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**ORIGINAL ARTICLE**

# Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome

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## ABSTRACT

**Objective:** The aim of this study is to determine the efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome.

**Study Design:** Randomized Control Trial

**Place and Duration:** The study was conducted at the emergency department of Lady Reading hospital Peshawar for the duration of six months during the period July to December 2020.

**Methods:** Total 150 patients suffering from acute respiratory distress syndrome were presented in this study. Patients were aged between 40-75 years. Patients' detailed demographics age, sex and body mass index were recorded after taking informed written consent. Patients were equally divided into-2 groups. Group I received corticosteroids and group II received placebo for 7-days of duration. At 28$^{th}$ day efficacy among both groups were assessed and compared in terms of low mortality, free from ventilator and reduction in complications. Complete data was analyzed by SPSS 24.0 version.

**Results:** There were 120 males (60 in each group) and 30 (15 in each group) were females. Mean age of the patients in group I was 59.14±6.45 years with mean BMI 25.88±3.42 kg/m$^2$ and in group II mean age was 58.38±7.46 years with mean BMI 26.41±3.54 kg/m$^2$.Smoking was the most common cause of ARDS, in group I among 40 (53.3%) patients and 42 (56%), followed by chronic lung disease 20 (26.7%) in group I and 19 (25.3%) in group II. After regular follow up, mortality rate among patients of group II was greater 18 (24%) as compared to steroids group 13 (17.3%) and frequency of ventilator free patients were higher among steroids group 39 (52%) as compared to placebo 31 (41.3%). We found that complications reduction in steroids group was greater with minimum recurrence rate.

**Conclusion:** We concluded in this study that the use of corticosteroids for persistent acute respiratory distress syndrome was effective and reliable in terms of low mortality and shorten the time of ventilation. Except this reduction in complications with minimum recurrence rate was found among patients those received steroids.

**Keywords:** Acute respiratory distress syndrome, Placebo, Corticosteroids, Efficacy, Ventilator

## INTRODUCTION

Acute respiratory distress syndrome (ARDS) is defined clinically by acute hypoxemic respiratory failure and is brought on by an inflammatory damage to the lungs [1]. Early exudative lung changes are followed by proliferative and fibrotic phases that demonstrate pathologically complicated modifications [2, 3]. In chronic ARDS, inflammation, proliferation of parenchymal cells, and abnormal collagen deposition all persist and may be amenable to corticosteroid therapy [4, 5].

Short regimens of high-dosage steroids in ARDS are not helpful [6, 7]. Lower steroid doses (1-2 mg/kg/day) over a longer period of time may improve the lungs while lowering systemic side effects, as previously proposed. This technique may improve outcomes in early ARDS, including death, according to recent evidence from a retrospective subgroup analysis of a clinical study and a small (n=91) prospective clinical trial [8, 9]. Initial observational studies in patients with advanced ARDS revealed a benefit as well [10, 11]. A short (n=24) randomized investigation of low dosage steroids in patients with severe ARDS for 7 days in 1998 found considerably lower ICU (0% vs 62%, p=0.002) and hospital mortality (12% vs 62%, p=0.03) by Meduri and colleagues [12].

This study, which was a multicenter, randomized trial of low dose steroids in 180 patients with at least seven days of ARDS, was done by the ARDS Clinical Trials Network because of the encouraging findings from the late stages of the disease [13]. The steroid-treated group was given methylprednisolone (2 mg/kg/day) intravenously for 14 days in this research. The dosage was subsequently lowered to 1 mg/kg/day for a further seven days before being gradually reduced to zero over the course of two to four days. During the first 28 days, individuals treated with steroids saw significant reductions in pulmonary inflammation, increased oxygenation, improved compliance of the respiratory system, and an increase in days without the use of a ventilator or shock. However, the mortality rates at 60 and 180 days in each group were practically comparable (29.2 percent vs. 28.6 percent and 31.5 percent vs. 31.9 percent , steroids vs. placebo). Infectious consequences were similar in both groups, although the steroid group had a higher occurrence of neuromuscular weakness. Steroids were linked to significantly poorer 60 and 180-day mortality in ARDS patients who were enrolled at least 14 days after the onset of the condition. However, mortality was not significantly lower with steroids in patients who were included between the seventh and thirteenth day after the beginning of ARDS.

It's not apparent whether corticosteroids have any side effects in persons with this condition. A meta-analysis of moderate-dose corticosteroids for sepsis did not

substantiate the observation that high-dose corticosteroids increase the incidence of secondary infections in patients with sepsis and ARDS,[14,15]. Corticosteroids may also cause diabetes, poor wound healing, psychosis, pancreatitis, and persistent muscular weakness with a decreased functional status. [16]

The efficacy and safety of this treatment were investigated in a multicenter, randomized, controlled trial. A moderate dose of methylprednisolone was given to patients with chronic acute respiratory distress syndrome in hopes of improving clinical outcomes without significantly worsening side effects, which was our hypothesis.

## MATERIAL AND METHODS

This randomized control trial was conducted at the emergency department of Lady Reading hospital, Peshawar for the duration of six months during the period July to December 2020. The study comprised of 150 patients of both genders. Patients' detailed demographics including age, sex and body mass index were recorded after taking informed written consent. Patients <25 years of age and those did not give any written consent were excluded from this study.

Patients were aged between 25-80 years. Patients were equally divided into-2 groups. Group I received corticosteroids and group II received placebo for 7-days of duration. Intravenous (methylprednisolone) diluted in 50 ml of 5 percent dextrose water or placebo (50 ml of 5 percent dextrose water), stratified according to hospital. Methylprednisolone was given as a solitary dose of 2 mg per kilogram of anticipated body weight, followed by 0.5 mg every 6 hours for 7 days, 0.5 mg every 12 hours for 7 days, and then a gradual lowering of the dosage. At 28$^{th}$ day efficacy among both groups were assessed and compared in terms of low mortality, free from ventilator and reduction in complications. Complete data was analyzed by SPSS 24.0 version.

## RESULTS

There were 120 males (60 in each group) and 30 (15 in each group) were females. . Mean age of the patients in group I was 59.14±6.45 years with mean BMI 25.88±3.42 kg/m$^2$ and in group II mean age was 58.38±7.46 years with mean BMI 26.41±3.54 kg/m$^2$. Smoking was the most common cause of ARDS, in group I among 40 (53.3%) patients and 42 (56%), followed by chronic lung disease 20 (26.7%) in group I and 19 (25.3%) in group II and misuse of alcohol among 15 (20%) and 14 (18.7%) in group I and II.(table 1)

Table 1: Demographically details of enrolled cases

| Variables | Steroids (75) | Placebo (75) |
|---|---|---|
| Mean age (years) | 59.14±6.45 | 58.38±7.46 |
| Mean BMI (kg/m$^2$) | 25.88±3.42 | 26.41±3.54 |
| **Gender** | | |
| Male | 60 (80%) | 60 (80%) |
| Female | 15 (20%) | 15 (20%) |
| **Causes** | | |
| Smoking | 40 (53.3%) | 42 (56%) |
| Chronic lung disease | 20 (26.7%) | 19 (25.3%) |
| Misuse of alcohol | 15 (20%) | 14 (18.7%) |

After regular follow up, mortality rate among patients of group II was greater 18 (24%) as compared to steroids group 13 (17.3%) and frequency of ventilator free patients were higher among steroids group 39 (52%) as compared to placebo 31 (41.3%). (table 2)

Table 2: Post-treatment comparison of mortality and outcomes among both groups

| Variables | Steroids | Placebo |
|---|---|---|
| **Mortality** | | |
| Yes | 13 (17.3%) | 18 (24%) |
| No | 62 (82.7%) | 57 (76%) |
| **Ventilator Free** | | |
| Yes | 39 (52%) | 31 (41.3%) |
| No | 36 (48%) | 44 (58.7%) |

We found that complications in steroids group was greater with minimum recurrence rate.(table 3)

Table 3: Comparison of complications and recurrence rate

| Variables | Steroids | Placebo |
|---|---|---|
| **Complications** | | |
| Yes | 20 (26.7%) | 25 (33.3%) |
| No | 55 (73.3%) | 50 (66.7%) |
| **Recurrence Rate** | | |
| Yes | 10 (13.3%) | 15 (20%) |
| No | 65 (86.7%) | 60 (80%) |

## DISCUSSION

When fluid accumulates in the lungs' air sacs, acute respiratory failure results. If this occurs, your lungs will be unable to deliver oxygen into your blood as they should. As a result, your organs are deprived of oxygen-rich blood and unable to operate. Acute respiratory failure can also occur if your lungs fail to eliminate carbon dioxide from your blood. Small blood arteries around your air sacs can fail to exchange carbon dioxide for oxygen, resulting in respiratory failure. Acute or chronic conditions are both possible. When you have acute respiratory failure, your body immediately shows the effects of a lack of oxygen. If it's not addressed right away, this kind of failure can be deadly.

In this randomized control study 150 patients of acute respiratory distress syndrome were enrolled. Patients were equally categorized into two groups. . Mean age of the patients in group I was 59.14±6.45 years with mean BMI 25.88±3.42 kg/m$^2$ and in group II mean age was 58.38±7.46 years with mean BMI 26.41±3.54 kg/m$^2$. Majority of the patients 120 (80%) were males in this study. These findings were comparable to the previous studies.[17,18] Smoking was the most common cause of ARDS, in group I among 40 (53.3%) patients and 42 (56%), followed by chronic lung disease 20 (26.7%) in group I and 19 (25.3%) in group II and misuse of alcohol among 15 (20%) and 14 (18.7%) in group I and II.[19]

In present study, mortality rate among patients of group II was greater 18 (24%) as compared to steroids group 13 (17.3%) and frequency of ventilator free patients were higher among steroids group 39 (52%) as compared to placebo 31 (41.3%). Methylprednisolone was studied in patients with ARDS in several major multicenter RCTs recently. These trials looked at the mortality, mechanical breathing time, and adverse event rates associated with corticosteroids. When Meduri et al.[20,21,22] looked at the

effects of methylprednisolone on systemic inflammation, they found that patients' ability to breathe on their own was improved, and mechanical ventilation was required for shorter periods of time. Rezk et al[23] found that giving methylprednisolone to ARDS patients for the first two days reduced the severity of lung injury, reduced systemic inflammation, and reduced the risk of hospital-acquired infection. Despite improvements in cardiac physiology, the study by Steinberg et al[24] did not support routine treatment of methylprednisolone against persistent ARDS.

We found that complications reduction in steroids group was greater with minimum recurrence rate.[25] Methylprednisolone has been studied and shown to have some promise as a treatment. It is an end-effector of the hypothalamic-pituitary-adrenal axis and one of the most important physiologic anti-inflammatory agents. Many genes involved in stress homeostasis are influenced by it. Methylprednisolone works by activating cytoplasmic heat shock protein–complexed glucocorticoid receptors in the cell. Furthermore, it interacts with active nuclear factor kB, preventing DNA binding and subsequent transcriptional activity. Methylprednisolone, on the other hand, may have side effects that outweigh its therapeutic benefits, such as psychological side effects, iatrogenic Cushing syndrome, infections, and osteoporosis. [26,27]

Corticosteroids were found to be safe and may have the potential to cut mortality and minimize the length of a patient's hospital stay. Corticosteroids use was not linked to an increased risk of adverse outcomes in ARDS patients, according to the findings. The effectiveness and safety of methylprednisolone against ARDS must be further characterized in well-designed and large-scale research.

## CONCLUSION

We concluded in this study that the use of corticosteroids for persistent acute respiratory distress syndrome was effective and reliable in terms of low mortality and shorten the time of ventilation. Except this reduction in complications with minimum recurrence rate was found among patients those received steroids.

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