

# “Modified Schirmer Test in Assessment of Salivary Flow Rate Among Patients on Antidepressants”: A Comparative Study

Manipal Shruthi<sup>1</sup>, Vathsala Naik<sup>2</sup>, Pooja Naik<sup>3</sup>, Raghavendra Kini<sup>4</sup>, Ashwini Avanti<sup>5</sup>, Supriya Bharti<sup>6</sup>

<sup>1</sup>Department of Oral Medicine and Radiology, Srinivas Institute of Dental Sciences, Mangaluru, Karnataka, <sup>2</sup>Department of Oral Medicine and Radiology, Bangalore Institute of Dental Sciences, Bengaluru, Karnataka,

<sup>3</sup>Department of Oral Maxillofacial Pathology and Microbiology, Srinivas Institute of Dental Sciences, Mangaluru, Karnataka,

<sup>4</sup>Department of Oral Medicine and Radiology, A. J. Institute of Dental Sciences, Mangaluru, Karnataka, <sup>5</sup>Department of Pediatric and Preventive Dentistry, MGM Dental College and Hospital, Kamothe, Navi Mumbai, Maharashtra, <sup>6</sup>Department of Oral Maxillofacial Pathology and Microbiology, Dr. B. R. Ambedkar Institute of Dental Sciences, Patna, Bihar, India

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## ABSTRACT

**Aims:** The objective of this study was to assess salivary flow rate (SFR) among healthy subjects or patients on antidepressant drugs such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) by using the “Modified Schirmer Test” (MST). To evaluate and correlate salivary flow rate by using MST and comparing it with the spitting method in patients on antidepressants and healthy control subjects. **Materials and Methods:** Data were collected from the patients visiting the dental college and the psychiatry department. A total of 105 subjects were included in the present study, dividing Group I as control, Group II as SSRIs, and Group III as TCAs. In all subjects, a screening questionnaire was recorded, SFR was determined by the spitting method, and MST was carried out in the morning. The MST was performed by placing a modified Schirmer tear strip (STS) on the floor of the mouth for all subjects, and readings were taken for 3 min. **Results:** The SFR value obtained among Group I by the spitting method was 0.83 ml at 5 min, and by the MST method was 34.97 mm at 3 min, with a *P* value of 0.860. The SFR value obtained among Group II by the spitting method was 0.47 ml at 5 min, and by the MST method was 26.25 mm at 3 min, with a *P* value of 0.001, which was highly significant. The SFR value obtained among Group III by the spitting method was 0.394 ml at 5 min, and by the MST method was 10.71 mm at 3 min, with a *P* value of 0.041, which was significant. **Conclusions:** A significant positive correlation was observed between the SFR value obtained by both the spitting method and MST. From our study, we can conclude that the MST can be used as an effective noninvasive tool to estimate SFR.

**KEYWORDS:** Flow rate, modified schirmer test, saliva, spitting method, SSRIs, TCAs

## INTRODUCTION

Saliva is called the “mirror of the body.” Since time immemorial, it has been portrayed as a unique yet complex body fluid, the adequacy of which plays an essential role in health, including the protective mechanisms involving lubrication and debridement of

the oral cavity.<sup>[1,2]</sup> The main mechanism of drug-induced xerostomia is an anticholinergic or sympatho-mimetic

**Address for correspondence:** Dr. Shruthi M., Department of Oral Medicine and Radiology, Srinivas Institute of Dental Sciences, Mukka, Surathkal, Mangaluru, Karnataka, India. E-mail: shruthim64@gmail.com

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action; thus, the drugs most commonly causing xerostomia include antihistamines, atropines, benzodiazepines, antipsychotics, and TCAs.<sup>[3]</sup>

Antidepressants are drugs that are advised for various diverse therapeutic reasons, which include psychiatric disorders, pain control, insomnia, cessation of smoking, substance abuse, and eating disorders. When patients take multiple drugs in combination, adverse effects such as decreased salivation changes in viscosity of saliva, orthostatic hypotension, and cardiotoxicity are found in certain groups of antidepressant medications.<sup>[4]</sup> There are various methods to estimate the quantitative and qualitative salivary secretion. In our study, MST was used to estimate the quantitative SFR among people who were prescribed two classes of antidepressant drugs, namely TCAs and SSRIs, and assess the burden of hyposalivation and quality of life of those individuals.

Salivary gland dysfunction may be characterized by either hyposalivation or hypersalivation. Hyposalivation refers to an objective reduction in salivary secretion, and hypersalivation or sialorrhea refers to an increased secretion of saliva.<sup>[5]</sup> Xerostomia is defined as a subjective complaint of dry mouth that may result from a decrease in the production of saliva.<sup>[6]</sup> Xerostomia is a familiar complaint among older age groups, and according to a study 30% of the general population aged 65 years and older experience xerostomia.<sup>[7]</sup>

Antidepressants such as TCAs compete and restrain the binding of Acetylcholine (ACh) to the muscarinic cholinergic receptors located in the salivary glands. The TCAs also inhibit the reuptake of norepinephrine and serotonin. Since the cholinergic and the alpha 1 adrenergic receptors control the flow of water and electrolytes in saliva, their prevention can induce hyposalivation and dryness of oral mucosa.<sup>[8-10]</sup> Some of the medications such as amitriptyline, imipramine, and doxepin, which belong to the TCA group, have high anticholinergic activity.<sup>[8]</sup>

Serotonin reuptake inhibitors are a newer class of antidepressants. The SSRIs block the reuptake of serotonin in the brain and make it more available to the synaptic receptors of the central nervous system. Citalopram and escitalopram have probable effects on serotonin uptake and less inhibitory action on norepinephrine and dopamine. Their xerogenic potential is lower than that seen with the TCAs.<sup>[8,11,12]</sup>

The aim of the study was to assess the SFR among healthy subjects and patients on antidepressant medication such as TCAs and SSRIs by using the

MST and further evaluate and correlate the SFR by comparing MST with the spitting method.

The aims of the study were as follows:

- 1) To assess SFR among healthy subjects and patients on antidepressant drugs such as TCAs and SSRIs using MST.
- 2) To evaluate and correlate SFR using MST and comparing it with the spitting method in patients on antidepressants and healthy control subjects.

## MATERIALS AND METHODS

Data were collected from 105 subjects visiting the department of psychiatry and the department of oral medicine and radiology. The subjects were divided into age- and sex-matched groups of 35 each. Healthy subjects in Group 1 were selected from patients visiting the department of oral medicine and radiology. Subjects in Groups II and III were selected from patients visiting the outpatient department of psychiatry

These groups are:

- Group 1: 35 Healthy subjects
- Group 2: 35 Patients on SSRIs
- Group 3: 35 Patients on TCAs

## METHODOLOGY

### Inclusion criteria

1. Patients were on antidepressant drugs such as TCAs and SSRIs for a minimum of three weeks and a maximum of one year. Patients chosen for the study were taking TCAs such as amitriptyline (amitone, amitril 10mg) and SSRIs such as Citalopram (C-PRAM 10mg) and Escitalopram (ESPAM, CITALOP-S 10mg).
2. Normal healthy patients without any other systemic diseases served as controls.

### Exclusion criteria

1. Patients on medications such as antihypertensives, anti-inflammatory, diuretics, antihistamines, muscle relaxants, and analgesics
2. Patients who are having Sjogren's syndrome (SS), multiple systemic diseases and those undergoing radiation therapy.

Approval for the study was granted by the Ethics Committee of AJ Institute of Medical Sciences (approval date: November 8, 2013, approval number: AJEC/Rev/76/ 2011–2012). The study had to conform to the standards of the Declaration of Helsinki and its subsequent revisions, and informed consent was obtained. Case histories were recorded for every

individual. The patients were screened for xerostomia, and questionnaires were given to all the patients. Out of 70 patients from Group 2 and Group 3, around 20 patients self-reported with xerostomia. All the participants in the study were advised not to chew or have beverages for a period of 1 h prior to the study, as it would stimulate the SFR. The examination was carried out in conducive climatic conditions (room temperature), between 8 am and 12 noon to avoid temperature and diurnal variations. The screening questionnaire was given to the patients for the assessment of xerostomia. Questionnaires were used to assess the patient's feeling of mouth dryness.

#### Assessment of xerostomia

1. Do you have difficulty in swallowing food?
2. Do you have to sip liquids to aid in swallowing?
3. Is the amount of saliva in your mouth "too little" most of the time?
4. Do you have less saliva than you used to?
5. Is it difficult to eat dry foods such as crackers or toast?
6. When was the last time you had a complete physical examination by your doctor?
7. How much water do you drink throughout the day?

Saliva was collected by the spitting method in Group 1 (healthy subjects), Group 2, and Group 3; this was a standard method and was compared with MST in all the groups. The SFR was tested by both MST and the spitting method for the evaluation and correlation of SFR among the study groups.

After assessing xerostomia, patients were managed by advising noncarcinogenic diet, staying hydrated, limiting caffeine and alcohol, vitamin C chewable tablets (limcee 500 mg).

#### MODIFIED SCHIRMER TEST

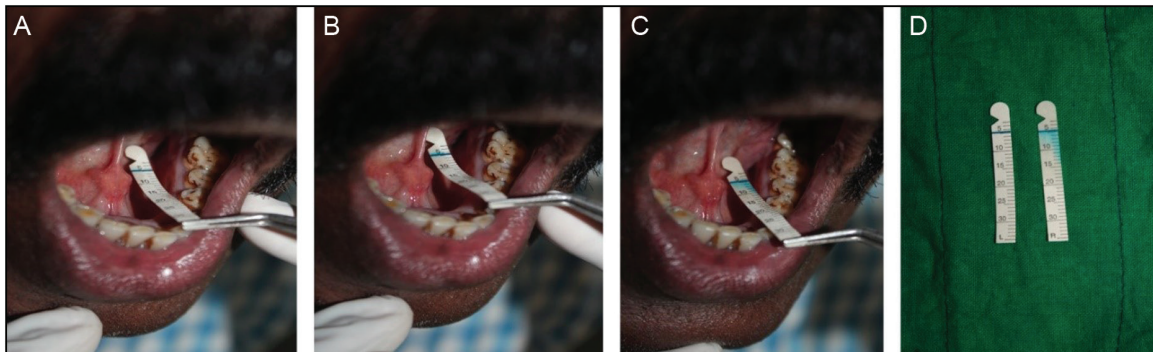
MST was performed to measure the unstimulated flow rate of saliva. The test was conducted by using an STS,

which is routinely used by ophthalmologists to measure the amount of wetness of the eye. A standardized commercially available STS (Eagle Vision, TN, USA) measuring 5 × 35 mm and having a graduated scale and blue color bar was used. The color bar gradually traveled along the graduated scale (1–35 mm), depicting the amount of fluid flow. The tests were conducted from 8 am to 12 noon, and the patients were advised not to drink or eat for 2 h before the test.

Before the commencement of the test, the patients were instructed to swallow all the saliva present in their mouth. Later, the patients were instructed to make their tongue touch their palate to prevent any contact with the strip. The strip was then held and positioned touching the floor of the mouth using a tweezer for 3 min. During the test, the strip would change color (white to blue) when it came in contact with the saliva [Figure 1]. Based on the study analyses done by Chen *et al.* and Shribang we also followed the same and kept the preset values of MST: If the reading was less than 15 mm, it was considered as hyposalivation in 3 min; if it was more than 15 mm in 1 min, it was considered as normal salivation; and if it was 35 mm in 1 min, it was considered as hypersalivation.

#### SPITTING METHOD

Before the commencement of the test, the patients were asked to swallow all the saliva. Once the test commenced, the patients were advised to limit the movement of their mouth to prevent them from swallowing the accumulated saliva. At the end of 5 min, the patients were instructed to spit out the pooled saliva into a sterile pre-weighed container. The quantity of the saliva was estimated by weighing the container before and after collection, assuming the specific gravity of the saliva to be 1 g/cm<sup>3</sup>. The SFR was estimated in g/min, which is approximately equivalent to ml/min. The normal unstimulated SFR was 0.1 ml/min or 0.5 ml/5min.



**Figure 1:** Placement and wettability of the strip in MST, (A) After 1 min, (B) After 2 min, (C) After 3 mins, and (D) Comparison of the strip before and after the test

## STATISTICAL ANALYSIS

For this SPSS software version 16.0 was used for statistical analysis of data. Analysis of variance (ANOVA) was applied to statistically determine the total number of patients, minimum age and maximum age, and estimated flow rate of saliva by the spitting method and MST. A chi-square test was applied to statistically determine the significant difference between gender and the distribution of MST at 3 min in three groups. Pearson's correlation coefficient was applied to determine the correlation between the spitting method and MST. Turkey HSD was applied to statistically determine multiple comparisons between groups. Fisher exact test was applied to estimate the percentage distribution of xerostomia among TCAs and SSRIs.

## RESULTS

The current study was carried out to measure the salivary rates of patients under two groups of antidepressant drugs, and the same were compared with sex- and age-matched control group individuals (healthy subjects). In age variants, Group I had a mean age of 40.86 years with a Standard Deviation (SD) as 13.46; Group II had a mean age of 40.74 years with an SD as 11.82; and Group III had a mean age of 44.37 years with an SD as 12.01;  $P = 0.38$  not significant. Among them, Group I had 40% male and 60% of female individuals; Group II had 40% male and 60% of female patients; and Group III had 34.3% male and 65.7% female patients.

The flow rate of saliva was calculated as ml for 5 min among the three groups, and it was assessed using two methods, namely the spitting method and MST. Table 1 presents the flow rate of saliva by the spitting method among Group I, Group II, and Group III.  $P < 0.046$  was significant.

In Table 2, SFR was assessed by MST in mm for 1, 2, and 3 min. All three groups had  $P < 0.001$ , which was highly significant.

Further SFR by MST was also categorized as 5–15 mm, 16–24 mm, and 25–35 mm at 3 min among experimental groups. Overall, the patients who had MST wettability at the end of 3 min at 5–15 mm were 36 (35%); at 16–24 mm, 5 (4.8%); and at 25–35 mm, 64 (60.2%).

**Table 1: Assessment of salivary flow rate by the spitting method for 5 min**

Group, N = 35	SFR Min., mL/min	SFR Max., mL/min	Mean	SD
Group I	0.51	0.86	0.83	1.34
Group II	0.41	0.54	0.47	0.29
Group III	0.31	0.31	0.39	0.39

$P < 0.046$

Table 3 demonstrates the MST after 3 min in three different groups.

The results of SFR thus obtained from the spitting method and MST among all the study groups were, in turn, compared and correlated to determine specificity and significance. Table 4 presents the comparison and correlation of the spitting method and MST. The SFR values obtained for Group I by the spitting method at 3 min was 0.83 ml and by the MST method was 34.97 mm at 3 min. Pearson co-efficient value ( $r$ ) was 0.032 with a  $P$  value of 0.860, which was not significant [Figure 2]. Group II by the spitting method was 0.47 ml at 5 min, and the MST method was 26.25 mm at 3 min. Pearson co-efficient value ( $r$ ) value was 0.520 with a  $P$  value of 0.001, which was highly significant [Figure 3]. Group III by the spitting method was 0.394 ml at 5 min, and the MST method was 10.71 mm at 3 min. Pearson co-efficient value ( $r$ ) value was 0.35 with a  $P$  value of 0.041, which was significant [Figure 4].

Comparison and correlation of MST values between different study groups were done. The MST value for Group I and Group II was 34.95 mm and 26.74 mm, respectively, with a mean difference of -8.21 mm and  $P < 0.001$  (highly significant); the MST value for Group I and Group III was 34.95 mm and 10.7 mm, respectively, with a mean difference of -24.27 mm and  $P < 0.001$  (highly significant); and the MST value for Group 2 and Group 3 was 26.74 mm and 10.7 mm, respectively, with a mean difference of -16.06 mm and  $P < 0.001$  (highly significant). The percentage distribution of xerostomia among patients in Groups II and III was found to be 25.7% and 100%, respectively.

## DISCUSSION

Saliva has antimicrobial properties; xerostomia can cause a dry and sticky sensation in the mouth, which causes difficulty in mastication, frequent sipping of water for deglutition, increased dental caries, cracked lips, and reduced ability of taste perception and smell.<sup>[6,13]</sup> The quantitative and qualitative analysis of formed saliva is based on subjective and objective data, derived from symptoms reported by the patient, clinical examination, and investigations.<sup>[14]</sup> The drugs that prevent neurotransmitters from binding to salivary gland membrane receptors, or that agitate ion transport pathways in the acinar cell may significantly affect the volume of salivary output. These types of drugs include sedatives, tranquilizers, antihistamines, antihypertensives, and antidepressants, such as TCAs, SSRIs, etc.<sup>[15]</sup> Antidepressants are a class of drugs used primarily for patients who have depression and anxiety disorders.<sup>[16]</sup> In our study, those who were on

**Table 2: Assessment of salivary flow rate using MST**

Assessment of MST	Wettability											
	After 1 min				After 2 min				After 3 min			
	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD
Group I	10.00	15	12.40	0.95	20	27	23.21	1.51	34	35	34.96	0.17
Group II	9.0	13	10.14	0.85	16	23	18.41	1.43	24	35	26.73	2.58
Group III	4.0	6	5.13	0.42	6	10	7.55	1.20	8	14	10.69	1.72

\**P* < 0.001**Table 3: MST values after 3 min in different study groups**

MST value, mm	Group I, %	Group II, %	Group III, %
5–15	0	1 (2.9%)	35 (100%)
16–24	0	5 (14.3%)	0
25–35	35 (100%)	29 (82.9%)	0

TCAs had low MST values than those on SSRIs and the control group.

In our study, MST helped us to distinguish the SFR between the control group and patients on antidepressants. Among patients on antidepressants such as SSRIs and TCAs, symptoms of xerostomia were present. The MST values of healthy control group I had a mean reading of 34.96, group II had 26.73, and group III had 10.69 at the end of 3 min. Chen *et al.* suggested that 15 mm at 3 min indicated hyposalivation.<sup>[17]</sup> A study conducted by Lopez and Jornet suggested a cutoff value of 43.3 mm at 5 min, presuming that the reading will be 26.00 at 3 min. Davis and Mark also used a strip for 5 min with a mean reading of 10.6 mm and for 3 min with a mean reading of 15.6 mm. Their reading was low based on the fact that saliva was collected from the single parotid duct.<sup>[18,19]</sup> Kumar *et al.* have used the MST to check hyposalivation in patients on antidepressants that had high sensitivity and specificity.<sup>[20]</sup>

The spitting method was performed along with MST. The mean SFR for 5 min among Group I was 0.83, Group II had 0.47, and Group III had 0.39. A similar study was conducted by Chen *et al.*, obtaining a value of 0.47 g/min.<sup>[18]</sup>

There are several methods to measure saliva in resting and stimulating condition. Saliva can be collected from an individual gland lashley cup that is used for saliva of the parotid region, and Schneyer's device is used for submandibular and sublingual saliva. Conventional methods are time-consuming and require devices to perform the tests that might not be readily available in dental clinics and hospitals. The usage of suction devices or catheters can cause irritation and discomfort to the patient.<sup>[21]</sup> Fontana *et al.* assessed the relationship between MST and other saliva collecting methods and evaluated the correlation between MST and the spitting

**Table 4: Comparison and correlation of salivary flow rate by spitting method and Modified Schirmer Test**

Group	SFR for 5 min	MST at 3 min	Pearson coefficient (r)	<i>P</i> value
Group I	0.83	34.96	0.32	<0.860
Group II	0.47	26.25	0.52	<0.001
Group III	0.39	10.71	0.35	<0.041

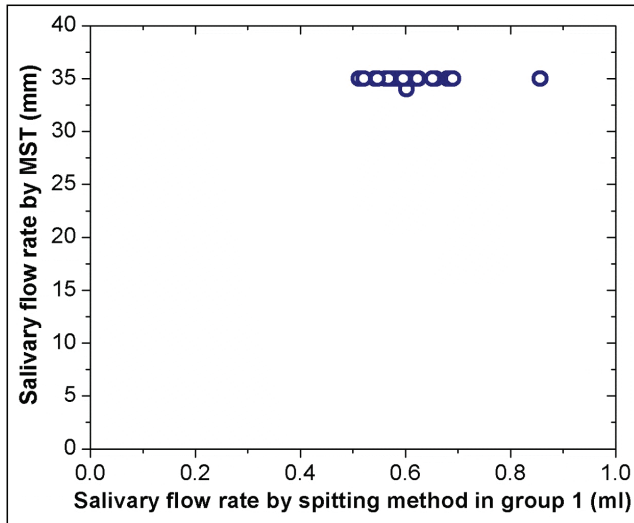
method. In our study, there was a correlation between MST and the spitting method in Group II and Group III; there was no correlation in the control group. The strip would reach the 35 mm marking before 3 min, and lack of standardization might be the reason for Group I not obtaining significant results. The study conducted by Chen *et al.* showed no significance in the control group due to lack of restriction of diet and liquid 1 h before the study.

Questionnaire is a good screening tool for ruling out xerostomia. In our study, Group II prevalence of xerostomia was 25.7% and Group III prevalence of xerostomia was 100%. So, this can be used to document hypofunction of the salivary gland.

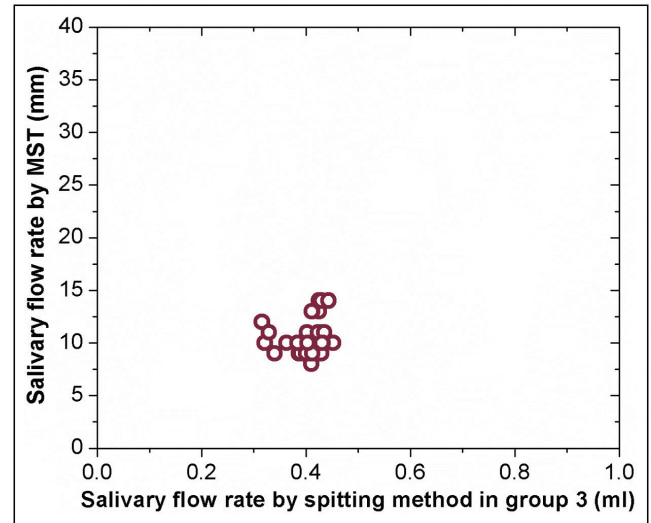
The MST was a noninvasive and less time-consuming chairside investigative tool that was used to assess the subjective and objective salivary discrepancies. Based on the results obtained, MST has the sensitivity and specificity to assess the SFR, which is comparative or even better than the conventional gold standard method such as the spitting method; it has the following advantages: the MST is simple, inexpensive, and readily available in sterilized packs for routine use in clinical settings. The MST helps in instant checking of medication effects on saliva. Hence, from our study, it can be considered that the MST can be used to assess SFR in patients who are on antidepressants.

## CONCLUSION

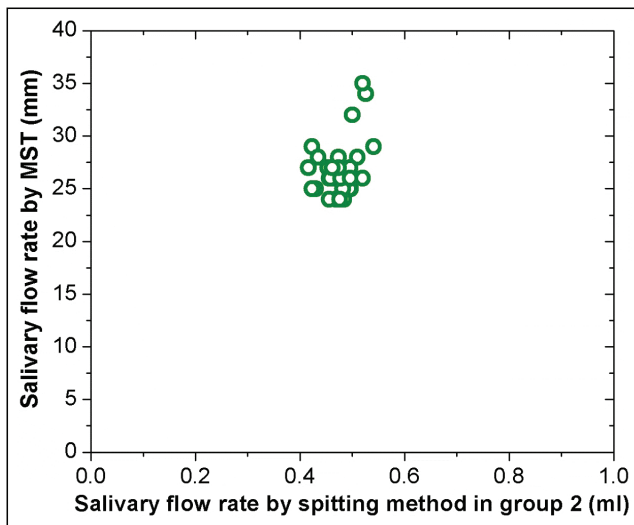
There are various methods to assess SFR, and the MST is one of them. The objective findings are more important than the subjective findings, as they are more reliable and accurate to assess the salivary gland function. Patients who are healthy and asymptomatic can be readily differentiated from those who suffer



**Figure 2:** Comparison and correlation of SFR by the spitting method and MST in Group I



**Figure 4:** Comparison and correlation of SFR by the spitting method and MST in Group III



**Figure 3:** Comparison and correlation of SFR by the spitting method and MST in Group II

from hyposalivation. Finally, summing up this method will help in the easy monitoring of those patients who have hyposalivation visiting dentists.

*Future Scope/Clinical Significance* It is a simple, noninvasive chairside investigation that can be routinely used in our daily practices. It takes less than 5 min to perform the test. It aids in monitoring the patients who have reduced salivary flow and in managing them accordingly.

The SFR can be assessed faster; the method is less cumbersome and well tolerated; and it is easy to dispose the saliva with the pouches available. There are many methods to check SFR. The results are instant and accurate. The strip is blue in color, which helps in

easy identification compared with other methods such as the spitting method and the Saxon test. The color change in the strip helps to investigate whether a person is having hyposalivation/xerostomia. The test can also be performed by the patient himself or herself during treatment.

The test strip that we have used in our study is a 4 cm strip that is calibrated in 1 mm intervals from 5 to 35 mm along its length and that has a rounded notch. The color change (blue) will be noticed when it is kept in the patient's mouth. By the change in color of the strip, accurate values can be obtained, which will help the clinician to diagnose xerostomia at the chairside investigation itself. The MST can be used as a routine chairside screening tool, to evaluate xerostomia and hyposalivation.

#### ACKNOWLEDGMENTS

Not applicable.

#### FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

#### CONFLICTS OF INTEREST

None of the authors have conflict of interest.

#### AUTHORS' CONTRIBUTIONS

Not applicable.

#### ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

Approval for the study was granted by the Ethics Committee of AJ Institute of Medical Sciences (approval date: November 8, 2013, approval number: AJEC/Rev/76/ 2011–2012) and confirming to the standards of the Declaration of Helsinki and its

subsequent revisions. All the procedures have been performed as per the Helsinki guidelines.

#### PATIENT DECLARATION OF CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

#### Data availability statement

Data availability and supplementary materials used in our study are available on request at AJ Institute of Dental Sciences after the embargo period. The additional data of this study are available from corresponding author upon reasonable request.

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