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Does drinking water influence hospital-admitted sialolithiasis on an epidemiological level in Denmark?

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ABSTRACT

Objectives: Sialolithiasis, or salivary stones, is not a rare disease of the major salivary glands. However, the aetiology and incidence remain largely unknown. Since sialoliths are comprised mainly of calcium phosphate salts, we hypothesise that drinking water calcium levels and other elements in drinking water could play a role in sialolithiasis. Owing to substantial intermunicipality differences in drinking water composition, Denmark constitutes a unique environment for testing such relations.

Design: An epidemiological study based on patient data extracted from the National Patient Registry and drinking water data from the Geological Survey of Denmark and Greenland retrieved as weighted data on all major drinking water constituents for each of the 3364 waterworks in Denmark.

All patient cases with International Statistical Classification of Diseases 10th Revision (ICD-10) codes for sialolithiasis registered between the years 2000 and 2010 were included in the study (n=3014) and related to the drinking water composition on a municipality level (n=98).

Primary and secondary outcome measures: Multiple regression analysis using iterative search and testing among all demographic and drinking water variables with sialolithiasis incidence as the outcome in search of possible relations among the variables tested.

Results: The nationwide incidence of hospital-admitted sialolithiasis was 5.5 cases per 100 000 citizens per year in Denmark. Strong relations were found between the incidence of sialolithiasis and the drinking water concentration of calcium, magnesium and hydrogen carbonate, however, in separate models (p<0.001). Analyses also confirmed correlations between drinking water calcium and magnesium and their concentration in saliva whereas this was not the case for hydrogen carbonate.

Conclusions: Differences in drinking water calcium and magnesium may play a role in the incidence of sialolithiasis. These findings are of interest because many countries have started large-scale desalination programmes of drinking water.

INTRODUCTION

Sialolithiasis is not a rare disease of the major salivary glands, although little is known about the aetiology and the incidence

Strengths and limitations of this study

- All patient cases in Denmark with International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes for sialolithiasis registered between the years 2000 and 2010 were included (n=3014) and related to the drinking water composition on a municipality level (n=98).
- The drinking water in Denmark displays substantial intermunicipality compositional differences in a country covering only a limited area of land and with a relatively genetically homogeneous population.
- The validity of the diagnoses was tested in a subsample (n=200) and showed no differences between low-incidence and high-incidence regions, indicating that systematic misclassification was not present in the data analysed.
- On a global scale, all information about the possible medical effects of changes to drinking water, including desalination and other modifying measures, will be valuable for high-level decision-making.
- The study is epidemiological, and therefore patient intrinsic factors, such as saliva secretion and saliva composition, and parameters regarding calcium metabolism and duct anatomy are unknown. Thus, the contributing role of such factors in addition to drinking water composition was not analysed.

on nationwide scales.[1–3] Since sialolithiasis occurs mainly unilaterally, patient intrinsic factors more than likely contribute to this disease.[4] The symptoms are swelling and pain, caused by obstruction of the physiological salivary flow and commonly meal related.[5][6] Although sialolithiasis is a benign condition that occurs mostly in the ducts of glandula submandibularis,[7] sialolithiasis can lead to painful inflammation of the salivary glands, sialadenitis,[8] which, if not spontaneously resolved, requires surgical treatment either by direct incision (sialodochotomy) or endoscopic removal of the stone (sialoendoscopy) or finally by excision of the gland.[9]

In other exocrine glands and the kidneys, the concentration of specific constituents

can influence stone formation,[10] and it therefore seems reasonable that similar relations could apply for sialo-lithiasis. Since sialoliths predominantly consist of calcium phosphate salts,[11] and as calcium in drinking water is associated with other diseases such as atopic dermatitis in childhood, colon cancer and dental caries,[12–15] it is tempting to speculate on an association between drinking water calcium levels and salivary stone formation. In some areas of Denmark, the drinking water contains considerable amounts of calcium,[15] and in these areas a substantial part of the daily calcium intake may arise from the intake of drinking water.

The main determinant of calcium in Danish drinking water, which is almost solely derived from groundwater, is the geochemical difference among aquifers

(figure 1A). Major differences among the country municipalities have previously allowed for analyses of strong associations with other diseases and drinking water composition, especially calcium and fluoride.[15] From this perspective, it is also possible that drinking water calcium is linked to sialolithiasis. In a pilot study, the incidence of sialolithiasis differed among the five main Danish regions (each comprising several municipalities) and the incidence was higher in the regions with high-calcium levels in the water than in regions with lower calcium levels (p<0.001). Consequently, we here aimed to test whether drinking water calcium and other ions may explain part of the variation of sialolithiasis on a municipality level (98 municipalities vs the 5 main regions) in Denmark.
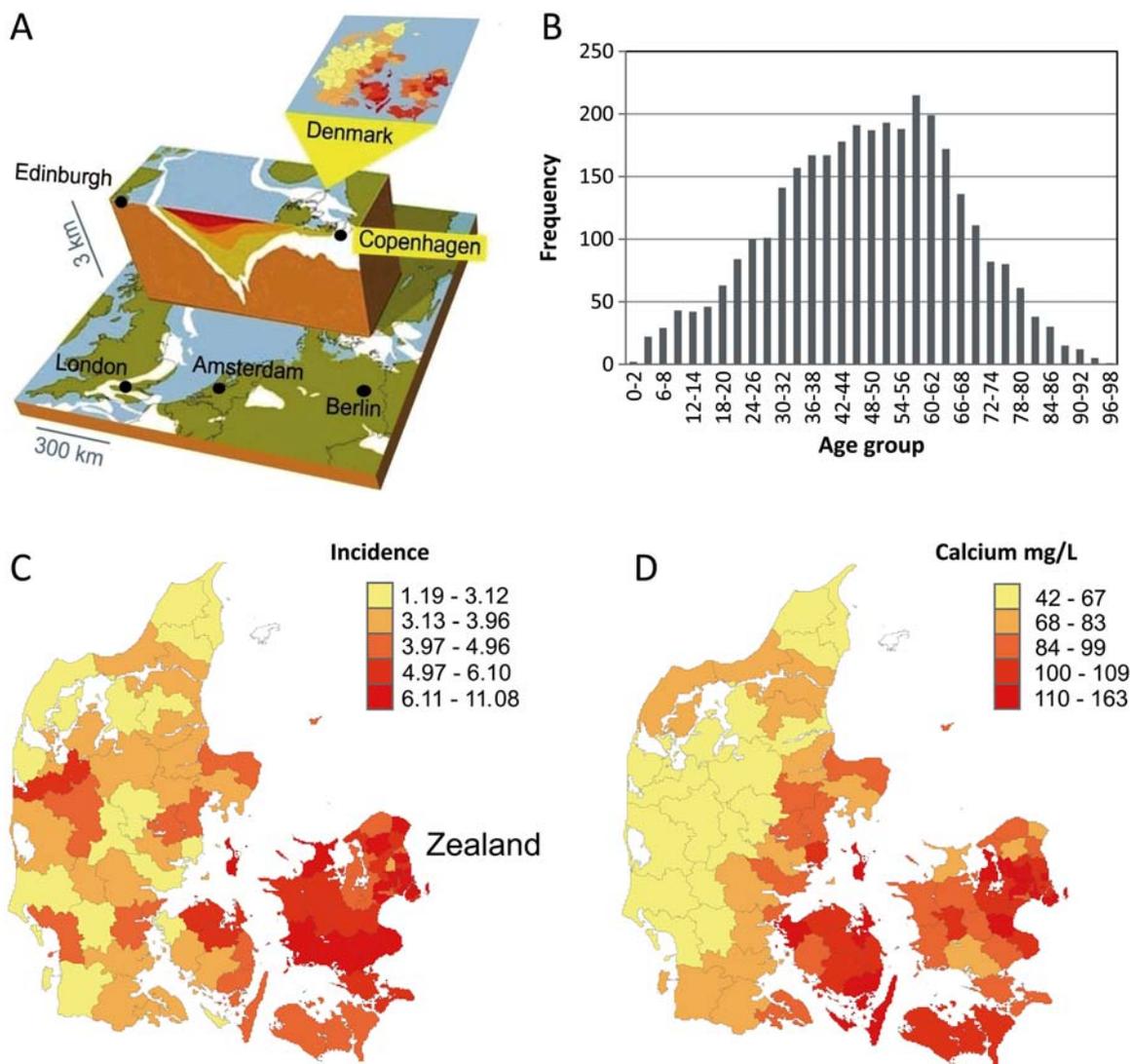
Figure 1 (A) The proximity of the limestone layer to the surface of the earth in Northern Europe with special focus on Denmark. (B) The frequency (2000–2010) of hospital-admitted sialolithiasis with respect to the age of the patient at the time of diagnosis. (C) The incidence (number of cases per 100 000 citizens per year) of hospital-admitted sialolithiasis in the 98 Danish municipalities and (D) the drinking water calcium levels (mg/L) in each of the municipalities. (C and D) Mean values (2000–2010) for each of the municipalities. For magnesium and hydrogen carbonate, the map covering the land of Denmark would be very similar to (D) for calcium.

MATERIALS AND METHODS

Data collection and validity

Data were extracted from the Danish National Patient Registry as all patient cases with International Statistical Classification of Diseases 10th Revision (ICD-10) codes for sialolithiasis registered between the years 2000 and 2010. Care was taken to avoid the same sialolith being counted more than once, such as for a patient diagnosed on more than one occasion (thus, duplicates were excluded). For each case, we recorded the age of the patient at the time of diagnosis, gender, hospital of treatment and municipality of residence during the past 3 years. To evaluate whether the validity of the sialolithiasis diagnosis was comparable among regions, we conducted a test sample on 100 patient records from a low-incidence region and 100 patient records from a high-incidence region. Only direct stone visualisation by the treating physician, or stones confirmed through imaging techniques, such as ultrasound, MRI, CT or X-ray, were accepted as an accurate diagnosis. Population size data were gathered from Statistics Denmark, which is the national governmental institute for statistics.

Drinking water composition and chemistry

Within the observation period of study, data on the average drinking water composition (20 variables) were retrieved from the Geological Survey of Denmark and Greenland (table 1). All chemical data were obtained as average concentrations (mg/L) from the year 2000 to 2010 for each of the waterworks in the 98 Danish municipalities. In total, data from 3364 waterworks were obtained, and a weighted average was calculated based on the total drinking water volume from each waterworks in the municipality in question and the total

Table 1 Standard chemical characteristics of Danish drinking water from 2000 to 2010 (mean and range)

	Mean	Range	Per cent of total
Physicochemical characteristics			
Evaporation residue (mg/L)	434	177–886	–
Ionic strength (mol/L)	0.010	0.004–0.023	–
pH	7.57	7.14–7.92	–
Water hardness (°dH)	16.0	7.4–30.0	–
Gases (mg/L)			
Aggressive carbon dioxide	4.6	0.0–77.2	0.8
Oxygen	8.8	6.0–10.6	1.6
Cations (mg/L)			
Ammonia and ammonium	0.06	0.01–0.39	<0.1
Calcium	91.2	42.0–163.0	16.4
Iron	0.13	0.02–2.91	<0.1
Magnesium	14.5	3.9–41.2	2.6
Manganese	0.06	0.01–1.82	<0.1
Potassium	3.6	1.3–10.5	0.6
Sodium	33.7	11.0–103.0	6.1
Anions (mg/L)			
Chloride	54.7	14.5–164.1	9.8
Fluoride	0.38	0.09–1.35	0.1
Hydrogen carbonate	287	112–427	51.6
Nitrate	4.15	0.63–23.97	0.7
Nitrite	0.02	0.00–0.10	<0.1
Inorganic phosphorus	0.03	0.01–0.09	<0.1
Sulfate	50.7	4.0–237.0	9.1
Organic compounds (mg/L)			
Organic carbon	1.86	0.62–9.43	0.3
Saturation indices as $\log_{10}$ (IAP/Ksp)			
Hydroxyapatite*	2.66	−1.82 to 6.05	–
Brushite†	−2.68	−3.45 to −2.12	–
Mg-whitlockite*	4.87	−4.04 to 11.58	–
Calcium carbonate*	0.26	−0.64 to 0.87	–
Octacalcium phosphate†	−5.35	−8.74 to −2.81	–
Fluorapatite*	7.91	3.25 to 11.47	–

Weighted average values for 20 standard chemical characteristics, as well as ionic strength and saturation indices, of Danish drinking water from 2000 to 2010 in the 98 Danish municipalities. The part of each ion and compound relative to the total amount of ions and compounds is given in the right hand column in per cent of total by weight. Saturation indices were determined by calculation.
*Denotes general (mean) supersaturation.
†General undersaturation. It should be noticed that the result for Mg-whitlockite is based on a temperature of 25°C. In addition to the total concentrations of all species, pH is known as well. For this reason, the hydrogen carbonate concentration was treated as variable, which seems justified as the value may easily change by exchange with the atmosphere.

drinking water consumption for the same municipality. Hydrogen carbonate was by far the most abundant ion, constituting more than half the constituents in the water by weight, followed by calcium, chloride, sulfate, sodium and magnesium (table 1). The term aggressive carbon dioxide, mentioned in table 1, is used by water suppliers and is a measure of the amount of carbon dioxide that will react with calcium carbonate to achieve calcium carbonate equilibrium.

Saturation indices were determined by computer programmes for an assumed drinking water temperature of $10°C$.[16 17] Solubility data for calcium phosphates at $10°C$ were retrieved from the National Bureau of Standards (NIST),[18–20] data on fluorapatite ($Ca_5(PO_4)_3F$) were retrieved at temperatures from $25°C$ to $50°C$,[21 22] and data for calcium carbonate ($CaCO_3$) were taken from Plummer and Busenberg.[23] The first two dissociation constants of the phosphate system were also retrieved from NIST,[24] whereas the third was obtained by non-linear extrapolation from additional data.[25] When not given at $10°C$ directly, values were obtained from $25°C$ and the standard enthalpy increment. We also considered magnesium whitlockite (Mg-whitlockite). Crystal structure determination has indicated it to be $Ca_9MgH(PO_4)_7$,[26] and its solubility product was determined under this assumption.[27] The following solubility products ($pKsp$) were found from the sources quoted: hydroxyapatite ($Ca_5(PO_4)_3OH$) 58.50, brushite ($CaHPO_4 2H_2O$) 6.61, Mg-whitlockite 122.33, calcium carbonate (calcite) 8.41, octacalcium phosphate ($Ca_4H(PO_4)_3 2.5H_2O$) 48.26, and fluorapatite 61.54. Nitrite was ignored due to its low concentration and iron was assumed to be $Fe(III)$ due to the presence of oxygen and high drinking water pH (table 1).

Statistical analyses

Primary statistical models were based on multiple regressions using iterative search and testing among the main 20 drinking water variables against the incidence of sialolithiasis in the 98 Danish municipalities as the outcome. One-way analyses of variance were used to study associations among incidence of sialolithiasis and each of the characteristics of the municipalities. Adjusted multiple linear regression models were fitted with incidence as the explained variable and water characteristics as explanatory variables. Models were adjusted for mean age, region and percentage of females in the population. One-to-one correlation analyses were conducted among all water characteristics to avoid misleading effects in the models and thus in order to rule out strong inter-relationships. Similar analyses were performed to test the effect of drinking water on human saliva composition. When assessing relations between drinking water composition and sialolithiasis incidence, patients who had not resided in the same municipality 3 years prior to diagnosis (n=390) were excluded in order to avoid bias from patients being exposed to drinking water in more than one municipality. The main statistical analyses were performed with SAS

V.9.3 and additional analyses with R.[28 29] The level of significance was set at $p<0.05$.

RESULTS

Incidence, epidemiology and data validity

A total of 3014 cases were recorded with a mean of 298 annual cases. For the obtained population size of 5 475 791 citizens (average size of the Danish population between years 2000 and 2010), the mean yearly incidence was 5.5 cases per 100 000 citizens nationwide (95% CI 5.3 to 5.5). Incidence was also calculated for men and women separately being 5.4 (CI 5.3 to 5.5) and 5.5/100 000/year (CI 5.4 to 5.6), respectively, with no significant difference between genders. The mean age at the time of diagnosis for patients with sialolithiasis was 48.2±18.3 years nationwide with the gender-specific values being males 46.9±17.3 and females 49.6 ±17.6 years, respectively, and with 75% of patients being between 36 and 61 years of age (IQR 26 years) at the time of diagnosis (figure 1B). Although some variation was present, the mean age among municipalities did not differ. Among all age groups, the lowest incidence of sialolithiasis was among children and adolescents. In the test sample, there was no difference in the validity of the sialolithiasis diagnosis between areas with low and high incidence (p=0.880).

The incidence differed considerably among municipalities in Denmark (p<0.001), ranging from 1.2 cases to as much as 11.1 cases per 100 000 citizens per year (figure 1C). The incidence was higher in the Zealand municipalities in eastern Denmark, where the calcium levels in drinking water are considerably higher compared with the western municipalities characterised by much lower levels of drinking water calcium (figure 1C). There were neither significant correlations between municipality size and incidence, nor between age and incidence. However, municipalities with higher incidence tended to comprise more females than males, although the incidence among females was not significantly higher than among males.

Drinking water and incidence

To evaluate associations between sialolithiasis incidence and drinking water composition, all 20 drinking water constituents were tested against incidence. Several constituents of drinking water were correlated with the incidence of sialolithiasis (table 2). Specifically, this was the case for calcium (p<0.001), magnesium (p<0.001), hydrogen carbonate (p<0.001), fluoride (p<0.001) and pH (p<0.001). However, strong positive inter-relationships were also identified among most drinking variables, especially among calcium, magnesium and hydrogen carbonate (p<0.001).

When fitting multiple regression analyses to adjust for mean age, female proportion, regions and drinking water pH, a model containing calcium could be developed that explains 50% (p<0.001) of the variation in

Table 2 Statistical models of Danish drinking water composition and sialolithiasis from 2000 to 2010

	Estimate	SD	T-Value	p Value
Calcium model				
Copenhagen region (east Zealand)	12.71	5.07	−1.40	0.165
Western Zealand region	16.09	4.84	3.32	0.001
North West Denmark region	−5.77	5.40	−1.07	0.289
South West Denmark region	0.11	4.12	0.03	0.979
Mean age	−1.43	0.73	1.96	0.054
Per cent females	475.77	261.49	1.82	0.072
Drinking water calcium	0.22	0.08	2.69	0.009
Drinking water pH	23.12	13.63	1.70	0.094
			Adjusted R^2 0.50	
Magnesium model				
Copenhagen region (East Zealand)	11.24	5.57	2.02	0.047
Western Zealand region	11.96	5.89	2.03	0.045
North West Denmark region	−4.41	5.41	−0.82	0.417
South West Denmark region	1.54	4.08	0.38	0.706
Mean age	−1.63	0.76	−2.14	0.035
Per cent females	492.66	263.31	1.87	0.065
Drinking water magnesium	1.84	0.80	2.29	0.024
Drinking water pH	8.76	11.63	0.75	0.454
			Adjusted R^2 0.49	
Hydrogen carbonate model				
Copenhagen region (East Zealand)	9.66	5.39	−1.79	0.077
Western Zealand region	9.16	5.98	1.53	0.130
North West Denmark region	−3.93	5.28	−0.74	0.459
South West Denmark region	−0.55	4.10	−0.13	0.893
Mean age	−1.65	0.74	−2.24	0.028
Per cent females	419.62	261.11	1.61	0.112
Drinking water hydrogen carbonate	0.09	0.03	3.06	0.003
Drinking water pH	17.33	12.08	1.43	0.155
			Adjusted R^2 0.51	

Estimates, t values, p values and adjusted R^2 values for three models relating drinking water calcium, magnesium and hydrogen carbonate levels to the incidence of hospital-admitted sialolithiasis in the years from 2000 to 2010 (ie, number of cases per 100 000 citizens per year) on a municipality level (n=98).

the incidence of sialolithiasis among municipalities (table 2 and figure 1C,D). The incidence of sialolithiasis was high in municipalities with high-calcium levels and vice versa. Adding pH to the analyses had some effect and pH was also positively related to the incidence of sialolithiasis. Fitting a similar model for magnesium, this ion was also positively related to the incidence of sialolithiasis with an explanatory power of 49% (p<0.001). A model containing hydrogen carbonate also explained 51% of the variation in the incidence of sialolithiasis with a positive relation (p<0.001). Finally, a model with calcium and magnesium, although neither could be significant at the same time, also returned an explanatory power of 51% for the incidence of sialolithiasis (p<0.001).

Drinking water and human saliva

The saturation indices for Danish drinking water are given in table 1. As shown, the drinking water was indeed supersaturated with respect to some of the main elements of sialoliths, namely hydroxyapatite and Mg-whitlockite. We further speculated that for a correlation to signify causality, it would require that the saliva

levels of the ions in question were affected by the drinking water levels of the same ions. So in order to determine which of the ions in drinking water could indicate such a causative relation, we reanalysed saliva data from patients with known drinking water composition from a previous study, performed on 255 healthy subjects distributed among 12 municipalities in Denmark.[30] We found saliva calcium levels to be positively and significantly correlated to drinking water calcium levels (r=0.19; p<0.004, unpublished). Also, saliva magnesium was significantly and positively correlated with drinking water magnesium levels (r=0.23; p<0.001; unpublished), whereas no relations were present with hydrogen carbonate, sodium, chloride, pH and the saliva levels of the same ions.

DISCUSSION

Sialolithiasis is painful and in recurrent and complicated cases, requiring surgical removal, a condition that will lead to loss of gland function with troublesome sequelae such as xerostomia. The surgical treatment of this condition by sialoendoscopy requires painstakingly devised

procedures that are complicated, expensive and time-consuming. Thus, from a quality-of-life as well as a socio-economic perspective, it is desirable to understand aetiological factors for future treatment and prevention of sialolithiasis.

In the current study, the incidence of hospital-admitted sialolithiasis in Denmark was 5.5 cases per 100 000 citizens, although with significant variation among municipalities. The variation in incidence in sialolithiasis among municipalities could not be explained by population size in the municipality, nor the age and gender distribution. However, by adjusting for influence from the region (the five main regions in Denmark), female gender and age, strong relations between incidence and several drinking constituents were obtained, including calcium, magnesium and hydrogen carbonate. After mathematical and statistical evaluation, all three models (calcium, magnesium and hydrogen carbonate; table 2) showed strong and statistically significant relations with the incidence of sialolithiasis. However, it cannot be determined which of the three models is the most important as strong inter-relationships among the ions in question exist. Therefore, analyses were performed on data from a previous study, showing that saliva levels of calcium and magnesium were affected by the drinking water levels of the same ions, whereas no relations were obtained with hydrogen carbonate.[30] We therefore excluded hydrogen carbonate as being related to the incidence of sialolithiasis.

With calcium comprising the major component of all sialoliths,[31] in the form of precipitated hydroxyapatite, subsequent to heterogeneous nucleation in ducts and glands, it seems to be the most likely ion for this relation to occur. Thus, in the municipalities with the highest drinking water calcium levels, the contribution of calcium from drinking water may be as much as 40% of the average calcium intake among Danes, although this value is much less in the western municipalities. As saliva is always supersaturated with respect to hydroxyapatite,[32] saliva calcium concentrations are higher in stone formers versus non-stone formers,[33] and saliva calcium levels are positively related to drinking water calcium levels,[30] the relation with this ion seems to be the most plausible despite calcium metabolism being a very well-regulated metabolic system in humans,[34] and the fact that not even in a study with experimental induced hypercalcaemia in a rat had any influence on the salivary glands in terms of formation of calcified deposits.[35] An uncontrolled factor, however, is the fraction of daily calcium intake derived from dairy products which could not be assessed in this study. For instance, an explanation for the effect of including the regions in the analyses may be that dairy products available for retail are normally derived from cows from within the same region. Thus, with the mammalian glands being exocrine, as are the salivary glands, an additional 'halo-effect' with calcium may arise from the intake of such products, adding further to the effect of drinking water calcium. Furthermore, the calcium-containing mineral brushite is also part of most sialoliths,[31] and saturation indices of this mineral will also increase with increased drinking water calcium levels, adding more evidence to calcium being the most important correlating factor.

Magnesium has often been identified as an inhibitor of hydroxyapatite formation,[36 37] but the magnesium concentrations in human saliva (0.3 mmol/L on average) are not sufficiently high to inhibit hydroxyapatite precipitation.[38] It therefore seems unlikely that there should be a negative interaction between calcium and magnesium. In contrast, magnesium constitutes parts of many sialoliths in the form of Mg-whitlockite,[31] and therefore this correlation coupled with the significant correlation between drinking water and saliva magnesium levels also seems causative. Thus, with normal saliva magnesium levels, precipitation of Mg-whitlockite is indeed likely.[39] The combination of high saliva calcium and magnesium concentrations will increase the pressure on precipitation of Mg-whitlockite even further, indicating a positive relation between the two ions. Thus, magnesium undoubtedly also influences sialolithiasis in some individuals, but not all, because Mg-whitlockite is not found in all sialoliths.[31]

It should be emphasised that the correlations, despite high-statistical significance, does not infer causality. This said, on the basis of a pilot study our a priori assumption was that calcium would be linked to sialolithiasis, which was confirmed in this study, given the strong relation between sialolithiasis and drinking water calcium, and also observed for magnesium, explaining half the variation among municipalities. Taken together, with these ions being prominent in sialoliths and that the drinking water calcium and magnesium content in a separate study is linked to the saliva ions content, we suggest that drinking water calcium and magnesium may play a role in sialolithiasis. Since external factors and patient intrinsic factors are also important, the drinking water calcium and magnesium content may be viewed as preconditions for sialolithiasis.

When comparing our observations with those of other studies, the incidence and municipality variation of hospital-admitted sialolithiasis was higher in Denmark than in the UK and Germany, despite Denmark being a much smaller country.[2 3] In western Denmark, most aquifers are situated within deep layers of sand as opposed to superficial layers of limestone in Zealand, giving rise to considerable differences in drinking water calcium (figure 1A,D) and magnesium levels (table 1). Although somewhat comparable, national patterns regarding calcium have also been found in the UK and Germany,[3 11 40] even though they showed much weaker or even no relations.[1] The more pronounced variation in Denmark may be related to major variations in drinking water composition in a country covering only a limited area of land and with a relatively genetically homogeneous population. The effect of the region could be due to socioeconomic differences or a representation of

different genes in the populations among the regions, as well as exposure to dairy products available at a retail level in the region in question. Furthermore, socioeconomic differences may contribute to the likelihood of seeking medical help as well as the fraction of people being treated in private ear, nose, and throat practice, which may also differ due to socioeconomic differences.

Even if assuming that drinking water constituents as calcium and magnesium served as a preconditioning to sialolithiasis, these could explain only half of the variation, indicating that the aetiology of sialolithiasis is indeed multifactorial. The fact that salivary stones are rarely bilateral (BLATT) argues against a systemic aetiology and rather points to local factors, such as saliva viscosity and duct anatomy. Furthermore, the rate of stone formation increases with decreased flow of saliva as seen after parasympathectomy,[41] and finally it is also observed that sialolithiasis is associated with the presence of bacteria.[42 43]

It is important to stress that since this study is epidemiological, patient-related parameters, for example, saliva secretion, saliva contents and duct anatomy, have not been registered. Therefore, the contributing role of such factors in addition to drinking water composition is unknown. Finally, the validity of the hospital diagnosis is characterised by some degree of uncertainty. Differences among hospital practices in the five regions may influence the results. Nonetheless, the validity of the diagnoses in the test sample (n=200) was comparable between low-incidence and high-incidence regions, so overall there is no reason to believe that systematic misclassification is present in the data analysed for this study.

CONCLUSIONS

The mean Danish incidence of hospital-admitted sialolithiasis was 5.5 cases and most frequent at 36–61 years of age. Strong correlations were found between incidence of sialolithiasis and drinking water calcium and magnesium. About half the variation among municipalities could be explained by drinking water calcium and magnesium ($p<0.001$), although in separate models. We therefore conclude that drinking water calcium and magnesium may play a significant role in sialolithiasis and may serve as a precondition for the disease. As the remaining half of the variation was not explained by drinking water constituents, this supports the notion of sialolithiasis as a disease with a multifactorial aetiology. For future perspectives, it is interesting that many countries have started large-scale desalination programmes, for example, in the Mediterranean area, Singapore and Australia, not because of health-related issues, but because of shortage of drinking water and because high drinking water calcium levels have a negative impact on water distribution supply systems, increasing the maintenance costs significantly.[44 45] Also in Zealand, similar programmes are now planned. It will therefore be interesting to see whether desalination brings changes to the incidence of sialolithiasis in the Zealand municipalities.

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