ORIGINAL ARTICLE

Dexamethasone versus Prednisolone in Relapse of Symptoms in Children with Acute Exacerbations of Asthma

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ABSTRACT

Objective: To determine effectiveness of single dose of oral dexamethasone with multiple doses of oral prednisolone in relapse of symptoms in children with acute exacerbations of asthma.

Study Design: This was a randomized controlled trial.

Place and Duration of Study: The study was conducted from 1st January to 31st December 2016 at the emergency department of Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad.

Materials and Methods: Total 302 patients were included in the study with 151 children in each group receiving either dexamethasone or prednisolone. Sampling technique was consecutive and non-probable. Children of age 2 to12 years with previous history of asthma diagnosed by a physician presenting with acute exacerbations in emergency were included after consent. After assessment of Pediatric respiratory assessment measure (PRAM) score by the study physician, the patient was either given a single dose of dexamethasone 0.3mg/kg with maximum dose of 12mg or 1mg/kg of oral prednisolone with maximum dose of 40mg followed by two doses for next 2 days after discharge. Patients were reassessed for PRAM score at day 4. The patients were then called at day 14 for the assessment of relapse of symptoms of asthma like cough, wheeze and breathing difficulty. Data was documented by the study physician on a proforma. SPSS version 20 was used for entry and analysis of data. Data was presented as mean with standard deviations. Percentage was calculated from descriptive variables. Chi-square test was used for nonparametric data. P value was significant if less than 0.05.

Results: There was no significant difference in relapse of symptoms of asthma on day 14 between dexamethasone and prednisolone.10 patients i.e. 6.6% in Prednisolone and 12 i.e. 7.9% in Dexamethasone group had relapse of symptoms of asthma on Day 14 with a 'p' value of 0.65 which was not significant.

Conclusion: Single dose dexamethasone is as effective as multiple doses of prednisolone as measured by relapse of symptoms in children with acute exacerbation of asthma.

Key Words: *Asthma, Dexamethasone, Prednisolone, Relapse.*

Introduction

Asthma is one of the common pediatrics illnesses.[1] It is a frequent cause of presentation in the emergency department and hospitalization. In children it is estimated that asthma causes an estimated loss of 14.4 million school days.[2] Asthma is a worldwide problem with an estimated 300 million affected individuals.[3] Global Initiative of Asthma (GINA) reports a prevalence of 4-5% in Pakistan.[4] Asthma is a chronic inflammatory disorder characterized by airway hyper responsiveness.[5] Bronchoconstriction leads to airway edema in response to certain triggers leading to cough, shortness of breath, chest tightness and wheeze along with variable limitation of expiratory airflow.[6] Patients with asthma experience exacerbations with worsening of their symptoms. In 2019 British Thoracic society (BTS) guidelines recommend inhaled β_2 agonist as first line treatment for asthma along with early use of steroids.[7] Systemic corticosteroids for shorter duration are mainstay for asthma exacerbations which are moderate to severe.[8] Corticosteroids decrease relapses of illness, admission to hospitals and the requirement for bronchodilators. The steroid recommended is prednisone/prednisolone orally for five days, as oral is as effective as intramuscular and intravenous route.[9] However; prolonged duration of treatment with prednisolone

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Funding Source: NIL; Conflict of Interest: NIL
Received: January 18, 2019; Revised: March 10, 2020
Accepted: March 16, 2020

for 3-5 days and its bitter taste leading to vomiting may decrease compliance with it.[10]Dexamethasone is tried as an alternative to prednisolone. It has a long half-life (36 to 72 hours) as compared to prednisolone (12 to 36 hours) so it requires fewer doses as compared to prednisolone.[10] Furthermore it tastes better and costs less. It can be given orally or via intramuscular route ensuring compliance.

A number of studies have published which compared single or two days per oral or intramuscular dexamethasone with 3 or 5 days of prednisone or prednisolone. There is increasing documentation that short duration of treatment with dexamethasone is as effective as prednisolone in asthma exacerbations which are mild or moderate in severity.

Asthma is a common illness in our community. Although there are multiple trials available in the literature to support equivalence of dexamethasone versus prednisolone, there is no study conducted in this regard locally. Secondly the available guidelines are still supporting use of prednisolone in asthma exacerbations. So we decided to carry out this comparative study in our local population in the emergency department to compare the relapse rate of symptoms in children with acute exacerbations of asthma receiving either oral dexamethasone or prednisolone.

Materials and Methods

It was a Randomized control trial conducted at the Emergency Department, Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad from 1st January 2016 till 31st December 2016.Total sample size was 302 cases and 151 patients were included in each group receiving either dexamethasone or prednisolone. Consecutive, non-probable sampling technique was used. Permission from the hospital ethical committee was taken before the commencement of study. Inclusion criteria was children of age 2 to 12 years, both male and female with previous history of asthma as diagnosed by a physician , who present with acute exacerbation of asthma in emergency department. Asthma exacerbation was interpreted as acute attack of asthma with symptoms of cough, wheeze, dyspnea and oxygen saturation of less than 95% and with Pediatric Respiratory Assessment measure(PRAM) score of more than or equal to 6.[11] This score takes into account 5 items to evaluate severity of asthma. Suprasternal retractions, scalane muscle contraction, air entry in chest, wheeze and oxygen saturation with individual score of 0-4 for each sign. Total score from 1-3 shows mild exacerbation, 4-7 shows moderate exacerbation and 8-12 reveals severe exacerbation of asthma. Patients with silent chest, cyanosis, drowsy, unable to verbalize, having marked tachycardia and respiratory distress, having known exposure to tuberculosis, fever more than 39.5C°,use of corticosteroids in previous 4 weeks and those having significant co-morbid were excluded from the study .

Eligible participants were identified during clinical consultation in emergency department and PRAM score was assessed by the study physician. Informed written consent was obtained from parents/guardians. Randomization was done by lottery method. The study physician was responsible for randomization, dispensing, accountability and collection of medicinal products and maintenance and documentation of patient's record and data. Study packs of the medicines were made; each labeled clearly with name of the medication "PREDNISOLONE" or "DEXAMETHASONE."The randomized patient was either given a stat dose 0.3mg/kg dexamethasone orally (maximum 12mg) or prednisolone orally in 1mg/kg dose (maximum 40mg) followed by two doses after discharge. If the patient was randomized to the group of dexamethasone that was the only dose. If the patient was randomized to have prednisolone, two doses were provided to the patient prior to discharge from emergency department for next two subsequent day intake to complete 3 days of treatment. Subjects and parents/guardians were trained to administer prednisolone on second and third day of treatment. Patients were asked to bring the empty (dose) packs on the fourth day and were reassessed for PRAM score .Patients were then called after two weeks and enquired about symptoms of relapse of asthma. A relapse was interpreted as a visit to physician for symptoms of wheeze, breathing difficulty and cough within two weeks of inclusion in the study.[10] Patients who vomited after oral steroids, whose condition deteriorated and required hospitalization, those did not appeared for Day 4 PRAM score reassessment or

were lost to follow up at two weeks were excluded from the study.

SPSS version 20 was used for entry and analysis of non-parametric data. Data was presented as mean with standard deviations. Percentage was calculated from descriptive variables. Chi- square test was used. P value was significant if less than 0.05.

Results

Total 302 patients were finally enrolled in the study and 151 children were included in each group. Regarding age of patients, 71 i.e. 47% in Prednisolone and 93 i.e. 61.5% in Dexamethasone group were between 2-7 years of age while 80 i.e. 52.9% in Prednisolone and 58 i.e. 38.4% in Dexamethasone group were between 8-12 years of age. Mean age was 7.48± 2.53 years in Prednisolone and 7.07± 2.16 in Dexamethasone group. 96 i.e. 63.5% in Prednisolone and 80 i.e. 52.9% in Dexamethasone group were male while 55 i.e. 36.4% in Prednisolone and 71 i.e. 47.02% in Dexamethasone group were female. PRAM Score for each patient either in the dexamethasone or prednisolone group at time of induction in study was calculated and distribution of all patients according to the score is shown in Table I. Majority of the patients either in dexamethasone or prednisolone group had a score of 9 or 10 at induction. No patient having PRAM score of 12 was included in either group because of associated co-morbidities.

Table I: Distribution of Patients According to Pram Score

Pram Score At Baseline	Dexamethasone Number (%)	Prednisolone Number (%)
6	12(7.9%)	10(6.6%)
7	22(14.5%)	19(12.5%)
8	19(12.5%)	23(15.2)
9	42(27.8%)	40(26.4%)
10	33(21.8%)	42(27.8%)
11	23(15.2%)	17(11.2%)
12	0	0
Total	151	151

The mean PRAM score at baseline was calculated as 8.90 ± 1.40 in Prednisolone and 8.86 ± 1.49 in Dexamethasone group. It was 0.92± 0.33 for Prednisolone and 0.96 ± 0.25 for dexamethasone group on 4th day of treatment. The mean change in PRAM score from baseline to reassessment at day 4 was 7.98 for prednisolone and 7.90 for dexamethasone group.

Only 10 patients i.e. 6.6% in Prednisolone and 12 patients i.e. 7.9% in Dexamethasone group had relapse of symptoms of asthma like cough, wheeze or breathing difficulty documented on day 14 follow up, whereas 141 i.e. 93.3% in Prednisolone and 139 i.e. 92% in Dexamethasone group had no relapse of symptoms. This difference was not statistically significant with 'p' value of 0.65.

Discussion

This study suggests that in children with acute exacerbation of asthma, there was no significant difference in relapse of symptoms either treated with prednisolone or dexamethasone on a 14th day follow up. Dexamethasone is as effective as prednisolone and can be used as an alternative to prednisolone in management of exacerbations of asthma. It requires lesser/fewer doses than prednisolone; effects are equivalent but not inferior to prednisolone.

The results of our study are comparable to a trial done by Cronin et al. comparing dexamethasone to prednisolone for acute exacerbations of asthma.[10] They concluded that a single oral dose of dexamethasone (0.3mg/kg) was non inferior to a 3 days treatment of prednisolone (1mg/kg/day) as measured by mean PRAM score on day 4.No significant difference was also observed in both groups receiving either dexamethasone or prednisolone in hospital admissions or number of return unscheduled visits after treatment to hospital. Keeney et al.in their analysis regarding risk of relapse of symptoms between dexamethasone and prednisolone at day 5 and 10-14 days found no significant difference.[12] However they included studies comparing both oral and intramuscular dexamethasone with oral prednisolone in their analysis.

A double blind, randomized controlled trial was conducted in India to compare the efficacy of oral dexamethasone to prednisolone in treatment of moderate exacerbation of bronchial asthma in children.[2] They also concluded that single dose of dexamethasone was as effective as three doses of prednisolone as no significant difference was observed in mean time in hours to attain a PRAM score of less than 2 and number of bronchodilator nebulization in both groups randomized to receive either dexamethasone or prednisolone.

Paniagua et al in a randomized, non-inferiority trial

compared efficacy of two doses dexamethasone (0.6 mg/kg/dose) to five days of oral prednisolone (1.5 mg/kg/day, followed by 1mg/kg/day on days 2-5) in children with asthma exacerbations.[13]Both groups showed no difference related to persistence of symptoms and unscheduled emergency department visits at day 7. They also suggested dexamethasone as an effective alternate to prednisolone.

A Cochrane review by Norman sell et al which reviewed 18 randomized studies comparing dexamethasone to prednisolone suggested a comparable (not superior) efficacy and safety of dexamethasone to prednisolone.[14] However, it suggested larger studies with oral steroids to make conclusions as different studies had used different doses and duration of steroids and different methodologies to measure results.

Our study suggests dexamethasone as a potential alternate for prednisolone. Longer half-life as compared to prednisolone leading to less frequent dosing, better taste, lesser cost and similar efficacy as documented by insignificant difference in relapses of both groups makes it a better alternative therapy.

Limitation of our study was small sample size in each group and only children of two to twelve years were included in our study so findings are required to be confirmed with a larger trial. Secondly this study was conducted in the emergency department of the hospital and further studies are required to apply this management to ambulatory outpatient clinics as well.

Conclusion

Single dose dexamethasone is as effective as multiple doses of prednisolone as measured by relapse of symptoms in children with acute exacerbation of asthma.

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