

Evaluation of cariogenic potential of dry powder inhalers: A case-control study

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ABSTRACT

Objective: Dry powder inhalers (DPIs) are commonly employed in the management of asthma and other diseases with airway obstruction. A causal relationship of DPI use and occurrence of dental caries has been speculated. The present case-control study was therefore designed to examine the potential link between dental caries and specific use of dry powder inhalers in patients with bronchial asthma. **Materials and Methods:** The present study was conducted on 100 asthmatic patients aged between 10 and 45 years who were using DPIs for at least one year. The control group ($n = 100$) was selected from non-asthmatic individuals and were matched with the study group with respect to age, gender, and socio-economic status. **Results:** The results revealed that asthmatic subjects exhibited higher occurrence of dental caries in comparison to control group, but the difference was statistically non-significant. The mean decayed, missing, and filled teeth (DMFT) indices scores in asthmatic and control group were found to be 1.71 ± 2.34 SD and 1.46 ± 1.89 SD ($P = 0.408$), respectively. Likewise, the mean decayed, missing, and filled surfaces (DMFS) indices scores in both the groups were 2.41 ± 3.84 SD and 2.34 ± 4.48 SD ($P = 0.90$). However, increased frequency of DPI use was associated with significant risk of caries ($P = 0.01$). It has been observed that oral rinsing after an inhaler use limited the occurrence of dental caries to a certain extent although was non significant. **Conclusions:** Dry powder inhaler use in patients with bronchial asthma was not associated with significant risk of dental caries.

KEY WORDS: Asthma, dental caries, dry powder inhalers

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INTRODUCTION

Inhalers are the safest and most effective mode of treatment in patients with asthma, and other chronic respiratory diseases. The inhalation route allows low doses of medication to be delivered directly to the site of action in the airways, significantly reducing systemic side effects compared with oral therapy.^[1] Inhaled medication such as β_2 -agonists and glucocorticosteroids can be taken either by using pressurised metered dose inhalers (MDIs) with or without spacer, dry powder inhalers (DPIs) and nebulisers.

DPI is a common form of inhaled drug delivery system being used in asthmatic patients. A significant proportion of DPI drug is, however, retained in the mouth,^[2] which may lead to local adverse effects such as dental caries.^[3] It has been suggested that asthmatic patients on prolonged use of DPIs have inherently lower oral pH than the normal population.^[4] A DPI contains sweeteners such as lactose monohydrate as carrier vehicle that has been shown to be cariogenic during low salivary flow.^[5] The lower pH of inhalers combined with salivary changes due to β_2 -agonists may potentially increase the risk of dental caries in asthmatics. Though couple of studies investigating a risk of dental caries in asthmatics have shown higher occurrence of caries,^[6-8] others could not show a relationship.^[9-12] Genesis of caries depends on dynamic factors that include a variety of environmental, sociodemographic, behavioural, microbiological, dietary/nutritional, and/or salivary risk factors.^[13] Since these factors may vary between populations of different countries, the results of western studies may not be extrapolated for Indian population. The present study was, therefore, conducted with an objective

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to assess the dental caries experience in asthmatic subjects using DPIs in Jaipur, Rajasthan, India.

MATERIALS AND METHODS

A case-control study was chosen which included 100 asthmatic patients in the age group of 10-45 years as a study group. All the participants fulfilled the diagnostic criteria of asthma, and were using DPIs for a period of at least one year, as directed by the physician. A control group of 100 non-asthmatic subjects was selected. They were matched for age, gender, and race with the study group. Both the groups were matched for the individuals who came from the geographical areas with a similar socio-economic profile. There were no appreciable differences in oral hygiene practices among the two groups. Informed consent was obtained from all the subjects before examination.

Demographic data along with medical records containing age, gender and race were recorded. A semi-structured interview regarding duration, frequency, and time of inhaler use was conducted as well as data related to oral hygiene practices and dietary habits were also collected. Examination was carried out with the patient seated on a normal chair, using a torch and sterile instruments. A single examiner performed the examinations throughout the study. The DMFT and DMFS indices suggested by Klein, *et al.*^[14] were used to assess the dental caries status of the individual. Decayed (D) tooth refers to a tooth with an obvious cavitation(s), catch with an explorer tip, discolored or undermined enamel, a temporary filling or a detectably softened floor or wall. A tooth with both permanent restoration(s) and decay is also regarded as a decayed tooth. Filled (F) tooth refers to a tooth with permanent restoration(s) without decay anywhere on the tooth. Only restorations placed due to previous decay are included in the DMFT index. Missing (M) tooth refers to a tooth that is considered as extracted or missing as a result of caries. Teeth that are absent congenitally, exfoliated naturally, or extracted due to reasons other than caries are not included.

The data was statistically analysed. The Mann-Whitney U test, Independent Sample *t*-test, one-way ANOVA, and Tukey's HSD tests were used to evaluate the dental caries experience based on various variables included in the study. A '*P*' value of <0.05 was considered as statistically significant.

RESULTS

The mean age of asthmatics was 26.82 ± 9.51 SD years with 65% of the individuals within the age group of 16-35 years and 51% of the sample being females. Almost half of the individuals in study group were using DPI since 1-2 years (40%) and the majority used the DPI once daily (69%). A total of 45% of the cases rinsed their mouth immediately after an inhaler use as directed by the physician.

In comparison to control group, DPI group showed higher number of decayed, missing and filled teeth and decayed, missing and filled surfaces (DMFT and DMFS). The prevalence of caries in study and control groups was 57% and 56% respectively (Odds ratio = 1.04, 95% CI = 0.59 - 1.82). The mean DMFT and DMFS scores in the study group were found to be 1.71 ± 2.34 SD and 2.41 ± 3.84 SD, respectively, as compared to indices scores among the controls to be 1.46 ± 1.89 SD and 2.34 ± 4.48 SD ($P > 0.05$) [Table 1, Figure 1]. However, the difference was not significant statistically.

Gender-wise comparison of the caries experience among the asthmatics was found to be statistically non significant. The subjects within the age group of 26-35 years showed higher mean DMFT and DMFS scores (2.56 ± 2.72 SD and 3.85 ± 4.67 SD, respectively).

The duration of DPI was not significantly linked to occurrence of caries. In terms of frequency of DPI use, the significant difference was observed. ($P = 0.01$) [Table 2].

The results revealed that rinsing of the oral cavity after an inhaler use reduced the dental caries scores in asthmatics, but the difference was not significant. The mean indices scores among the rinsing group were 1.22 ± 1.69 SD (DMFT) and 1.73 ± 2.44 SD (DMFS) [Table 1].

Table 1: Comparison of DMFT and DMFS scores in study and control group

Scores	Group	N	Mean	Z
DMFT	Study*	100	1.71±2.34	0.829
	Control*	100	1.46±1.89	<i>P</i> =0.408
	No rinsing (study)	55	2.10±2.71	1.47
	Rinsing (study)	45	1.22±1.69	<i>P</i> =0.139
DMFS	Study*	100	2.41±3.84	0.118
	Control*	100	2.34±4.48	<i>P</i> =0.906
	No rinsing (study)	55	2.96±4.63	1.60
	Rinsing (study)	45	1.73±2.44	<i>P</i> =0.293

DMFT: Decayed, missing and filled teeth, DMFS: Decayed, missing and filled surfaces. *Odds ratio = 1.04, 95% CI = 0.59 - 1.82

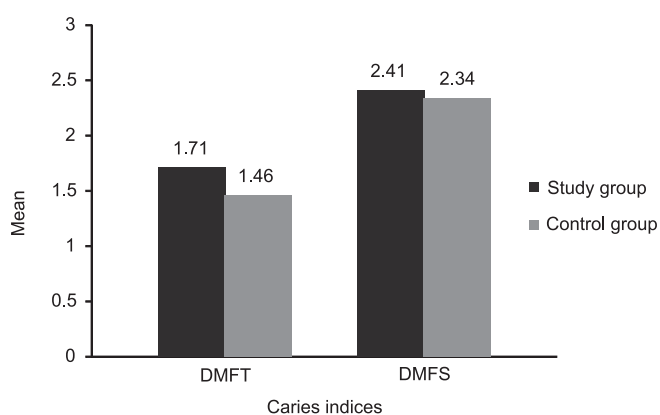


Figure 1: Mean DMFT and DMFS indices scores in study and control group are marked on the Y-axis on the graph. It clearly depicts the increased scores of dental caries in study group using DPI

Table 2: Multiple comparisons of DMFT and DMFS scores in study group based on duration and frequency of dry powder inhaler use

Dependent variable	(I)	N	Mean	(J)	Mean difference (I-J)	P
DMFT						
(Duration in yrs)	1<2	40	1.40±1.70	2<3	-0.39	0.968
				3<4	-0.18	0.999
				4-5	-1.22	0.669
				>5	-0.60	0.912
	2<3	24	1.79±3.25	3<4	0.20	0.999
				4-5	-0.83	0.910
				>5	-0.20	0.999
	3<4	12	1.58±2.42	4-5	-1.04	0.871
				>5	-0.41	0.991
				>5	0.62	0.973
	4-5	8	2.62±2.72	>5	0.62	0.973
				>5	0.62	0.973
>5				0.62	0.973	
(Duration in yrs)	1<2	40	2.05±3.41	2<3	-0.61	0.973
				3<4	-0.03	1.000
				4-5	-0.82	0.982
				>5	-0.88	0.939
	2<3	24	2.66±5.23	3<4	0.58	0.993
				4-5	-0.20	1.000
				>5	-0.27	1.000
	3<4	12	2.08±2.71	4-5	-0.79	0.992
				>5	-0.85	0.979
				>5	-0.06	1.000
	4-5	8	2.87±3.09	>5	-0.06	1.000
				>5	-0.06	1.000
>5				-0.06	1.000	
DMFT (Frequency)	1X	69	1.81±2.53	2X	0.54	0.721
				3X	1.81	0.523
				4X	-4.68	0.023*
				4X	-5.23	0.011*
	2X	26	1.27±1.37	3X	1.26	0.791
				4X	-5.23	0.011*
				4X	-6.50	0.011*
	3X	3	0.00±0.00	4X	-6.50	0.011*
				4X	-6.50	0.011*
	4X	2	6.50±0.70	4X	-6.50	0.011*
				4X	-6.50	0.011*
	DMFS (Frequency)	1X	69	2.50±4.13	2X	0.37
3X					2.49	0.686
4X					-4.50	0.358
4X					-4.50	0.358
2X		26	2.11±3.07	3X	2.11	0.800
				4X	-4.88	0.307
				4X	-4.88	0.307
3X		3	0.00±0.00	4X	-7.00	0.192
				4X	-7.00	0.192
4X		2	7.00±0.00	4X	-7.00	0.192
				4X	-7.00	0.192

*Significant, **highly significant. DMFT: Decayed, missing and filled teeth, DMFS: Decayed, missing and filled surfaces

DISCUSSION

In the present case-control study, the score of dental caries was higher in the group using DPI, though it was not significant statistically. In subgroup analysis, four time use of DPI showed increased caries score. Mouth rinsing after DPI use was associated with lower score of dental caries although non significant. The large variation obtained in caries indices scores of the subjects would result in difficulty in detecting statistically significant differences. It has been suggested that any association between asthma and dental caries may occur primarily in younger children with no such evidence as child matures.^[6] Highly significant caries indices scores seen in asthmatics between the age of 26-35 years in the present study could be best understood due to certain factors including diet, lack of access to preventive, and

therapeutic dental services, lack of awareness, poor oral hygiene practices, and longer duration of asthma disease and its medication.

In DPI, micronized drug is blended with larger carrier particles called excipient, as a dry powder mix. Excipient improves handling, dispensing, and metering of the drug. Apart from providing bulk, it also improves the taste of the medication.^[15] Currently, lactose is the main excipient used in DPIs in the range of 12.5-25 mg per dose. Other sugars such as mannitol and glucose have also been used as alternatives to lactose.^[16,17] Lactose is considered least cariogenic among the other sugars, but has been proved to cause potential demineralization of the tooth enamel and root dentin leading to dental caries.^[18-20] It has been suggested that the inherent pH value is lower for the lactose-based DPIs and their mean titratable acidity being significantly higher, rendering them potentially cariogenic.^[21] Although another study investigated the demineralizing potential of inhalers in subsurface enamel and they found no significant cariogenic effect.^[22] This could explain the non-significant result obtained in the present study, although slightly higher indices scores had been observed in study group as compared to controls.

It is usually recommended that the patients must adequately rinse the mouth with neutral pH or basic mouth rinses (milk, water, sodium fluoride 0.05% mouth rinses) immediately after using an inhaler, especially before bedtime. This is to wash away the medication deposits and counteract the acidic pH of the inhalers. In the present study, 62% of the individuals in study group used inhaler at bedtime only, out of which nearly half of them rinsed their mouth following its use. Overall, 45% of the asthmatics adopted this practice and have shown to have reduced caries experience as compared to the non-rinsing group. It can, therefore, be stated that oral rinsing must be encouraged among the patients using DPI.

In the present study, all the asthmatics were being medicated with dry powder formulation containing both β_2 -agonists and corticosteroids. It has been suggested that prolonged use of β_2 -agonists is associated with diminished salivary production and secretion, and thus an increased frequency of caries.^[23] There is a reduction in flow rates of whole and parotid saliva by 26% and 36%, respectively.^[24] Since salivary buffering capacity has been lost, an acidic environment is encouraged and persists longer. This in turn encourages growth of aciduric bacteria such as lactobacilli and *Streptococcus mutans*. These bacteria grow in the acid conditions and continue to metabolize carbohydrate in the low pH environment. The stage is set for uncontrolled carious attack.^[25] Inhaled corticosteroids are weak organic acids and generally are not metabolized by oral bacteria. However, they pose a pH threat when sugar-based inhalers are used.^[21] Since all the patients in study group were using the lactose-based dry powder inhalers, thus their role as being potentially

cariogenic in addition to the medication effects could not be neglected.

The duration, frequency, and time of inhaler use often change over time based on varying severity of the asthma disease owing to seasonal variations. One of the strengths of present study was, however, that only those subjects were considered who regularly used DPIs for at least one year. The recurrent episodes of wheezing, breathlessness, chest tightness and coughing, are seen particularly at night or in the early morning in asthmatics.^[26] Accordingly the majority of the individuals in the present study used the inhaler at bedtime and/or morning time. The cariogenic activity increases during the night due to lower salivary flow and lack of masticatory movements. However, the results revealed that time of inhaler use over a day had no observable effect on the caries experience. It had been reported that asthmatic subjects using the inhalers for more than 4 years showed increased caries indices scores. This could be explained due to the long term use of dry powder inhaler containing fermentable carbohydrates or due to direct effect of the asthma medication itself. The highly significant result between dental caries and frequency can be attributed to the increased usage of dry powder inhaler. The subjects who used the inhaler four times daily had increased indices scores, but this finding could not be generalized to the overall study group as it included a very small sample size.

CONCLUSIONS

Within the parameters of this study, it is concluded that there is no significant association between dental caries and prolonged use of dry powder inhalers among patients with bronchial asthma. Further studies are recommended that include the salivary and plaque pH analysis following a DPI use to explore their acidogenic effect, preferably with a longitudinal design.

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