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The effect of duration of treatment with inhaled steroids on asthma control in children

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Original Article

Abstract

BACKGROUND: Corticosteroids are the first line of treatment for asthma by inhibiting airway inflammation. Therefore, the present study was performed to evaluate the effect of duration of treatment with inhaled steroids on asthma control in children.

METHODS: This retrospective study was performed on children under 12 years of age in 2021. Children with asthma referred to the specialized clinic of Qods Hospital, Qazvin City, Iran, were included in the study. 90 children were assigned to two groups of 45 subjects, one group with inhaled steroids treatment for one month, and the other group with inhaled steroids treatment for three months. One month after the end of treatment in both groups, patients' clinical and paraclinical symptoms were re-evaluated. SPSS software and an independent t-test were used to compare the groups.

RESULTS: Body mass index (BMI) in the percentile was between 3 to 97 kg/m^2 (76.3%). The duration of treatment was more than one month in 85.6% of children and up to one month in 14.4% of children. The mean recurrence time was 14 days in both groups. The effect of treatment duration on the return of clinical symptoms was the same in both groups. The duration of treatment was not effective in controlling asthma (P > 0.05).

CONCLUSION: Recurrence of asthma symptoms was observed in both groups at two and three months. Therefore, the duration of inhaled steroid use did not affect the duration of symptom recurrence.

KEYWORDS: Steroids; Asthma; Children

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Introduction

Asthma is a reversible obstruction of small and large airways due to the increased sensitivity of the airways to various immunological and non-immunological stimuli, which manifests itself in the form of repeated and intermittent attacks of cough, shortness of breath, chest tightness, and wheezing.[1] The worldwide increase in the prevalence of asthma has made it a major public health concern.[2] The prevalence of asthma in children has been reported from 0% to 2% in India and up to 20.3% in Costa Rica by Shariat et al.[3] Mattiuzzi and Lippi showed that nearly 17 million Americans suffered from asthma.[4] Parisi et al.[5] and Hassanzadeh et al.[6] expressed that the incidence of asthma was reported at 43.12 million new cases per year, while in the same year, the prevalence and mortality were 272.68 million cases and 0.49 million deaths, respectively. Asthma is the most common chronic disease in children and affects more than 10% of the child population and is one of the main reasons for children to go to the

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emergency room, be hospitalized, and for absenteeism from school.[1] Corticosteroids have anti-inflammatory effects and their main mechanism is to activate glucocorticoid receptors. The anti-inflammatory effects of corticosteroids are through phospholipase A2 inhibitory proteins and lipocortins. They inhibit arachidonic acid and control the biosynthesis of prostaglandins and leukotrienes.[7] Use of inhaled corticosteroids in recommended doses in some children causes a decrease in growth or a decrease in the function of the adrenal gland. Regular use of inhaled corticosteroids also prevents the risk of reduced growth or decreased adrenal function.[8,9]

The main approach in the treatment of asthma is to reduce airway inflammation by minimizing exposure to inflammatory stimuli, daily use of anti-inflammatory drugs, and controlling conditions that can make asthma worse.[10] Inhaled corticosteroids are a gold standard and the first line of airway asthma treatment. They prevent irreversible harmful pathological changes.[11]

Saad and Moursi showed that the budesonide inhalation by children had a positive effect on long-term asthma treatment.[10] Kachroo et al. reported that largest reductions in severe asthma in children were associated with inhaled corticosteroid treatment.[11]

In summary, due to the high prevalence of asthma in children and adolescents, and the high costs of this disease for families and society, it seems necessary to pay more attention to children and adolescents with this disease. The aim of this research was to investigate the effect of duration of treatment with fluticasone propionate dry powder inhaler (DPI), fluticasone propionate pressurized metered-dose inhaler (pMDI), and hydrofluoroalkane (HFA) on asthma control in children. The present study will be of particular importance to evaluate the effect of duration of treatment with inhaled steroids on asthma control in children.

Methods

This was a retrospective study in 2021 (Qazvin City, Iran), based on hospital information with random sampling which was performed by examining the files of children aged 5-12 years. In this experiment, children who had been referred to the specialized clinic of Qods Hospital, Qazvin City, and showed clinical signs of asthma, and also were diagnosed with moderate and severe asthma after clinical and paraclinical examinations, were included in the study.

Confounding factors were considered in the exclusion criteria including chronic cough syndrome due to upper airway disorder, other lung diseases such as bronchiectasis, respiratory infections, suffering from cardiovascular disease (CVD), respiratory tract infections, foreign body aspiration, bronchopulmonary dysplasia, cystic fibrosis, and prototypical disorder of respiratory cilia.

The variables of age, genus, body mass index (BMI),[9] duration of return of asthma symptoms, and experimental group of patients were recorded. The subjects were randomly divided into two treatment groups.

Considering the prevalence of asthma in Iran (8.9%)[2] (P = 0.134), 95% confidence interval (CI) (Z = 1.96), and sampling accuracy of 90% (d = 0.1), the sample size for each experimental group was estimated as 45 patients (total: 90 patients) who were randomly selected from the patients' files. After examining the patients, seven samples were added.

$$n = \frac{z^2\, p(p-1)}{d^2}$$

$$\mathrm{n} = \frac{1.96^2 \times 0.134 \times (1 - 0.134)}{0.1^2} \cong 45$$

The randomization list was also generated online (https://www.sealedenvelope.com/simple-randomiser/v1/lists) considering the total sample size and block size. One randomization

was performed by the random block method and considering four blocks. Blocked randomization is for the purpose of making sure that exactly equal number of participants are included in the intervention and control groups at consecutive but equal time intervals. The first group was treated with inhaled steroids DPI, pMDI, and HFA [100-205 micrograms (mcg)] (Jaber Ebne Hayyan Pharmaceutical Company, Tehran, Iran) for one month (no oral medication was received).

The second group was treated with inhaled steroids DPI, pMDI, and HFA (100-205 mcg) (Jaber Ebne Hayyan Pharmaceutical Company) for three months (no oral medication was received).

The dose for each patient was determined based on the patient's age and weight. The parents were taught how to use inhaled steroids for children.[3] Children were treated for three months. During this period (three months), clinical and paraclinical symptoms of patients were re-evaluated every month in both groups.

The collected data were entered into the SPSS software (version 21, IBM Corporation, Armonk, NY, USA). Descriptive findings were calculated using relative frequency as well as the mean and standard deviation (SD). An independent t-test was used to compare groups with a significance level of less than 0.05 (ethics code: IR.QUMS.REC.1399.265).

Results

The mean age of children was 11.9 ± 3.8 years and the age range was 5-18 years. The majority of the children were boys (56.7%), and in terms of BMI, in the percentile between 3-97 kg/m^2 (76.3%). The treatment's mean duration for children took 8 weeks (two months). The duration of treatment was more than one month in 83 (85.6%) children and up to one month in 14 (14.4%) children (Table 1).

The mean recurrence time was 14 days in both groups (14.4 ± 6.09 for less than a month group and 14.40 ± 6.08 for more than a month group, t = 0.01, P = 0.98). The effect of treatment duration on the return of clinical symptoms was not significant and the mean duration of return of symptoms was the same in both groups (respiratory distress was considered a clinical symptom of asthma).

Table 1. Demographic information of children with asthma in this study (After examining the patients, seven samples were added)

Variable	Value
Age (year)	11.9 ± 3.8
Duration of treatment (week)	8.0 ± 2.9
BMI (kg/m^2) (less than 3 percentile)	5.0 ± 5.2
BMI (kg/m^2) (percentile between 3 and 97)	74.0 ± 76.3
BMI (kg/m^2) (percentile more than 97)	18.0 ± 18.6
Gender	
Girls	42 (43.3)
Boys	55 (56.7)

Data are presented as mean ± standard deviation (SD) or number and percentage
BMI: Body mass index

Discussion

In this study, the effect of duration of treatment with inhaled steroids on asthma control in children was considered. Data from 97 children with moderate and severe asthma in the present study showed that the duration of treatment in more than 83 (85.6%) children was more than one month and in 14 (14.4%) children was up to one month. Hosseininasa et al. in Iran showed that inhaled drugs were the most common asthma control drugs in children in Iran and the pattern of use of inhaled drugs and the factors affecting it were effective in treating and controlling the disease.[1] In this study, the mean and SD of patients' age was 7.58 ± 4.01 years. The mean age of children in our study was 11.9 ± 3.8 years, which was almost the same over a period of time. Moreover, in the study of Hosseininasa et al., more than 95% of patients were taking anti-asthma drugs at the time of the study. In patients taking asthma medications, 86.6% took inhaled medications alone or in combination with oral asthma medications. In patients taking inhaled drugs,

22.2% used one drug, 58.7% used two drugs, and 19.1% used three or more drugs. Despite the high satisfaction of parents with the effectiveness of inhaled drugs to control asthma in children, concerns about its side effects, duration and treatment of the disease, and its cost were among the main concerns of parents. Additionally, in children with disease duration of more than four years, the frequency of using inhaled drugs was higher than children with disease duration of four years or less**.** The results of our study showed that the average length of treatment in children was two months. The duration of treatment was more than one month in 83 children and a maximum of one month in 14 children. Studies have shown that the frequency of use of inhaled drugs and the duration of the disease of more than 4 years was significantly higher in children older than 7 years. The pattern of drug use varies with age, and in patients with longer duration of illness, the disease is usually more severe; therefore, the use of inhaled drugs and the length of treatment are higher.[1] In another study conducted by Elkout et al. in the United Kingdom (UK), 62% of patients aged 5-12 years with asthma used inhaled corticosteroids, which was higher than children in other age groups. Therefore, the frequency of use of inhaled drugs in children is higher and the duration of the disease is longer. Parents are concerned about the side effects of inhaled medications in children with asthma and prefer oral asthma medications. Concerns about inhaled drugs in Iran are higher than in other countries. Parents' worries are negatively correlated with adherence to treatment.[12] Therefore, due to the high concerns about the use of inhaled drugs, adherence to treatment is usually low, between 30% and 70%, and the effectiveness of the drug can vary depending on the adherence to treatment. Educating parents about asthma and its medications can reduce concerns about the use of these medications and lead to increased long-term use of inhalers and better disease control.[1] In the present study, the number of boys and girls was 55 and 42, respectively. As in our study, boys outnumbered girls with asthma in a study by Assadi et al.[13] Among the children aged 6-7 years studied by Assadi et al., there were 350 boys and 211 girls. Besides, there were 236 boys and 370 girls, in the group of 13-14 years. A study by Heidarzade et al. in Iran reported that the mean age of children with asthma was 8.82 ± 2.75 years. Among the children studied, 33 were girls (41.3%) and 47 (58.7%) were boys; the number of boys was more than girls as in our study.[14] Asthma can range from mild in childhood to widespread asthma with various pathologies in adulthood. Studies have found differences in the prevalence of asthma by gender. In adulthood, asthma is more common in women than in men. In addition, women have more severe asthma than men. Severe asthma is a type of asthma that does not respond well to standard asthma treatments. The defined symptoms are more severe than normal asthma symptoms and can last for a long time. People with severe asthma often find their symptoms persistent and difficult to control. This type of asthma occurs when adequate asthma control is not achieved even with high-dose treatment with inhaled corticosteroids and additional controllers [long-acting beta-agonists (LABAs), montelukast, and/or theophylline] or with oral corticosteroid therapy (for at least six months a year); in addition, reduction in treatment does not exist. Additional medications that can be used include tiotropium, omalizumab [for immunoglobulin E (IgE)-mediated asthma], and azithromycin (for non-eosinophilic asthma). Anti-interleukin-5 (IL-5) or receptor antibodies may soon be approved for the treatment of severe eosinophilic asthma.[15] The role of sex hormones in respiratory tract inflammation, smooth muscle contraction, mucus production, and airways associated

with asthma pathogenesis has been proven. The increase in asthma symptoms in women from puberty is greater than in boys in adulthood, but in childhood, these symptoms are more in boys. Testosterone is associated with improved systemic and airway inflammation, but estrogen and related type 2 (Th2) helper cell (T2) increased airway inflammation, and women increase interleukin-17A (IL-17A)-mediated airway inflammation compared to men. In general, ovarian hormones increase and testosterone reduces inflammation of the airways in asthma.[16] The mean BMI results in our study showed that BMI less than the 3rd, between 3rd and 97th, and more than 97th percentile were considered 5, 74, and 18 kg/m^2, respectively. In 2020, a study in Iran by Kang et al. found that childhood asthma and obesity were major public health problems. This relationship was significant for both men and women. 18% of children with asthma were classified as overweight and 13.5% of them were obese in 7.5% and 6% of non-asthmatic people, respectively. The results of this study showed that there was a relationship between asthma symptoms and obesity in children.[17] Therefore, any attempt to control weight in children with asthma may be beneficial.[17] In another study, Han et al. reported that among children with asthma, children with a BMI above normal were more likely to need high-dose inhaled steroids and had slower psychotherapy.[18] Obesity has risen dramatically among children in many parts of the world, especially in North America. Children with obesity are at higher risk for asthma, which is currently one of the most common chronic diseases among children. The consequences of obesity include respiratory muscle dysfunction due to chest tightness, obesity-related circulatory inflammation of the lungs, and obesity-related diseases.[18] Furthermore, common dietary characteristics in different countries may lead to obesity and asthma, decreased physical activity, and genetic changes that increase the susceptibility to obesity and asthma. Obesity in children with asthma is associated with greater airflow obstruction and a mildly decreased response to inhaled corticosteroids.[2,3,19] Obesity seriously endangers or increases the risk of disease in children. Interventions that encourage daily physical activity, weight loss, normalization of nutrient levels, and monitoring the consequences of obesity should be considered by health care providers who control obese children with asthma.[20-22]

Limitations: The limitations of this study include small number of children and non-cooperation of parents in most cases. Moreover, it is better to follow-up the treatment in different groups and in different number of months.

Conclusion

The results of the present study showed that the mean duration of relapse was 14 days in both groups and the duration of treatment for clinical relapse was not significant. The duration of treatment is not effective in controlling asthma. Since asthma is a chronic disease, its control is affected by various factors, such as age, genetic factors, living conditions, status and living environmental conditions, physical condition, or other underlying diseases from which a person suffers.

Conflict of Interests

Authors have no conflict of interests.

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