Changes in the chemical composition of mineralised teeth in children after antineoplastic treatment

Ewa Krasuska-Sławińska1, Bożenna Dembowska-Bagińska2, Agnieszka Brożyna2, Dorota Olczak-Kowalczyk1, Elżbieta Czarnowska4, Agnieszka Sowińska4

1Department of Paediatric Dental Surgery, Children’s Memorial Hospital, Warsaw, Poland
2Department of Paediatric Oncology, Children Memorial Hospital, Warsaw, Poland
3Department of Paediatric Dentistry, Warsaw Medical University, Poland
4Department of Pathology, Children Memorial Hospital, Warsaw, Poland

Introduction

Antineoplastic treatment directly and indirectly affects permanent teeth in children and adolescents.

Chemotherapy and the complications it causes, such as malnutrition, malabsorption, or metabolic disorders, may lead to improper tooth development and frequent severe caries in patients during and after antineoplastic treatment [1–7]. Dental abnormalities occur also more frequently in patients who have undergone chemotherapy during odontogenesis. Chemotherapeutics used in early childhood may also be responsible for carious lesions in mineralised dental tissues, which may promote caries. According to the literature, the calcium-to-phosphorus ratio affects the hardness of enamel. The higher the ratio, the lower the enamel mineralisation. Fagrell et al. and Jalevik et al. established that the calcium to phosphorus ratio was higher in demineralised than in healthy enamel [8, 9]. Furthermore, trace elements also affected the size of enamel prisms, which in their turn determined enamel hardness [10]. The occurrence of trace elements was also related to the susceptibility of mineralised tissues to caries [10, 11]. The negative impact of chemotherapeutics and of the complications they cause on teeth is not fully known and there are no studies on the chemical composition of permanent mineralised teeth extracted after antineoplastic treatment. The comparative microanalysis of the chemical composition of teeth extracted from patients after chemotherapy may help to answer the question of why children after antineoplastic treatment are much more prone to developing caries than generally healthy children, and it may hint at potential treatments.

Aim of the study

The study aimed to determine the extent to which chemotherapy leads to enamel mineralisation in children who undergo antineoplastic treatments.

Material and methods

Samples analysed microscopically included:
• five permanent teeth extracted due to complicated caries, without peri-apical inflammatory changes, from patients who completed antineoplastic treatment (aged 14.8 ±3.2 years; group 1);
• five teeth extracted due to orthodontic treatment, from generally healthy patients (aged 15.6 ±2.3 years; group 2).
Patients received different chemotherapy regimens, including vincristine, etoposide, cisplatin, 5-fluorouracil, cyclophosphamide, and doxorubicin. Three patients started antineoplastic treatment after removing fully formed teeth, including two patients with fully formed crowns.

The extracted teeth were rinsed under running water, mechanically cleaned from soft tissues, cut lengthwise, and kept in ethanol. Dental cross-sections were visualised with a stereo microscope (SZX16, Olympus) and, after applying carbon dust with an ionic duster (JEC 530 Auto Carbon Coat er, Jeol), with a scanning electron microscope (JSM-7600F Jeol). Chemical elements in the different parts of the enamel, dentine, cementum, and interior of the canal were analysed with energy-dispersive X-ray spectroscopy (EDS; Oxford X-Max) together with an electron microscope.

The analysis was performed with a magnification of 250×, at 15kV at fixed voltage measurement points (n = 6 for each area), as shown in Fig. 1.

The chemical composition was presented as mean element mass contents (arithmetic mean ± standard deviation) of elements prevailing in the assessed tooth areas in children after chemotherapy (group 1) and in generally healthy children (group 2). The calcium-to-phosphorus ratio for subsequent dental tissues was also calculated for both groups. The results were statistically analysed with the U Mann-Whitney test. Significance was set at p ≤ 0.05.

Results

The microanalysis of the chemical composition of enamel within the opaque areas in children after chemotherapy showed that levels of phosphorus were statistically significantly lower than in healthy enamel. The calcium-to-phosphorus ratio in these areas was 1.851 ±0.524. It was higher in the teeth of patients after chemotherapy (1.760 ±0.232) than in those of controls (1.694 ±0.011) (Fig. 2).

The mass contents of trace elements (Cl, Mg, and Na) within the opaque areas were higher in patients treat-
ed with chemotherapeutics than in macroscopically unchanged enamel after chemotherapy or in healthy enamel (Table 1).

The enamel mass content of Mg was also higher in patients after chemotherapy than in controls, while that of Cl was lower. Na levels were also assessed in both groups (Table 2).

Furthermore, the enamel of two teeth after chemotherapy tested positive for zinc (Zn) (Fig. 3), whereas healthy enamel did not.

Chlorine and a lower magnesium level were detected in the dentine of patients after chemotherapy when comparing to controls (Table 3).

Chlorine was detected in the cementum of patients after chemotherapy and sulphur was also detected in two teeth. Sulphur was not detected in any of the teeth in the controls (Table 4, Fig. 4).

The surface of the interior of the canal in the post chemotherapy group contained statistically insignificantly less calcium and phosphorus than the surface of the canal in controls (Table 5). Chlorine (Cl) was also detected in the inner wall of the canal in teeth after chemotherapy, but not in healthy teeth.

Discussion

The analysis of the chemical composition of various tooth areas in children and adolescents after antineoplastic treatment indicated a lower calcium level (Ca) and an increased calcium to phosphorus ratio in enamel, when compared to controls. The level of magnesium (Mg) decreased; chlorine (Cl) was detected in dentine; trace amounts of sulphur (S) and important amounts of chlorine (Cl) were detected in the cementum of certain teeth, when compared to controls.
the region of the city of Szczecin than in that of children living
and plant-based foods have been decreasing. Opalko et al.
trialised regions, levels of magnesium contained in animal
orthodontic treatment [17]. The level of Mg in enamel could
determined that the level of magnesium in carious enamel
responsible for more severe caries in that group. Amr et al.
group after chemotherapy than in controls, which could be
study, the level of Mg in dental enamel was higher in the
release of these elements to acids and therefore also to caries. In the present
ments could promote caries [10, 11, 15, 16]. Magnesium (Mg)
controls, with slightly higher results in the former. These ele-
identified defects during tooth mineralisation.

Hydroxyapatite, a crucial enamel component, is mainly
comprising of calcium and phosphorus. The normal Ca level in healthy enamel is between 36.5 and 40.0 mass percent,
depending on age, and the normal phosphorus (P) level is between 17.25 and 18.25 mass percent [12]. A study reported
levels at 32.68 mass percent for Ca and 17.48 for P [12].
However, the Ca level increased with age [13].

The present analysis of enamel established a Ca level at 35
mass percent in children not treated with chemotherapeut-
icks, and at 34.67 mass percent in children treated with
chemotherapeutics; therefore considerably higher than in adult
This did not confirm the generally suggested tendency
carries. Therefore, the prevalence of Zn detected in the
enamel of patients after chemotherapy and not detected
controls remained unclear.

Many studies have emphasised that even a low level of
trace elements could impact the size of the formed enamel
prisms, determining their hardness, and therefore their
resistance to acids [10, 11]. Such trace elements as lead (Pb),
titanium (Ti), manganese (Mn), selenium (Se), chromium (Cr),
and nickel (Ni) affected the crystal structure of hydroxyapa-
tites [10].

Such trace elements as fluorine (F), aluminium (Al), iron
(Fe), selenium (Se), and strontium (Sr) were detected in teeth
at a low risk of caries; manganese (Mn), copper (Cu), and cad-
mium (Cd) were detected in teeth at a high risk of caries. In
the mean time, the levels of fluorine (F), strontium (Sr), po-
tassium (K), and aluminium (Al) were higher in healthy than
in carious enamel, and the level of silicon (Si) was higher
in carious enamel [11]. In the present study, fluorine was detect-
ed in one patient after chemotherapy and in one control, and
silicon only in one patient after chemotherapy. No other trace
elements were detected in the enamel in both groups.

When considering the impact of trace elements on enam-
el mineralisation, it is important to note that because of fluct-
ations in the levels of other elements, which ranged from
very low to very high, averaging the results could lead to in-
terpretation errors [20, 12]. Divergences between the chemi-
cal composition of carious and healthy teeth could also result
from environmental factors (diet and pollution), the impact
of other diseases, different patient ages in subsequent stud-
ies, and the use of different measurement tools. The main dentine components — calcium, inorganic phosphorous, and
fluorine — play a key role in tooth demineralisation and rem-
nineralisation [21, 22].

Pawlicki et al. assessed the chemical composition of dentine [13] and found lower mass percentage of calcium
(21.76—25.82 depending on age group) and phosphorous
(7.91—15.20) than in the present study. The present calcium
and phosphorus mass percentages in outer dentine was
higher than in the interior of the canal. These results dif-
ered from those of Magnus et al. [22], who compared Ca
and P mass percentages in both outer dentine and in the
interior of the canal. Chlorine was detected in the dentine
of teeth after chemotherapy but not in that of controls. How-

<table>
<thead>
<tr>
<th>Chemical element</th>
<th>Patients after chemotherapy (group 1)</th>
<th>Controls (group 2)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca</td>
<td>26.870 ±9.839</td>
<td>33.420 ±2.789</td>
<td>0.4034</td>
</tr>
<tr>
<td>P</td>
<td>17.472 ±6.247</td>
<td>19.528 ±0.698</td>
<td>0.8345</td>
</tr>
<tr>
<td>Na</td>
<td>1.326 ±1.192</td>
<td>1.594 ±0.873</td>
<td>0.4034</td>
</tr>
<tr>
<td>Cl</td>
<td>0.234 ±0.265</td>
<td>-</td>
<td>0.1797</td>
</tr>
<tr>
<td>Mg</td>
<td>1.444 ±0.897</td>
<td>5.320 ±7.106</td>
<td>0.2492</td>
</tr>
<tr>
<td>O</td>
<td>46.106 ±8.916</td>
<td>42.236 ±0.755</td>
<td>0.8345</td>
</tr>
</tbody>
</table>
ever, according to Jalevik et al., chlorine did not affect tooth mineralisation [9].

Brodzikowska assessed the mass percentage of these elements in healthy and carious cementum (23). She established that the calcium mass percentage (38.1) was higher than in the present study (23). Furthermore, carious cementum contained less Ca (33.1) than healthy cementum. Brodzikowska also showed that the phosphorous mass percentage was higher in both healthy (18.08) and carious (17.02) cementum than in the present group 1 (14.47), but higher than in the present group 2 (19.48). In the present study, the calcium to phosphorus ratio in the cementum of children after chemotherapy was higher (2.92) than Brodzikowska’s ratio in healthy cementum (2.12). For controls, the calcium to phosphorus ratio (1.76) was lower than Brodzikowska’s. It is difficult to compare the present study to the existing ones because there are no publications reporting on the element composition in teeth extracted after antineoplastic treatment. Höltta and Maclenod analysed teeth extracted from patients after chemotherapy with a microscope, however they only determined the morphology of mineralised tissues [5, 24].

The present X-ray analysis of the chemical composition of mineralised dental tissues showed that multidrug antineoplastic treatments in childhood, together with the complications they cause, including malnutrition, malabsorption, and metabolic disorders, could considerably impact developmental anomalies, caries, and their severity. It could be caused by abnormal calcium and phosphorus levels and the prevalence of trace elements in these tissues. Since antineoplastic treatments are complex and may impact oral health in numerous ways, studies on this impact should be continued.

In conclusion, antineoplastic treatment, and the complications it causes, in childhood may lead to a decrease in the calcium-to-phosphorus ratio and also modify the levels of these elements in mineralised teeth. Antineoplastic treatments and concurrent disorders could also have an impact on the levels of trace elements. A higher predisposition to caries in children after oncological treatment could result from modifications in the chemical composition of teeth.

The authors declare no conflict of interest.

References


Address for correspondence

Ewa Krasuska-Slawańska
The Children’s Memorial Health Institute
Al. Dzieci Polskich 20
04-730 Warsaw, Poland
e-mail: e.krasuska@czd.pl

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