Effects of methyl prednisolone in early ARDS

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Received 25 November 2012; accepted 25 February 2013
Available online 19 March 2013

KEYWORDS
Methyl prednisolone; ARDS

Abstract
Introduction: Glucocorticoid induced down-regulation of systemic inflammation in ARDS is associated with a significant improvement in pulmonary and extrapulmonary organ dysfunction and a reduction in duration of mechanical ventilation and ICU length of stay [1].

We aimed in this study to evaluate the effect of methyl prednisolone when used early in ARDS.

Patients and methods: We studied 27 patients with ARDS, we divided them randomly into two groups the first group consists of 18 patients received methyl prednisolone and the other group consists of 9 patients did not receive it. All patients were subjected daily to: history taking and clinical examination, Chest X-ray, routine blood investigation (CBC–LFT–RFT–electrolytes), ABG, Serum lactate, INR, fibrinogen, and aptt, CRP, protein C, protein S, and D-dimer at the beginning and at the end of study.

Results: After 7 days there were significant improvements of clinical parameters (pulse, temperature, and systolic blood pressure), peep (one parameter from lung injury score), lactate, D-dimer, AST, and a highly significant improvement of creatinine in the methyl prednisolone group when compared to the control group. After 14 days from starting treatment there were significant improvements of clinical parameters (pulse and systolic BP), ventilator parameters (FIO2, peep, PEEP, AST, ALT, GGT, CRP, protein C, protein S, and D-dimer).
Introduction

In ARDS, the evolution of systemic and pulmonary inflammation in the first week of mechanical ventilation determines the physiologic progression (resolving vs. unresolving) and outcome of the disease [2].

The lung injury score (LIS) quantifies the physiologic respiratory impairment in ARDS through the use of a 4-point score based on the levels of positive end-expiratory pressure (PEEP), ratios of PaO2 to fraction of inspired oxygen (FIO2), the static lung compliance, and the degree of infiltration present on chest radiograph [9].

Patients failing to improve the LIS or its components by day 7 of ARDS (unresolving ARDS), contrary to improvers, have persistent elevation in circulating and BAL levels of inflammatory cytokines and chemokines, markers of alveolo-capillary membrane permeability [5] and fibrogenesis (dysregulated systemic inflammation) [3], and a higher mortality [4].

Glucocorticoid induced down-regulation of systemic inflammation in ARDS is associated with a significant improvement in pulmonary and extrapulmonary organ dysfunction and a reduction in duration of mechanical ventilation and ICU length of stay. [1]

We aimed in this study to evaluate the effect of methyl prednisolone in early ARDS regarded to outcome, incidence of infection, organ dysfunction, D-dimer, CRP, protein C and protein S.

Patients and methods

This study was performed in Farwaneya Hospital Kuwait October 2011–October 2012 in ICU department, we divided the 27 patients with ARDS randomly into two groups the first group consists of 18 patients received methyl prednisolone and the other group consists of 9 patients received normal saline in the same manner of methyl prednisolone.

Inclusion criteria

1. All patients must get criteria of ARDS.
2. All patients must be on mechanical ventilation.
3. Methyl prednisolone must be started randomly in first 48 h.

Exclusion criteria

1. PaO2/FIO2 more than 200
2. Patients were not on mechanical ventilation.

Conclusion

We conclude that methyl prednisolone when used on first 2 days in ARDS patients improves the LIS, decreases the systemic inflammation, earlier extubation from mechanical ventilation, and decreases the incidence of hospital acquired infection.

Methyl prednisolone dosing [1]

Methylprednisolone was mixed in 240 mL of normal saline solution and administered daily as an infusion at 10 mL/h and changed to a single oral dose when enteral intake was restored. A loading dose of 1 mg/kg was followed by an infusion of 1 mg/kg/d from day 1 to day 14, 0.5 mg/kg/d from day 15 to day 21, 0.25 mg/kg/d from day 22 to day 25, and 0.125 mg/kg/d from day 26 to day 28. If the patient was extubated between days 1 and 14, the patient was advanced to day 15 of drug therapy and tapered according to schedule.

ARDS criteria (Bernard et al. 1994)

1. PaO2/FIO2 less than 200
2. Bilateral pulmonary infiltrates
3. PAWP less than 18 mmHg

* Data was analyzed using SPSS (Statistical Package for Social Sciences) version 15. Qualitative data was presented as number and percent. Comparison between groups was done by Chi-Square test. Data was presented as mean ± SD. Paired t-test was used for comparison within groups. Student t-test was used to compare between two groups. P < 0.05 was considered to be statistically significant.

Results

There were no significance difference between the methyl prednisolone and control groups in all parameters except peep, ps, and fibrinogen were significantly higher in the methyl prednisolone group when compared with the control group before starting of methyl prednisolone. O2sat, PaO2, pCO2, HB, and creatinine were higher in the control group when compared with the methyl prednisolone group in the same time (see Table 1).

There were significant improvements of pulse, temperature, systolic blood pressure, peep, lactate, D-dimer, creatinine, and
effects of methyl prednisolone in early ARDS

There were significant improvements of pulse, temperature, systolic BP, FIO2, peep, RR, O2sat, lactate, WBCs, AST, ALT, GGT, fibrinogen, and CRP in the methyl prednisolone group at the beginning of study and 7 days later (see Table 4).

There were significant improvements of pulse, temperature, systolic BP, FIO2, peep, RR, O2sat, PaO2, INR, APTT, lactate, WBCs, platelets, creatinine, bilirubin, AST, ALT, GGT, fibrinogen, and CRP in the methyl prednisolone group at the beginning of study and 7 days later (see Table 4).

There were significant improvements of pulse, temperature, systolic BP, FIO2, peep, RR, O2sat, PaO2, INR, lactate, WBCs, platelets, creatinine, bilirubin, AST, ALT, GGT, fibrinogen, CRP, D-dimer, and CX-ray in the methyl prednisolone group at the beginning of study and at the end of study. And the rate of infection increased significantly in the control group (see Table 5).

There were no significant changes in the control group at the beginning of study and 7 days later (see Table 6).

There were significant decreases of temperature, HB, protein C and protein S in the control group pre and at end of study (see Table 7).

Discussion

The American-European Consensus Conference defines ARDS as:[8]

- Acute onset of respiratory symptoms
- Chest radiograph with bilateral infiltrates
- Pulmonary artery wedge pressure (PAWP) of less than 18 mmHg (indicating no evidence of left heart failure)
- ARDS: PaO2/FIO2 ratio < 200 mmHg

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic data, clinical data, ventilator parameters, ABG, biochemical examination and chest X-ray in methyl prednisolone group and control group in the first day of study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases (n = 18)</td>
<td>Control (n = 9)</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>16 (88.9%)</td>
</tr>
<tr>
<td>Female</td>
<td>2 (11.1%)</td>
</tr>
<tr>
<td>Cause</td>
<td></td>
</tr>
<tr>
<td>HAP</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>CAP</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>Comorbid</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>1</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>3</td>
<td>6 (33.3%)</td>
</tr>
<tr>
<td>CXR-before</td>
<td>3.67 ± 0.49</td>
</tr>
<tr>
<td>Pulse</td>
<td>104.33 ± 17.99</td>
</tr>
<tr>
<td>Temperature</td>
<td>37.92 ± 0.75</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>127.50 ± 17.64</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>67.00 ± 6.70</td>
</tr>
<tr>
<td>FIO2</td>
<td>91.67 ± 12.49</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>67.00 ± 6.70</td>
</tr>
<tr>
<td>Ps</td>
<td>15.83 ± 1.92</td>
</tr>
<tr>
<td>O2sat</td>
<td>95.17 ± 2.75</td>
</tr>
<tr>
<td>PaO2</td>
<td>100.28 ± 14.80</td>
</tr>
<tr>
<td>PaCO2</td>
<td>114.89 ± 18.79</td>
</tr>
</tbody>
</table>

AST in the methyl prednisolone group 7 days from the date of mechanical ventilation when compared to the control group.

And there was a significant increase of PaCO2 in the control group (see Table 2).

There were significant improvements of pulse, systolic BP, FIO2, peep, RR, O2sat, lactate, creatinine, WBCs, AST, GGT, CRP, and CX-ray, with earlier extubation from mechanical ventilation and improvement of mortality in the methyl prednisolone group when compared with the control group at the end of study, and there were significant decreases of protein C and protein S in the control group (see Table 3).
In ARDS, the evolution of systemic and pulmonary inflammation in the first week of mechanical ventilation determines the physiologic progression (resolving vs. unresolved) and outcome of the disease. [2]

Glucocorticoid treatment-induced down-regulation of systemic inflammation in ARDS is associated with a significant improvement in pulmonary and extrapulmonary organ dysfunction and a reduction in duration of mechanical ventilation and ICU length of stay. [1]

We aimed in this study to evaluate the effect of methyl prednisolone when used early in ARDS.

In this study we found no significance difference between methyl prednisolone group and control group before the introduction of methyl prednisolone in relation to demographic data, etiology of ARDS, comorbidity, chest X-ray and most of clinical parameters, ventilator parameters, and biochemical investigation and this mean that the both groups were comparable.

After 7 days there were significant improvements of clinical parameters (pulse, temperature, and systolic blood pressure), peak (one parameter from lung injury score), lactate, D-dimer, and AST, and highly significant improvement of creatinine in the methyl prednisolone group when compared to the control group. This agreed with (Meduri et al.[1]) who studied 91 patients with severe early ARDS (< 72 h), 66% with sepsis. Patients were randomized (2:1 fashion) to methylprednisolone infusion (1 mg/kg/d) vs. placebo. The duration of treatment was up to 28 days and found patients with methyl prednisolone achieving the primary end point of a 1-point reduction in LIS.

After 14 days from starting the treatment there were significant improvements of clinical parameters (pulse, and systolic BP), ventilator parameters (FIO2, peep, and RR), systemic inflammation markers organ functions (O2sat, lactate, creatinine, WBCs, AST, and GGT) and CRP. And a significant improvement of CX-ray, and earlier extubation from mechanical ventilation and improvement of mortality in the methyl prednisolone group when compared with the control group, improvement of mortality reflection to improvement of clinical status, oxygenation, inflammatory markers and early extubation of this group. And there were significant decreases of protein C and protein S in the control group. This indicate worse clinical outcomes, including death, fewer ventilator-free days, and more non pulmonary organ failures in this group. [6]

In the methylprednisolone group after 7 days from the beginning of the drug there were significant improvements of clinical parameters (pulse, temperature, and systolic BP), ventilator parameters (FIO2, peep, RR, and ps), two parameters of three measured LIS (FIO2, PaO2, and peep) and systemic inflammatory markers (CRP and organ functions).

After 28 days and found patients with methyl prednisolone achieving the primary end point of a 1-point reduction in LIS.
before, CX-ray, and the incidence of infection was significantly lower in the same group. And this agreed with (Anname et al. [7]) who conclude that Long course of low dose corticosteroids reduced 28-day all-cause mortality, and intensive care unit and hospital mortality, and decreased incidence of infection.

We conclude that methyl prednisolone when used on first 2 days in ARDS patients improves the LIS, decreases the systemic inflammation, earlier extubation from mechanical ventilation, and decreases the incidence of hospital acquired infection.
References


