MINERAL ANALYSIS OF GIANT SUBMANDIBULAR GLAND SIALOLITHS IN COMPARISON WITH PATIENT'S SERUM PARAMETERS: A CLINICAL STUDY

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ABSTRACT

BACKGROUND

Sialoliths often referred to as salivary calculi constitute 0.45% in regular clinical practice and mainly characterize the ducts of parotid and submandibular salivary glands. Sialolith is composed of both organic and mineral substances. However, only few studies exist on the characterization and distribution of the inorganic and organic matter in the sialolith. In our study, we aim at correlating the patient's serum characteristics to the inorganic materials in the sialolith in order to deduce an association between the two.

METHODS

14 patients were included in study (11 males and 3 females). Only patients with sialoliths in submandibular gland proper were included and those with sialoliths in ducts were excluded. Radiological investigations and confirmation of provisional diagnosis was done followed by blood tests that were given in fasting state. Removal of submandibular gland along with sialolith was done under general anaesthesia through submandibular approach. The excised gland and sialolith were sent to lab for histopathological and mineral analysis respectively. The results of both serum values and mineral analysis of sialolith were compared statistically.

RESULTS

The mean age group of the entire study group was 52.5 ± 8.7 years. Submandibular gland sialoliths were found on the right side in 8 patients (57.14%). The mean dimensions of the submandibular gland sialolith measured from the CT scan was: supero-inferiorly 19 ± 8.7 mm, antero-posteriorly 20.4 ± 8.1 mm, and medio-laterally 9.4 ± 4.7 mm. All the sialoliths that were included in study were more than 1.5 cm which is regarded as giant in size. The histopathological examination was suggestive of chronic sialadenitis in all cases. The average weight of all salivary stones was found to be 1107.9 ± 503.2 mg.

CONCLUSIONS

There seemed to be very little or no correlation between the increased serum values and the presence of the corresponding inorganic substance in the sialolith. Thus, the propensity for sialolith formation is attributed to tortuous course of the salivary ducts and consistency of salivary flow seem to be the majorly proven factor and cannot be substituted for any other justifications till date.

KEYWORDS

Mineral Analysis, Sialolith, Submandibular Gland.

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BACKGROUND

Salivary Calculi also designated as a sialolith is commonly associated with the ducts of parotid and submandibular gland. The prevalence of sialoliths of the Wharton duct is estimated to range between 60-80% due to its salivary properties and course. The encounter of a sialolith in clinical practice is decreed to be about 0.45%.[1]

The sialolith is composed of both organic and mineral substances. Mineral phase is predominated by carbonate containing hydroxyapatite crystals which are structured as lamellar increments. These minerals either predominate in

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the centre or the periphery of the sialolith and distribution of mineral phase is essential to disintegrate the stone. Globules of organic matter have been found on external fracture surfaces, and polished cross-sections of sialoliths.[2,3] However, only few studies exist on the fraction and distribution of the inorganic and organic matter in the sialolith. In our study an interdisciplinary approach was used to analyse the sialolith both histologically for organic content and biochemically for its inorganic content which would aid in understanding the concrement and throw light on its management strategies. The serum characteristics of a patient suffering from sialolith have been discussed very sparsely in literature. In our study we investigate to correlate the serum characteristics and their association with sialolith formation in individuals.

METHODS

This study was carried out from June 2011 to October 2016. Patients who suffered from submandibular sialoliths and reported for the very first time were included in the study with an inclusion age range of 20-70 years. Sialoliths of other major salivary glands were not a part of this study and patients with systemic disorders and recurrent sialoliths were excluded from the study. Sialoliths from the submandibular ducts were also excluded from the study because of the tortuous and anti-gravity course of the duct which itself may influence in formation of a submandibular gland duct sialolith. Hence, Sialoliths only from submandibular gland proper were included in the study. A total of 14 cases (11 male and 3 female) were considered for the study. The patient's history was recorded followed by clinical examinations. Radiographic examination was done for confirmation of provisional diagnosis by Orthopantomogram (OPG) (Figure 1). It was followed by Cone Beam Computed Tomography (CBCT) scan or plain CT (Computed Tomography) scans for measuring sialolith in all three dimensions. (Figure 2, 3, 4 and 5)

Serum Collection

2 ml of peripheral blood were drawn from subjects using standardized phlebotomy procedures after 10 hours of fasting and collected blood was allowed to clot. Blood samples were collected without anticoagulant into 10 ml centrifuge tubes and allowed to coagulate for 1 hour at room temperature. Sera were separated by centrifugation in a cooling centrifuge at 1500 rpm for 10 minutes at -4^{0}C and all specimens were immediately aliquoted, frozen, and stored at -80^{0} C freezer. No more than one freeze-thaw cycle was allowed for each sample. The sera collected were quantitatively analysed for constituents like serum calcium, bicarbonate, sodium, potassium, chloride, phosphorus, magnesium, uric acid, total cholesterol and total bilirubin.

Surgical Technique

All patients were treated under general anaesthesia after obtaining informed consent in their regional language. The patients were intubated using naso-endotracheal intubation. Marking of the skin was done prior to the infiltration of vasoconstrictors. The incision marking was given 3 cm below the inferior border of mandible to preserve marginal mandibular nerve. The length of incision was approximately 5 cm (Figure 6). Normal saline with adrenaline was injected below the skin at the surgical site to reduce operative bleeding and also to get better cleavage planes of tissues while dissection. After the skin incision, subcutaneous tissue was incised and deeper to this, Platysma was identified and carefully incised. Superficial layer of deep cervical fascia is carefully incised followed by identification of facial artery and vein which was then ligated (Figure 7). With the help of Hayes Martin manoeuvre, the ligated facial vessels is slung superiorly due to which marginal mandibular branch of facial nerve gets preserved. Deeper dissection is then carried out. Superficial part of submandibular gland is identified and freed from anterior belly of digastric muscle and also lateral surface of mylohyoid muscle. The free edge of the mylohyoid muscle is then identified and retracted superolaterally to expose the Lingual nerve, Hypoglossal nerve and Wharton's duct. The sub-mandibular gland is then retracted inferiorly to identify the submandibular ganglion that is then divided to free the lingual nerve with a care so that the tie doesn't lie across the main nerve. The Wharton's duct is then divided after identification of hypoglossal nerve. The duct is divided and ligated close to the floor of the mouth (Figure 8). Then submandibular gland was retracted inferiorly, and then facial artery is identified running superomedial to the gland. The facial artery is again ligated here as it crosses the digastric muscle. The gland along with the sialolith is then completely excised following the dissection across the posterior belly of digastric muscle (Figure 9 and 10). The deeper layers were sutured with 3-0 Vicryl (Polyglactin 910) and subcuticular sutures were placed on skin using 4-0 or 5-0 Prolene (poly propylene) suture (Figure 11). The skin sutures were removed after 7 days, regular follow-up of the patients were done for a period of one year. The excised submandibular gland along with sialolith was sent for histopathological analysis and mineral analysis respectively. There were no signs of infection, wound dehiscence or facial nerve weakness in any of the cases.

RESULTS

The study sample included 14 patients with a follow up period of one year. They were in total 11 male patients (78.57%) and 3 female patients (21.43%). The mean age group of the entire study group was 52.5 ± 8.7 years. Submandibular gland sialoliths were found on the right side in 8 patients (57.14%) and the rest were of left side. The mean dimensions of the Submandibular gland Sialolith measured from the CT scan was: supero-inferiorly 19 ± 8.7 mm, antero-posteriorly 20.4 ± 8.1 mm, and medio-laterally 9.4 ± 4.7 mm (Table 1). All the sialoliths that were included in study were more than 1.5 cm which is regarded as Giant in size and can be termed as Megalith according to the classification by Broadner et al. The histopathological examination revealed that all the excised salivary gland showed atrophy of salivary acini with sparse chronic inflammatory infiltrate suggestive of chronic sialadenitis. The average weight of the stones was found to be 1107.9 ± 503.2 mg. Elemental calcium was present in all the cases. 10 patients (71.4%) had Calcium oxalate. Whereas only 42.8% of patients (6 patients) had non oxalate calcium. Two patients had both oxalate and non-oxalate calcium. Among the 14 patients, eight patients (57.14%) had carbonate in the sialolith, 12 patients (85.7%) had sodium traces, 9 patients (64.2%) had potassium traces, 11 patients (78.57%) had chloride traces and 7 patients (50%) had phosphates, 7 patients (50%) had magnesium, 5 patients (35.7%) had uric acid. None of the patients had cholesterol and bilirubin in sialoliths (Table 2). Serum values of the respective patients were also taken pre operatively to ascertain any correlation between the two (Table 3). Both the inorganic mineral constituents as well as increase in corresponding serum values were compared statistically using SPSS software version 21 using Chi Square tests. None of the constituents in sialoliths showed any statistical significance in relation to increased corresponding serum value of the patient.

Case No.	Age	Gender	Side	Single/ Multiple	Size of Sialolith/s in mm as per CBCT			Weight of Sialolith/s in Milli Grams
					Antero- Posterior	Supero-Inferior	Medio- Lateral	
1	43	Male	Right	Single	31	11	5	1065
2	52	Male	Right	Single	27	14	6	1100
3	40	Male	Left	Single	30	6	6	840
4	66	Male	Right	Multiple	8	30	11	1925
5	52	Male	Right	Multiple	12	28	14	970
6	46	Male	Left	Single	24	15	9	850
7	55	Female	Left	Single	12	16	7	450
8	41	Male	Right	Single	19	5	4	660
9	70	Male	Left	Single	30	33	20	2250
10	57	Female	Right	Single	28	24	15	1650
11	55	Female	Left	Multiple	11	27	8	790
12	47	Male	Right	Multiple	17	21	11	980
13	55	Male	Left	Single	23	18	6	1200
14	56	Male	Right	Multiple	14	18	10	780

Table 1. Demographic Data and Details of Submandibular Sialolith

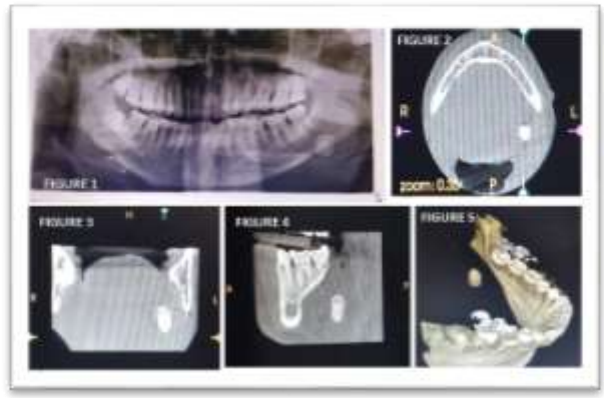

Figure 1. Orthopantomogram Showing Sialolith of Submandibular Gland Region on Left Side.
Figure 2. Axial View of Sialolith in CT Scan.
Figure 3. Coronal View of Sialolith in CT Scan.
Figure 4. Sagittal View of Sialolith in CT Scan.
Figure 5. Three-Dimensional Reconstruction of Sialolith in Relation to Mandible

Figure 6. Skin Marking of Incision 3 cm Below the Inferior Border of the Mandible.
Figure 7. Identification and Ligation of Facial Vessels.
Figure 8. Identification and Ligation of Wharton's Duct after Retracting Gland Inferiorly.

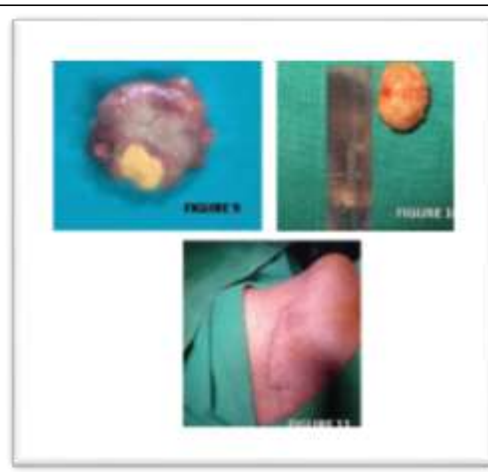

Figure 9. Excised Submandibular Salivary Gland Along with Sialolith.
Figure 10. Submandibular Gland Sialolith.
Figure 11. Skin Closure with Subcuticular Suturing

Mineral in Sialolith	Case No.													
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Calcium Oxalate	✓	✓	×	✓	✓	✓	✓	✓	×	×	✓	✓	✓	×
Non - Oxalate Calcium	×	×	✓	×	×	×	×	✓	✓	✓	×	✓	×	✓
Carbonate	×	✓	✓	×	×	×	✓	✓	✓	✓	×	✓	×	✓
Sodium	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	✓	✓	✓	×
Potassium	✓	×	×	✓	×	✓	✓	✓	✓	×	✓	✓	×	✓
Chloride	×	✓	✓	✓	✓	✓	×	×	✓	✓	✓	✓	✓	✓
Phosphates	✓	×	×	✓	✓	×	✓	×	×	✓	×	✓	×	✓
Magnesium	×	✓	✓	×	×	✓	×	✓	×	×	×	✓	✓	✓
Uric Acid	✓	✓	×	×	×	✓	×	×	✓	×	×	×	✓	×
Cholesterol	×	×	×	×	×	×	×	×	×	×	×	×	×	×
Bilirubin	×	×	×	×	×	×	×	×	×	×	×	×	×	×

Table 2. Mineral Analysis of the Submandibular Gland Sialoliths

Serum Value	Case No.													
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Calcium (9-11 mg/dL)	9.5	10.1	9.8	8.9	10.2	10.5	9.7	9.6	9.3	10.3	10.9	10.5	9.7	9.3
Bicarbonate (18-30 mEq/L)	28	25	25	25	19	23	27	28	29	20	22	21	27	25
Sodium (135-147 mEq/L)	137	139	140	134	145	142	143	147	140	140	136	143	140	139
Potassium (3.5-5.5 mEq/L)	4.0	4.2	3.8	3.7	5.2	5.4	5.4	3.8	4.3	5.2	4.4	5.0	4.9	4.2
Chloride (98-106 mEq/L)	99	101	100	102	106	105	105	99	101	106	101	99	104	102
Phosphorus (3-4.5 mg/dL)	3.8	3.7	3.5	4.2	4.3	4.3	3.9	3.8	4.2	4.5	4.8	3.3	3.7	3.9
Magnesium (1.8-3.6 mg/dL)	1.9	2.5	2.8	1.9	2.9	3.5	3.3	2.0	3.5	2.9	2.0	2.8	3.2	2.0
Uric Acid (2-5 mg/dL)	2.5	2.8	3.9	3.2	7.2	4.0	3.3	2.9	2.2	3.6	4.2	6.5	4.2	5.1
Total Cholesterol (< 225 mg/dL)	157	180	245	145	155	150	198	180	215	220	163	238	172	195
Bilirubin Total (<1 mg/dL)	0.7	0.4	0.5	0.3	0.2	0.3	0.3	0.5	0.7	0.4	0.8	0.5	0.7	0.9

Table 3. Serum Parameters

DISCUSSION

Mineral composition of the sialolith comprises mainly of inorganic constituents like carbonated calcium, phosphates and organic constituents such as proteins and glycoproteins and lipids. In contrast to popular belief, a higher content of protein or organic matter in the sialolith makes it resistant to management. With this in mind, the present study aims at studying the constituent content in a sialolith and its clinical implications.[4,]

Larger stones have increased mineral content, the major composition of which seemed to be carbonates. In accordance to previous studies conducted by Kraaij et al,[5] this study also presented the stones with largest dimensions with more carbonate content. This supports the theory of concentric growth of the sialolith around a central core of amorphous substances. The mineral layers are deposited in a laminated fashion around the sialolith. With increase in size there is increase in laminated layers with carbonate and different degrees of mineralization.[5]

The weight of a sialolith is correlated with age of the patient and previous results have shown that there is significant association between these two factors. The serum levels of circulating minerals have been cited as an explanation for this association. With increasing age of the patient, studies have shown a significant decrease in serum phosphate levels.[6,7]

The inhibitory action of phosphates on crystallization is widely documented. With rising age and depleting serum phosphate levels the crystallization of sialoliths goes unchecked and leads to larger and heavier stones. In our study we did not find any huge association but the phosphate content in older individuals in the sialoliths were larger compared to the younger age group, thus we conclude that heavier sialoliths in older patients may be attributed to the longer time period of development in these cases.[8]

The reason for oxalate and carbonates to be the major mineralized contents of the sialolith is attributed to the fact that these resist easy solubility to treatment that the stones are subjected too. This is also one major drawback of studying the mineral content conventionally; easily soluble minerals are lost during procedural handling.[9]

In order to overcome this drawback a serum analysis was done for the same patients to understand how serum properties contributed to the formation of a sialolith. No significant changes were detected between serum values and the mineral composition of these patients.

In our study 71.4% population had oxalated calcium which is more commonly seen in stones reminiscent of the kidney and has a propensity to occur in male patients. Salivary stones being more common in men can be justified on the same basis as renal stones owing to the increased serum testosterone level and deposition of oxalate.[10]

CONCLUSIONS

The most important limitation of the present study was its dependence on historically collected data with regards to medical examination of the individuals and lack of spectrophotometric analysis to understand the constitutional distribution of the mineral and organic content.

Despite these, it is evident that the mineral or inorganic content do not vary drastically with medical status or serum levels of minerals in these patients in spite of increasing age. The propensity for sialolith formation is attributed to tortuous course of the salivary ducts and consistency of salivary flow seem to be the majorly proven factor and cannot be substituted for any other justifications till date.

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