ECRONICON OPEN ACCESS

EC DENTAL SCIENCE
Research Article

An Evaluation of the Effects of Antidepressant Drugs on Unstimulated Sialochemistry

Annette Milton B[1]* and Ajay Bhambal[2]

[1]*Associate Professor, Department of Oral Medicine and Radiology, People's College of Dental Sciences and Research Centre, People's University, Bhopal, Madhya Pradesh, India*

[2]*Professor and Head, Department of Preventive and Public Health Dentistry, People's College of Dental Sciences and Research Centre, People's University, Bhopal, Madhya Pradesh, India*

***Corresponding Author**: Annette Milton B, Associate Professor, Department of Oral Medicine and Radiology, People's College of Dental Sciences and Research Centre, People's University, Bhopal, Madhya Pradesh, India.

Received: September 13, 2019; **Published:** October 22, 2019

Abstract

Introduction: 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 composition.

Purpose of the Study: 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 unstimulated sialochemical alterations between patients with depressive disorders and on antidepressant drugs.

Materials and Methods: Whole unstimulated saliva was collected from patients suffering from depressive disorders and were on antidepressant drugs for at least a month. The sialochemical parameters were determined using suitable methods.

Results: A significant increase in the levels salivary amylase, calcium, total protein and urea were observed in patients- especially in those administering Tricyclic (TCAs) and Tetracyclic (TeCAs) antidepressants.

Conclusion: From the present study, it was observed that cyclic antidepressants produced significant alteration in the sialochemical constituents of saliva.

Keywords: *Depression; Depressive Disorders; Sialochemical Analysis; Sialochemistry; Unstimulated Saliva*

Abbreviation

TCAs: Tricyclic Antidepressants; SSRIs: Selective Serotonin Reuptake Antidepressants; TeCAs: Tetracyclic Antidepressants; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders-IV

Introduction

In India, about 10 million people suffer from depressive disorders, the prevalence rate being recorded as 31.2 for every 1000 individuals. Depressive disorders, worldwide, may rank second by the year 2020. A significant impairment of all personal hygiene may occur due a depressive episode which in turn may result in altered salivary composition. All psychotropic drugs, even those of the latest generation, present side effects.

Sialochemistry provides qualitative information on certain important parameters of saliva which are used for diagnostic and research purposes. It's also a cost-effective and simple diagnostic methods. The present scenario has prompted this study to estimate the changes in the salivary composition of some important salivary parameters in patients on antidepressant drugs.

Purpose of the Study

The present study was a hospital- based clinical cross-sectional study which was conducted in Bhopal, the soul of Madhya Pradesh, India. It was done to assess the relationship of bring about a comparison of unstimulated sialochemical alterations between patients with depressive disorders and on some commonly administered antidepressant.

Materials and Methods

Settings and design

The present study was a hospital- based clinical cross-sectional study which was conducted in Bhopal, the heart of Madhya Pradesh, India. The survey period extended over a period of one year, from March 2018 to March 2019. 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.

Criteria for patient selection

After a detailed explanation about the nature of research, its objectives, methods and the inconvenience this methodology could cause, the research participants siSgned a free and informed consent form authorizing their voluntary participation in the research.

A total of 50 normal volunteers, of either gender, above 15 years and below 45 years of age were chosen for this study. They were clinically diagnosed depressive disorders and had been on antidepressant drugs for a minimum of 1 month {i.e. Tricyclic antidepressants (TCAs), Selective serotonin reuptake antidepressants (SSRIs) and Tetracyclic antidepressants (TeCAs)}. 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 three months.

Clinical assessment

Self- administered questionnaire was developed to identify the patient data. It included age, sex, diagnosed diseases and presence.

Assessment of depression: The patients coming to the outpatient department 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 [1]. For patients who were using psychotropic drugs, data about the medication, including duration and dosage were recorded.

Data collection of saliva samples

Borosil vials with lid were autoclaved and pretagged with an identification number. The closed vials were used to collect and transport the samples from the hospitals to the laboratories for analysis. Cold sterilized disposable funnels were given to each patient along with the vials to aid in 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 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 wash their mouths, sit in a relaxed position and 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. Samples containing visible blood were discarded. The samples were assembled in the ice box and taken to the biochemistry laboratory where they were processed on the same day or stored at -20°C and analyzed within 24 hours after collection.

Biochemical analyses

Unstimulated whole saliva was analyzed biochemically for α- amylase, calcium, sodium, potassium, total proteins and urea. The data obtained in this study were statistically analyzed by using Unpaired Student's t-test.

Results

Estimation of α-amylase between 3 different antidepressant drugs

Table 1 shows the variations in unstimulated α- amylase levels among patients taking different antidepressant drugs. The patients on TeCAs showed increased α- amylase levels (861841.2 ± 286353.9 U/L) when compared to those taking TCAs (568423.1 ± 390621.8 U/L) and SSRIs (301242.4 ± 354690.6 U/L). The unstimulated results between those in TCAs and TeCAs ($p < 0.0001$, $p = 0.0245$ respectively). The results between TCAs and SSRIs were not statistically significant ($p = 0.0508$).

Parameter	Group	Mean	SD	t-Value	D/F	P-value	Results
Amylase	TCA	568423.10	390621.80	2.03	31	P = 0.0508	NS
	v/s SSRI	301242.40	354690.60				
	SSRI	301242.40	354690.60	5.23	35	P < 0.0001	S
	v/s TeCA	861841.20	286353.90				
	TCA	568423.10	390621.80	2.38	28	P = 0.0245	S
	v/s TeCA	861841.20	286353.90				

Table 1: *Comparision of α- amylase with 3 different antidepressant drugs.*

Estimation of calcium between 3 different antidepressant drugs

Table 2 compares the calcium levels in unstimulated saliva. The values of TCAs and SSRIs ($p = 0.0052$) and TCAs and TeCAs ($p < 0.0001$) were statistically significant to each other but no statistical significant difference was found between the values of SSRIs and TeCAs ($p = 0.2915$). The mean unstimulated calcium values for TCAs were 7.2 ± 0.56, for SSRIs 9.8 ± 3.09 and for TeCAs 10.7 ± 1.49.

Parameter	Group	Mean	SD	t-value	D/F	P-value	Results
Calcium	TCA	13.18	0.56	3.01	31	P = 0.0052	S
	v/s SSRI	11.30	3.09				
	SSRI	11.30	3.09	1.07	35	P = 0.2915	NS
	v/s TeCA	21.53	1.49				
	TCA	13.18	0.56	8.02	28	P < 0.0001	S
	v/s TeCA	21.53	1.49				

Table 2: *Comparision of calcium with 3 different antidepressant drugs.*

Estimation of sodium between 3 different antidepressant drugs

Table 3 shows statistically significant differences in the unstimulated salivary sodium levels between SSRIs and TeCAs and between TCAs and TeCAs ($p < 0.0001$, $p = 0.0252$ respectively). Conversely, the results between TCAs and SSRIs were not significant statistically ($p = 0.613$). The mean values of TeCAs (21.53 ± 1.21) appeared raised when compared to the mean TCA (13.18 ± 14.58) and SSRI (11.295 ± 6.34) values.

Parameter	Group	Mean	SD	t-value	D/F	P- value	Results
Sodium	TCA v/s SSRI	13.18	14.58	0.51	31	P = 0.6130	NS
		11.30	6.34				
	SSRI v/s TeCA	11.30	6.34	6.54	35	P < 0.0001	S
		21.53	1.21				
	TCA v/s TeCA	13.18	14.58	2.36	28	P = 0.0252	S
		21.5	1.21				

Table 3: *Comparision of sodium with 3 different antidepressant drugs.*

Estimation of potassium between 3 different antidepressant drugs

Table 4 shows statistically significant difference between the unstimulated potassium values of TCAs and SSRIs (p = 0.02) and between SSRIs and TeCAs (p < 0.0001). However, there was no significant change between TCAs and TeCAs (p = 0.376). The mean values recorded for TCAs, SSRIs and TeCAs were 28.15 ± 22.42, 15.94 ± 1.11 and 23.11 ± 5.29 respectively.

Parameter	Group	Mean	SD	t-value	D/F	P-value	Results
Potassium	TCA v/s SSRI	28.15	22.42	2.45	31	P = 0.0200	S
		15.94	1.11				
	SSRI v/s TeCA	15.94	1.11	5.93	35	P < 0.0001	S
		23.11	5.29				
	TCA v/s TeCA	28.15	22.42	0.90	28	P = 0.3760	NS
		23.11	5.29				

Table 4: *Comparision of potassium with 3 different antidepressant drugs.*

Estimation of total proteins between 3 different antidepressant drugs

Table 5 shows only the values of unstimulated total protein between TCAs and TeCAs to be statistically significant (p = 0.0207). There was no significant variation between TCAs and SSRIs and between SSRIs and TeCAs (p = 0.362 and p = 0.0908) respectively. The mean values for TCAs, SSRIs and TeCAs were 989.23 ± 755.42, 773.85 ± 579.71 and 509.65 ± 254.87 respectively.

Parameter	Group	Mean	SD	t-value	D/F	P-value	Results
Total Proteins	TCA v/s SSRI	989.23	755.42	0.93	31	P = 0.3620	NS
		773.85	579.71				
	SSRI v/s TeCA	773.85	579.71	1.74	35	P = 0.0908	NS
		509.65	254.87				
	TCA v/s TeCA	989.23	755.42	2.45	28	P = 0.0207	S
		509.65	254.87				

Table 5: *Comparision of total proteins with 3 different antidepressant drugs.*

Estimation of Urea between 3 different antidepressant drugs

Table 6 estimates the mean unstimulated salivary urea among Group III patients to be 65.38 ± 25.83 in TCAs, 40.83 ± 7.59 in SSRIs and 43.4 ± 5.42 in TeCAs. Between TCAs and SSRIs (p = 0.0003) and between TCAs and TeCAs (p = 0.0019), the differences were statistically significant but there was no statistical alteration between SSRIs and TeCAs (p = 0.2517).

Parameter	Group	Mean	SD	t-value	D/F	P-value	Results
Urea	TCA v/s SSRI	65.38	25.83	4.02	31	P = 0.0003	S
		40.83	7.59				
	SSRI v/s TeCA	40.83	7.59	1.17	35	P = 0.2517	NS
		43.40	5.42				
	TCA v/s TeCA	65.38	25.83	3.43	28	P = 0.0019	S
		43.40	5.42				

Table 6: *Comparision of urea with 3 different antidepressant drugs.*

The present study was done to assess the effect of 3 commonly used antidepressant drugs on specific biochemical parameters in unstimulated whole saliva. Significant associations between the drugs and sialochemical parameters were observed. Severity of changes in the qualitative analysis was observed among Group III patients. The results were tabulated along with statistical analysis.

Discussion

50 patients suffering from depressive disorders and on medication were considered for the study. They were within the age range of 15 - 45 years. The mean age was 37 years. The results showed that most of the patients were in the third decade of life.

Estimation of α-amylase between 3 different antidepressant drugs

The above results showed that salivary α- amylase was significantly increased in patients using tricyclic and tetracyclic groups of antidepressant drugs as compared to those taking selective serotonin reuptake inhibitors.

The present study is analogous with Mörnstad H, von Knorring L and Holmgren FS [2,3] who studied the effects of antidepressants on unstimulated 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 L and Mörnstad H [4] also found that maprotiline (TeCA) ($p < 0.01$) gave a strong increase in the activity of unstimulated values of salivary amylase as compared to amitriptyline (TCAs) ($p < 0.05$) and zimelidine (SSRI) ($p< 0.001$) in the saliva composition.

Almeida PDV., *et al.* [5] stated that that though TCAs modify the salivary component of α- amylase, no significant changes were observed among patients taking SSRIs ($p > 0.05$). Chiappelli F [6] 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 HP [7] 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.

Estimation of calcium between 3 different antidepressant drugs

Results of the present study showed statistically increased unstimulated levels of calcium in Group III patients. The calcium values of patients on TeCAs (in unstimulated saliva) were increased when compared to that of SSRIs.

The unstimulated salivary calcium levels of the present study were concurrent with von Knorring L., *et al.* [8] where there was no significant change in patients on TeCAs (imipramine) (mean = 0.34 ± 0.03) and SSRIs (zimelidine) (mean= 0.36 ± 0.03). Almeida PDV., *et al.* [5] 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 anticholinergics like antihistaminics and tricyclic antidepressants. Calcium and phosphate neutralize acids that would otherwise compromise tooth mineral integrity [9].

Estimation of sodium between 3 different antidepressant drugs

In the present study, the mean unstimulated sodium levels in unstimulated saliva of patients administering SSRIs had the lowest values when compared to TeCAs and TCAs.

Mörnstad H., *et al.* [3] found significant increase in the concentration of unstimulated sodium in SSRI (zimelidine) when compared to TeCA (maprotiline) ($p < 0.05$). von Knorring L., *et al.* [8] also found no significant change in the unstimulated salivary sodium levels in patients on TeCAs (imipramine) (mean= 23.6 ± 5.0) and SSRIs (zimelidine) (mean= 32.3 ± 7.3).

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, though there was no significant change in the normal concentration of sodium in unstimulated saliva, there was a definite reduction in their concentration due reduced whole salivary flow rate.

Estimation of potassium between 3 different antidepressant drugs

In unstimulated whole saliva, the potassium levels were lowered. TeCAs had the maximum stimulated salivary potassium levels.

However, von Knorring L., *et al.* [8] found no significant change in the unstimulated salivary potassium levels in patients on TeCAs (imipramine) (mean = 23.8 ± 0.9) and SSRIs (zimelidine) (mean = 23.9 ± 0.8).

The major ions (cations sodium, potassium, calcium, chloride and bicarbonate) are the main contributors to the osmolality of saliva, which is approximately half that of plasma.

Estimation of total proteins between 3 different antidepressant drugs

The present study showed statistically significant increase in the whole salivary total protein in unstimulated saliva.

The present study was consistent with the findings of von Knorring L., *et al* [4,8]. However, studies done by Mörnstad H., *et al.* [3] stated that there was pronounced increase (50%) in the concentration of unstimulated 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 the 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 the drugs stimulate the alpha- and beta- receptors in the salivary glands and subsequently cause an increase in the concentration of proteins [2].

Estimation of urea between 3 different antidepressant drugs

Patients on Tricyclic antidepressants produced augmented salivary urea levels as compared to those taking Tetracyclic antidepressants and selective serotonin reuptake inhibiters.

Almeida PDV., *et al.* [5] 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 have stated that plaque carcinogenicity may be inversely related to salivary urea concentrations [10]. Dawes C [11] 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 literature due to differences in study population, methodology and the parameters used. However, attempts have been made to compare various studies and reasons for observations have been suggested.

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 sialochemical alterations in a few important parameters among 50 patients with depressive disorders who were on medication for at least 1 month. The effect of three antidepressant 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.

The results revealed that most of the patients with depressive disorders fell into the age slot of 31 - 45 years of life. Salivary qualitative parameters and 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 patients-especially in those administering Tricyclic (TCAs) and Tetracyclic (TeCAs) antidepressants.
- Salivary electrolytes like sodium and potassium did not show much change.

Conclusion

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. A follow up study might be suggested to throw light on the fate of saliva after the patient has been relieved from treatment and also if the effect of these drugs, on saliva, transient or has it caused irreversible damage.

Bibliography

1. Semple D and Smyth R. "Oxford Handbook of Psychiatry". 2nd edition. Oxford University Press Inc., New York. (2005): 223-277.

2. Mörnstad H., *et al*. "Acute effects of some different antidepressant drugs on saliva composition". *Neuropsychobiology* 15.2 (1986): 73-79.

3. Mörnstad H., *et al*. "Long-term effects of two principally different antidepressant drugs on saliva secretion and composition". *Scandinavian Journal of Dental Research* 94.5 (1986): 461-470.

4. von Knorring L and Mornstad H. "Saliva secretion rate and saliva composition as a model to determine the effect of antidepressant drugs on cholinergic and noradrenergic transmission". *Neuropsychobiology* 15.3-4 (1986): 146-154.

5. Almeida PDV., *et al*. "Effects of antidepressants and benzodiazepines on stimulated salivary flow rate and biochemistry composition of the saliva". *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 106.1 (2008): 58-65.

6. Chiappelli F., *et al*. "Salivary biomarkers in psychobiological medicine". *Bioinformation* 1.8 (2006): 331-334.

7. Lawrence HP. "Salivary Markers of Systemic Disease (): Non invasive Diagnosis of Disease and Monitoring of General Health". *Journal of the Canadian Dental Association* 68.3 (2002): 170-174.

8. von Knorring L and Mornstad H. "Qualitative changes in saliva composition after short term administration of imipramine and zimelidine in healthy volunteers". *Scandinavian Journal of Dental Research* 89.4 (1981): 313-320.

9. Damle. "Saliva and oral health". Text book of paediatric dentistry. Arya (Medi) Publishing House (2009): 244-249.

10. Dibdin GH and Dawes C. "A mathematical model of the influence of salivary urea on the pH of fasted dental plaque and on the changes occurring during a cariogenic challenge". *Caries Research* 32.1 (1998): 70-74.

11. Dawes C and Dibdin GH. "Salivary concentrations of urea released from a chewing gum containing urea and how these affect the urea content of gel-stabilized plaques and their pH after exposure to sucrose". *Caries Research* 35.5 (2001): 344-353.

Volume 18 Issue 11 November 2019