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# Association of serum electrolytes and smoking with salivary gland stone formation

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*Abstract.* To further define potential factors that may contribute to stone formation in salivary glands (sialolithiasis), a retrospective chart review was performed of patients diagnosed with sialolithiasis between March 1, 1998 and February 29, 2012. Information on salivary gland stone number, location and size, medical history, medications, and serum electrolyte levels were collected. Associations between electrolyte levels and stone characteristics (such as stone number and size) were examined. Fifty-nine patients were identified; their median age was 58 years (range 25–89 years) and most were male (95%). Salivary stones were most commonly located in the submandibular glands (83%). Thirty-five patients (59%) had a smoking history, with 16 (27%) reported as current smokers. There was a significant association between current smoker status and stone size (mean largest stone size 12.4 ± 8.8 mm vs. 7.5 ± 4.8 mm in current smokers vs. non-smokers; $P = 0.03$). Serum sodium levels ($r = 0.32$, $P = 0.014$) and serum potassium levels ($r = 0.31$, $P = 0.017$) showed significant positive correlations with stone size. While the aetiology of sialolithiasis remains unclear, smoking (which can contribute to reduced saliva flow) and higher serum sodium levels (which can reflect volume depletion) are associated with larger salivary stones.

Key words: sialolithiasis; patient factor; smoking; diuretics; serum electrolyte levels.

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Sialolithiasis is a common salivary gland dysfunction due to stone formation, occurring mostly in the submandibular salivary glands.[1] Stone formation in the salivary gland can lead to recurrent pain and infection. The majority of patients for whom the stone cannot be removed or destroyed inside, require surgical excision of the salivary gland.[2] However, these surgeries are done under general anaesthesia and place branches of the facial nerve, hypoglossal nerve, and lingual nerve at risk.[3] Understanding the pathophysiology of stone formation may help to prevent stone formation and allow patients to avoid invasive surgical procedures.

Although the aetiology and pathogenesis of sialolithiasis is not clear, several theories have been proposed from the analysis of extracted stones.[4,5] Generally, the composition of a salivary stone contains both organic and inorganic components. The organic substances comprise cellular debris, glycoproteins, and mucopolysaccharides and the inorganic outer layer can be made up of calcium carbonates and phosphates.[6,7] Salivary stasis, or even decreased salivary flow, has been indicated as a contributing factor to the development of salivary stones.[7,8]

Additionally, inflammation, or sialadenitis, has been associated with the formation of salivary stones.[9,10] Patient factors, such as tobacco smoking, reduced fluid intake, and the use of medications that diminish salivary output, have already been proposed to influence the salivary flow rate and inflammation in salivary glands.[4,9] Interestingly, when compared to normal individuals, the stasis of salivary flow has also been found in alcoholic individuals, due to histopathological changes in serous acini from major and minor salivary glands.[11]

Additionally, decreased salivary flow, or salivary stasis, can contribute to the formation of salivary stones through the accumulation of ions that have a role in the precipitation, accumulation, and aggregation of salivary stones; for example, salivary stasis has been shown to contribute to the precipitation of calcium ($Ca^{2+}$).[12] Although the concentration of electrolytes such as $Ca^{2+}$ in saliva has been shown to be directly associated with stone formation,[13] there is a lack of information on serum electrolyte levels. Thus, the serum concentrations of particular electrolytes, which might influence their salivary levels,[14] require investigation.

Accordingly, the present study was performed to analyze some of the common patient factors (such as tobacco smoking and alcohol use) and the serum electrolyte levels that may be associated with the size and number of salivary gland stones, using retrospective data from salivary stone patients.

## Materials and methods

A retrospective chart review was performed to identify all patients seen with a diagnosis of sialolithiasis between March 1, 1998 and February 29, 2012 (*International Classification of Diseases, Ninth Revision*, ICD-9, 527.5). To identify patients with a diagnosis of sialolithiasis, all charts were meticulously reviewed and any patient found not to have salivary stones on imaging or direct visualization by an oral surgeon or otolaryngologist was excluded.

Information was then gathered with regards to demographics (age at time of chart review and sex), number of stones, stone location and size, medical history, medications, and serum electrolyte levels. For patients with multiple stones, the size of the largest stone was also recorded. Current use of alcohol and current smoking were recorded as smoking or alcohol consumption at or near the time of diagnosis; smoking history and history of alcohol use were recorded as any smoking or alcohol use now or in the past. The serum electrolyte levels obtained closest to the time of diagnosis were recorded: sodium ($Na^{+}$), calcium ($Ca^{2+}$), magnesium ($Mg^{2+}$), potassium ($K^{+}$), chloride ($Cl^{-}$), bicarbonate ($HCO_3^{-}$), and phosphate ($PO_4^{3-}$). Patient medications were also recorded, such as diuretics, antihistamines, and antidepressants.

Data were recorded in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). The statistical analysis was performed using SAS version 9.3 (SAS Institute, Cary, NC, USA). Between-group comparisons were made using the binomial test, Fisher's exact test, the $\chi^2$ test, or the independent samples *t*-test. Statistical comparisons between the study cohort and population figures for smoking were completed using $\chi^2$ analysis with Yates' correction. Associations between two continuous variables were examined using Pearson correlation. A *P*-value of less than 0.05 was considered to be statistically significant.

## Results

In total, 59 patients with salivary gland sialolithiasis were identified. Within this population, there were 56 men (95%) and three women (5%) ($P < 0.0001$ for equal proportions). The median age of the cohort was 58 years (range 25–89 years). Within the cohort, 45 patients (76%) had one stone and 14 patients (24%) had more than one stone ($P < 0.0001$ for equal proportions). Fourteen patients (24%) were found to be using diuretics, with hydrochlorothiazide and furosemide being the most frequently used. Fifty-three patients (90%) had a history of sialadenitis; the history of sialadenitis was unknown for six (10%) patients. Consistent with past studies,[7,15] the most common stone location was found to be the submandibular salivary gland (83%; Table 1). Among the 49 patients with submandibular sialolithiasis, 47 were men and two were women. Salivary stones were found in the left submandibular gland in 18 patients (37%) and in the right submandibular gland in 28 patients (57%); three patients (6%) had bilateral disease. The difference between left and right laterality was not significantly different from 50% ($P = 0.18$).

Smoking history was positive in 35 (59%) subjects, negative in 20 (34%), and unknown in four (7%). Current smoking was positive in 16 (27%), negative in 39 (66%), and unknown in four (7%). A positive history of alcohol use was found in 30 patients (51%); 25 patients denied using alcohol (42%) and four subjects (7%) had an unknown alcohol use history. Twenty-three patients (39%) were current alcohol users and 30 patients (51%) denied using alcohol; the current alcohol use status was unknown for six patients (10.2%).

*Table 1.* Overall cohort characteristics.

| | No. (%) |
|---|---|
| Sex | |
| Male | 56 (95) |
| Female | 3 (5) |
| Total | 59 ($P < 0.0001$ for equal proportions)[a] |
| No. of stones | |
| 1 | 45 (76) |
| >1 | 14 (24) |
| Total | 59 ($P < 0.0001$ for equal proportions)[a] |
| Diuretic use | |
| No | 45 (76) |
| Yes | 14 (24) |
| Stone location | |
| SMG | 49 (83) |
| Parotid | 8 (13) |
| Minor | 1 (2) |
| SMG + parotid | 1 (2) |

SMG, submandibular gland.
[a] Binomial test.

To determine the predisposition of reduced salivary flow due to salivary gland infection/inflammation caused by smoking or alcohol use,[9] the associations of stone size with current alcohol use, history of alcohol use, smoking history, and current smoking was examined using analysis of variance; patients for whom the current or historical smoking or alcohol status was unknown were excluded. There was no significant association for stone size among patients who had a smoking history and those who did not. Interestingly, the stones of patients who were current smokers were significantly larger than those of patients who were not current smokers ($P = 0.03$), with a mean of 12.4 and 7.5 mm, respectively. Alcohol use (current or prior) and diuretic use were not significantly correlated with stone size (Table 2).

A $\chi^2$ analysis with Yates' correction was used to determine whether there was an association between the number of stones (1 vs. >1) among diuretic users, or confirmed smoking or alcohol use (current and history), excluding subjects with unknown smoking or alcohol status. No significant difference was found for each of these comparisons. Among diuretic users, five (36%) developed more than one stone, as did nine (20%) of those