



Original Article

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

Zunnera Rashid Chaudhry^{1*}, Sabeen Shakir¹, Sana Rasheed², Erum Rashid³, Hifza Noor Lodhi⁴ and Naima Shakeel⁵¹Department of Pharmacology, Akhtar Saeed Medical College, Rawalpindi, Pakistan²Department of Physiology, Ameer-Ud-Din Medical College, Lahore, Pakistan³Department of Biochemistry, Watim Medical College, Rawalpindi, Pakistan⁴Department of Physiology, Rashid Latif Khan University, Lahore, Pakistan⁵Department of Physiology, Postgraduate Medical Institute, Ameer-Ud-Din Medical College, Lahore General Hospital, Lahore, Pakistan

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*Corresponding Author:

Zunnera Rashid Chaudhry
Department of Pharmacology, Akhtar Saeed Medical College, Rawalpindi, Pakistan
zunnerach@gmail.comReceived Date: 18th April, 2024Acceptance Date: 28th May, 2024Published Date: 31st May, 2024

ABSTRACT

Corona virus an infectious disease caused by SARS-CoV-2 virus that lower hemoglobin level leading to worsening of the conditions. The respiratory symptoms are treated by steroids and patients are rapidly recovered. **Objective:** To study the effect of high and low doses of dexamethasone on hemoglobin level in COVID-19 infected patients. **Methods:** This experimental study was carried out in Rawal Institute of Health Sciences, Islamabad and Pakistan Institute of Medical Sciences, Islamabad between May 2021 to Sep 2021 on 100 adult male and female of COVID-19 patients having blood hemoglobin level < 10 g/dl. For different doses of dexamethasone patients were divided into two groups of 50 patients in each group. Blood samples were taken on day 01 and day 15 for hemoglobin analysis. Mean and standard deviation of both groups was calculated and p-value of < 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. Mean Hemoglobin (Hb) levels of both groups were compared on day 01 and day 15 respectively. The comparison of Hb levels showed a significant difference on day 15, there was a marked increase in Hb levels in the group which was taking 12mg/day of dexamethasone as compared to the group which was taking 6mg/day of dexamethasone (P-value < 0.05). **Conclusions:** Administration of high doses of Dexamethasone caused a pronounced increase in hemoglobin levels in COVID-19 patients.

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. 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 6.67% 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 \pm standard deviation (mean \pm 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.

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

Presenting Complaints	Group 1 (n=50) N (%)	Group 2 (n=50) N (%)
Cough	33 (66%)	41 (82%)
Fever	40 (80%)	49 (98%)
Increased Heart Rate	50 (100%)	48 (96%)
Fatigue	50 (100%)	50 (100%)

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

Groups	Day 1 (Serum Hb) g/dL	Day 15 (Serum Hb) g/dL	p-Value
Group 1	8.95 ± 0.497	8.99 ± 0.562	0.64
Group 2	8.07 ± 0.32	9.46 ± 0.67	0.00 *

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 $p < 0.05$.

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

Test (g/dl)	Time Points	Group 1	Group 2	p-Value
Serum Hb	Day 1	8.95 ± 0.497	8.07 ± 0.32	0.00
	Day 15	8.99 ± 0.562	9.46 ± 0.67	0.00

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

Groups (n=100)	Hb (g/dl) Day 01	Hb (g/dl) Day 15	Increase in Hb (%)
Group 1 (n=50)	8.95 ± 0.497	8.99 ± 0.562	0.4 %
Group 2 (n=50)	8.07 ± 0.32	9.46 ± 0.67	17%

DISCUSSION

In our study we have seen that at the time of admission 100 % of the patients presented with fatigue and 98% of them presented with increased heart rate. 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. Salari 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 12 mg 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 12 mg /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.

Bahsoun A *et al.*, said that one of the beneficial outcomes of steroids is that they reduce morbidity, mortality and have anti-inflammatory effect preventing further complication in COVID-19 patients [19, 20]. In our study we have seen that high dose of dexamethasone caused more increase in hemoglobin level compared to low dose Karam D *et al.*, used high dose of steroids for correction of anemia and concluded that hemoglobin level was not improving but after increasing the dose of steroids there was improvement in the hemoglobin levels [20, 21]. The steroids are used in multiple blood disorder diseases and it was seen that they increase red cell production Ashley R *et al.*, in one of his research said that dexamethasone augments hemoglobin by increasing the expansion and average size of erythrocyte colony forming units causing increase in red cell production [21, 22]. A study conducted on the physiological and pharmacological effects of corticosteroids suggested that the increase in blood hemoglobin by steroids may be due to retarding or reducing phagocytosis of erythrocytes [23]. Steroids improve hemoglobin and correct anemia this may be due to their effect on bone marrow causing an increase in erythropoiesis [24]. In this study although the patients were using pain killers and antibiotics for the treatment of corona but their hemoglobin levels and symptoms improved rapidly after taking steroids. In future we can recommend steroids to be added in the treatment of anemia and correction of hemoglobin level.

CONCLUSIONS

Dexamethasone in high doses of 12mg /day caused more improvement in hemoglobin levels lowered by corona virus compared to low dose of dexamethasone 6mg/day in COVID-19 infected patients.

Authors Contribution

Conceptualization: ZRC

Methodology: ZRC, SS¹, SS², SS³, NS

Formal analysis: ZRC, SS¹, SS², SS³, ER, HNL

Writing, review and editing: ZRC, SS¹, SS², SS³, ER, HNL

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

- [1] Keam S, Megawati D, Patel SK, Tiwari R, Dhama K, Harapan H. Immunopathology and immunotherapeutic strategies in severe acute respiratory syndrome coronavirus 2 infection.

- Reviews in Medical Virology. 2020 Sep; 30(5): e2123. doi: 10.1002/rmv.2123.
- [2] Li H, Wang Y, Ji M, Pei F, Zhao Q, Zhou Y *et al.* Transmission routes analysis of SARS-CoV-2: a systematic review and case report. *Frontiers in Cell and Developmental Biology*. 2020 Jul; 8: 618. doi: 10.3389/fcell.2020.00618.
- [3] Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP *et al.* A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military Medical Research*. 2020 Dec; 7: 1-23. doi: 10.1186/s40779-020-0233-6.
- [4] Rahman HS, Aziz MS, Hussein RH, Othman HH, Omer SH, Khalid ES *et al.* The transmission modes and sources of COVID-19: A systematic review. *International Journal of Surgery Open*. 2020 Jan; 26: 125-36. doi: 10.1016/j.ijso.2020.08.017.
- [5] Hopp MT, Domingo-Fernández D, Gadiya Y, Detzel MS, Schmalohr BF, Steinbock F *et al.* Unravelling the debate on heme effects in COVID-19 infections. *bioRxiv* 2020 Jun; 10: 2020-06. doi: 10.1101/2020.06.09.142125.
- [6] Cavezzi A, Troiani E, Corrao S. COVID-19: hemoglobin, iron, and hypoxia beyond inflammation. A narrative review. *Clinics and Practice*. 2020 May; 10(2): 1271. doi: 10.4081/cp.2020.1271.
- [7] Mehta J, Rolta R, Mehta BB, Kaushik N, Choi EH, Kaushik NK. Role of Dexamethasone and Methylprednisolone Corticosteroids in Coronavirus Disease 2019 Hospitalized Patients: A Review. *Frontiers in Microbiology*. 2022 Feb; 13:813358. doi: 10.3389/fmicb.2022.813358.
- [8] Seo SJ and Priefer R. Dexamethasone Mechanism in Inflammatory Immune Mediated Disease and its Application in Treating 2019 Coronavirus Disease (COVID-19). *Medical Research Archives*. 2020 Dec; 8(12): 2020. doi: 10.18103/mra.v8i12.2267.
- [9] Zhang G, Su L, Wu W, Qiao Q, Gao S, Zhang Y *et al.* Efficacy of different doses of corticosteroids in treating severe COVID-19 pneumonia. *Virology Journal*. 2024 Mar; 21(1): 74. doi: 10.1186/s12985-024-02345-7.
- [10] Salari N, Khodayari Y, Hosseinian-Far A, Zarei H, Rasoulpoor S, Akbari H, Mohammadi M. Global prevalence of chronic fatigue syndrome among long COVID-19 patients: A systematic review and meta-analysis. *BioPsychoSocial Medicine*. 2022 Oct; 16(1): 21. doi: 10.1186/s13030-022-00250-5.
- [11] Saeed U, Uppal SR, Piracha ZZ, Khan AA, Rasheed A, Zaheer H, Aftab Z, Uppal R. Effectivity analysis of SARS-CoV-2 nasopharyngeal swab rapid testing kits in Pakistan: A scenario of inadequate COVID-19 diagnosis. *Research Square*. 2021 Mar. [Preprint].
- [12] Shiravi AA, Saadat M, Abdollahi Z, Miar P, Khanahmad H, Zeinalian M. Vitamin D can be effective against COVID-19 and other similar viral infections: a review on molecular aspects. *Zenodo*. 2020 Mar; 92(2): 134-146. doi: 10.1024/0300-9831/a000676.
- [13] Paul P, Maiti D, Adhikary T. Iron deficiency anemia-An updated overview. *International Journal of Research in Pharmacy and Pharmaceutical Sciences*. 2021 Sep; 6(4): 28-33.
- [14] Miwa T, Hatano Y, Kochi T, Aiba M, Toda K, Goto H, *et al.* Spur cell anemia related to alcoholic liver cirrhosis managed without liver transplantation: a case report and literature review. *Clinical Journal of Gastroenterology*. 2020 Oct; 13: 882-90. doi: 10.1007/s12328-020-01142-3.
- [15] Russell L, Uhre KR, Lindgaard AL, Degn JF, Wetterslev M, Sivapalan P *et al.* Effect of 12 mg vs 6 mg of dexamethasone on the number of days alive without life support in adults with COVID-19 and severe hypoxemia: the COVID steroid 2 randomized trial. *The Journal of the American Medical Association*. 2021 Nov; 326(18): 1807-17.
- [16] Anai M, Akaike K, Iwagoe H, Akasaka T, Higuchi T, Miyazaki A *et al.* Decrease in hemoglobin level predicts increased risk for severe respiratory failure in COVID-19 patients with pneumonia. *Respiratory Investigation*. 2021 Mar; 59(2): 187-93. doi: 10.1016/j.resinv.2020.10.009.
- [17] Nóbrega F, Mauad VA, Borducchi DM. Does COVID-19 really impact on the oxy-hemoglobin dissociation curve? *eJHaem*. 2020 Nov; 1(2): 604-7. doi: 10.1002/jha2.126.
- [18] Russo A, Tellone E, Barreca D, Ficarra S, Lagana G. Implication of COVID-19 on erythrocytes functionality: red blood cell biochemical implications and morpho-functional aspects. *International Journal of Molecular Sciences*. 2022 Feb; 23(4): 2171. doi: 10.3390/ijms23042171.
- [19] Bahsoun A, Fakhir Y, Zareef R, Bitar F, Arabi M. Corticosteroids in COVID-19: pros and cons. *Frontiers in Medicine*. 2023 Aug; 10: 1202504. doi: 10.3389/fmed.2023.1202504.
- [20] Karam D, Swiatkowski S, Purohit P, Agrawal B. High-dose steroids as a therapeutic option in the management of spur cell haemolytic anaemia. *Case Reports*. 2018 Jan; 2018: bcr-2017. doi: 10.1136/bcr-2017-223281.
- [21] Ashley R, Yan H, Wang N, Hale J, Dulmovits BM, Papoin J, Olive M, Udeshi N, Carr S, Vlachos A, Lipton JM. Glucocorticoids Induce the Maintenance and Expansion of an Immature CFU-E Erythroid

- Progenitor Population in Humans. *Blood*. 2019 Nov; 134: 943. doi: 10.1182/blood-2019-130710.
- [22] Al-Ansari RY, Alromaih L, Osman M. Steroid induced hypertriglyceridemia in pregnant women with immune thrombocytopenia-case report. *Annals of Medicine and Surgery*. 2022 May; 77: 103636. doi: 10.1016/j.amsu.2022.103636.
- [23] NB, Bonne TC, Sørensen H, Bejder J. Glucocorticoids accelerate erythropoiesis in healthy humans—should the use in sports be reevaluated?. *Medicine and Science in Sports and Exercise*. 2023 Feb; 55(7): 1334-1341. doi: 10.1249/MSS.0000000000003156.
- [24] Hsu RJ, Yu WC, Peng GR, Ye CH, Hu S, Chong PC *et al.* The role of cytokines and chemokines in severe acute respiratory syndrome coronavirus 2 infections. *Frontiers in Immunology*. 2022 Apr; 13: 832394. doi: 10.3389/fimmu.2022.832394.