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Original Research

Sialochemical Analysis: Windfall to the Oral Physician (A Hospital-based Clinical Cross-Sectional Study in Depressive Disorders)

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***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 biochemical composition of some important salivary parameters. The present study was conducted in Bhopal, the heart of Madhya Pradesh, India. It was done to assess the relationship and bring about a comparison of certain selective sialochemical alterations between normal and subjects with depressive disorders.

Materials and Methods: The research participants signed a free and informed consent form authorizing their voluntary participation in the research. A total number of 150 subjects were selected and were distributed equally between 3 groups - Group I (normal), Group II (subjects with depressive disorders who were only on psychiatric counseling) and Group III (subjects with depressive disorders who were on medication for at least 1 month). The effect of three antidepressant drugs, which were commonly prescribed by the psychiatrists were considered for the study. Stimulated whole saliva was analyzed biochemically for α-amylase, calcium, sodium, potassium, total proteins, and urea.

Results: Stimulated salivary calcium and total protein levels were found to be statistically significant among all three groups ($P < 0.0001$). Salivary amylase levels between Groups II and III and between Groups I and III ($P < 0.0001$) was statistically significant while the salivary urea levels between Groups I and II and between Groups I and III were found to be statistically significant ($P < 0.0001$). However, there was no statistical difference in their sodium and potassium levels.

Conclusions: It was observed that drugs do affect the salivary composition. It was observed that cyclic antidepressants produced significant alteration in the sialochemical constituents of saliva as compared to tricyclic antidepressants and tetracyclic antidepressants.

Key Words: Depression, sialochemistry, stimulated saliva

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]

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 changes in the salivary composition in patients on antidepressants and on psychiatric counseling in order to develop cost-effective and simple diagnostic methods.

Sialochemistry thus provides qualitative information on certain important parameters of saliva, which is used for diagnostic and research purposes.[3-6] Although a growing number of dental and medical doctors are discovering that 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 in dental offices. All psychotropic drugs, even those of the latest generation, present side-effects. The present scenario has prompted this study to estimate the composition of certain important salivary parameters in patients on antidepressants or on psychiatric counseling in order to develop cost-effective and simple diagnostic methods.

Aim

The aim was to investigate the sialochemical variations in healthy and patients with depressive disorders.

Objectives

1. To compare the qualitative differences of stimulated saliva

between healthy individuals and depressed patients.
2. To check for correlation between important biochemical parameters in saliva.
3. To compare these results with other studies and see for differences in the results.

Ethical consideration

The entire study protocol had been approved by The Ethical Committee of People's College of Dental Sciences and Research Center and affiliated to Barkatullah University of Bhopal.

Study setting and schedule of the survey

The present study had been conducted in Bhopal, the capital city of Madhya Pradesh. The survey period extended over a period of 1 year and 2 months, from May 2009 to July 2010.

Materials and Methods

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.

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

Criteria for patient selection

Subjects who were physically healthy had no depressive symptoms disorders and were not on any medication for any systemic diseases were selected as a study Group I. While patients with complaints of depressive symptoms, and were either under psychiatric counseling or had been on antidepressant drugs for a minimum of 1 month, comprised Groups II and III, respectively. The exclusion criteria included deleterious habits, systemic disorders related to salivary gland physiology, menopause, hysterectomy and radio/chemotherapy in the head and neck region in the last 3 months.

Determining sample size

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.

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.

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 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.

Data collection of saliva samples

Equipments and materials used

Borosil vials with lid were autoclaved and pretagged with an identification number. The closed vials were used to collect and transport the samples from hospitals to the laboratories for analysis. Cold sterilized disposable funnels were given to each patient along with the vials to aid in the collection. A polystyrene box half-filled with dry ice cubes was used to transport the clinical samples to the biochemistry laboratory for analysis. A deep freezer with provision of maintaining the temperature at −20°C was used to store the samples.

Standardization and method for collecting clinical data

All samples were taken between the hours of 9:00-11:30 am. Samples were collected from patients by direct draining method. 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), and tooth brushing, practice physical exercises or be under great physical stress for at least 1 h prior to sample collection. The subjects were instructed to wash their mouths, sit in a relaxed position and chew on sterile rubber bands of standard size. Saliva was allowed to accumulate in the mouth and drained through a funnel into vials over a period of 10 min.[1,7] Samples containing visible blood were discarded.

Storage and transport of salivary samples

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

Biochemical analyses

Stimulated salivary α-amylase and calcium activity were determined with the help of colorimetric method and specific Autopak kits, while sodium and potassium concentration were determined with a photochromometer at 540 nm within 10 min. Total protein concentration was estimated using the end-point method. Urea in the saliva was determined with autopak kit (ultra violet method or the enzymatic method).

Demographic and laboratory data gathered were sorted, tabulated and subjected to appropriate statistical analysis with the consult of a statistician. The data so obtained was compiled systematically. A master table was prepared, and the total data were subdivided and distributed meaningfully and presented as individual tables along with graphs.

Results

The present study was conducted in Bhopal, Madhya Pradesh, with a view to assess and bring about a comparison of sialochemical alterations in selected important parameters in unstimulated whole saliva.

A total of 150 subjects were chosen for the study, which comprised of subjects with clinically diagnosed depressive disorders; i.e., those who were not on medication, those who were on antidepressant drugs (i.e., tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs] and tetracyclic antidepressants [TeCAs]) and control group.

The following observations were tabulated along with statistical analysis.

Estimation of α-amylase

Table 1 shows the mean stimulated salivary amylase levels in Group I (138947.6 ± 109250.3), Group II (101900 ± 44548.8) and Group III (527685.8 ± 358656.7) patients. There was statistically significant differences between all the three groups, i.e. the values between Groups I and II, Groups II and III and between Groups I and III were $P = 0.029$, $P < 0.0001$, and $P < 0.0001$, respectively.

Table 1: Comparison of stimulated whole salivary α-amylase levels between Groups I, II, and III.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
α-amylase (U/L)	Group I versus Group II	111766.00	78183.94	0.73	98	*P*=0.469	NS
		133338.00	194706.78				
	Group II versus Group III	133338.00	194706.78	6.61	98	*P*<0.0001	S
		561312.94	414583.36				
	Group I versus Group III	111766.00	78183.94	7.53	98	*P*<0.0001	S
		527685.80	358656.7				

SD: Standard deviation, S: Significant, NS: Non significant, D/F: Degrees of freedom

Estimation of α-amylase between 3 different antidepressant drugs

Table 2 shows that among Group III patients, the mean stimulated α-amylase levels in patients on TCAs were 707039 ± 310995, on SSRIs were 310995 ± 3988243 and on TeCAs were 645465 ± 178254. The stimulated results for α-amylase was statistically significant only between patients on TCAs and SSRIs and between SSRIs and TeCAs ($P = 0.005$ and $P < 0.003$, respectively). The results between TCAs and TeCAs were not statistically significant ($P = 0.502$).

Estimation of calcium

Table 3 shows that the stimulated calcium values among all groups were statistically significant when compared to each other, respectively ($P < 0.0001$). The mean stimulated calcium values for Group I was 2.52 ± 1.83, for Group II was 7.44 ± 3.86, and for Group III was 10.91 ± 3.87, respectively.

Estimation of calcium between 3 different antidepressant drugs

Table 4 estimated the stimulated salivary calcium values between all the drugs, i.e., between TCAs and SSRIs ($P < 0.0001$), between SSRIs and TeCAs ($P = 0.0322$) and between TCAs and TeCAs ($P < 0.0001$) to be statistically significant to each other. The mean values of TCAs, SSRIs and TeCAs obtained were 15.82 ± 1.77, 10.07 ± 3.34, and 8.15 ± 1.28, respectively.

Estimation of sodium

The stimulated salivary sodium levels in Table 5 and shows

Table 2: Comparison of stimulated whole salivary α-amylase between three types of antidepressant drugs.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
α-amylase (U/L)	TCA versus SSRI	707038.50	313508.70	3.02	31	*P*=0.0050	S
		310994.50	3988243.00				
	SSRI versus TeCA	310994.50	3988243.00	3.19	35	*P*=0.0030	S
		645464.70	178253.90				
	TCA versus TeCA	707038.50	313508.70	0.68	28	*P*=0.5017	NS
		645464.70	178253.90				

SD: Standard deviation, S: Significant, NS: Non significant, TCA: Tricyclic antidepressant, SSRI: Selective serotonin reuptake inhibitor, TeCA: Tetracyclic antidepressants, D/F: Degrees of freedom

Table 3: Comparison of stimulated whole salivary calcium between Groups I, II, and III.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Calcium (mg/dl)	Group I versus Group II	2.52	1.83	8.14	98	*P*<0.0001	S
		7.44	3.86				
	Group II versus Group III	7.44	3.86	4.50	98	*P*<0.0001	S
		10.91	3.87				
	Group I versus Group III	2.52	1.83	13.87	98	*P*<0.0001	S
		10.91	3.87				

SD: Standard deviation, S: Significant, NS: Non significant, D/F: Degrees of freedom

statistically significant differences between Groups I and II ($P < 0.0001$) and between Groups I and III ($P < 0.0001$) when compared with Groups II and III ($P = 0.091$). The mean value of Groups I, II, and III were 29.04 ± 13.83, 16.93 ± 5.43, and 14.92 ± 6.31, respectively.

Estimation of sodium between 3 different antidepressant drugs

Table 6 shows that among Group III patients, the stimulated whole saliva sodium levels was found to be statistically significant between SSRIs and TeCAs and between TCAs and TeCAs ($P = 0.0003$, $P = 0.0006$, respectively). The results between TCAs and SSRIs were not significant statistically ($P = 0.5195$). The mean value of TeCAs (19.394 ± 3.07) was more when compared to the mean values of TCA (13.51 ± 5.28) and SSRI (12.03 ± 7.0).

Table 4: Comparison of stimulated whole salivary calcium between three types of antidepressant drugs.

Parameter	Group	Mean	SD	*t* value	D/f	*P* value	Results
Calcium (mg/dl)	TCA versus SSRI	15.82	1.77	5.70	31	*P*<0.0001	S
		10.07	3.34				
	SSRI versus TeCA	10.07	3.34	2.23	35	*P*=0.0322	S
		8.15	1.28				
	TCA versus TeCA	15.82	1.77	13.78	28	*P*<0.0001	S
		8.15	1.28				

SD: Standard deviation, S: Significant, TCA: Tricyclic antidepressant, SSRI: Selective serotonin reuptake inhibitor, TeCA: Tetracyclic antidepressants, D/F: Degrees of freedom

Table 5: Comparison of stimulated whole salivary sodium between Groups I, II, and III.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Sodium (mg/dl)	Group I versus Group II	29.04	13.83	5.76	98	*P*<0.000	S
		16.93	5.43				
	Group II versus Group III	16.93	5.43	1.71	98	*P*=0.091	NS
		14.92	6.31				
	Group I versus Group III	29.04	13.83	6.57	98	*P*<0.0001	S

SD: Standard deviation, S: Significant, NS: Non significant, D/F: Degrees of freedom

Table 6: Comparison of stimulated whole salivary sodium between three types of antidepressant drugs.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Sodium (mg/dl)	TCA versus SSRI	13.51	5.28	0.65	31	*P*=0.5195	NS
		12.03	7.00				
	SSRI versus TeCA	12.03	7.00	4.02	35	*P*=0.0003	S
		9.39	3.07				
	TCA versus TeCA	13.51	5.28	3.84	28	*P*=0.0006	S
		9.39	3.07				

SD: Standard deviation, S: Significant, NS: Non significant, TCA: Tricyclic antidepressant, SSRI: Selective serotonin reuptake inhibitor, TeCA: Tetracyclic antidepressants, D/F: Degrees of freedom

Estimation of potassium

As shown in Table 7, the stimulated salivary potassium levels between Groups II and III ($P = 0.006$) and between Groups I and III ($P < 0.0001$) had statistically significant differences when compared to each other. However, Groups I and II showed no statistical significant difference ($P = 0.4211$). The mean stimulated values for salivary potassium in Group I was 28.26 ± 9.09, in Group II 25.86 ± 18.96, and in Group III 17.31 ± 10.35, respectively.

Estimation of potassium between 3 different antidepressant drugs

Table 8 shows statistically significant differences between all the stimulated potassium values of TCAs, SSRIs, and TeCAs ($P < 0.0001$). The mean values recorded for TCAs, SSRIs, and TeCAs were 12.02 ± 1.02, 15.46 ± 0.94, and 28.77 ± 7.17, respectively.

Estimation of total proteins

As shown in Table 9, all the three groups were statistically significant when compared to each other ($P < 0.0001$). The mean values for stimulated salivary total proteins was increased in Group III patients (654.94 ± 518.7) when compared to Group I (mean = 158.1 ± 37.6) and Group II (mean = 338.26 ± 167.6).

Estimation of total proteins between 3 different antidepressant drugs

Table 10 found only stimulated total protein values between TCAs and TeCAs ($P = 0.001$) and between SSRIs and TeCAs ($P = 0.016$) to be statistically significant. However, there was no

Table 7: Comparison of stimulated whole salivary potassium between Groups I, II, and III.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Potassium (mg/dl)	Group I versus Group II	158.12	37.61	7.41	98	*P*<0.0001	S
		338.26	167.62				
	Group II versus Group III	338.26	167.62	4.11	98	*P*<0.0001	S
		654.94	518.72				
	Group I versus Group III	158.12	37.61	6.75	98	*P*<0.0001	S
		17.31	10.35				

SD: Standard deviation, S: Significant, D/F: Degrees of freedom

Table 8: Comparison of stimulated whole salivary potassium between three types of antidepressant drugs.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Potassium (mg/dl)	TCA versus SSRI	12.02	1.02	9.95	31	*P*<0.0001	S
		15.46	0.94				
	SSRI versus TeCA	15.46	0.94	8.24	35	*P*<0.0001	S
		28.77	7.17				
	TCA versus TeCA	12.02	1.02	8.32	28	*P*<0.0001	S
		28.77	7.17				

SD: Standard deviation, S: Significant, TCA: Tricyclic antidepressant, SSRI: Selective serotonin reuptake inhibitor, TeCA: Tetracyclic antidepressants, D/F: Degrees of freedom

significant variation between TCAs and SSRIs ($P = 0.096$). The mean values for TCAs, SSRIs, and TeCAs were 1003 ± 656.2, 676.7 ± 439.1, and 362.8 ± 286.4, respectively.

Estimation of urea

Table 11 shows the mean values for stimulated salivary urea in Group I was 25.91 ± 12.07, in Group II 33.32 ± 15.7, and 39.69 ± 14.8 in Group III. The *t*-test results between all the groups were found to be statistically significant to each other. The values between Groups I and II, between Groups II and III and between Groups I and III were $P = 0.01$, $P = 0.04$, and $P < 0.0001$, respectively.

Estimation of urea between 3 different antidepressant drugs

Table 12 shows that among the three antidepressant drugs, the values between TCAs and SSRIs ($P = 0.0001$) and between TCAs and TeCAs ($P = 0.0001$) were statistically significant to each other. The differences were, but there was no statistical alteration between SSRIs and TeCAs ($P = 0.2517$). The mean stimulated salivary urea was estimated to be 60.22 ± 10.71 in TCAs, 34.58 ± 7.6 in SSRIs, and 30.02 ± 6.48 in TeCAs.

Table 9: Comparison of stimulated whole salivary total protein between Groups I, II, and III.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Total proteins (mg/dl)	Group I versus Group II	153.70	197.77	6.26	98	*P*<0.0001	S
		331.18	571.52				
	Group II versus Group III	331.18	571.52	4.78	98	*P*<0.0001	S
		740.02	571.52				
	Group I versus Group III	153.70	197.77	7.24	98	*P*<0.0001	S
		654.94	518.72				

SD: Standard deviation, S: Significant, D/F: Degrees of freedom

Table 10: Comparison of stimulated whole salivary total proteins between three types of antidepressant drugs.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Total proteins (mg/dl)	TCA versus SSRI	1003.46	656.24	1.72	31	*P*=0.0957	NS
		676.70	439.12				
	SSRI versus TeCA	676.70	439.12	2.52	35	*P*=0.0163	S
		362.82	286.40				
	TCA versus TeCA	1003.46	656.24	3.61	28	*P*=0.0012	S
		362.82	286.40				

SD: Standard deviation, S: Significant, NS: Non significant, TCA: Tricyclic antidepressant, SSRI: Selective serotonin reuptake inhibitor, TeCA: Tetracyclic antidepressants, D/F: Degrees of freedom

Table 11: Comparison of stimulated whole salivary urea levels between Groups I, II, and III.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Urea (mg/dl)	Group I versus Group II	25.91	12.07	2.65	98	*P*=0.0095	S
		33.32	15.70				
	Group II versus Group III	33.32	15.70	2.09	98	*P*=0.0394	S
		39.69	14.80				
	Group I versus Group III	25.91	12.07	5.10	98	*P*<0.0001	S
		39.69	14.80				

SD: Standard deviation, S: Significant, D/F: Degrees of freedom

Discussion

Sialochemical analysis

α-amylase

The stimulated salivary amylase in all the three Groups of this study were found to be statistically significant when compared to one another ($P = 0.0287$, $P < 0.0001$, and $P < 0.0001$, respectively). Group III patients had increased levels of stimulated salivary amylase when compared to other two groups.

Comparison of α-amylase levels among the three antidepressant drugs In Group III

The maximum increase in salivary α-amylase in Group III patients was seen in patients on TCAs (707039 ± 310995) followed by TeCAs (645465 ± 178254) and then those on SSRIs (310995 ± 3988243).

The above results showed that salivary α-amylase was significantly increased in Group III patients of which TCAs and TeCAs drugs showed a greater rise in the amylase as compared to those taking SSRIs.

The present study is analogous with Mörnstad *et al.*[7,8] who studied the effects of antidepressants on stimulated saliva. Those on short-term administration of the drugs had no significant change in the amylase levels in both amitriptyline (TCA) and zimelidine (SSRI), while significant increase in the amylase levels were observed in long-term users of maprotiline (TeCA) as compared to zimelidine (SSRI) ($P < 0.05$). von Knorring and Mörnstad[9] also found that maprotiline (TeCA) ($P < 0.01$) gave a strong increase in the activity of both stimulated values of salivary amylase as compared to amitriptyline (TCAs) ($P < 0.05$) and zimelidine (SSRI) ($P < 0.001$) in the saliva composition. In another study on the acute effects of these antidepressant drugs, Mörnstad *et al.*[8] found a significant increase in the levels stimulated salivary

Table 12: Comparison of stimulated whole salivary urea between three types of antidepressant drugs.

Parameter	Group	Mean	SD	*t* value	D/F	*P* value	Results
Urea (mg/dl)	TCA versus SSRI	60.22	10.71	8.06	31	*P*<0.0001	S
		34.58	7.60				
	SSRI versus TeCA	34.58	7.60	1.94	35	*P*=0.0600	NS
		30.02	6.48				
	TCA versus TeCA	60.22	10.71	9.59	28	*P*<0.0001	S
		30.02	6.48				

SD: Standard deviation, S: Significant, D/F: Degrees of freedom, NS: Non-significant, TCA: Tricyclic antidepressant, SSRI: Selective serotonin reuptake inhibitor, TeCA: Tetracyclic antidepressants

amylase in subjects taking amipramine (TCA) ($P < 0.001$) as compared to maprotiline (TeCA) ($P < 0.05$) and zimelidine (SSRI) which also matched with the findings in the present study. de Almeida Pdel *et al.*[10] stated that though TCAs modify the salivary component of α-amylase, no significant changes were observed among patients taking SSRIs ($P > 0.05$). Chiappelli *et al.*[11] stated that salivary α-amylase was a more sensitive and specific measurement than blood pressure or heart rate in healthy adult subjects and are predictive of plasma norepinephrine levels. He also stated that α-adrenergic agonists stimulate salivary α-amylase levels without increasing salivary flow. Lawrence[12] stated that salivary α-amylase act as receptor for the adhesion of several species of oral streptococci onto the hydroxyapatite crystals of the tooth and contributes to the formation of dental plaque.

Calcium

The stimulated level of salivary calcium in Group III was increased as compared to Groups I and II.

Comparison of calcium levels among the three antidepressant drugs in Group III

Patients on TeCAs (mean = 8.15 ± 1.28) had decreased calcium levels when compared to SSRIs (mean = 10.07 ± 3.34) and TCAs (mean = 15.82 ± 1.77).

In another study done by Mörnstad *et al.*[8] the concentration of stimulated calcium showed 10% increase in SSRI (zimelidine) in a single dose experiment as compared to TeCA (maprotiline) ($P < 0.05$). The stimulated salivary calcium levels of the current study was analogous with Mörnstad *et al.*[9] on the acute effects of three antidepressant drugs where the most pronounced increase were recorded after the intake of TCA (amitriptyline) when compared to SSRI (zimelidine) ($P < 0.01$) and TeCA (maprotiline) ($P < 0.05$). de Almeida Pdel *et al.*[10] stated that although TCAs modify the salivary component of calcium, no significant changes were observed in patients taking different types of SSRIs ($P > 0.05$).

Increased calcium levels have been recorded with the use of anti-cholinergics like anti-histaminics and TCAs. Calcium and phosphate neutralize acids that would otherwise compromise tooth mineral integrity.[13]

Sodium

The stimulated whole saliva in Group III (mean = 14.92 ± 6.31) patients had reduced sodium levels when compared to Group I (mean = 29.04 ± 13.83) and Group II (mean = 16.93 ± 5.43).

Comparison of sodium levels among the three antidepressant drugs in Group III

Among the patients of Group III, the mean stimulated sodium in SSRIs (12.03 ± 7.0) was decreased when compared to TCAs (13.51 ± 5.28) and TeCAs (19.4 ± 3.07).

The present study also synchronized with Mörnstad *et al.*[7] who found a significant increase in the stimulated concentration of sodium due to TeCAs (maprotiline) and TCAs (amitriptyline) when compared to SSRI (zimelidine) ($P < 0.05$).

Salivary sodium levels are the one of the main contributors to the osmolarity of saliva, which is approximately half that of plasma. As the flow rate of both whole and ductal saliva increases, the concentrations of proteins, sodium, chloride and bicarbonate rise while the levels of phosphate and magnesium fall. Variable sodium concentrations at different flow rates depend on changes during duct passage. Thus, there was a definite reduction in the stimulated values of Group III patients due reduced whole salivary flow rate.

Potassium

The stimulated salivary potassium levels of patients in Group III (mean = 17.31 ± 10.35) was significantly reduced when compared to Groups I (mean = 28.26 ± 9.09) and II (mean = 25.86 ± 18.96). All the three drugs in Group III showed statistical increase in stimulated salivary potassium levels ($P < 0.0001$) when compared to each other.

Comparison of potassium levels among the three antidepressant drugs in Group III

The patients on TeCAs (mean = 28.77 ± 7.17) had maximum potassium levels when compared to SSRIs (mean = 15.46 ± 0.94) and TCAs (mean = 12.02 ± 1.01).

Dawes[14] stated that stimulated flow rate decrease potassium concentrations. Similar features were also observed in our study. The stimulated values of the present study were concurrent with studies done by Mörnstad *et al.*[8] where the concentration of stimulated potassium showed 50% increase in patients on TeCA (maprotiline) as compared to SSRI (zimelidine) ($P < 0.05$). However, in another study done by Mörnstad *et al.*[7] on the acute effects of three antidepressant drugs found that statistically significant increase in the stimulated salivary potassium levels were recorded after the intake of TCA (amitriptyline) when compared to SSRI (zimelidine) and TeCA (maprotiline) ($P < 0.01$). The major ions (cations sodium, potassium, calcium, chloride, and bicarbonate) are the main contributors to the osmolarity of saliva, which is approximately half that of plasma.

Total proteins

The stimulated total proteins of whole saliva had statistical significance when compared to each other ($P < 0.0001$). Group III patients (mean = 654.94 ± 518.72) had increased total protein levels when compared to Group I (mean = 158.12 ± 37.61) and Group II patients (mean = 338.26 ± 167.62).

Comparison of total proteins levels among the three anti-depressant drugs in Group III

In Group III, patients taking TCAs (mean = 1003.46 ± 656. 24) had amplified values and the least was found in TeCAs (mean = 362.82 ± 286.4). The present study was consistent with the findings of von Knorring and Mörnstad *et al.*[9]

However, studies done by Mörnstad *et al.*[8] stated that there was pronounced increase (50%) in the concentration of stimulated total proteins in patients on either acute ($P < 0.001$) or long-term ($P < 0.05$) antidepressants like TeCA (maprotiline) as compared to SSRI (zimelidine).

The reason for increased total protein levels maybe because of interference to the buffering capacity leading to precipitation of total proteins in the saliva. TCAs and TeCAs both are inhibitors of noradrenaline reuptake. It is believed that both drugs stimulate the alpha- and beta-receptors in the salivary glands and subsequently cause an increase in the concentration of proteins.[15]

Urea

The stimulated whole salivary urea among all the three Groups in the current study had statistical significance when compared to one another. Group III patients (mean = 39.69 ± 14.8) showed enhanced stimulated urea values when compared with Group I (mean = 25.91 ± 12.07) and Group II patients (mean = 33.32 ± 15.7).

Comparison of urea levels among the three antidepressant drugs in Group III

Among the medicated patients, TCAs (mean = 60.22 ± 10.71) produced augmented whole salivary urea levels in stimulated cases. TCAs had significantly amplified urea levels, then followed by SSRIs (mean = 34.58 ± 7.6) and the least in TeCAs (mean = 30.02 ± 6.48).

Weighing the results of stimulated whole saliva, patients with depressive disorders who were either on medication or on counseling, held a higher concentration of urea with values inclining more toward those in Group III.

de Almeida Pdel *et al.*[10] stated that although TCAs modify the salivary component of urea, no significant changes were observed in patients taking different types of SSRIs ($P > 0.05$).

Literature has stated that plaque carcinogenicity may be inversely related to salivary urea concentrations. Dawes and Dibdin[15] stated that urea is a substrate for base formation by dental plaque. The level of urea in saliva is directly proportional to the level in blood. A slight increase in salivary urea concentration might reduce the development of caries.

Although salivary urea is an important biochemical parameter for the control of caries, limited literature is available with regard to this component.

Direct comparisons could not be made between the findings of the present study and studies reported in the literature due to differences in the study population, methodology and the parameters used. However, attempts have been made to compare various studies and reasons for observations have been suggested. A significant increase in the levels salivary amylase, calcium, total protein, and urea were observed, especially in patients who had been taking TCAs and TeCAs. The study showed a selectivity of the action of SSRIs as compared to TCAs (non-selective) and TeCAs. It also showed that there is a difference in drawing conclusions with other study groups in different settings.

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 sialochemical alterations in stimulated 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 anti-depressive drugs (namely TCAs, SSRIs and TeCAs), which were commonly prescribed by the psychiatrists, were considered for the study.

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

A significant increase in the levels salivary amylase, calcium, total protein, and urea were observed in Group III patients, especially in those administering TCAs and TeCAs.

Salivary electrolytes like sodium and potassium did not show much change.

To conclude, antidepressant drugs do affect the salivary composition. 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 alteration in the sialochemical constituents of saliva. The action of SSRIs was selective and did not cause as much variation in the saliva composition as compared to TCAs and TeCAs and thus can be a better drug to treat the disease.

Significance

The holistic approach to health is currently widely advocated as a prerequisite for successful outcomes in patient care. A significant impairment of all personal hygiene may occur due to the depth of a depressive episode which in turn may result in a total lack of oral hygiene-salivary biochemical parameters may be altered, and the patient may complain of dry mouth, increased rate of dental caries and periodontal disease.

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