Evaluation of Sialometric Analysis of Patients Suffering from Depressive Disorders

Annette Milton B, Bhambal A, Nair P

People's College of Dental Sciences and Research Centre

Bhopal, Madhya Pradesh, India.

Corresponding Author

Annette Milton B

People's College of Dental Sciences and Research Centre

Bhopal, Madhya Pradesh, India.

E-mail: 11drann@gmail.com

Citation

Annette Milton B, Bhambal A, Nair P. Evaluation of Sialometric Analysis of Patients Suffering from Depressive Disorders. *Kathmandu Univ Med J* 2015;50(2):134-9.

ABSTRACT

Background

Depressive disorders, worldwide, may rank second by the year 2020. In India; about 10 million people suffer from depressive disorders, the prevalence rate being recorded as 31.2 for every 1000 individuals. A significant impairment of all personal hygiene may occur due a depressive episode which in turn may result in altered salivary flow.

Objective

The present study was a hospital- based clinical cross-sectional study which was conducted in Bhopal, the heart of Madhya Pradesh, India. It was done to assess the relationship of bring about a comparison of sialometric alterations between normal and subjects with depressive disorders.

Method

The survey period extended over a period of one year and two months, from May 2009 to July 2010. It was conducted in Bhopal, Madhya Pradesh, Central India. A sample size of 150 individuals, 50 of each group, was taken in the study. Whole salivary flow rates were determined by gravimetric method (i.e. in millilitres per minute). The Tenovuo criterion was used, to which numerical scores (SFI) were attributed.

Result

Results showed that the unstimulated salivary flow rates between patients of Group I and Group III ($p< 0.0001$) and between Group II and Group III ($p < 0.0001$) were statistically significant. The study also showed statistically significant relation between subjective and objective oral dryness (chi 2= 55.789, df= 6 and $p< 0.0001$).

Conclusion

It was observed that subjective sensation of dry mouth may exist even in the presence of normal salivary flow rates. This might be acknowledged as a psychophysiological expression of depression and may not necessarily reflect actual salivary gland function. The lack of secreted mucins rather than the quantity of saliva may play a role in the genesis of xerostomia.

KEY WORDS

Depression, sialometry, sialometric analysis, subjective oral dryness, unstimulated saliva, xerostomia.

INTRODUCTION

Depressive disorders rank fourth as causes of disability worldwide and may rank second by the year 2020. Prevalence of depressive symptoms may be as high as 30% in the general population with women being twice as likely to be affected as men.[1] In India; about 10 million people suffer from depressive disorders. The prevalence rate for depression in India in the year 2001 was recorded as 31.2 for every 1000 individuals.[2]

A holistic approach to health is currently widely advocated as a prerequisite for successful outcomes in patient care. A significant impairment of oral hygiene may occur due to the depth of a depressive episode - salivary flow may be reduced and patient may complain of dry mouth, increased rate of dental caries and periodontal disease. Although saliva provides an easily available, non-invasive diagnostic medium for a rapidly widening range of diseases, saliva sampling unfortunately, has not yet become a routine laboratory procedure. All psychotropic drugs, even those of the latest generation, present side effects. The present scenario has prompted this study to estimate the salivary flow rate levels in patients on antidepressants and on psychiatric counselling in order to develop cost-effective and simple diagnostic methods. Sialometry thus provides quantitative information of the flow rates of saliva which are used for diagnostic and research purposes.[3-6]

The aim of this study was to investigate the sialometric variations in healthy and depressed patients and the objectives were to compare the quantitative differences of unstimulated saliva between healthy individuals and depressed patients and to check for correlation between hyposalivation and subjective oral dryness. The latter was further subdivided as those under medication and those who were on psychiatric counseling only.

METHODS

I. Study Type And Study Design:

The present study was a hospital- based clinical cross-sectional study. An attempt was done to assess and bring about a comparison of sialometric alterations in unstimulated saliva between normal (Group I) and subjects with depressive disorders who were either only on psychiatric counseling (Group II) or on medication for at least 1 month (Group III). The effect of three antidepressive drugs {namely Tricyclic antidepressants (TCAs), Selective serotonin reuptake inhibitors (SSRIs) and Tetracyclic antidepressants (TeCAs)}, which were commonly prescribed by the psychiatrists, were considered for the study.

II. Place and Duration of Study:

The present study was conducted in Bhopal, the heart of Madhya Pradesh. The survey period extended over a period of one year and two months, from May 2009 to July 2010.

III. Sample Size and Sampling Method:

This was a hospital based cross- sectional study. Sample size was calculated by using the following formula.

$$n = \frac{t^2 \times p(1-p)}{m^2}$$

n = required sample size

t = confidence level at 95% (standard value of 1.96)

p = estimated prevalence of depressive illness in the project area

m = margin of error at 5% (standard value of 0.05)

Using this formula, the sample size calculated. A sample size of 150 individuals, 50 of each group were taken in the study.

IV. Method of Data Collection:

• Standardization of Total Saliva Collection:

All samples were taken between the hours of 9:00 -11:30 am. Samples were collected from patients coming to the department of oral medicine and radiology, People's College of Dental Sciences and Research Centre and from the department of psychiatry and psychiatric counselling, Gandhi Medical College and Associated Hospitals, Bhopal. Those candidates who fulfilled the criteria of any of the three groups were selected for this study. The individuals were asked to refrain from eating, drinking (except water), tooth brushing, practice physical exercises or be under great physical stress for at least 1 hour prior to sample collection. The subjects were instructed to sit in a relaxed position in an ordinary chair. All samples were collected in pretagged and preweighed sterile universal collection vials. Samples containing visible blood were discarded. The samples were assembled in a polystyrene box with dry ice and then taken to the biochemistry laboratory at People's College of Medical Sciences and Research Centre, Bhopal. They were processed on the same day they were collected or stored at -20oc and analysed within 24 hours after collection.

• Equipments and Materials Used:

An analytic scale was used to measure weight of the pretagged vials with lid before and after the collection of saliva. Borosil vials with lid were sterilized in an autoclave prior to any test. Each vial was then pretagged with an identification number. The closed vials were used to collect and transport the samples from the hospitals to the laboratories for analysis. The mass of the universal collection vial with cap was measured, before and after the sample collection, with the help of analytic scale. Plastic funnels which were cold sterilized were given to each patient along with the vials to aid in collection. After the procedure, they were discarded. Stimulated whole saliva samples were obtained by mechanical stimulus, using sterilized rubber bands of standard size (1 cm in diameter).

Test-tube racks were used for placing the test-tubes before and after collection.

A 10 x10 inch sized polystyrene box was half- filled with dry ice cubes. This was used to transport the clinical samples to the biochemistry laboratory for analysis. A deep freezer with provision of maintaining the temperature at -20oc was used to store the samples.

• Method for collecting clinical data:

Unstimulated whole saliva was collected from all subjects by direct draining method into the pre weighed and pretagged vials. Each participant was first asked to wash his/her mouth, allow saliva to accumulate in the mouth and then to expectorate through a funnel into a sterile vial usually once every 60 seconds over a period of 10 minutes.[1,2]

Storage and Transport of Salivary Samples:

The samples were wiped with tissue paper and then assembled in a polystyrene box with dry ice. This was immediately transported to the biochemistry laboratory at the People's College of Medical Sciences, Bhopal where it was stored at -21o c. The samples were analysed on the same day or within 24 hours. Unused samples were discarded after 24 hours to avoid contamination and inaccurate estimates.

V. Ethical Consideration and Patient Consent:

The entire study protocol had been approved by *The Ethical Committee of People's College of Dental Sciences and Research Centre* and affiliated to Barkatullah University of Bhopal. After a complete and detailed explanation about the nature of research, its objectives, methods and anticipated benefits and the inconvenience this methodology could cause, the research participants signed a free and informed consent form authorizing their voluntary participation in the research.

VI. Inclusion and Exclusion Criteria:

Subject groups:

A total number of 150 subjects were included. Three different study groups selected were as follows:

1. Study group I

2. Study group II

3. Study group III

1. Study group I / Control group:

The study group comprised of 50 normal volunteers, of either gender, above 15 years and below 45 years of age.

• *Inclusion criteria:*

i. Subjects who were physically healthy and were well oriented in time, space and person.

ii. Subjects who had no depressive symptoms or depression disorders.

iii. Subjects who were not on any medication for any systemic diseases.

iv. Subjects who had willingly signed the consent form prior to the study.

• *Exclusion Criteria:*

i. Patients with systemic disorders related to salivary gland physiology.

ii. Patients with a history of menopause and hysterectomy.

iii. Patients with a history of radiotherapy/chemotherapy in the head and neck region in the last three months.

iv. Smokers, alcohol users and illicit drug users.

2. Study group II:

This study group consisted of 50 patients of both sexes and were between 15 to 45 years of age.

• *Inclusion Criteria:*

i. Patients who were physically healthy and had come to the department of psychiatry with complaints of depressive symptoms.

ii. Patients who were either under psychiatric counselling or had come to the psychiatric out- patient department for consultation.

iii. Patients who had not taken any psychosomatic drugs so far.

• *Exclusion Criteria:*

i. Patients on any type of psychotropic drugs.

ii. Patients suffering from systemic conditions related to salivary gland disorders.

iii. Patients with a history of menopause and hysterectomy.

iv. Patients with a history of radiotherapy/chemotherapy in the head and neck region in the last three months.

v. Smokers, alcohol users and illicit drug users.

3. Study group III:

This study group consisted of 50 patients and were between 15 to 45 years of age.

• *Inclusion criteria:*

i. Patients who had been diagnosed and were undergoing treatment in the Department of psychiatry and psychiatric Counselling, for either depressive disorders/ disease.

ii. Patients who had been on antidepressant drugs for a minimum of 1 month.

• *Exclusion Criteria:*

i. Patients with systemic disorders related to salivary gland physiology.

ii. Patients with a history of menopause and hysterectomy.

iii. Patients with a history of radiotherapy/chemotherapy in the head and neck region in the last three months.

iv. Smokers, alcohol users and illicit drug use.

VII. PROTOCOLS FOLLOWED (if any):

CLINICAL ASSESSMENT:

• Self- administered questionnaire

A preliminary case history of the individuals according to a self- administered questionnaire was developed to identify the patient data which included: age, sex, diagnosed diseases and presence of any acute illness, regularly prescribed medication or over-the- counter medication.

• Questionnaire for Subjective Oral Dryness

A questionnaire constructed especially for this study was used to determine the subjective presence or absence of oral dryness and their related symptoms. It was established with a scale of present or absent to the symptoms related by the patient. The questionnaire was given to the patients prior to sample collection.

• Assessment of Depression:

The patients coming to the outpatient department of the hospital were first shown to the psychiatrist. The type of depression was assessed by using the *DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) SCALE* for depression.

For patients who were using psychotropic drugs, data about the medication, including duration and dosage were recorded.

• Laboratory Procedures- Sialometric Analysis:

In the present study, whole salivary flow rates were determined by gravimetric method (i.e. in millilitres per minute). The pretagged borosil vials with lid were measured on the assuming that the specific gravity of saliva is 1 and that 1 gram mass is equal to 1 ml of saliva. The difference in the vial mass before and after collection, divided by the time period of 10 minutes, gave the salivary flow rate expressed in ml/min. The Tenovuo criterion was used, to which the following numerical scores (SFI) were attributed.[1]

VIII. STATISTICAL ANALYSIS AND SOFTWARE USED:

Unpaired Student t-test was used to compare the sialometric levels of unstitmulated saliva between groups I, II& III and between the 3 antidepressive drugs of group III.

Chi square test of correlation was used to study the levels of oral dryness in group II.

RESULTS

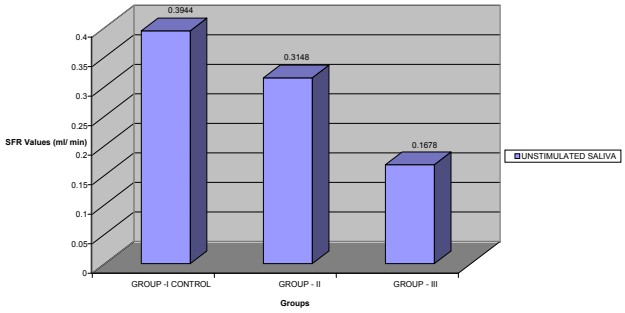
The present study was done to assess the effects of depression and antidepressant drugs on the sialometric parameter of unstimulated whole saliva. Significant associations between Group I, Group II and Group III were observed. Severity of changes was observed among Group III patients. The results were tabulated along with statistical analysis.

Sialometric Analysis:

Table 1 and Graph 1 show variation in the unstimulated salivary flow rates between the three groups. Group III (0.168± 0.057) (mean ± SD) had reduced salivary flow when compared to Group I (0.394±0.28) and Group II (0.315± 0.19). Unstimulated salivary flow rates between patients of Group I and Group III ($p< 0.0001$) and between Group II and Group III ($p < 0.0001$) were statistically significant. Though a slight decrease was noted in the rates of Group II when compared to Group I, tests did not show statistical significance ($p= 0.0967$).

Table 1. Comparison of Sialometric Analysis of Unstimulated Whole Saliva between Group I, Group II and Group III patients.

	GROUP	Mean	SD	t-value	d/f	P- Value	Results
FLOW RATE (ml/min)	Group I v/s Group II	0.39 0.31	0.28 0.19	1.68	98	P=0.0967	NS
	Group II v/s Group III	0.31 0.17	0.19 0.06	5.24	98	P<0.0001	S
	Group I v/s Group III	0.39 0.17	0.28 0.06	5.67	98	P<0.0001	S



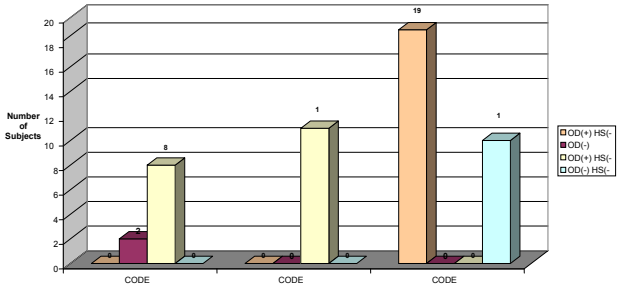
Graph 1. Comparison of Unstimulated Salivary Flow Rates between Group I, Group II and Group III patients.

Estimation of Oral Dryness and Hyposalivation:

Table 2 and Graph 2 shows the relation between subjective oral dryness and hyposalivation in Group II patients. Among 50 subjects, 16 (32%) males and 19 (38%) females experienced subjective oral dryness in Group II patients. 20 (40%) had both subjective oral dryness feeling and hyposalivation, 18 (36%) had subjective oral dryness feeling but no hyposalivation, 2 (4%) had no feeling of oral dryness but had hyposalivation and 10 (20%) had no oral dryness with no decrease in salivation. The relation between subjective and objective oral dryness was found to be statistically significant (chi 2= 55.789, d.f= 6 and $p<0.0001$).

Table 2. Relation between subjective feeling of oral Dryness and Hyposalivation in Group II patients.

	x^2 value	d/f	P-value	Result
Whole Unstimulated Saliva	55.789	6	P < 0.0001	S



Unstimulated whole salivary flow rate and subjective oral dryness feeling in Group II patients

Graph 2. Comparison of subjective feeling of Oral Dryness and Hyposalivation in Group II patients.

DISCUSSION

The present study results showed that there was statistically significant difference in the unstimulated salivary flow rate between patients of Group I and Group III (p< 0.0001) and between Group II and Group III (p < 0.0001). The salivary flow rate of Group III patients was significantly reduced when compared to Group I and Group II.

The mean values of unstimulated saliva in Group I in the present study correlated with the findings of Andersson et al (mean= 0.39), Becks & Wainwright (mean 0.32) and Heintze et al (0.36).[7]

In Group III, there was statistically significant difference between patients taking TCAs and SSRIs (p< 0.0001) and between patients taking TCAs and TeCAs (p= 0.0006). However, no difference was observed between patients taking SSRIs and TeCAs (p= 0.0939). Patients on TCAs had the lowest unstimulated salivary flow rate as compared to those taking SSRIs and TeCAs. This is because of the anticholinergic properties of TCAs which is in accordance with a previous study conducted by Cooper TB et al.[8]

Arnold SE et al. found similar significant depressions in salivary flow when the effects of three TCAs (amitriptyline, desipramine and doxepin) were compared.[9]

Studies done by Palmai G et al. & Mörnstad H et al. stated that the most pronounced reduction in the salivary flow rate was at rest.[10,11] TCA caused a more pronounced reduction than SSRIs. Imipramine (TCAs) reduced salivation by 12% and zimelidine (SSRIs) by 45.2%.

Oral dryness and Hyposalivation in Unstimulated saliva:

16 (32%) males and 19 (38%) females experienced subjective oral dryness in Group II patients. Considering the unstimulated salivary flow rate, 20 (40%) had both subjective oral dryness feeling and hyposalivation, 18 (36%) had subjective oral dryness feeling but no hyposalivation, 2 (4%) had no feeling of oral dryness but had hyposalivation and 10 (20%) had no oral dryness with no decrease in salivation. The relation between subjective and objective oral dryness was found to be statistically significant (p<0.0001).

This study correlated with Nederfors T et al. who concluded that xerostomia is not necessarily reflected in the actually measured flow rates.[12] The cause can be contributed to either water or metabolite loss; damage to salivary glands and interference with neural transmission.[13-15]

Bergdahl M and Bergdahl J also stated that not only medication but psychological factors could be associated with hyposalivation or subjective oral dryness.[5] Subjective oral dryness could be associated with depression, trait anxiety, perceived stress, state anxiety and female gender; while age and medication could play an important role in individuals with hyposalivation. Direct comparisons could not be made between the findings of the present study and studies reported in literature due to differences in study population.

The present study revealed reduction in the salivary flow rate in patients who had been under various antidepressant medications (mainly TCAs) for depressive illness. There was a significant relationship between the subjective feeling of oral dryness and objective reduction in the flow.

CONCLUSION

The present study was a hospital- based clinical cross-sectional study which was conducted in Bhopal, the heart of Madhya Pradesh. An attempt was done to assess and bring about a comparison of sialometric alterations in unstimulated saliva between normal (Group I) and subjects with depressive disorders who were either only on psychiatric counseling (Group II) or on medication for at least 1 month (Group III). The effect of three antidepressive drugs {namely Tricyclic antidepressants (TCAs), Selective serotonin reuptake inhibitors (SSRIs) and Tetracyclic antidepressants (TeCAs)}, which were commonly prescribed by the psychiatrists, were considered for the study.

Salivary quantitative alterations in their levels were assessed among the three groups. The results were compared and correlated. The present study depicted the following outcome:

i. There was reduction in the unstimulated salivary flow rate in Group III patients especially those who had been administering Tricyclic antidepressants (TCAs).

ii. It was found that subjective oral dryness feeling in patients with depressive illness was not always associated with decrease in the salivary flow rate.

To conclude, antidepressant drugs do affect the salivary flow. These discrepancies could be due to pharmacokinetic and pharmacodynamic implication, the study group selected and the bioavailability of drugs. From the present study, it was observed that cyclic antidepressants produced significant sialometric alterations in saliva.

REFERENCES

1. Tenovo J. Human saliva: Clinical chemistry and microbiology. Volume 1.© 1989 by CRC Press Inc., Boca Raton, Florida.
2. Tenovo J. Human saliva: Clinical chemistry and microbiology. Volume 2.© 1989 by CRC. Press Inc. Boca Raton, Florida.
3. Kalk WWI, Vissink A, Spijkervet FKL, Bootsma H, Kallenberg CGM and Amerongen AVN. Sialometry and sialochemistry: Diagnostic tools for Sjögren's syndrome. *Ann Rheum Dis* 2001; 60: 1110-16.
4. Kalk WWI, Vissink A, Stegenga B, Bootsma H, Amerongen AVN and Kallenberg CGM. Sialometry and sialochemistry: a non-invasive approach for diagnosing Sjögren's syndrome. *Ann Rheum Dis* 2002; 61: 137-44.
5. Bergdahl M and Bergdahl J. Low unstimulated salivary flow and subjective oral dryness: Association with medication, anxiety, depression and stress. *J Dent Res.* 2000; 79(9): 1652- 58.
6. Michels LFE. Diagnosis of salivary gland disorders. Graamans K & Van Den Akker HP (Eds) 1991. Kluwer academic publishers. Netherlands. 139-61.
7. Dawes C. Physiological factors affecting salivary flow rate, oral sugar clearance and the sensation of dry mouth in man. *J Dent Res* 1987; 66: 648-53.
8. Cooper TB, Bark N and Simpson GM. Prediction of steady state plasma and saliva levels of desmethlimipramine using a single dose, single time point procedure. *Psychopharmacology.* 1981; 74: 115-21.
9. Arnold SE, Kahn RJ, Faldetta LL, Laing RA and Mcnair DM. Tricyclic Antidepressants and Peripheral Anticholinergic Activity. *Psychopharmacology.*1981; 74: 325-28.
10. Palmai G, Blackwell B, Maxwell E and Morgenstern F. Patterns of salivary flow in depressive illness and during treatment. *Brit J Psychiat.* 1967; 113:1297-1308.
11. Mörnstad H, Knorring LV, Forsgren L and Holmgren S. Long-term effects of two principally different antidepressant drugs on saliva secretion and composition. *Scand J Dent Res.* 1986; 94:461-70.
12. Nederfors T, Isalsson R, Mornstad H, Dahlof C. Prevalence of Perceived Symptoms of Dry Mouth In An adult Swedish population- relation to age, sex and pharmacotherapy. *Community Dent Oral Epidemiol.* 1997; 25:211-6.
13. Nederfors T. Xerostomia and hyposalivation. *Adv Dent Res.* 2000; 14: 48- 55.
14. Thelin WR, Brennan MT, Lockhart ML, Singh ML, Fox PC, Papas AS and Boucher RC. The oral mucosa as a therapeutic target for xerostomia. *Oral Diseases.* 2008; 14, 683-9.
15. Mathew RJ, Weinman M and Claghorn JL. Xerostomia and Sialorrhea in Depression. *Am K. Psychiatry.* 1979;136: 11.