**INTRODUCTION**

Asthma is a common chronic disease [1,2]. The World Health Organization (WHO) considers asthma as the most important chronic respiratory disease of the childhood [3]. The prevalence of asthma is reportedly increasing [3,4]. This disease is more common in prepubertal boys than in girls, with the peak prevalence between ages of six and 11 years [4]. Asthma was suggested as a risk factor for increased susceptibility to caries first in the 1970s [1]. Since then, many studies have assessed the role of asthma itself along with anti-asthmatic agents in increasing the prevalence of caries [4-11]. Some studies have shown that asthma or its medications can increase the risk of dental caries [4,6-8,10] since they affect the salivary flow and the composition and pH of the saliva and can therefore increase the susceptibility to caries [1]. In addition, decreased salivary flow results in proliferation of lactobacilli and Streptococcus mutans and subsequent development of caries [10]. Nevertheless, studies have reported conflicting results [4-11]. Eloot et al, [5] did not find any association between asthma medications and increased risk of caries. Wogelius et al, [11]...
found no increased risk of caries in deciduous teeth of asthmatic children. With the debatable results, it seems that more studies in this area are imperative. In addition, studies designed to evaluate the effect of the form of asthma drugs on caries susceptibility are scarce. This study was conducted to evaluate the effects of different types and forms of antihistaminic medications and the duration of drug intake on the severity of dental caries in children with asthma.

MATERIALS AND METHODS
This cross-sectional study was conducted in Asthma and Allergy Department of Children’s Medical Center in Tehran, Iran. Eighty-five children between three to 12 years old who had been diagnosed with asthma by means of taking medical history, clinical examination and spirometry were chosen by non-simple random sampling. Sample size was calculated based on a similar previous study [12]. The children had to be under supervision and treatment with asthma medications. The participants did not have any other systemic disease and were not taking any medication interfering with asthma drugs. Patients taking their asthma medication irregularly or discontinuing it without the physician’s order were not included.

This study was approved by the Ethical Committee of Children’s Medical Center (code number: 4703). Written informed consent was obtained from the parents or legal guardians of patients and they were ensured about the confidentiality of information. The participants and their parents were interviewed first and the data were collected using questionnaires. Demographic information included patients’ age and sex. Next, we asked them about their disease and types and forms of medications used for controlling the disease (antihistamines, beta 2 agonists and corticosteroids in the form of spray, tablets or syrup) and finally the daily frequency and duration of drug intake. In the next step, a set of questions were asked regarding oral hygiene and health. They were asked whether they brushed and flossed their teeth daily, had regular dental visits, performed fluoride therapy or not, and the amount of sugar-rich foods consumed daily. Also, they were asked if they felt any dryness in their oral mucosa. The qualitative data were expressed by percentage and the quantitative data were expressed as mean and standard deviation. A qualified dentist examined all the children and recorded their oral mucosal condition, occlusion and number of decayed, missing and filled teeth (dmft for primary teeth and DMFT for permanent teeth) according to the WHO criteria [13]. Hence, for children with primary dentition dmft and for children with mixed dentition dmft plus DMFT were recorded. Dental clinical examination was performed using a dental explorer and a dental mirror under daylight conditions. No radiographs were taken. The patients were encouraged to receive dental treatment especially preventive care.

Statistical analysis:
To evaluate the effect of drugs on the number of decayed and filled teeth and the dmft/DMFT index in presence of confounders (age, sex, regular dental visits, tooth brushing and dental flossing, fluoride therapy and sugar-rich food consumption), we used the stepwise linear multivariate regression analysis. The data were analyzed using SPSS version 16 (SPSS Inc., IL, USA) and P<0.05 was considered statistically significant.

RESULTS
A total of 85 asthmatic patients aged between three to 12 years with a mean age of 6.19±1.92 years were evaluated; 74% were males.

Pharmacotherapy:
From the three forms of asthmatic drugs (syrup, tablets, spray), 34.1% used one form, 50.6% used two and 12.9% used all three forms. The distribution of different drug forms used and the most commonly used drugs in each form are
Table 1: Frequency distribution of different drug forms used and the most commonly used drug in each form

| Drug form | Percentage | Most commonly used drug (%) |
|-----------|------------|-----------------------------|
| Spray     | 11.8%      | Cetirizine (77.3) Salbutamol (69.3) |
| Tablet    | 64.7%      | Cetirizine (56.7) Ketotifen (33.4) |
| Syrup     | 40.1%      | Cetirizine (44.4) Ketotifen (22.2) |

shown in Table 1. About 49.4% had a history of using asthma medications for more than one year and 34% of the patients were using these drugs for more than two years.

**Oral hygiene:**
Only half the patients used toothbrushes regularly, and use of dental floss was reported by four children only. About 22% of patients had overt sugar consumption. Only 20% had regular dental visits. Fluoride therapy was performed for 36.5%; only three of them performed fluoride therapy in a dental office.

**Oral health condition:**
Over half the children suffered from dry mouth; nevertheless, 96.5% showed normal oral mucosa in clinical examination. Inflammation of the oral mucosa was seen in only three children. Most children (95.3%) had class I occlusion and no patient had class III occlusion. The mean dmft/DMFT in children in this study was 3.95±3.42 and thus caries prevalence was estimated to be 78.8%.

**DMFT/dmft scores:**
The dmft/DMFT scores were lower in girls than boys but showed no significant difference (P=0.702). Also, we found no significant difference in dmft/DMFT scores among different age groups. Table 2 shows the association between the dmft/DMFT scores and the intake of different drug forms, frequency of usage and duration of drug intake.
There was an inverse correlation between the number of syrup bottles consumed and the dmft/DMFT score, which was not significant (P=0.20), and a significant association was found between the number of tablets used and the dmft/DMFT score (P=0.006). There were no correlations between the number of consumed sprays and dmft/DMFT (P=0.923), duration of drug therapy (P=0.907) and the type of medication including B2 agonist, antihistamines, steroids or a combination of all (P=0.907). The frequency percentage of different drug protocols is demonstrated in Table 3.

**DISCUSSION**
The present study compared different forms of asthma medications and showed that tablets significantly increased the severity of dental caries even in presence of confounders. Most patients were under combination therapy with a number of drugs rather than single-drug therapy, and in all three forms of syrup, tablets and inhaler. Cetirizine was the most commonly prescribed drug. There was no significant difference in dmft/DMFT score among different types of medications (beta2 agonist, antihistamines, steroids and different combinations). Ersin et al, [4] showed that the type of asthma medication had no effect on salivary flow, pH or the buffering capacity of the saliva, which was somewhat in accordance with our findings. On the other hand, the form of antihistamine used was demonstrated to be effective on the severity of caries. In this regard, it is important to consider the significant effect of tablet form of asthma medications on development of caries. In 2007, Shashikiran et al, [9] demonstrated that salbutamol inhalers caused a significant increase in caries followed by salbutamol tablets. In this study, as opposed to tablets, inhalers were not cariogenic. Orally administered tablets, which compared to inhalers, deliver a higher dose of drug and have more side effects, are usually used for children with more severe form of asthma [14,15]. This
could explain why children taking tablets showed higher dmft/DMFT scores. According to Reddy et al. [7] the consumers of syrup showed the highest caries prevalence rate, which was not in accordance with our results. Santos et al. [15] reported that use of inhaled corticosteroids increased the risk of dental caries. Kargul et al. [16] showed that inhaler drugs used to treat asthma decreased the pH of the saliva. However, Tootla et al. [17] found that none of the inhalers were capable of demonstrating an acidogenic response below the critical pH. Among all forms of drugs, antihistamines were prescribed the most. These drugs can reduce the salivary secretion by 50% and increase the viscosity of the saliva [18] while reducing the protective antibacterial effect of the saliva [3]. A lower salivary flow rate was found in the asthma group compared to the control group in the studies by Ryberg et al., [8] and Stensson et al [19]. All these data are compatible with our findings.

Asthma duration had no effect on the severity of dental caries in our study. This finding is in accordance with that of Eloot et al., [5] showing that asthma duration and drug consumption did not affect the risk of development of caries. Boskabady et al., [20] did not find any significant correlation between dental caries and the duration of disease in asthmatic patients either. On the other hand, some researchers [4,6,21] suggest that duration of intake and dose of medications are correlated with prevalence of caries in asthmatics. Prolonged course of treatment caused an increase in Streptococcus mutans count and subsequently the development of caries in a study by Botelho et al [21]. Moreover, Milano et al., [6] found a positive relationship between the frequency of taking drugs and caries prevalence. Ersin et al., [4] discovered a negative relationship between the duration of medication intake and the pH of the saliva. They noticed that as the duration of medication use increased, the pH of the saliva decreased.

They concluded that the duration of medication intake can be considered as a risk factor for development of dental caries. Half of the patients reported to brush their teeth regularly, consume sugar-rich foods reasonably and perform fluoride therapy in our study. Mazzoleni et al., [22] reported superior oral health habits and more frequent tooth brushing and usage of fluoride in asthmatic children. Eloot et al., [5] did not report a significant difference in bleeding index and the amount of plaque in asthmatic patients in comparison with healthy controls. There were some limitations that need to be acknowledged regarding the present study.

Table 2: Relationship between different drug forms and DMFT/dmft* independently and in presence of confounders**

| Drug form | DMFT/dmft  | P-value (independent sample test) | P-value (in presence of confounders)** |
|-----------|------------|-----------------------------------|--------------------------------------|
| Syrup     | 3.09±3.356/4.93±3.269 | 0.013 | 0.048 β=-1.584 |
| Tablet    | 4.53±2.991/3.63±3.623 | 0.225 | 0.040 β=+1.640 |
| Spray     | 4.00±3.545/3.60±2.413 | 0.651 | 0.886 β=-0.167 |

* Decayed, missing, filled teeth
** Sex, age, duration of disease, tooth brushing, sugar consumption, fluoride therapy, mouth dryness
SD: Standard deviation

Table 3: Frequency percentage of different drug protocols prescribed

| Drug type | AH | AH+BE | AH+CO | AH+CO+BE | CO | CO+BE | BE | Total |
|-----------|----|-------|-------|----------|----|-------|----|-------|
| Percentage| 4.7| 12.9  | 12.9  | 1.2      | 11.8| 54.1  | 2.4| 100   |

AH: Antihistamines
BE: Beta2 agonist
CO: Corticosteroids
We did not include a control group (healthy subjects), since the aim of this study was to compare the caries prevalence in asthmatic children taking different medications. Collecting information via questionnaires may cause memory bias. However, this method has been used for years in respiratory disease studies and has been successful in collecting useful data. WHO criteria were used for detecting caries and no radiographs were taken. Although use of these criteria could reduce the possible bias, the lesions are diagnosed at the level of cavitation. The findings of this study cannot be generalized to the entire population of asthmatic children, because all patients were recruited from a specific medical center.

CONCLUSION

In conclusion, there was an association between asthma medications and the severity of dental caries and this association was mainly due to the form of medications taken (tablets) rather than different types of drugs or a combination of them. The duration of taking these drugs does not seem to have any effect on this issue. Considering the limited number of patients who had fluoride therapy and the importance of preventive strategies in asthmatic children, parents of asthmatic children should be advised to take preventative measures for their children.

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