Original Article

A Comparative Study between Intramuscular and Oral Methylprednisolone Acetate in the Treatment of Asthma Exacerbation Following Discharge from the Hospital

Kishore Kumar K[1], Sai Samrat K[2], Sony Reddy S[3]

[1] Assistant Professor
[2, 3] Junior Resident
Department of
Pulmonary Medicine
Chalmeda Anand Rao
Institute of Medical Sciences
Karimnagar-505 001.
Telangana, India.

CORRESPONDENCE :

[1] Dr.K.Sai Samrat
Junior Resident
Department of Pulmonary Medicine
Chalmeda Anand Rao
Institute of Medical Sciences
Karimnagar-505 001
Telangana, India.
E-mail: saisamratk.78@gmail.com

ABSTRACT

Aims and Objectives: To compare the efficacy of long acting Intamuscular methylprednisolone to tapering oral doses of methylprednisolone in reducing the relapse rates in adult asthmatic patients discharged from the hospital following an exacerbation.

Materials and Methods: This comparative study was conducted in the Department of Pulmonology in Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar from November 2015 to June 2017. This comparative study was conducted on 100 known asthma patients having asthma exacerbations.

Results: 10 day relapse rates are 14.58% (95% CI=4.6% to 24.56%) and 14.28% (95% CI=4.48% to 24.08%) with intramuscular and oral methylprednisolone preparations respectively. 21 day relapse rates are 18.75% (95% CI = 7.71% to 29.79%) and 20.40% (95% CI=9.12% to 31.68%) with intramuscular and oral methylprednisolone respectively.

Conclusion: Single-dose IM methylprednisolone administered to adult asthmatic patients at ED discharge appears to be a viable therapeutic alternative to a course of oral methylprednisolone.

Keywords: Asthma exacerbation, intramuscular methylprednisolone, oral methylprednisolone, relapse

INTRODUCTION

Asthma is a common, chronic respiratory disease affecting 1-18% of the population in different countries.[1] It is characterised by pulmonary symptoms like breathlessness, wheezing, cough and chest tightness, reversible airway obstruction, and evidence of bronchial hyper-reactivity.

Asthma is the 14th most important disorder in the world in terms of extent and duration of disability. 334 million people worldwide suffer from asthma. Among them 8.6% of young adults (aged 18-45) experience asthma symptoms. The burden of asthma is greatest for children aged 10-14 and the elderly aged 75-79.2.

The prevalence of asthma has increased dramatically and asthma is now regarded as a major public health problem. There is sufficient evidence from meta-analysis[3] to support the administration of steroids to patients who have been discharged from emergency department following treatment for asthma exacerbations.

Despite the proven therapy with steroids, the relapse rates for asthmatic patients remain high.[4] A single IM dose of a long acting corticosteroid may offer the advantage of sustained drug level, eliminating the need for a pharmacy visit, and may reduce non- adherence.[5, 6]

Earlier work[6] has suggested a role for corticosteroids with a depot-repository release given via the IM route in

asthmatic patients who have been discharged from the ED. Although these previous studies have reported results ranging from a 20% difference in relapse rate at 7 to 10 days favouring IM administration to a 6% difference favouring oral administration, none achieved statistical significance, and all were accompanied by wide confidence intervals (CIs).

Consequently, the question of whether the IM repository administration of corticosteroids is of greater, less, or equal efficacy when compared to oral administration of corticosteroids has not yet been answered.

So, we have taken up this study to compare the efficacy of long acting Intamuscular methylprednisolone to tapering oral doses of methylprednisolone in reducing the relapse rates in adult asthmatic patients discharged from the hospital following an exacerbation.

MATERIALS AND METHODS

The present study was conducted in the department of pulmonology, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar from November 2015 to June 2017. This study was a prospective, comparative study conducted on 100 known asthma patients having asthma exacerbations.

The patients were enrolled from emergency department (ED) after completion of their emergency therapy according to the inclusion and exclusion criteria.

Inclusion Criteria

1. Both males and females
2. Age 18-45 years
3. Peak expiratory flow rate (PEFR) of less than or equal to 70% predicted during the hospital visit, and a minimum PEFR of 40% predicted

Exclusion Criteria

1. Patients with other chronic lung diseases
2. Known or suspected bacterial pneumonia
3. History of systemic corticosteroid therapy in the past month
4. Who had a current illness precluding use of corticosteroids
5. Who currently used Theophylline, Mast cell stabilizers, or Inhaled anticholinergic
6. Patients with Methylprednisolone allergy

STUDY METHOD

Patients fulfilling the inclusion and exclusion criteria were included in the study. Written, informed consent was taken from all the study participants. Initial peak expiratory flow rate was recorded by using a peak flow meter. All patients received the standard emergency department treatment for Asthma exacerbations. Patients were considered for discharge if their clinical status was stable and Peak flow rates were more than 60% predicted. At the time of discharge from the emergency department, the patients were prescribed inhalers and systemic steroids. The first patient in the study was given intramuscular methylprednisolone 160 mg single dose.

The second patient in the study was instructed to take 8-day oral tapering doses of Methylprednisolone. The subsequent patients were given intramuscular and oral preparations alternately (i.e., odd numbers in the study received intramuscular corticosteroid and even numbers received oral corticosteroid). The protocol for oral Methylprednisolone tapering was as follows: day 1, 32 mg; day 2, 32 mg; day 3, 24 mg; day 4, 24 mg; day 5, 16 mg; day 6 16 mg; day 7, 8 mg; day 8, 8 mg (total oral methylprednisolone dose 160 mg).

The injection was reconstituted in the emergency department and administered by an emergency department nurse. Patients receiving the oral tapering dose were instructed to start oral therapy when they arrive home. They were given written instructions in English and Telugu explaining the study and how to take oral methylprednisolone.

Before discharge, patients were interviewed regarding history of asthma, smoking, and asthma medications. Contact numbers of the participants and their family members were taken and follow up was done regularly for 21 days.

The primary end point of the study was relapse, which is defined as the need to seek unscheduled care at the doctor's clinic or ED for symptoms of persisting or worsening asthma within 10 days of ED discharge. The secondary end point was relapse between 11 and 21 days. Additional information obtained during the follow-up period was pain, swelling or bruising at the injection site.

Permission to conduct the study was obtained from Institutional Ethics committee(IEC), Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar. Informed oral consent was obtained from all patients.

RESULTS

Table 1 : The Study Sample

Total Number of Patients included in the Study	100
Patients Excluded	3
Total Study Sample	97
Causes of Exclusion	
Patients Excluded	2
Total Study Sample	1

Table 2: Age distribution

Age in Years	Count
20-24	12 (12.37%)
25-29	15 (15.46%)
30-34	20 (20.62%)
35-39	19 (19.59%)
40-45	31 (31.96%)

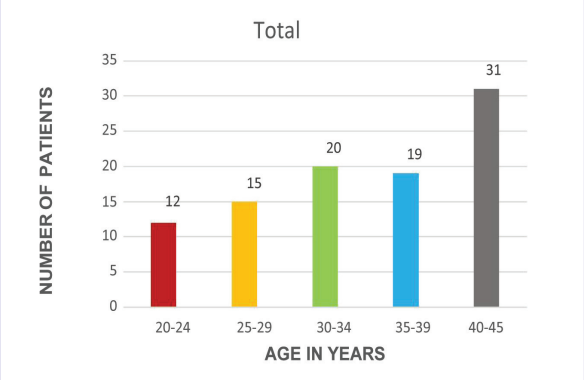

FIGURE 1: Age distribution

The age group of patients presenting in this study are 12 (12.37%) in 20-24 age group, 15 (15.46%) in 25-29 age group, 20 (20.62%) in 30-34 age group, 19 (19.59%) in 35-39 age group, 31 (31.96%) in 40-45 age group. The mean age at presentation was 34±7 years.

Table 3: Sex Distribution

Sex	Count
Male	42 (43.3%)
Female	55 (56.7%)

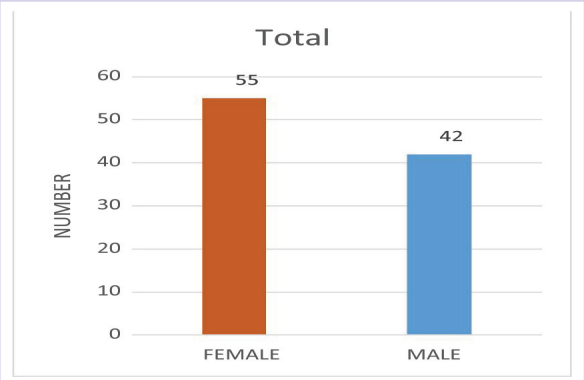

Figure 2: Sex Distrtibution

In this study, 42 (43.3%) are male and 55 (56.7%) are female.

Table 4 : Duration of Asthma in Years

Duration in Years	Count
0-9	28(28.9%)
10-19	53(54.6%)
20-29	15(5.5%)
30-39	1(1%)

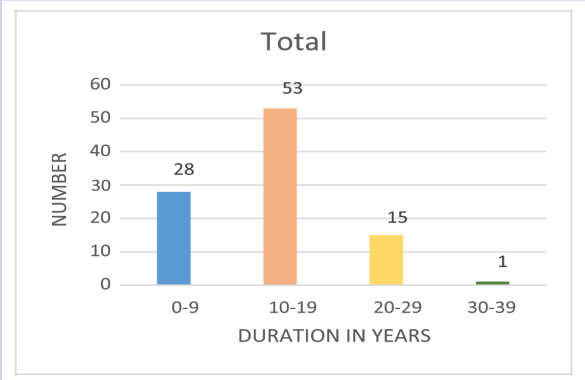

Figure 3: Duration of Asthma in Years

The majority of patients (54.6%) in the sample group are suffering from asthma since 10-19 years. mean duration of asthma is 12.55 ± 6.4years.

Table 5 : PEFR Percentage Predicted at the Time of Hospital Visit

PEFR percentage predicted	Count
<50%	33(34%)
>50%	64(66%)

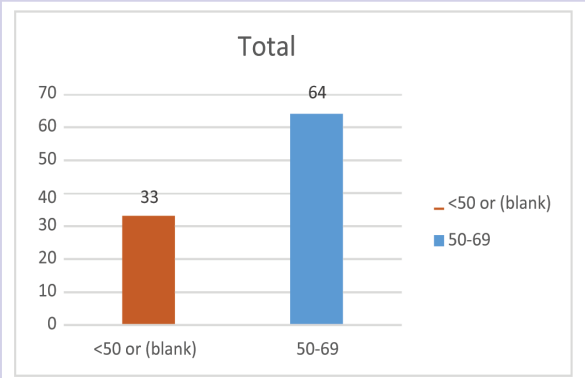

Figure 4 : PEFR Percentage Predicted at the time of hospital visit

At the time of admission, 33 patients (34%) have a predicted PEFR of less than 50% and 64 patients (66%) have a predicted PEFR of more than 50%. The mean PEFR is 276.4± 42 L/min

Table 6 : Relapse Rate at 10 Days

Relapse Rate	Intramusular Methylprednisolone	Oral Methylprednisolone
10 Days	14.58% (7/48)	14.28%(7/49)
	(95% CI=4.6% to 24.56%)	(95% CI=4.48% to 24.08%)

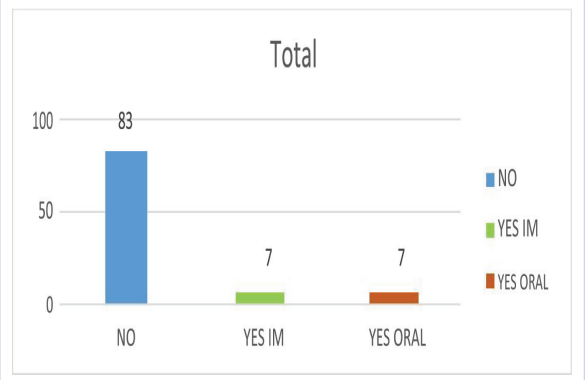

Figure 5 : Relapse rate at 10 days

10 day relapse rates are 14.58% (95% CI = 4.6% to 24.56%) and 14.28% (95% CI=4.48% to 24.08%) with intramuscular and oral methylprednisolone preparations respectively. 7 out of 48 patients had relapse in IM group. 7 out of 49 patients had relapse in oral group.

Table 7 : Relapse Rate At 21 Days

Relapse Rate	Intramusular Methylprednisolone	Oral Methylprednisolone
at 21 Days	18.75%(9/48)	20.40%(10/49)
	(95% Ci= 7.71% To 29.79%)	(95% Ci=9.12% To 31.68%)

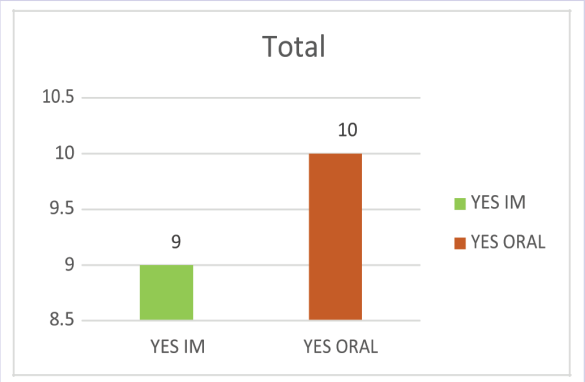

Figure 6 : Relapse rate at 21 days

21 day relapse rates are 18.75% (95% CI=7.71% to 29.79%) and 20.40% (95% CI=9.12% to 31.68%) with intramuscular and oral methylprednisolone respectively. 9 out of 48 patients had relapse in IM group. 10 out of 49 patients had relapse in oral group.

DISCUSSION

The results of the present study suggests that a single dose of depot methylprednisolone injection is a viable therapeutic alternative for the treatment of asthma patients who have been discharged from the pulmonary medicine department.

In the present study, out of 97 patients analysed, total number of patients who had relapse of asthma are 19 (19.6%), 9 relapses in the IM group and 10 in the oral group. On the 10th day, the total number of relapses in both intramuscular and oral methylprednisolone groups were found to be nearly the same. Seven members had relapse of asthma in both the groups.

The 10th day relapse rates in the intramuscular and oral group was 14.58% (95% CI=4.6% to 24.56%) and 14.28% (95% CI=4.48% to 24.08%) respectively. The difference in relapse rates was 0.3%. Although the oral preparation of methylprednisolone seems to be having better therapeutic effect on 10th day, the findings were not significant (p=0.803).

On the 21st day, the total number of relapses in intramuscular methylprednisolone group was nine (9/48) and in the oral methylprednisolone group was ten (10/49). Relapse rate in the intramuscular group and oral group was 18.75% (95% CI=7.71% to 29.79%) and 20.40% (95% CI=9.12% to 31.68%) respectively. The difference in the relapse rate was -1.65%. At 21 days, although the results favoured the intramuscular group, the findings were not significant (p=0.933).

This results were similar to other studies published earlier to the initiation of the present study although the percentage relapse rates was different in different studies.

Lahn et al[7] compared the efficacy of long acting IM methylprednisolone 160 mg depot preparation with 8-day oral tapering of a total dose of 160mg oral methylprednisolone in 190 adult asthmatic patients who were discharged from the ED following standardized treatment for exacerbation. They reported a relapse rate of 14.1% and 13.6% in the IM and oral group respectively with a difference in relapse rates of 0.5% and CI of -9.6 to 6%. They concluded that Intramuscular depot preparation of methylprednisolone appears to be a viable therapeutic alternative to a course of oral methylprednisolone in preventing relapses of asthma. The results of the present study is consistent with the results of Lahn et al, although the relapse rates are slightly differing. The p value was found to be not-significant in both the studies.

Table 8 : Comparison between present study and Lahn et al

Reference	Treatment Group	Follow uP	Relapse (%)
Lahn et al, 98 2004	Methylprednisolone acetate, 160mg IM, versus Methylprednisolone, 32mg PO with an 8-day taper	21 days	18.5% vs. 22.7% P= not significant
Present study	Methylprednisolone acetate, 160mg IM, versus Methylprednisolone, 32mg PO with an 8-day taper	21 days	18.75% vs. 20.40% P= not significant

Hoffman and Fiel[8] compared 7-day relapse rates among 18 asthmatic patients who had been discharged from an ED who were randomized to either a single 80-mg intramuscular dose of methylprednisolone or a 7-day oral taper of methylprednisolone. These authors reported no relapses in the IM group versus a 20% relapse rate among the orally treated patients. Although the 95% CI (-45 to 5%) surrounding the 20% difference in relapse rate favoured intramuscular over oral administration of methylprednisolone, the findings were not statistically significant and were too imprecise to support the conclusion that the IM route was superior. The major differences in the relapse rates may be due to the differences in the sample taken included in the study. They found intramuscular methylprednisolone was as effective as oral methylprednisolone in preventing relapse of asthma.

Table 9: Showing comparison between present study and Hoffman et al

Reference	Treatment Group	Follow uP	Relapse (%)
Hoffman et al, 99 1988	Methylprednisolone acetate, 80mgIM, vs. methylprednisolone, 32mg BID PO with an 8-day taper	5-7 days	20.0% vs. 0%, P= not significant
Present study	Methylprednisolone acetate,160mg IM, versus methylprednisolone,32mg PO with an 8-day taper	21 days	18.75% vs. 20.40% P= not significant

Lee et al [9] conducted a randomized controlled trial and compared 7-day relapse rates among 52 asthma patients who had been discharged from an emergency department. They were randomized to one of the following three arms: seventeen patients received a single 10-mg intramuscular dose of dexamethasone; nineteen patients received an 8-day oral taper of dexamethasone; and sixteen patients received placebo administered both intramuscular and orally. These authors reported a 6% relapse rate among the IM administration patients versus no relapses in the oral administration group (difference in relapse rate, 6%). The 95% CI of -5 to 17% indicated that these findings trended in a direction that was the opposite of the data from the study by Hoffman and Fiel, but were also neither statistically significant nor sufficiently precise to support the conclusion that the oral route was superior to an IM injection.

Table 10: Comparison between present study and Lee et al

Reference	Treatment Group	Follow up	Relapse (%)
Lee et al., 100 1992	Dexamethasone, 10 mg IM, Vs. dexamethasone, 1.5 mg BID PO with an 8-day taper, vs. double placebo (IM and PO)	7 days	5.9% vs. 6.2%, P=not significant
Present study	Methylprednisolone acetate,160mg IM, versus methylprednisolone,32mg PO with an 8-day taper	21 days	18.75%vs. 20.40% P= not significant

Combining relapse rates of Hoffman and Fiel and Lee et al in a subset meta-analysis of oral versus IM corticosteroid administration, Rowe et al [10] reported a pooled odds ratio of 0.82 (95% CI, 0.05 to 13.77), indicating that there was no detectable quantitative or statistical difference between the two routes of administration. Despite the close proximity of the odds ratio to the null of 1.00, the width of the confidence interval bounding this point estimate indicates that either the intramuscular or oral route might still be associated with clinically important, although undetected, differences in relapse rates.

Schuckman et al [11] compared relapse rates at 7 to 10 days among 168 asthmatic patients who had been discharged from an ED, and had been randomized either to a single 40-mg IM dose of triamcinolone or to 5 days of prednisone therapy at 40 mg/d without a taper. Of the 154 patients

available for analysis, there were no differences between the two patient groups with regard to demographics, smoking history, weight, or symptom severity. Mean initial peak flows were 244±64 L/minute for the triamcinolone group and 245±83 L/minute for the prednisone group. Fifty percent of the study patients were current smokers.

These authors reported a 9% relapse rate in the IM group versus a 15% relapse rate among those allocated to oral administration. Although the 95% CI (16 to 5%) surrounding the 6% difference in relapse rates slightly favoured IM over oral administration, this finding was not statistically significant. Despite the increased precision, which was driven by the larger sample size of the study by Schuckman et al, the CIs remained too wide to support the inference that the two routes of administration possessed equivalent efficacy.

These authors concluded, however, that a single IM dose of dexamethasone appeared to be an "attractive alternative" when compliance with an oral regimen was of concern.

Table 11: Comparison between present study and Shuckman et al

Reference	Treatment Group	Follow Up	Relapse (%)
Shuckman et al., 1998	Triamcinolone diacetate 40 mg IM, Vs. prednisone, 40 mg/d PO for 5 days	7 days	9.0% vs.14.5% P=not significant
Present study	Methylprednisolone acetate, 160mg IM, versus methylprednisolone, 32mg PO with an 8-day taper	21 days	18.75%vs. 20.40% P= not significant

CONCLUSION

Single-dose IM methyl prednisolone administered to adult asthmatic patients at ED discharge appears to be a viable therapeutic alternative to a course of oral methylprednisolone. Long acting repository preparations offers an advantage of sustained drug level, eliminating the need for a pharmacy visit, and may reduce non-adherence.

CONFLICT OF INTEREST :

The authors declared no conflict of interest.

FUNDING : None

REFERENCES

1. Global Initiative for Asthma. Global strategy for asthma management and prevention. Global Initiative for Asthma. 2015: 2. *Available from: www.ginaasthma.org.*
2. McCaig LF, Burt CW. National hospital ambulatory medical care survey: 2001 emergency department summary. *Advance Data from Vital and Health Statistics.* 335. National Center for Health Statistics, 2003:1-36.
3. Rowe BH, Spooner CH, Ducharme FM, et al. Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database syst Rev.* 2003; (3):CD000195.
4. Emerman CL, Woodruff PG, Cydulka RK, Gibbs MA, Pollack C V, Camargo CA. Prospective multicenter study of relapse following treatment for acute asthma among adults presenting to the emergency department. MARC investigators. Multicenter Asthma Research Collaboration. *Chest.* 1999; 115(4):919–27.
5. Yeung M, O'Connor S a, Parry DT, Cochrane GM. Compliance with prescribed drug therapy in asthma. *Respir Med.* 1994; 88(1):31-5.
6. Thomas EJ, Burstin HR, O'Neil AC, Orav EJ, Brennan TA. *Ann Emerg Med.* 1996; 27(1):49–55.
7. McNamara RM, Rubin JM. Intramuscular methylprednisolone acetate for the prevention of relapse in acute asthma. *Ann Emerg Med.* 1993; 22(12):1829-1835 .
8. Hoffman IB, Fiel SB. Oral vs repository corticosteroid therapy in acute asthma. *Chest.* 1988; 93(1):11-13.
9. Lahn M, Bijur P, Gallagher EJ. Randomized clinical trial of intramuscular vs oral methylprednisolone in the treatment of asthma exacerbations following discharge from an emergency department. *Chest.* 2004; 126(2):362-8.
10. Hoffman IB, Fiel SB. Oral vs repository corticosteroid therapy in acute asthma. *Chest.* 1988; 93(1):11-3.
11. Lee CH, Lee CJ, Lan RS, Tsai YH, Chiang YC, Wang WJ, et al. Repository dexamethasone in the treatment of acute bronchial asthma. *Chang Gung Med J.* 1993; 16(1):25-9.
12. Rowe BH, Spooner CH, Ducharme FM, Bretzlaff JA, Bota GW. Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database syst Rev.* 2007; 18(3):CD000195.
13. Schuckman H, DeJulius DP, Blanda M, Gerson LW, DeJulius AJ, Rajaratnam M. Comparison of Intramuscular Triamcinolone and Oral Prednisone in the Outpatient Treatment of Acute Asthma: A Randomized Controlled Trial. *Ann Emerg Med.* 1998; 31(3):333-8.