moderate to severe acute respiratory distress syndrome in our data set. Use of early neuromuscular blockage did not provide any added benefit in reduction of mortality in patients studied for two years in our critical care unit.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

KIQ & TM: Data acquisition, data analysis, critical review, approval of the final version to be published.

AA & AMB: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

HS & RI: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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