

## Effect of Using Methylphenidate on Salivary Flow Rate and Salivary Buffering Capacity in Children with Attention-deficit/Hyperactivity Disorder

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### ABSTRACT

**Objective:** Most drugs used to treat attention-deficit/hyperactivity disorder treatment can affect saliva secretion. Methylphenidate is the most commonly prescribed drug for the treatment of attention-deficit/hyperactivity disorder and was approved for use in children over the age of 6 years. However, limited information is available on the use and long-term adverse effects of methylphenidate in preschool children (< 6 years). We explored the effects of methylphenidate on salivary flow rate and salivary buffering capacity during treatment for attention-deficit/hyperactivity disorder.

**Methods:** Children who were diagnosed with attention-deficit/hyperactivity disorder by expert psychiatrists, under medical treatment, and those who had no other systemic diseases were included. Stimulated saliva samples were collected before prescription of methylphenidate and after 15 days, 30 days and 3 months of regular drug intake. The samples were analysed for *Streptococcus mutans*, as well as salivary buffering capacity and salivary flow rate. Twenty children (age range, 6–15 years) with attention-deficit/hyperactivity disorder were included.

**Results:** The mean salivary buffering capacity value at month 3 was significantly lower than that at baseline and at day 15. Regarding the distribution according to salivary flow rate, statistically significant differences were found between baseline and the first month and between baseline and month 3. These results indicate that methylphenidate consumption in children with attention-deficit/hyperactivity disorder leads to reduced salivary buffering capacity and salivary flow rate after 3 months of follow-up.

**Conclusion:** Parents should be informed about necessary preventive dental treatments to minimize the negative oral and dental effects of long-term drug use in children.

**Keywords:** Attention-deficit/hyperactivity disorder, methylphenidate, salivary buffer capacity, salivary flow rate.

### INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is among the most common neuro-behavioural problem in children aged between 6 and 17 years. The estimated prevalence in the United States is 2%–18% (1). Learning disabilities, mood and anxiety disorders, substance abuse, and impaired academic and social functioning are observed in children and adolescents with ADHD, and these conditions unfavourably influence their lives. It has been reported that 60%–80% of ADHD symptoms persist in adulthood and that ADHD is present in 4%–4.5% of adults (1).

Treatment of ADHD includes drug therapy, behavioural therapy or a combination. Early and effective treatment in children may be associated with better prognosis and lead to fewer problems in adulthood (1). Drugs approved by the Food and Drug Administration for the treatment of ADHD include stimulants (considered first-line agents) such as methylphenidate and amphetamines and non-stimulants (considered alternative agents) such as atomoxetine and extended-release alpha-2 agonists (guanfacine and clonidine) (1). Methylphenidate is the most commonly prescribed drug for the treatment of ADHD and was approved for use in children over the age

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of 6 years (2). However, limited information is available on the use and long-term adverse effects of methylphenidate in preschool children (< 6 years) (3).

Most drugs used for the treatment of ADHD (stimulants, non-stimulants, alpha-2 agonists, tricyclic antidepressants, and bupropion) directly and indirectly affect the oral environment of patients (1). While some may experience xerostomia, the subjective feeling of dry mouth, others do not (4). It is important to understand the side effects of drugs involved in medication to decrease the negative outcomes to oral health. Salivary flow rate (SFR) and salivary buffering capacity (SBC) can be easily affected by such drugs. We explored the effects of methylphenidate, which is the most common drug used to treat ADHD, on SFR and SBC in children with ADHD.

## SUBJECTS AND METHODS

The study was approved by the Marmara University Scientific Research Ethics Committee (approval no. MAR-YÇ-2009-0112). Children who were being treated at Erenköy Hospital for Mental and Nervous Diseases, Istanbul, Turkey and who were diagnosed with ADHD by expert psychiatrists, under medical treatment, and had no other systemic diseases were included in the present study. The written consent forms were obtained from the parents of all children. Children who did not regularly attend control visits or those who did not regularly use their drugs were excluded. Examinations of the oral cavities of all children included in the study were performed in the hospital by the same dentist using a mirror and a periodontal probe. In accordance with the World Health Organization (WHO) criteria, the number of decayed, filled, and extracted teeth was assessed and the decayed, missing, and filled teeth (DMF-T) index scores were used for permanent teeth, whereas the decayed, filled teeth (df-t) index score was used for deciduous teeth (5). The families of the children were asked to complete a questionnaire, which was developed to obtain information on the demographic characteristics and oral hygiene habits of children.

The children had a standard breakfast to measure the stimulated salivary rate. Saliva samples were collected between 9:00 a.m. and 10:00 a.m. During this procedure, the children were asked to chew pre-weighed (2 g) paraffin wax for 5 minutes and then to spit the saliva together with the paraffin wax into a test tube. Salivary flow rate was recorded as amount in ml in 5 minutes. Stimulated saliva samples were collected from children before prescription of methylphenidate and after

15 days, 30 days and 3 months of regular intake. The samples were analysed for *Streptococcus mutans* using Saliva-Check Mutans (GC Corp., Tokyo, Japan) and SBC was measured using Saliva-Check BUFFER (GC Corp., Tokyo, Japan). Required saliva samples were collected in accordance with the directions specified by the manufacturer of the chair-side kits.

## Statistical analysis

Statistical analyses were performed by the Number Cruncher Statistical System (NCSS; NCSS Inc., Kaysville, UT, USA) 2007 package program. In addition to descriptive statistical methods (mean, standard deviation, median, interquartile range), the Friedman test was used for repeated measurements of multiple groups, Dunn's multiple comparison test was used for subgroup comparisons, and McNemar's test was used to compare qualitative data. A  $p$ -value < 0.05 was considered statistically significant.

## RESULTS

The present study included 20 children (age, 6–15 years) diagnosed with ADHD. The oral health characteristics of the children including frequency of tooth brushing, DMF-T index score and df-t index score are presented in Table 1.

Table 1: Characteristics of the children with attention-deficit/hyperactivity disorder

Characteristics	
Age, year	9.40 ± 2.64
Gender	
Boy	2 (10.0)
Girl	18 (90.0)
Frequency of tooth brushing	
Once or more daily	12 (60.0)
2–6 times weekly	5 (25.0)
Once weekly	3 (15.0)
DMF-T index score	1.20 ± 1.80
df-t index score	2.90 ± 3.52

Data are presented as mean ± standard deviation or number (%), where appropriate.

DMF-T: decayed, missing, filled teeth; df-t: decayed, filled teeth.

The SBC, SFR and pH values of salivary samples are presented in Table 2. The mean SBC value at month 3 was significantly lower than that at baseline ( $p = 0.048$ ) and at day 15 ( $p = 0.045$ ); no significant differences were observed between the values at other time points ( $p > 0.05$ ). There were no differences in *S. mutans* values.

Table 2: Salivary measurements of the children with attention-deficit/hyperactivity disorder

	Baseline	15 <sup>th</sup> day	1 <sup>st</sup> month	3 <sup>rd</sup> month	<i>p</i>
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	
<b>Salivary buffering capacity</b>	9.1 ± 2.56 <sup>a</sup> 11 (6.5–12)	9.5 ± 2.42 <sup>a</sup> 10 (8–12)	8.8 ± 2.09 10 (6.5–10)	8.6 ± 2.52 <sup>b,c</sup> 10 (8–10)	0.020
<b>Salivary pH</b>	7.46 ± 0.23 7.5 (7.2–7.6)	7.47 ± 0.25 7.6 (7.25–7.6)	7.51 ± 0.26 7.6 (7.4–7.6)	7.5 ± 0.24 7.6 (7.25–7.6)	0.607
	n (%)	n (%)	n (%)	n (%)	
<b>Salivary flow rate</b>					
Normal	15 (75.0)	10 (50.0)	7 (35.0) <sup>b</sup>	7 (35.0) <sup>b</sup>	<i>p</i> = 0.008
Low	5 (25.0)	9 (45.0)	13 (65.0)	13 (65.0)	
Very low	0 (0.0)	1 (5.0)	0 (0.0)	0 (0.0)	

<sup>a</sup>Different from the 3<sup>rd</sup> month.

<sup>b</sup>Different from the baseline.

<sup>c</sup>Different from the 15<sup>th</sup> day.

SD = standard deviation; IQR = interquartile range.

## DISCUSSION

The main finding of the present study is that methylphenidate, which is the most commonly used drug for ADHD, has adverse effects on SFR and SBC in children with ADHD that may negatively influence oral health. Various adverse effects and drug–drug interactions are in question for the treatment of ADHD. The frequency of treatment-associated adverse effects, the majority of which are mild or moderate, ranges between 58% and 78% and the rate of drug discontinuation due to adverse effects is lower than 25% (6).

In a systematic review of medication-induced salivary gland dysfunction, all studies reviewed mentioned xerostomia as a main adverse effect of the assessed medications, with no objective measurements of SFRs (7). In the present study, SFR and SBC were measured objectively to evaluate the effects of methylphenidate, which is a commonly prescribed central nervous system stimulant for ADHD patients. Daily use of this medication for 3 months had negative effects on SBC and SFR.

Children with ADHD are considered to have special health care needs (SHCNs). Children with SHCN require nearly twice the amount of oral health care attention than children without SHCN (8). Bimstein *et al* (9) compared the oral characteristics of children receiving treatment for ADHD (*n* = 25) with those of healthy children receiving no drugs (*n* = 127). They determined that toothache, bruxism, bleeding gums and oral trauma were more common in children with ADHD; however, there were no significant differences between healthy children and children with ADHD in terms of plaque accumulation, gingival inflammation, calculus, oral hygiene compliance, dental caries experience, and unmet dental needs. They suggested that behavioural characteristics

of ADHD children may have unfavourable effects on oral health and that specific strategies focusing on this issue are required. Broadbent *et al* (10) performed conditional logistic regression analyses on 128 case–control pairs matched in terms of age, sex, and ethnic and socioeconomic status, and found that when fluoride history, medical problems, diet and self-reported oral hygiene were controlled, the risk of having a high DMF-T score was approximately 12 times higher in children with ADHD than in those without it. Kohlboeck *et al* (11) reported that non-cavitated caries lesions were positively associated with the presence of hyperactivity/inattention based on logistic regression analyses. In the present study, DMF-T index scores were 1.20 ± 1.80 in children with ADHD, which is within the limits according to data from WHO, which suggests that the DMF-T index score should not be more than 3 in children aged 12 years.

Several physical, biological, environmental, behavioural, and lifestyle factors may affect the formation of caries, including high numbers of cariogenic bacteria, insufficient salivary flow, inadequate exposure to fluoride, poor oral hygiene, inappropriate methods of feeding infants, and poverty (12). Saliva provides protection against dental caries, erosion, attrition, abrasion, candidiasis, and abrasive mucosal lesions by forming a protective layer in the mouth (13). It also enables the clearance of sugar and acids; contains buffer, urea, and antifungal and antibacterial factors; and enhances the resistance of mucosa against abrasive lesions (14). It is also rich in calcium, phosphate and acid-buffering agents, which helps reduce the incidence of dental caries (13).

Xerostomia is a common subjective complaint of dryness in the mouth (15). Its major causes include use

of medications and head and neck radiation therapy. It is the most common side effect (80%) of the prescribed medications in the United States (16). Human salivary secretion and its regulation, involving facilitatory and inhibitory influences from higher brain centres and synergistic interactions between the two divisions of the autonomic nervous system, are complex processes that require a rich blood supply (17, 18). The most commonly reported classes of medication that result in hyposalivation are antidepressants, antipsychotics, antihistamines, muscarinic receptor,  $\alpha$ -receptor antagonists, antihypertensive (eg, diuretics,  $\beta$ -blockers and angiotensin-converting enzyme inhibitors), bronchodilators, and skeletal muscle relaxants (7, 19–21).

Current drugs used for the treatment of ADHD include stimulants and non-stimulants, and methylphenidate is a stimulant drug considered as an indirect dopamine agonist that acts by blocking the reuptake of the neurotransmitter dopamine and dextroamphetamine (22). Xerostomia is mentioned in the literature as one of the adverse effects of methylphenidate (23). While some authors have reported that methylphenidate causes dry mouth (24), others have not observed any change in SFR associated with this drug (25).

Hyposalivation or xerostomia reduces SBC, thus making the oral cavity more acidic (25); it also reduces oral clearance and allows the metabolism of cariogenic bacteria. Increased adhesion of cariogenic bacteria to the tooth surface and a decrease in oral pH caused by hyposalivation promotes the formation of caries. Sakeenabi and Hiremath (26) demonstrated that the mean caries score was significantly correlated with SBC and SFR in 6-year-old school children. Animireddy *et al* (27) reported that the physicochemical properties of saliva (SFR, pH, buffering capacity and viscosity) of 4- to 12-year-old children were associated with caries, and SBC and SFR were significantly higher in children without caries. On the other hand, Rosenberg *et al* reported that the prevalence of dental caries is higher in children with ADHD, and that decreased salivary flow due to pharmacological treatment does not appear to be responsible (28).

Patients with hyposalivation tend to have higher levels of *S. mutans* and lactobacilli, which are caries pathogens (26, 29). Oral bacteria play an important role in the formation of dental caries (28). Salivary microbial tests are used to measure caries risk to detect cariogenic microorganisms such as *S. mutans*, lactobacilli, *Actinomyces* spp. and *Candida* spp. Hidas *et al* (29) observed no difference between children with ADHD (receiving and not receiving drugs) and healthy children in terms of oral

levels of *S. mutans* and lactobacilli. In the present study, children with ADHD taking methylphenidate did not show a change in *S. mutans* levels after 3 months.

## CONCLUSION

Children with ADHD taking methylphenidate showed a reduced SBC and SFR after 3 months of follow-up. This finding is important as it may unfavourably influence oral-dental hygiene and accelerate the formation of caries. Parents should be informed about the necessary preventive dental treatments to minimize oral and dental negative effects of long-term drug use in children. Dental professionals should make recommendations to prevent and reduce symptoms and to improve oral health quality of life.

## AUTHORS' NOTE

The authors declare that they have no competing interests.

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