Original Article

High Doses of Dexamethasone Improved Hemoglobin Levels Lowered by Corona Virus in COVID-19 Infected Patients

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INTRODUCTION

The global pandemic disease COVID-19 caused by “SARS-CoV-2” virus presented with flu and common cold like symptom mainly effecting the respiratory tract, If not treated properly leads to death. This positive RNA strand coronavirus produces cytokines and chemokine's damage lungs and causes cough with fever [1]. Coronavirus targets the ACE-2 receptors for entering in host cell mucosa, after replication, it damages the respiratory passage, lungs, trachea, pharynx, nasal cavity and conjunctiva [2]. The mode of transmission of this virus is by contact with infected individual, droplets and aerosol [3, 4]. Hemoglobin contains porphyrin on which coronavirus damages and gains porphyrin required for its replication. The deranged hemoglobin are unable to deliver oxygen to the tissues [5]. Coronavirus binds and interacts with the receptors located on red blood cells and causes further destruction of hemoglobin and reduces oxygen supply [6]. Steroids have effective role in controlling and reducing the symptoms of COVID-19 patients. One of the corticosteroid with similarity to natural hormones is dexamethasone. It has anti-inflammatory effects relieves respiratory symptoms, itching, rhinitis and asthma in coronavirus infected patients.
patients. It also inhibits expression of inflammatory proteins and transcription factors necessarily for cell proliferation [7, 8]. Different doses of dexamethasone ranging from 6-12mg once daily are used for treating respiratory and allergic symptoms in COVID-19 patients [9]. Dexamethasone also improves hemoglobin level. Steroids increases blood hemoglobin level in the body by stimulating the synthesis of a hormone erythropoietin which leads to increased production of red blood cells and hemoglobin [10].

The present study was conducted to see the effect of high dose of dexamethasone in improving blood hemoglobin levels compared to low dose in coronavirus infected patients.

**METHODS**

After approval from the ethical committee of RIHS Islamabad with reference no: RIHS-REC/ 062/21 dated: 29-01-21. This study was carried out in Rawal Institute of Health Sciences, Islamabad and Pakistan Institute of Medical Sciences, Islamabad from May 2021 till September 2021. It is an experimental study conducted on 100 adult patients suffering from COVID-19 disease. The sample size was calculated by using expected prevalence of COVID-19 in Pakistan was 6.87% by taking 5% margin of error and 95% confidence interval [11]. Male and female patients with low hemoglobin (<10 g/dl) were included. The patient with anemia due to blood disorders, or diseases causing anemia were excluded. Blood hemoglobin was seen from the records on the day of admission. Patients with blood hemoglobin level less than 10 g/dl were considered anemic and selected. Prior to study, all the patients provided informed consent. Patients were taking dexamethasone prescribed by the physician. On the basis of the doses, patients were divided into two groups with 50 patients in each group. Group 1 was taking dexamethasone in a dose of 6 mg once daily and group 2 was taking dexamethasone 12 mg once daily. Blood hemoglobin was analyzed on day 01 and on day 15 after taking dexamethasone Change in blood hemoglobin level was recorded. Data were entered using SPSS version 26.0. Results were given in mean ± standard deviation (mean ± SD). Hemoglobin levels on day 01 and day 15 of both groups were compared by applying unpaired t-test and paired sample t-test was used to find out difference of mean hemoglobin of each group before and after taking the dexamethasone. P value < 0.05 was considered significant.

**RESULTS**

At the time of admission 74% of the patients had a cough, 89% of the patients presented with fever, 98% had increased heart rate whereas, 100% of the patients presented with the complaint of fatigue. Group wise distribution of presenting complaints was in table 1.

In table 2, Group 1 levels of serum hemoglobin on day 15 were compared with day 01 their mean were 8.99 ± 0.562 g/dl versus 8.95 ± 0.497 g/dl, a slight increase was observed but the difference was not significant with a p-value of 0.64 i.e., p>0.05. However group 2 showed a remarkable increase in hemoglobin levels when recorded on day 15 as compared to day 01, i.e., 9.46 ± 0.67 g/dl versus 8.07 ± 0.32 g/dl. The difference was observed as significant with a p<0.05.

**Table 1:** Presenting Complaints of Patients in Group 1 and 2 at the Time of Admission

<table>
<thead>
<tr>
<th>Presenting Complaints</th>
<th>Group 1 (n=50) N (%)</th>
<th>Group 2 (n=50) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>33 (66%)</td>
<td>41 (82%)</td>
</tr>
<tr>
<td>Fever</td>
<td>40 (80%)</td>
<td>49 (98%)</td>
</tr>
<tr>
<td>Increased Heart Rate</td>
<td>50 (100%)</td>
<td>48 (96%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>50 (100%)</td>
<td>50 (100%)</td>
</tr>
</tbody>
</table>

In table 2, Group 1 levels of serum hemoglobin on day 15 were compared with day 01 their mean were 8.99 ± 0.562 g/dl versus 8.95 ± 0.497 g/dl, a slight increase was observed but the difference was not significant with a p-value of 0.64 i.e., p>0.05. However group 2 showed a remarkable increase in hemoglobin levels when recorded on day 15 as compared to day 01, i.e., 9.46 ± 0.67 g/dl versus 8.07 ± 0.32 g/dl. The difference was observed as significant with a p<0.05.

**Table 2:** Comparison of Effect of Dexamethasone (6mg and 12mg)/Day in Individual Groups on Serum Hemoglobin Levels in Covid 19 Patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>Day 1 (Serum Hb) g/dL</th>
<th>Day 15 (Serum Hb) g/dL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>8.95 ± 0.497</td>
<td>8.99 ± 0.562</td>
<td>0.64</td>
</tr>
<tr>
<td>Group 2</td>
<td>8.07 ± 0.32</td>
<td>9.46 ± 0.67</td>
<td>0.00 *</td>
</tr>
</tbody>
</table>

P Value <0.05 = Significant(*)
P Value >0.05 = Non Significant(NS)
1n=50, Results are expressed as mean (Paired t test)

On day 01 the hemoglobin level of group -1 was 8.95 ± 0.497 g/dl and group 2 was 8.07 ± 0.32 g/dl. The difference among the two groups was observed significant having p<0.01 with a p<0.05.

In table 3, day 15 showed the hemoglobin level of group 1 was 8.99 ± 0.562 g/dl and group 2 was 9.46 ± 0.67 g/dl. A significant rise was observed on comparing the two groups with p<0.05.

**Table 3:** Comparison of Effect of Dexamethasone (6mg and 12mg)/Day among Two Groups on Serum Hemoglobin Levels in Covid 19 Patients

<table>
<thead>
<tr>
<th>Test (g/dl)</th>
<th>Time Points</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Hb</td>
<td>Day 1</td>
<td>8.95 ± 0.497</td>
<td>8.07 ± 0.32</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>Day 15</td>
<td>8.99 ± 0.562</td>
<td>9.46 ± 0.67</td>
<td>0.00</td>
</tr>
</tbody>
</table>

P Value <0.05 = Significant(*)
P Value >0.05 = Non Significant(NS)
1n=50, Results are expressed as mean (Unpaired t test)

The result below shows on day 01 the hemoglobin level of group 1 was 8.95 ± 0.49 g/dl and hemoglobin level of group 2 was 8.07 ± 0.32 g/dl after taking 6 mg and 12 mg of Dexamethasone There was improvement in the hemoglobin levels in both groups. There is 0.4 % increase in hemoglobin level in group 1 and 17 % increase in hemoglobin level in group 2 patients after two weeks. The percentage improvement in hemoglobin levels is seen in table 4.
Table 4: Percentage Increase in Hemoglobin Levels in Both Groups on Day 15

<table>
<thead>
<tr>
<th>Groups (n=100)</th>
<th>Hb (g/dl) Day 01</th>
<th>Hb (g/dl) Day 15</th>
<th>Increase in Hb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=50)</td>
<td>8.95 ± 0.497</td>
<td>8.99 ± 0.562</td>
<td>0.4 %</td>
</tr>
<tr>
<td>Group 2 (n=50)</td>
<td>8.07 ± 0.32</td>
<td>9.46 ± 0.87</td>
<td>17%</td>
</tr>
</tbody>
</table>

Discussion
In our study we have seen that at the time of admission 100% of the patients presented with fatigue and 98% of them were using pain killers and antibiotics for the treatment of respiratory symptoms, relieves body aches and pains. Although fatigue and increased heart rate are also seen in corona patients but since these patients had hemoglobin level less than 10 g/dl and are anemic these two symptoms increased to such a high percentage. Safari N et al., in one of his research said that the global prevalence of chronic fatigue is 45.2% in corona patient [10]. In one of the study it is said that coronavirus causes inflammation of heart leading to increased heart rate [12, 13]. The causes of fatigue and increased heart rate in anemic patient are low hemoglobin levels leading to reduced oxygen delivery causing tiredness and fatigue. To provide oxygen to the rest of the body the heart works rapidly, increasing heart rate [14]. In our experimental study we have seen the effect of high and low doses of dexamethasone for two weeks and noted the changes in hemoglobin levels. Karam D et al., in one of his research used high doses of steroids for two weeks and suggested that high doses caused the improvement in hemoglobin levels [14, 15]. We have seen the effect of 6mg and 12mg of dexamethasone in COVID-19 infected patient. Russell L et al., used the same doses of dexamethasone in coronavirus infected patients and concluded that rapid improvement in symptoms was seen in patients taking high doses compared to low dose [15, 16]. From our results we have seen although there was insignificant difference in hemoglobin levels in group 1 patients on day 01 and day 15 but on finding out the percentage increase in hemoglobin level after two weeks of taking 6mg/day of dexamethasone there is 0.4% increase in hemoglobin level. In group 2 anemic patients they had significant difference on day 01 and day 15 but after taking 12mg/day of dexamethasone for two weeks there was 17% increase in hemoglobin levels. A research conducted by Anai M et al., on hemoglobin levels in corona virus infected patients, concluded that in severe infection there is reduction in hemoglobin level reduced oxygen delivery, further worsening the conditions [16, 17]. After destruction of red blood cells corona virus acts on the hemoglobin and deranges its structure. Nóbrega F et al., and Russo A et al., in one of his study said that coronavirus acts on the beta chain of hemoglobin and code its protein, the hemoglobin oxygen transport ability is lowered and there is more hypoxia [17-19]. Steroids have shown a positive effect in COVID-19 patients leading to rapid recovery and improvement in the symptoms. They improve the respiratory symptoms, relieves body aches and pains, and increase heart rate [14]. In our study we have seen that at the time of admission 100% of the patients presented with fatigue and 98% of them were using pain killers and antibiotics for the treatment of respiratory syndrome coronavirus 2 infection. Dexamethasone and Hemoglobin in COVID-19

References
Chaudhry ZR et al.,


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