DOI: https://doi.org/10.53350/pjmhs22164121

ORIGINAL ARTICLE

Comparative Efficacy of High Dose Dexamethasone (8 mgx TDS) vs Low Dose Methylprednisoslone (100 mgx BD) Therapy in Patients with Covid Pneumonia

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ABSTRACT

Background: Around one and half years ago in the December of 2019 a flu like disease emerged in the city Wuhan located in China. This was termed by WHO as a global pandemic due to its rapid widespread.
Aim: To compare the efficacy of high dose dexamethasone (8 mgx tds) vs low dose methylprednisoslone (100 mgx bd) therapy for two weeks, in resolution of acute inflammatory markers in patients with covid pneumonia.
Study Design: Quasi experimental study.
Methodology: Patients (n=72) with an age range of 18-70 years with Covid 19 PCR positive having Covid associated pneumonia were enrolled. Group 1 containing 36 patients receiving high dose dexamethasone (8 mgx TDS) and group 2 with 36 participants receiving low dose methylprednisolone (100 mgx BD). Inflammatory markers (CRP, ESR and Ferritin) were recorded on Day 1 (T1) on day 7 (T2) and day 14 (T3). Patients who required ventillatory support and those who died was also recorded.All this information was recorded on Performa. Data was analyzed using SPSS version 26.
Results: Mean age of the patients was 50.11±11.7 years. When we compared the inflammatory markers among group 1 and group 2 at T1, T2 and T3 no statistically significant difference was obtained**.**
Conclusion: It was concluded that high dose dexamethasone and low dose methylprednisoslone therapy for two weeks were equally effective in resolution of acute inflammatory markers in patients with covid pneumonia.
Keywords: Covid, Pneumonia, High Dose Steroids and Inflammatory Markers.

INTRODUCTION

Around one and half years ago in the December of 2019 a flu like disease emerged in the city Wuhan located in China. This than was termed by World health organization as a global pandemic due to its rapid widespread occurrence on 12th March 2020 . This Covid-19 pandemic was latter recognized as a global health crisis after the outbreak of influenza in the year 1918[1]. This deadly disease has affected over 216 million individuals worldwide out of which around 4.9 million have died due to adverse effects associated with this virus[2].

Coronaviruses are single stranded, enveloped RNA viruses. On the basis of phylogenetics these viruses are grouped into four categories; alpha (α) coronavirus, beta (β) coronavirus, gamma (γ) coronavirus, and delta (δ) coronavirus[3]. Symptoms associated with SARS-CoV include fever, cough usually dry, dyspnea leading to the development of lower respiratory tract infection. Patients who were infected with this virus soon developed pneumonia, which progressed to pulmonary edema, acute respiratory distress syndrome and respiratory failure. Pneumonia associated with covid 19 is divided into mild, moderate and severe based on various clinical and radiological findings[4]. Usually the largest number of patients suffered from mild disease and recovered uneventfully. Around 19% of the individuals progressed to severe pneumonia and 14 % ended up having critical condition[5].

Antiviral and anti-inflammatory medications have been increasingly researched by the clinicians in the resolution of symptoms associated with covid 19 infection, due to its underlying pathophysiology. Uncontrolled replication of virus in the host cells and in turn a surge in the expression of immunomodulatory cells resulting in massive activation of cytokines results in a condition known as cytokine storm[6]. Corticosteroids have been previously utilized in the treatment of various inflammatory conditions (such as asthma, rheumatoid arthritis etc) owing to its proven anti inflammatory effects. Due to its increasing prevalence and debilitating effect on the quality of life of the patients, we designed this study.

Received on 10-09-2021
Accepted on 20-03-2022

The objective of the study was to compare the efficacy of high dose dexamethasone (8mgx tds) vs low dose methylprednisoslone (100mgx bd) therapy for two weeks, in resolution of acute inflammatory markers in patients with covid pneumonia.

METHODOLOGY

Present study was a quasi experimental study. Informed consent was taken from the patients or guardians prior to enrolling the patients into the study after permission from Ethical Review Board. Patients were divided into mild, moderate and severe pneumonia based on the clinical and laboratory findings. In the mild disease there is documented fever and upper respiratory disturbance with no hypoxic event and infiltration of xray chest. In moderate condition there is hypoxia (oxygen saturation <94%) and less than 50% infiltrates on chest x-ray. In severe condition patients usually need mechanical ventillatory support and may land up in multi organ damage.

Patients with an age range of 18-70 years with Covid 19 PCR positive having Covid associated pneumonia (moderate and severe only) admitted in the Covid ward, who never had to take corticosteroids in the past due to any medical condition were included into the study. Patients having severe immune compromised states such as HIV or those requiring immunosuppression therapies including corticosteroids (such as asthma, arthritis, Systemic lupus erythematosus) along with pregnant females were excluded from the study. Non-probability consecutive sampling technique was utilized in the data collection procedure. Patients were divided into two groups. Group-1 containing 36 patients receiving high dose dexamethasone (8 mgx TDS) and group-2 with 36 participants receiving low dose methylprednisolone (100mgx BD). Baseline investigations were repeated on day 7 (T2) and day 14 (T3). All this information was recorded on Performa.

Statistical Analysis: Data was analyzed using SPSS version 26.0. Mean and SD was calculated for variables such as Age, ferritin level, ESR level and CRP levels at T1, T2 and T3. Percentage and Frequency was calculated for variables (categorical) such as gender, requirement of ventillatory support

and outcome of the patient. Data Normality was assessed using Shapiro wilk test, which showed a parametric distribution of data. Comparison of efficacy of high dose dexamethasone (8 mgx tds) vs low dose methylprednisoslone (100 mgx bd) in resolution of acute inflammatory markers (CRP, ESR, FERRITIN) was carried out using Paired samples T test. Requirement of ventillatory support and outcome of patients among the two groups was assessed using chi square test. P-value of ≤0.05 was considered to be significant.

RESULTS

Out of total 72 patients 42(58.3%) were male and 30(41.7%) were female. Mean age of the patients was 50.11±11.7 years. Age range of the patients was 26 – 73 years. 55(76.4%) patients improved while 17(23.6%) died. 58(80.6%) patients never required ventillatory support however 14(19.4%) patients had to be put on ventilator during the study period. Group-1 had male predominance and group-2 showed female predominance (figure-1). However this difference was not statistically significant.

Inflammatory markers before, during and after treatment with dexamethasone and methylprednisolone were presented as mean ± SD (table-1).

Table-1: Mean values of inflammatory markers in 2 groups at T1, T2 and T3.

Parameter	Group-1			Group-2		
	T1	T2	T3	T1	T2	T3
CRP (mg/L)	136.60 ± 7.7	87.03 ± 6.9	24.64 ± 8.1	134.11 ± 6.9	89.2 ± 12.2	22.54 ± 5.0
Ferritin(ng/l)	930.05±58.5	566.83±134.2	342.36±93.89	906.02±64.4	459.5 ± 102.5	267.05 ± 74.9
ESR (mm/h)	74.94 ± 5.8	38.55 ± 7.7	22.75 ± 4.2	73.7 ± 4.9	39.58 ± 8.0	20.36 ± 3.9

The inflammatory markers among group 1 and group 2 at T1, T2 and T3 showed a significant reduction in values (table-2). Paired sample comparison of pre (T1) and post (T3) values of CRP, Ferritin and ESR revealed a statistically significant reduction in both groups (after treatment with dexamethasone as well as methyl prednisolone). However, There was no significant difference in efficacy of both treatment modalities in reduction of these inflammatory markers.

Table 2: Comparison of inflammatory markers before and after treatment with Steroids

Variables	Mean ± SD		p-value
	Dexamethasone	Methylprednisolone	
T1(pre treatment)			
CRP	136.60 ± 7.7	134.11 ± 6.9	0.6
Ferritin	930.05 ± 58.5	906.02 ± 64.4	0.04*
ESR	74.94 ± 5.8	73.7 ± 4.9	0.4
T3(post treatment)			
CRP	24.64 ± 8.1	22.54 ± 5.0	0.8
Ferritin	342.36 ± 93.89	267.05 ± 74.9	0.8
ESR	22.75 ± 4.2	20.36 ± 3.9	0.6

*Statistically Significant

Out of total 36 patients in group 1, 6 (16.67%) required ventilator and in group 2, 8(22.2%) required ventillatory support. However this difference was not statistically significant (p=0.7). Outcome among two groups is compared in Table-3.

Table 3: Comparison of Outcome of patients among groups

Groups	Death	Betterment	p value
Dexamethasone	8	28	0.5
Methylprednisolone	9	27	

DISCUSSION

Disease progression in covid 19 is associated with the severity of ongoing inflammatory response[7,8]. This response can be measured using various inflammatory biomarkers such as procalcitonin, c reactive protein, erythrocyte sedimentation rate, interleukin-6[9]. Cheng et al and Gao et al associated these inflammatory markers with severe covid 19 symptoms[10,11]. However these results were contradicted by the studies conducted by Zhang et al and Chen et al who found no significant correlation of these biomarkers with Covid 19 disease and symptoms[12,13].

In our study inflammatory markers (CRP, Ferritin, ESR) reduced in patients of both groups, those receiving dexamethasone and methyl prednisoslone. However this difference is not statistically significant. There was a slightly greater decrease in group 2 patients. Similar results were portrayed by Rana et al in his study, in which CRP before and after dexamethasone dosage was reduced from 110.34 mg/L to 19.54 mg/L as compared to the methylprednisolone receiving group which showed CRP reduction from 108.6 mg/L to 43.8 mg/L[14]. Fatima et al conducted a similar study where she followed the patients for 5 days and documented the reduction in CRP after giving dexamethasone and methylprednisolone. CRP reduced from 139.5 to 73.9 in dexamethasone receiving group and in methylprednisolone group the reduction was from 129.8 to 59.07[15].

Recovery trial conducted in UK on more than 4000 patients is the largest database available till now on Covid 19 patients. They compared outcome of dexamethasone with standard care protocol and found out that 22.9% patients in dexamethasone group expired which was relatively small as compared to the 25.7% mortality rate in the standard care group[16]. Outcomes and efficacy of methylprednisolone was studied in a retrospective cohort study carried out by Wang et al in Wuhan. He demonstrated a significant reduction in mortality and morbidity in patients who received methylprednisolone as compared to those who didn't[17].

A triple blind randomized clinical trial was conducted by Ranjbar et al[7]. He concluded that methylprednisolone demonstrated better clinical status scores as compared to dexamethasone. Pinzon et al in his study concluded that treatment of covid pneumonia with high dose methylprednisolone significantly reduced the recovery time and inflammatory markers as compared to dexamethasone[19]. Limitations of our study were that there was no control group. Blinding was not carried out for the participants or the observers. Long term follow up of these patients should have been carried out for the proper validation of the results and also that would help in the long term effects and safety of these medications in treating pneumonia associated with Covid 19 infection.

Limitations: Our study had limitations like financial constraints, lack of resources, genetic workup and short duration of study.

CONCLUSION

It was concluded that high dose dexamethasone and low dose methylprednisoslone therapy for two weeks were equally effective in resolution of acute inflammatory markers in patients with covid pneumonia.

Authors' Contribution: SAAG&NKN: Conceptualized the study, analyzed the data, and formulated the initial draft, **SHT&IR:** Contributed to the proof reading, **RS,MUR&TL:** Collected data.

Conflict of Interest: None to declare

Financial Disclosure: None

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