A population study of oligodontia and its correlation to signs and symptoms from ectodermal organs in young individuals in Sweden.

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Introduction
Recent reports have shown that many individuals with oligodontia also have signs and symptoms from other ectodermal organs. In a Norwegian patient material of 68 individuals with oligodontia, 57% had disturbances in either hair, nails and/or sweat production, and whole salivary secretion rates were lower than in a control group (Nordgarden et al, 20011). These reports gave the implication that some individuals with oligodontia had an ectodermal dysplasia (ED) syndrome. Signs and symptoms in rare disorders in general often vary in a Bell curve fashion from very mild to very evident (Bergendal, 20012). Although many of the ED syndromes are among the most well known heritable syndromes, defined clinical criteria and cut-off points for the respective signs and symptoms are lacking. The definition of an ED syndrome is the presence of two or more of the following symptoms: trichodysplasia, dental anomalies, onychodysplasia and dyshidrosis (Pinheiro and Freire-Maia, 19943). In a case presentation of one male person with hypohidrotic ED, hypoplasia and aplasia of major salivary glands was reported by Nordgarden et al, 19984. Nordgarden et al, 20035, established that individuals with ectodermal dysplasia often have reduced salivary secretion rates. In her thesis (Nordgarden, 20046), the diagnosis oral ectodermal dysplasia was suggested when teeth and salivary glands exclusively are affected. Schalk van der Weide19927, suggested the diagnosis of oligodontia to be divided into Oligodontia /I for isolated oligodontia and Oligodontia /S for oligodontia as part of a syndrome, since there is an overrepresentation of individuals with a diagnosis of a heritable syndrome among individuals with oligodontia. A search on features in the London Dysmorphology Database (LDDB, Oxford Medical Databases, Oxford University Press, 2000) results in 142 syndromes matching the search term oligodontia.

The population prevalence of oligodontia, defined as the congenital absence of six or more permanent teeth, third molars excluded, was reported by Hobkirk and Brook,19808 to occur in about one in fifteen individuals with hypodontia, giving a population prevalence of 0.3%. Poulsen and Rolling, 20022, reported the prevalence in a large Danish sample to be 0.16%, and Nordgarden et al, 200210, in a study of agenesis of teeth in 18-year olds in two counties in Oslo, Norway, found 8 individuals with oligodontia, giving a prevalence of 0.084%. In a study of 196 patients with oligodontia reported from specialist clinics in the Netherlands the prevalence was 0.08% (Schalk van der Weide, 19927).
Aim
It was the aim of the present study to establish the prevalence of oligodontia in a population study in three counties in Sweden and to investigate ectodermal signs and symptoms in order to suggest anamnestic and clinical criteria for involvement of ectodermal organs. The study protocol was approved by the ethics committee at the University of Linköping, Sweden.

Materials and methods
Inclusion criteria for the study were oligodontia, defined as agenesis of six or more permanent teeth, third molars excluded, in children born 1981-1994 in three Swedish counties. Exclusion criteria were radiation therapy to the jaws during the first years in life.

Sample
An inquiry was sent to all clinics in the Public Dental Service, PDS, in three countries in Sweden (the counties of Östergötland, Jönköping and Kalmar) with a total population of 900 000, which constitute about one tenth of the total Swedish population. More than 95% of the children in these counties get their regular dental care in the PDS.

No data on children with oligodontia could be obtained by computerized search from patient records. In a mailed inquiry to all PDS clinics, the dental teams were asked to report all children they could recall to fulfil the inclusion criteria. The reported children were asked to participate in a clinical study comprising a panoramic radiograph, clinical photographs, a structured interview focusing on symptoms from ectodermal organs, testing of salivary secretion rates and a blood sample for later genetic investigation. The parents, or the children when 18 years or older, gave written consent to participation in the study.

Saliva testing
Salivary secretion rates were tested using regular clinical routines: resting whole saliva was collected for 15 minutes and stimulated whole saliva for 5 minutes in a graduated measuring glass. Volume per minute was then calculated. The testing procedures were preferably performed in the morning, but examination time was coordinated for best convenience for the participants and also afternoon appointments were accepted. A salivary flow rate of less than 0.7 ml/min for stimulated whole saliva and/or 0.1 ml/min for resting whole saliva were used as cut off points for impaired salivary function (Fox et al 1987).

Structured interview on ectodermal signs and symptoms
A structured interview focusing on questions about symptoms from ectodermal organs was worked out and tried by all four examiners in a small number of children with tooth agenesis. The interview contained four questions about skin problems, four questions about sweating problems, and one question each whether the hair and nails were normal or not. After completion of the structured interview and the saliva sampling, the examiners were asked to judge whether in their opinion the individual had an ectodermal dysplasia syndrome.
Results

Examined individuals and prevalence of oligodontia

From the inquiry 164 individuals with oligodontia were identified. Two individuals who had been given radiation therapy to the jaws during their first year in life were excluded from the study. Thus the number of individuals with oligodontia was 162, 91 girls and 71 boys, 56% and 44 % respectively. Population figures of the age-groups born 1981 to 1994 in the three counties were obtained from Statistics Sweden, in all 179,716 children, giving a prevalence of oligodontia of 0.090%. When contacted for participation in the clinical study, 33 declined to participate, 2 could not co-operate to the examinations, and 4 had moved. Thus 123 (76 %) of the children with oligodontia accepted to participate in the clinical study. They were 71 girls (58 %) and 52 boys (42 %). The age and gender of identified and examined individuals with oligodontia are shown in Fig. 1.

In 7 out of 14 of the reported age-groups, 12- to 18 year-olds, the numbers of reported individuals were higher than in the younger and older age-groups. If calculated from the total numbers of 12-18 year-olds, 90,863, the prevalence of oligodontia in these age groups was 0.115 %. When divided on county level the prevalence figures for the whole material were 0.144, 0.072, and 0.060 respectively.

Tooth agenesis

The number of missing teeth varied from 6 to 20, with a mean of 8.3 for all identified individuals. The number of missing permanent teeth is shown in Fig 2. More than half of the individuals, 90 (55.6%), were missing six or seven permanent teeth. One out of ten individuals with oligodontia, 16 individuals or 9.9 % was missing more than 12 teeth. Agenesis of individual teeth is shown in Fig 3. The teeth most commonly missing were the second premolars of the upper and lower jaw, followed by the upper lateral incisors; these teeth constituted half of the missing teeth, 51.3%. The upper central incisors were not found missing in any individual. The study group comprised nine individuals with a known diagnosis of a syndrome; six had Down’s syndrome, one ichthyosis, one incontinentia pigmenti, and one had Prader-Willi syndrome. The number of missing teeth in individuals with a syndrome varied from 6 to 16 with a mean of 8.8. No classical case of hypohidrotic ectodermal dysplasia was found among the examined individuals.

One or more of the permanent incisors were missing in 65% of all individuals with oligodontia. Out of 72 individuals missing eight teeth or more, 77.8% were missing one or more incisors, and out of 51 individuals missing nine or more teeth 84.3% were missing one or more incisors. Seventeen per cent were missing only premolars and 10% were missing all premolars (and other teeth).

Ectodermal signs and symptoms

Data on symptoms from salivary glands, sweat glands, skin, hair, and nails were collected. Salivary function was recorded through clinical testing of salivary flow rates and for the other ectodermal organs through answers to the questions in the structured interview. Criteria for an impaired function were established after compilation of the results with reference to which question had the best discriminative potential (Table 1).

Four individuals could not co-operate to any of the two salivary tests and three could not co-operate to one of the tests. Therefore, data on ectodermal signs and symptoms are calculated on the results from 116 individuals. Of these, 56 (48.3%)
individuals had no and 60 individuals (51.7%) had one or more sign or symptom from ectodermal organs in addition to oligodontia.

The structured interview comprised four questions about skin problems. A positive answer to the question "Do you at present have eczema?" was chosen as criterion for symptoms from the skin. The other questions on symptoms from the skin were found not to be discriminative; the examinations were performed during the winter season and a majority of the children considered their skin to be dry. Of the four questions on sweating, a negative answer to the question "Do you sweat normally?" was chosen as criterion for symptom of reduced sweating capacity. The answer to this question was usually given after the other questions about sweating had been answered, ("Did you have episodes of fever cramps as a child?", "Can you participate in PE lessons in school?" and "Can you sit in the sun as long as your friends?") and often after discussion of symptoms related to reduced sweating. Negative answers to the question "Do you consider your hair to be normal?" and "Are your nails normal?" were chosen as criteria for symptoms from the hair and nails, respectively. The most common ectodermal symptom was decreased salivary secretion rates, which was found in 37 individuals (31.9%); in 21 cases as a single symptom and in 16 cases in combination with one or more other symptoms. The second most common symptom was skin problems reported by 22 (19.0%), followed by reduced sweating reported by 12 (10.3%) individuals. Abnormal nails were reported by 6 (5.2%) and abnormal hair by 5 (4.3%) individuals, (Table 1.). Of the 60 individuals, who had additional ectodermal symptoms 40 had one, 19 had two, and one had four more symptoms from sweat glands, hair, nail, skin, and salivary glands in addition to oligodontia (Table 2 and Fig 4). In all, 19 individuals (15.4%), 13 girls and six boys, fulfilled the criteria for symptoms from sweat glands, hair or nails; five of them had a known diagnosis of a heritable syndrome.

After completion of the structured interviews the examiners answered the question "Do you think the patient has an ectodermal dysplasia syndrome?". The examiners anticipated 19 of the children to have an ED syndrome.

Discussion

In this population study in individuals born 1981-94, representing 900 000 inhabitants, 162 individuals with oligodontia were identified giving a prevalence of 0.090%. There were methodological difficulties in carrying out a true population study. The identification of individuals with oligodontia depended upon the memory of all the PDS teams in the three counties involved. The diagnosis of oligodontia is usually not established until the age of eight to ten years, why some individuals could be missing in the younger age groups. The older age groups, 19 years and older, do not belong to the children’s dental service, and often move from the area where they grew up for studies or work. This could be some explanation to why there were fewer individuals reported in the youngest and oldest age groups. The prevalence of oligodontia was much lower in two of the three counties, probably due to a lower level of familiarity with inquiries and research projects. From one of the counties no individual, and from another county only one individual with a heritable syndrome was reported, as contrasted to eight from the third county. These are some of the reasons why the identified individuals do not represent all individuals with oligodontia and the reported prevalence reflects an underrepresentation and is anticipated to be too low. Schalk van der Weide, 1992, in a patient material reported a prevalence of 0.08% and Nordgarden, 2002, in a smaller population study in one age group, reported a prevalence of 0.084%. Poulsen and Rolling, 2001, reported the prevalence of oligodontia to be 0.16% in a study where data
from Danish schoolchildren were combined with data from earlier studies, and this large material to date represents the most complete Nordic sample. A British study reported oligodontia to occur in one out of fifteen individuals with hypodontia, giving a prevalence of 0.3%, (Hobkirk and Brook 1980). This points to possible variations in different countries.

The mean number of missing teeth in all 162 identified individuals was 8.3, and in the nine individuals with a known syndrome the number of missing teeth was 8.8. In a large Dutch material of 196 individuals with oligodontia, 62 patients with Oligodontia/S were missing significantly more teeth than patients with Oligodontia/I (Schalk van der Weide, 1992), however, this material was not a population study. The pattern of missing teeth was similar to what has been presented in earlier studies (Schalk van der Weide, 1992, Bergendal & Olgart, 1996, Bergendal et al, 1998). The teeth most frequently missing were second premolars followed by maxillary lateral incisors, these teeth constituted a little more than half of the missing teeth, as opposed to the findings by Rolling & Poulsen, 2001, who reported these teeth to represent two out of three missing teeth in individuals with oligodontia. The upper central incisors were not missing in any of the individuals.

Seven of the individuals could not co-operate to saliva testing, four of them had Down’s syndrome and one had Prader-Willi syndrome. Therefore, signs and symptoms from ectodermal organs in addition to missing teeth were reported in 116 of the individuals. No other ectodermal sign or symptom beside oligodontia was found in 48.3%, and one to four signs and symptoms from ectodermal organs were found in 51.7%. The most common sign was low salivary secretion found in 31.9%. Low salivary secretion rates and dry skin/exema have been described as co-existing symptoms in persons with oligodontia by Nordgarden et al. 2001, a finding which is validated by the present study. Testing of salivary flow is strongly recommended in individuals with oligodontia, since most of individuals with an inborn low salivary secretion will not subjectively perceive dryness of the mouth. Forty individuals had one, 19 had two, and one had four signs and symptoms from other ectodermal organs in addition to teeth. The diagnosis oral ED, suggested by Nordgarden 2004 when symptoms from teeth and salivary glands are present, was found in one in three, 31.9% of individuals with oligodontia in this study. According to the definition of an ED syndrome, two or more of the four tissues hair, teeth, nails and sweat glands should be affected. Missing teeth was the inclusion criterion in this study, and of the five organs studied, only three are among the criteria for an ED syndrome. Nineteen individuals (15.4%), five of them with a diagnosis of a syndrome, had subjectively perceived symptoms from hair, nails and/or sweat glands in the present population study, in contrast to 57% in a patient material where clinical signs and symptoms were recorded (Nordgarden et al, 2001). When individuals with oligodontia were investigated for subjectively perceived ectodermal symptoms and signs of low salivary secretion, more than half had one or more sign or symptom from the five tested organs, and one in six individuals fulfilled the criteria of an ED syndrome. This indicates that a revision of the criteria for ED syndromes could be a future option, even if the full picture will not be known until a better understanding of the molecular genetics in ED syndromes is achieved. Until then, dry skin/exema, and low salivary secretion should be recognised as concomitant symptoms in oligodontia.
References


Fig 1. Age and gender in 162 individuals with oligodontia

Fig 2. Number of missing teeth in 162 individuals with oligodontia
Fig 3. Agenesis of individual teeth in 162 individuals with oligodontia.

Fig 4. Self-reported symptoms from ectodermal organs and clinically tested salivary flow rates in 116 individuals with oligodontia.
Table 1. Frequency of ectodermal symptoms in 116 individuals with oligodontia (7 individuals could not cooperate to one or both salivary tests).

<table>
<thead>
<tr>
<th>Ectodermal organ sign/symptom</th>
<th>individuals who fulfill criteria no</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>56</td>
<td>43.3</td>
</tr>
<tr>
<td>Salivary glands(^1)</td>
<td>37</td>
<td>31.9</td>
</tr>
<tr>
<td>Skin(^2)</td>
<td>22</td>
<td>19.0</td>
</tr>
<tr>
<td>Sweat glands(^3)</td>
<td>12</td>
<td>10.3</td>
</tr>
<tr>
<td>Nails(^4)</td>
<td>6</td>
<td>5.2</td>
</tr>
<tr>
<td>Hair(^5)</td>
<td>5</td>
<td>4.3</td>
</tr>
</tbody>
</table>

\(^1\) Unstimulated whole saliva < 0.1 ml/min and/or stimulated whole saliva < 0.7 ml/min.
\(^2\) Answered yes to the question: “Do you at present have excess?”
\(^3\) Answered yes to the question: “Do you have normal sweat capacity?”
\(^4\) Answered yes to the question: “Are your nails normal?”
\(^5\) Answered yes to the question: “Is your hair normal?”

Table 2. Number of ectodermal symptoms in 116 individuals with oligodontia (7 individuals could not cooperate to one or both salivary tests).

<table>
<thead>
<tr>
<th>Number of symptoms from ectodermal organs</th>
<th>Number of individuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>56 (48.3 %)</td>
</tr>
<tr>
<td>1</td>
<td>40 (34.5 %)</td>
</tr>
<tr>
<td>2</td>
<td>19 (16.4 %)</td>
</tr>
<tr>
<td>4</td>
<td>1 (0.9 %)</td>
</tr>
</tbody>
</table>

116 (100.1 %)