Effect of hypertension on salivary pH, salivary flow and buffering capacity: An in-vivo study

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Abstract

Introduction: Hypertension is a highly prevalent cardiovascular disease, which affects over 1 billion people worldwide. Although more than 70% of hypertensive patients are aware of the disease, only 23.49% are treated, and fewer (20%) achieve control.

Aim of the study: to evaluate the influence of hypertension on pH of saliva, saliva flow rate and buffer capacity in individuals.

Material and methods: The subjects were categorized into the following four groups: Group 1- normal blood pressure (SBP of <140 mmHg and DBP of<90 mmHg) without medication; Group 2- normal blood pressure with antihypertensive medication; Group 3- hypertension (SBP of _140 mmHg and/or DBP of_90 mmHg) without medication; Group 4- hypertension with antihypertensive medication. Blood pressure measurements were taken by an automated sphygmomanometer (HEM-7120; Omron). Unstimulated whole saliva (USS) was collected by the spitting method, pH and buffering capacity was determined using a buffering capacity were estimated using GC Saliva Check Kit (GC Asia Dental Pvt. Ltd. Singapore, 508724).

Results: The DBP and SSFR were significantly higher in men than women. USSFR was almost equal in both males and females. 57.7% of analyzed subjects comprised individuals with normal blood pressure, 12.3% of these subjects took antihypertensive medication. 17.3% of all subjects included individuals taking antihypertensive medication. Statistically significant difference was not observed for hypertension or intake of antihypertensive medication and unstimulated or stimulated salivary flow rate. However, a statistically significant difference was observed for the pH of unstimulated among the four groups.

Conclusion: In conclusion, the contributory factors in maintaining the integrity of oral cavity is salivary flow rate, pH and the buffering action of the saliva. Use of anti-hypertensive medications effects pH of un-stimulated saliva which can be lead to many oral detrimental changes.

Keywords: Hypertension, Salivary pH, Salivary flow, Buffering capacity.

Introduction

Saliva is secreted by three pairs of major and numerous minor salivary glands, which are exocrine glands. It is a very dilute fluid, composed of waters, variety of electrolytes including sodium, potassium, calcium, magnesium, bicarbonate, and phosphates. It also contains immunoglobulins, proteins, enzymes, mucins, and nitrogenous products. Salivary function includes lubrication and protection, buffering action and clearance, maintenance of tooth integrity, antibacterial activity, and taste and digestion.\(^1\) The normal pH of saliva is 6 to 7 which is slightly acidic and pH can range from 5.3 (low flow) to 7.8 (peak flow).\(^2\) Bicarbonate, phosphate, urea, amphoteric proteins and enzyme acts as buffering system in which bicarbonate is most important buffering system, it diffuses into plaque and acts as a buffer by neutralizing acids. Moreover, it generates ammonia to form amines, which also serve as a buffer by neutralizing acids.\(^3\) On average, unstimulated flow rate is 0.3 mL/min and stimulated flow rate is, at maximum, 7 mL/min, any unstimulated flow rate below 0.1 mL/min is considered hypofunction.\(^4\) Hypofunction of stimulated salivary flow is not a normal age-related change. Reduced flow may result from a number of different conditions, such as dehydration, Sjogren’s syndrome, diabetes mellitus,
neurological and cognitive disorders, and multiple medications.\textsuperscript{6,7}

Hypertension is a highly prevalent cardiovascular disease, which affects over 1 billion people worldwide. Although more than 70\% of hypertensive patients are aware of the disease, only 23.49\% are treated, and fewer (20\%) achieve control. Hypertension is defined as systolic and diastolic blood pressures with values >140mmHg and >90mmHg respectively, the prevalence of which varies by age, race, and education.\textsuperscript{8} Hypertension exerts a substantial public health burden on cardiovascular health status and healthcare systems in India. The rates for hypertension in percentage are projected to go up to 22.9 and 23.6 for Indian men and women, respectively by 2025.\textsuperscript{5}

Hypertension and use of anti-hypertensive medications has definitive effect on pH of stimulated saliva which can be attributed to many oral detrimental changes. Hence, there is a necessity to monitor blood pressure for reconstruction and maintenance of oral health. Saliva is gaining popularity as a diagnostic tool for evaluating physiologic and pathologic conditions by virtue of its ease of collection method, non-invasiveness and low cost.\textsuperscript{9} Thus, the aim of the present study is to evaluate the influence of hypertension on pH of saliva, saliva flow rate and buffering capacity in individuals.

**Materials and Methods**

This study is a cross-sectional study done in KVG Dental College and hospital for a period of one year (June 2018-july 2019). This study was undertaken with the understanding and written consent of each subject and according to ethical principles, the study was approved by the Ethical Committee of the institution. The subjects in this study were patients visiting outpatient department for dental treatment. 213 subjects were considered after reviewing the inclusion and exclusion criteria. A prior consent was taken from the subjects, their past medical and current medications histories were recorded by the endodontists. Considering the subject’s blood pressure and the antihypertensive drugs which they were taking at the time of visit, the subjects were categorized into the following four groups: Group 1- normal blood pressure (SBP of <140 mmHg and DBP of<90 mmHg) without medication; Group 2- normal blood pressure with antihypertensive medication; Group 3- hypertension (SBP of _140 mmHg and/or DBP of_90 mmHg) without medication; Group 4- hypertension with antihypertensive medication. Patients having diabetes mellitus, any other systemic diseases, or who are on radiotherapy and chemotherapy dosages were excluded from the study. Consequently, data were collected and analyzed from 165 subjects.

Blood pressure measurements were taken by an automated sphygmomanometer (HEM-7120; Omron) to avoid inter-examiner variability after the person had been seated comfortably for at least 5 min. Subjects with either an SBP of _140 mmHg or DBP of_90 were defined as having hypertension according to the ACC/AHA Guidelines -2017.

Unstimulated whole saliva (USS) was collected by the spitting method (Matsuda et al, 2009). Salivary samples were collected between 10 AM and 3 PM. Patient was advised not to smoke, brush their teeth, and eat for 2 hrs. before saliva collection to minimize the effects of diurnal variability in salivary composition. The subjects remained quietly seated on a chair before the measurements and were asked to swallow all of the saliva in their mouths. Soon after, the subjects were asked to refrain from swallowing for 5 min and then to expectorate the accumulated saliva into a collection cup. Stimulated saliva (SS) was collected by the mastication method (Ikebe et al, 2006). The subjects were asked to collect all of the saliva in their mouths, chew a measured amount of paraffin wax for 30 secs, and then spit into a collection cup. Subjects were asked to continue chewing the wax for an additional 5 minutes, expectorating every 15 - 20 seconds in the collection cup. Subjects were left alone during collection of the saliva, volume of liquid in the cup excluding froth and recorded. Unstimulated and stimulated salivary flow rates (USSFR and SSFR) were expressed in ml min\textsuperscript{-1}

Immediately after saliva collection, pH and buffering capacity was determined using a buffering capacity were estimated using GC Saliva Check Kit (GC Asia Dental Pvt. Ltd. Singapore, 508724). For pH evaluation, a pH test strip was immersed in the saliva for 10 seconds and compared for colour change with a testing chart. The buffer strip was removed from the
foil package and placed onto an absorbent tissue with the test side up. Using pipette, sufficient saliva was drawn from the collection cup and dispense one drop onto each of the 3 test pads. Immediately the strip was turned around to 90 degrees to soak up excess saliva on absorbent tissue. (This is to prevent the excess saliva from swelling on the test pad and possibly affect the accuracy of the result). When the test pads started to change the colour, immediately and after 2 minutes, the final result were calculated by adding the points according to the final colour of each pad.

Data analyses were performed using SPSS Version 13.0 for Windows (SPSS, Inc., Chicago, IL, USA). A P-value of <0.05 was considered statistically significant.

Results
The demographic details, and the characteristic taken under study is discussed in Table 1. 213 subjects participated in this study, out of which 42.73% were males, 57.2% were females. The DBP and SSFR were significantly higher in men than women. USSFR was almost equal in both males and females. 57.7% of analyzed subjects comprised individuals with normal blood pressure, 8.1% (Group 1 and 2) of these subjects took antihypertensive medication. 17.3% (Group 1,2,3&4) of all the subjects included individuals taking antihypertensive medication. Seventy four percentage (74%) of subjects were taking calcium channel blocker i.e amlodipine antihypertensive medication, 20% were taking angiotensin II receptor blockers and 6% were taking angiotensin converting enzyme inhibitor. 73% were taking only one antihypertensive medication and 27% were taking two medications, out of the subjects taking antihypertensive medication. When the subjects were categorized into four groups by blood pressure and medication, there were no significant differences in the sex ratio, mean age among the four groups. Although there was no significant difference in the USSFR, SSFR, or SS pH among the groups, the USS pH showed a significant difference (p=0.001), (Table 2). Multiple comparison using tukey’s test (Group 1 vs Group 3:P = 0.001, Group 1 vs Group 4: P = 0.005) demonstrated that Groups 3 and 4 hypertensive subjects revealed a significantly lower USS pH than that of the Group 1-normal blood pressure without medication group.

Table 1: Distribution of study participants in relation to their characteristics recorded in the study (n = 213)

| Variables                  | Male (91)   | Female (122) | Total          | P Value |
|----------------------------|-------------|--------------|----------------|---------|
| Age (years)                | 59.2±7.4    | 58.09± 8.44  | 58.57± 8.03    | 0.32    |
| Systolic (SBP)             | 136.61 ±13.24 | 137.07± 13.82 | 136.87±13.55   | 0.808   |
| Diastolic (DBP)            | 84.59±5.68  | 84.08±6.50   | 84.3± 6.1      | 0.55    |
| Buffering Capacity         | 9.92 ±1.5   | 9.51± 1.59   | 9.68± 1.57     | 0.06    |
| USSFR (ml min_1)           | 1.59±0.43   | 1.59±0.49    | 0.34 ±0.33     | 0.9     |
| pH of Unstimulated Saliva  | 6.6±0.53    | 6.6±0.51     | 6.60 ±0.52     | 0.917   |
| pH of stimulated Saliva    | 7.82±0.3    | 7.81±0.43    | 7.78±0.33      | 0.25    |
| SSFR (ml min_1)            | 0.35±0.41   | 0.34± 0.25   | 1.59±0.46      | 0.879   |

Table 2: Shows distribution of various variables in each group

| Age (years) | Normal blood pressure without medication n =113 | Normal blood pressure with anti-hypertensive n = 10 | Hypertension without medication n = 63 | Hypertension with anti-hypertensive n = 27 | P-value |
|-------------|-------------------------------------------------|---------------------------------------------------|---------------------------------------|------------------------------------------|---------|
|             | 58.7±8.13                                       | 55.5± 6.02                                        | 58.92± 8.09                           | 58.14±8.30                               | 0.637   |
| Systolic (SBP) | 126.6± 6.92                                    | 125.60± 5.64                                      | 151.0 ± 4.89                          | 151.03± 4.86                             | <0.001** |
| Diastolic (DBP) | 81.77±5.66                                     | 81.30± 5.47                                      | 87.17 ± 9.5                           | 89.25 ± 5.02                             | <0.001** |
| Buffering Capacity | 9.97±1.52                                      | 9.8± 1.54                                        | 9.91±1.50                             | 9.8±1.62                                 | 0.59    |
Discussion
The study evaluates adults who were hypertensive and who took either no medication or only antihypertensive medication. Two major steps are involved in salivary fluid secretion; 1) an acinar stage 2) the transport of saliva through the duct system where the concentrations of the constituents are changed, resulting in a final hypotonic saliva with respect to plasma due to action of various ion channels and transporters such as calcium activated chloride and/ or HCO channel, the Na+/K + cl cotransporter, the Ca activated K+ channel, the Na+/H+ exchanger. Few antihypertensive drugs such as diuretics and hydrochlorothiazide mainly act on the ion channels for reducing the blood pressure. Diuretics also act on the small mucous glands, hampering the production of mucous, a most important protector to the oral mucosa. In the present study subjects were mostly under stage 1-2 of hypertension and were taking calcium channel blocker, ACE inhibitor and Angiotensin –II inhibitors. In a study done by Ship et, it was concluded that the stimulated parotid gland flow rates in the Hydrochlorothiazide medicated group were lower than in the normotensive and hypertensive groups, but were still within the normal ranges of saliva production. The results in our study showed that salivary flow rate had no significant association with hypertension or antihypertensive medication which is similar to a study done by Sankar et al. Study done by Streckfus CF et al. and Niedermeier W et al. also had similar findings. De Matos et al concluded that salivary flow rate will decrease chiefly as a medication side effect, but it has not clarified about the relationship between salivary flow rate and antihypertensive medications. A reason for this could be that people taking antihypertensive are unaware of their decreased salivary flow as saliva is often a neglected body fluid and therefore little real data have been obtained for the study. In the present study, regardless of antihypertensive medication, the pH of unstimulated saliva was significantly lower in the group with hypertension than in the group with normal blood pressure. With an increase in blood pressure both systolic and diastolic, the pH of unstimulated saliva became more acidic. The cause effect relationship was thus established here between increase in blood pressure and the acidic salivary ph. A similar study was done by Wong et al where he concluded that the blood pressure influences the general condition in several ways. Saliva is composed of electrolytes, including sodium, potassium, calcium, magnesium, bicarbonate, and phosphates. The most important buffering system of saliva is bicarbonate which maintains the neutrality of the salivary ph. The demineralization and remineralization of enamel and dentin is affected by the buffering capacity of the saliva. Dawes et al concluded that bicarbonate concentration and the salivary pH has a direct relationship, as the bicarbonate concentration decreases due to decrease in flow, the pH of saliva is also lowered. There was no significant difference in salivary flow rate among each group in this study. The cleansing action of saliva on tooth surface prevents caries. Bassoukou et al concluded that unstimulated saliva pH is closely related to the oral buffer capacity to the caries risk, further these are in agreement with a study conducted by Browne et al and Scully et al. Prashanthi B et al concluded that patients on diuretic medication which is antihypertensive have a higher prevalence of xerostomia, periodontitis, dental caries and mucosal lesions when compared with that in the control group individuals. An important risk factor for dental/oral health is decrease in ph. Johansson I et al and Saelbröm A-K et al concluded that the decreased buffering capacity due to more acidic pH resulted increased incidence of dental caries which supports the present study which is similar to our study. Prashanth K et al demonstrated that there was

| USSFR (ml min^-1) | 0.37±0.37 | 0.31±0.08 | 0.31±0.25 | 0.33±0.37 | 0.73 |
|------------------|-----------|-----------|-----------|-----------|-----|
| pH of Unstimulated Saliva | 6.69±0.48 | 6.54±0.58 | 6.39±0.50 | 6.74±0.55 | <0.001** |
| pH of stimulated Saliva | 7.97±0.31 | 7.72±0.32 | 7.84±0.51 | 7.87±0.38 | 0.352 |
| SSFR (ml min^-1) | 1.59±0.50 | 1.57±0.09 | 1.51±0.39 | 1.53±0.49 | 0.08 |
an association of gingival and periodontal pathology in hypertensive patients.

**Conclusion**

In conclusion, the contributory factors in maintaining the integrity of oral cavity is salivary flow rate, pH and the buffering action of the saliva. Use of antihypertensive medications effects pH of un-stimulated saliva which can be lead to many detrimental changes in oral cavity. In older adults, monitoring of blood pressure is required for maintenance of oral health. There was no significant association of either hypertension or antihypertensive medication with salivary flow rate in this study. Diminished pH of unstimulated saliva and thus acidity of the oral cavity was related to hypertension rather than antihypertensive medication. More research would be needed for confirming the flow rate alterations in hypertensive patients.

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**Conflict of Interest**

None.

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