Original Research Article

Comparison of effects of oral methylprednisolone with oral prednisolone in Acute Exacerbations of COPD

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Abstract

Background: Exacerbations are common in Chronic Obstructive Pulmonary Disease. Corticosteroids are the mainstay of therapy for treatment of acute exacerbation of COPD. In the present study we compared the effects of 32mg oral methylprednisolone and an equivalent dose of 40mg oral prednisolone in patients with AECOPD. **Methodology:** This was an analytical, experimental study conducted on 44 inpatients of AECOPD at a tertiary care centre in central India over a period of one and a half years. Patients were divided into two groups: Group A received 32mg methylprednisolone and Group B received 40 mg prednisolone for five days. **Results:** Both methylprednisolone and prednisolone were equally effective in relieving AECOPD symptoms at the end of day 5 (Group A: 72.2% vs Group B: 86.4%, p = 0.26). Mean length of hospital stay was similar in both the groups (Group A: 9.09 days vs Group B: 8.77 days, p = 0.68). There was no difference in the number of patients who failed treatment in both the groups (Group A: 72.7% vs Group B: 86.4%, p>0.26). The number of days on O_2 was similar in both the groups (Group A: 5.55 days vs Group B: 5.14 days, p = 0.46). O_2 free days was also similar in both the groups (Group A: 3.55 days vs Group B: 3.64 days, p = 0.64). Majority of the patients did not have any adverse effect (Group A: 59.9% vs Group B: 72.7%, p = 0.051). **Conclusion:** Prednisolone and Methylprednisolone had similar effects in AECOPD.

Keywords: AECOPD, prednisolone, methylprednisolone, LOHS.

Introduction

Exacerbations are common in Chronic Obstructive Pulmonary Disease. An exacerbation is described as worsening or flareup of symptoms of COPD. Acute exacerbations are frequent cause of hospitalization and significantly affect quality of life of an affected individual[3]. Exacerbations are associated with cumulative worsening of lung function over a period of time[12]. Corticosteroids are the mainstay of therapy for treatment of acute exacerbation of COPD. Corticosteroids improve the symptoms of COPD by reducing systemic inflammation and associated airway narrowing, thereby, improving oxygenation and lung function (FEV1). Corticosteroids also help in reducing length of hospital stay[6]. Though, corticosteroids are beneficial in management of AECOPD, they are associated with various adverse effects such as hypertension, raised blood glucose levels, fluid retention, delirium etc[13]. Very few studies have directly compared the effects of two different oral corticosteroids on clinical outcomes in patients with Acute Exacerbation of COPD. The present study was, therefore, conducted at a tertiary care centre to compare the effects of oral methylprednisolone with that of an equivalent dose of oral prednisolone in patients with AECOPD.

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Material and Methods

Study Design

This was a prospective analytical, experimental study done at a tertiary care centre in central India, from December 2019 to May 2021. After approval from the Institutional Ethical Committee, the study was registered in clinical trial registry of India (approval No. CTRI/2020/05/025292).

Patients over 40 years of age diagnosed with Acute Exacerbation of COPD and admitted in Pulmonary Medicine ward were included in the study. Patients of COPD with Pneumonia, pneumothorax, cardiac disease, history of asthma, those not giving consent , those unable to take oral corticosteroid , those on corticosteroid within the past 1 month and patients who had hospital stay less than 5 days were excluded from the study. Forty four patients with AECOPD were included in the study.

Socio demographic characteristics such as age, gender, residence, socioeconomic status were noted. Detailed clinical history regarding COPD, duration of COPD, history and duration of smoking, frequency of exacerbation, family history of COPD were documented. Acute exacerbation of COPD was defined according to the GOLD 2019 guidelines. Severity of COPD was defined according to Burge et al scale (2003).

Classification of severity of COPD according to Burge S et al (2003)[4]

A scale for exacerbation severity incorporating exacerbations managed at home and in hospital.

Table 1: Classification of severity of COPD

Mild	An exacerbation treated with antibiotics but no systemic corticosteroid. If no blood gases are available theabsence of respiratory failure is assumed
Moderate	An exacerbation treated with parenteral corticosteroids with or without an antibiotic. If no blood gases areavailable the absence of respiratory failure is assumed
Severe	Type 1 respiratory failure with hypoxaemia but no carbon dioxide retention or acidosis; Pa,O2v8 kPa (60 mmHg) and Pa,CO2v6 kPa (45 mmHg)
Very severe	Type 2 respiratory failure, compensated with hypoxia, carbon dioxide retention but no acidosis; Pa,O2v8 kPa(60 mmHg), Pa,CO2w6 kPa (45 mmHg) and hydrogen ion concentrationv44 nM (pHw7.35)
Life-threatening	Type 2 respiratory failure, decompensated with acidosis and carbon dioxide retention; Pa,CO2w6 kPa (45 mmHg)and hydrogen ion concentrationw44 nM (pHv7.35)

After explaining the nature and purpose of study written consent were obtained from all the study participants. Assignment of the group was done by systematic randomization which matched patients in terms of age, sex and severity of COPD.

•**Group A** - received 32mg/d methylprednisolone for 5 days.

•**Group B** - received equivalent dose of prednisolone equal to 40mg/d for 5 days;

Both the groups received similar treatment for AECOPD.

All patients received nebulized bronchodilators and systemic antibiotics. Glucometer blood sugar charting was done three times daily. Before breakfast, 2hr after lunch and 2hr after dinner. Oral cavity of patients were examined daily. Patients were questioned about difficulty in micturition and any gastric symptoms.

At the end of therapy symptom relief, length of hospital stay, treatment failure and adverse events were compared in the two groups.

Statistical analysis

Data was compiled and analysed using IBM SPSS software version 20. Categorical variables were expressed as frequency and proportions whereas continuous variables were expressed as mean and SD. Chi square test was applied to assess the difference in proportions between two groups whereas difference in mean between two groups was assessed using independent t test. P value less than 0.05 was considered statistically significant.

Results

The mean age in both groups was similar (Group A 58.95 ± 9.21 years, Group B 61.45 ± 9.41years p>0.05). Majority of the patients in group A were 61 to 70 years of age whereas in group B, patients were equally distributed in all age groups. There was no difference in the age composition between the two groups. In the age group ≥ 70 years Group B had more patients than Group A. More than 80% of the patients irrespective of treatment groups were males. The gender composition was similar (p>0.05). (Table – 2)

Table 2: Baseline characteristics of the study population

		Group A (n =22)	Group B (n=22)	P value
Age (years)	≤ 50	5 (22.7%)	5 (22.7%)	0.19
	51 – 60	6 (27.3%)	5 (22.7%)	
	61 – 70	10 (45.5%)	6 (27.3%)	
	≥ 70	1 (4.5%)	6 (27.3%)	
	Mean ± SD	58.95 ± 9.21	61.45 ± 9.41	
Gender	Male	18 (81.8%)	20 (90.9%)	0.38
	Female	4 (18.2%)	2 (9.1%)	
Mean SpO2 at Admission		84	85	0.57

Relief of symptoms was assessed at the end of day five of steroid treatment. We observed that majority of the patients had symptom relief at the end of day five (Group A 72.7% vs Group B 86.4%, p = 0.26). Equal number of patients in both the groups had symptom relief at the end of steroid course. (Table – 3)Mean length of hospital stay was similar in both the groups (Group A 9.09 days vs Group B 8.77 days, p = 0.68) .(Table - 3) There was no difference in the number of patients who failed treatment in both the groups (Group A: 6 patients vs. Group B: 3 patients, p = 0.26). (Table - 3)

Table 3: Comparison of relief of symptoms, length of hospital stay and treatment failure between the two treatment groups

		Group A (n =22)	Group B (n=22)	P value
Relief of symptoms	No	6 (27.3%)	3 (13.6%)	0.26
	Yes	16 (72.7%)	19 (86.4%)	
LOHS	Mean ± SD	9.09 ± 3.84	8.77 ± 5.53	0.68
Treatment failure	No	16 (72.7%)	19 (86.4%)	0.26
	Yes	6 (27.3%)	3 (13.6%)	

Majority of the patients did not have any adverse effect. The only adverse effect in patients on prednisolone was hyperglycemia. Hyperglycemia was less frequent with methylprednisolone than with prednisolone. However, patients on methylprednisolone had other adverse effects, which were not seen with prednisolone, such as gastritis, oral candidiasis and UTI. (Table – 4)

Table 4: Comparison of adverse effects

Adverse effects	Group A (n =22)	Group B (n=22)
Gastritis	2 (9.1%)	0 (0)
Hyperglycemia	2 (9.1%)	6 (27.3%)
Oral Candidiasis	2 (9.1%)	0 (0)
UTI	3 (13.6%)	0 (0)
None	13 (59.1%)	16 (72.7%)
P value	0.051	

Discussion

This was a prospective, analytical, experimental study done at a tertiary care centre in central India to compare the effects of two different oral corticosteroid in AECOPD. Forty four AECOPD patients were included in the study done over a period of one and a half years from December 2019 to May 2021.

Mean age of patients with COPD in methylprednisolne group was 58.95 ± 9.21 years and that in prednisolne group was 61.45 ± 9.41 years (p = 0.19). Majority of the cases with AECOPD were elderly. More than 80% of the patients in both the groups were males.

Relief of symptoms was assessed at the end of day five of steroid treatment. We observed that five days of oral steroid was adequate in achieving relief of symptoms. Equal number of patients in both the groups had significant symptom relief with a five day course of either steroid. In the REDUCE trial, five days of systemic glucocorticoid was non-inferior to 14 days of conventional treatment with systemic glucocorticoid[7]. Ardestani et al (2017) observed similar efficacy of methylprednisolone and dexamethasone in providing symptomatic relief, although methylprednisolone seemed to work better on cough predominant patients and dexamethasone in sputum predominant patients[1].Treatment failure was infrequent with both the steroids. There was no difference in the number of patients who failed treatment in both the groups (Group A: 6 patients vs Group B: 3 patients, p>0.26). Only four out of 40 patients in Ceviker et al study failed five days systemic corticosteroid therapy. These patients required an extended duration of steroids[5].Though corticosteroids are beneficial in providing immediate symptomatic relief, they are associated with certain side effects[14]. In our study, majority (29/44 patients) did not have any adverse effect. The only side effect in patients on prednisolone was hyperglycemia. Six patients in the prednisolone group developed hyperglycemia. Hyperglycemia was less frequent with methylprednisolone (2 out of 22 patients). However, patients on methylprednisolone had other adverse effects, which were not seen with prednisolone, such as gastritis, oral candidiasis and UTI. These adverse effects were not seen with prednisolone, probably, because of small sample size.Leuppi et al (2013) observed that patients on **7** day short course corticosteroid therapy compared to longer conventional 14 day therapy had lower risk of hyperglycemia and hypertension. This was attributed to low cumulative dose of prednisolone[7]. In our study all patients received five days of oral corticosteroid. Hence, hyperglycemia was uncommon.Niewoehner et al (1999) studied 271 patients of AECOPD**.** Hyperglycemia was the most common adverse event associated with systemic corticosteroid followed by secondary infection and myopathy. In this study patients received longer course of steroid of either 2 weeks or 8 weeks[9].Since we used shorter regimen of steroid, secondary infection and myopathy were not seen.

Myopathy and secondary infections are more frequent at higher doses and longer duration of steroids[9].Both the treatment strategies were equally effective in improving oxygen saturation. The mean duration of oxygen therapy (Group A: 5.55 days vs Group B: 5.14 days, p = 0.46) and oxygen free days (Group A: 3.55 days vs Group B: 3.64 days, p = 0.64) were also identical between the two groups.In a study by Li et al (2003) mean SpO_2 improved within 7 days of methyl prednisolone and dexamethasone therapy, but the improvement was significantly better in methyl prednisolone group[8]. Renil et al (2020) studied 64 patients of AECOPD. One group (32 patients) was given methylprednisolone and the other group (32 patients) prednisolone**.** They found that methylprednisolone was better than prednisolone at improving oxygen saturation[10].Previous studies have shown that corticosteroids reduced length of hospital stay in AECOPD[10,13].In our study we found that mean Length of Hospital stay was similar in both the groups (Group A: 9.09 days vs Group B: 8.77 days, p = 0.68). In a study by Aggarwal et al (2021)**,** 97 patients of AECOPD in emergency department, were randomly divided into two groups. 50 patients in Group 1 received intravenous hydrocortisone followed by oral prednisolone for 2 wks and 47 patients in Group 2 received intravenous methylprednisolone followed by Oral methylprednisolone. The emergency department length of stay was similar in both the groups (11.7 ± 6.96 hours in Group A and 13.5 ± 9.18 hours in Group B, p = 0.285)[2].Our study has certain limitations. Small sample size inhibits the generalization of the study. Other confounding variables like smoking history, occupation etc. were not matched / accounted for in this study.

Conclusion

Both 32 mg oral methyl prednisolone and 40 mg oral prednisolone are equally effective in AECOPD. Since, the efficacy, treatment failure, length of hospital stay and adverse events were similar with both methylprednisolone and prednisolone. Five days of either steroid may be used in AECOPD.

References

1. Ardestani ME, Kalantary E, Samaiy V, Taherian K. Methyl prednisolone vs dexamethasone in management of COPD exacerbation; a randomized clinical trial. Emergency. 2017;5(1).
2. Aggarwal P, Wig N, Bhoi S. Efficacy of two corticosteroid regimens in acute exacerbation of chronic obstructive pulmonary disease. Int J Tuberc Lung Dis. 2011 May;15(5):687-92.
3. American Thoracic Society. 2018 Available from: http://livebetter.org
4. Burge S, Wedzicha JA. COPD exacerbations: definitions and classifications. European Respiratory Journal. 2003 Jun 1;21(41 suppl):46s-53s.
5. Ceviker Y, Sayiner A. Comparison of two systemic steroid regimens for the treatment of COPD exacerbations. Pulm Pharmacol Ther. 2014 Apr;27(2):179-83.
6. GOLD COPD 2021 strategy | Independent professional body guideline | Guidelines [Internet]. Available from: https://www.guidelines.co.uk/respiratory/gold-copd-2021-strategy/455088. article
7. Leuppi JD, Schuetz P, Bingisser R, Bodmer M, Briel M, Henzen C, Leibbrandt Y, Maier S, Miedinger D. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. JAMA. 2010;309(21):2223-31.
8. Li H, He G, Chu H, Zhao L, Yu H. A step-wise application of methylprednisolone versus dexamethasone in the treatment of acute exacerbations of COPD. Respirology. 2003;8(2):199-204.
9. Niewoehner DE, Collins D, Gross NJ, Light RW, Anderson P, Morgan NA. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. New England Journal of Medicine. 1999 ;340(25):1941-7.
10. Niewoehner DE. The role of systemic corticosteroids in acute exacerbation of chronic obstructive pulmonary disease. Am J Respir Med. 2002;1(4):243-8.
11. Renil CS, Tom N, Rahul R, Chacko1 BK, George D, Mathews SM. Comparison of efficacy of methyl prednisolone and prednisolone oral therapy in exacerbation of chronic obstructive pulmonary disease. World J. Phar. & Pharmaceutical Sci. 2020; 9 (4); 553-60.
12. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. Chest. 2000 May;117(5 Suppl 2):398S-401S.
13. Walters JA, Tan DJ, White CJ, Gibson PG, Wood-Baker R, Walters EH. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2014 Sep 1;(9):CD001288.
14. Yasir M, Goyal A, Bansal P, Sonthalia S. Corticosteroid Adverse Effects. 2021 Jul 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021:1.

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