

# Effects of the Enamel Erosion Caused by Certain Antipyretic and Analgesic Medicines for Children

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## 일부 어린이 해열·진통제의 유치 법랑질 부식효과

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This study was conducted to provide basic understanding regarding possible enamel erosion by three kinds of first-aid antipyretic and analgesic medicines over a period of time, with comparison and analysis of the resulting deciduous teeth surface and microhardness changes. The analysis was performed using energy dispersive X-ray spectroscopy (EDX) and scanning electron microscope (SEM) to examine the surface erosion and changes. The Kruskal-Wallis test show differences in surface erosion and changes after 3, 5 and 8 days of treatment as well as before and after the treatment in each group. According to the results, there was no significant difference in the early deciduous teeth enamel surface microhardness ( $p > 0.01$ ). However there were significant changes after 3, 5, and 8 days ( $p < 0.01$ ). Calcium (Ca) and phosphorous (P) analysis using EDX showed significant differences in the enamel characteristics according to each tissue area after 8 days ( $p < 0.05$ ), but there was no significant difference in any of the areas for P content ( $p > 0.05$ ). In the surface observation with the SEM treatment with Children's Tylenol<sup>®</sup> tablet, which has the lowest pH, looked the roughest, followed by Brufen syrup for children and Children's Tylenol<sup>®</sup> suspension. Based on these results, it should be considered that antipyretic and analgesic medicines for children, which have lower pH values, may cause tooth erosion. Hence, it is necessary to give special attention to oral hygiene in young children or infants by brushing their teeth after such drugs are administered.

**Key Words:** Antipyretics · analgesics, Deciduous tooth, Tooth erosion

## Introduction

Current selling drugs such as Children's Tylenol<sup>®</sup> suspension, Children's Tylenol<sup>®</sup> tablet, and Brufen syrup for children belong to over-the-counter drugs in antipyretic·analgesic medicines for children. These ingredients include sucrose and aspartame as well as main component to release pain, especially, Hwang et al.<sup>1)</sup> reportedly said

that sweetening agents used to take medicine for infants or children without inconvenience could induce caries in the event of long-term dose. Moreover, 75.7% of parents would use a fever reducer to relieve their children's fever, awakening the children, which is not helpful for their health<sup>2)</sup>. Meanwhile, enamel and dentin of deciduous teeth are thinner than those of permanent teeth, while its dental pulp is bigger than the others'. These features trigger fast

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caries<sup>3)</sup>, and decrease in salivation in one's sleep augments enamel erosion<sup>4)</sup>.

Dental erosion refers to loss of dental hard tissues by acid in the chemical process<sup>5)</sup>. Its cause can be divided as intrinsic and extrinsic factor. The former includes nervous or spontaneous vomit, and gastrointestinal disorder; the latter, dietary factors e.g., soda like coke and vitamin C in acid foods, fruits<sup>6)</sup>, and energy drink containing low pH or citric acid<sup>7,8)</sup>, carbonated water<sup>9)</sup>. Another can be occupational dental erosion caused by job environment, the place to be dealt with acid<sup>4)</sup>.

Based on various factors which cause dental caries, syrup development has been conducted, among them, according to Lee et al.<sup>10)</sup>, decayed permanent teeth surfaces index (DS index) of the group who took the syrup for asthma treatment showed significance higher than those who did not. Furthermore, the longer they took the syrup, the higher decayed permanent teeth index (DT index) appeared. Costa et al.<sup>11)</sup> said that the syrup with antihistamine reduced the hardness of primary enamel. When it comes to the research of enamel's microhardness caused by lower pH, Ahn<sup>12)</sup> reported that 4 kinds of syrups dropped the plaque pH to its critical acidity to render enamel delime, or pH 5.5 after being put in the oral cavity. Valinoti et al.<sup>13)</sup> told that bovine enamel exposed to 3 kinds of children's syrups demonstrated erosive pattern by means of a scanning electron microscope. In addition, Sunitha et al.<sup>14)</sup> said inappropriate use of liquid medicines would have enormous potential to induce dental caries as syrups such as antipyretic·analgesic medicines, cough syrup with 10% of sucrose made experimental plaque's pH lower. Lots of pre-researches were progressed, but decalcification's aspects and quantitative analysis of minerals have not yet researched, just with a few literatures related with acidity, acidogenic ability and causes of dental caries.

Therefore, this research aimed to provide basic information on the possibility of dental erosion by medicines for children by applying 3 kinds of antipyretic·analgesic medicines for children in over-the-counter drugs for children as time passed, and by comparing·analyzing deciduous teeth's surface and microhardness changes.

## Materials and Methods

### 1. Experimental materials

The experimental group contained Children's Tylenol<sup>®</sup> suspension (Janssen Korea Inc., Seoul, Korea), Children's Tylenol<sup>®</sup> tablet (Janssen Korea Inc.), Brufen syrup for children (Samil-Pharm. Co. Ltd., Seoul, Korea), and distilled water was used as its control group.

Used deciduous teeth were 20 sound anterior primary and posterior primary molars teeth caries, restoration, and prostheses in 3-month odontectomy, respectively.

### 2. Methods

#### 1) Specimen fabrication

This study was approved by institutional review board of Eulji University (EU15-11). Remaining tissue and dental calculus in used deciduous teeth were scaled and 5-second prophylaxis was performed with pumice without fluorine and glycerin. Prophylaxis-based deciduous teeth were buried by anhydrite to expose their crown and cut with diamond disk (NTI-Kahla GmbH, Kahal, Germany) and then, labial side of anterior primary teeth and buccal posterior primary molars were placed toward the upper part and filled in with orthodontic resin (Dentsply International Inc., York, PA, USA), fixing in 2×3 mm size. The surface of enamel was polished with LaboPol-5 (Struers, Copenhagen, Denmark), supplying water into it as 600, 1,200, 4,000 grit, gradually.

#### 2) Immersion and incubation

Total 96 pieces, 24 by each group were prepared. During 8 days, 4 times a day, 20 minutes by each session, they were immersed in antipyretic·analgesic medicines for children and distilled water, and then immersed in artificial saliva (Kolmar Korean, Seoul, Korea) to apply pH circulation model for the rest.

#### 3) Measurement of endogenous pH

To keep constant temperature, 3 kinds of antipyretic·analgesic medicines for children were placed in room temperature for 6 hours, and then divide them into 50 ml beakers. Each beaker contains 20 ml of the liquids and was

stirred, measured using pH Meter (pH meter EcoMet, Seoul, Korea). The process was repeated three times by each group to calculate average.

#### 4) Measurement of microhardness on surface of deciduous teeth's enamel

With micro vickers hardness (Hmv-2<sup>®</sup>; Shimadzu, Kyoto, Japan), fine hardness of them was measured, weighting 100 g for 5 seconds. Prepared 180 pieces were measured from the three areas of incisal edge and occlusal margin. For this experiment, 96 pieces with more than 300 VHN (Vickers hardness number) of their average hardness were selected.

#### 5) Quantitative analysis of calcium (Ca) and phosphorus (P) on the enamel surface of deciduous teeth using energy dispersive X-ray spectroscopy (EDX)

In terms of quantitative analysis of Ca and P as time goes, total 16 pieces were used by classifying identified teeth into 4 groups for maintaining certain term. Dried pieces were carbon-taped to stub and coated as 150 nm, using ion sputter (E-1030; Hitachi, Ibaraki, Japan). After then, with EDX (Ex-220; Hoeiba, Japan), under 15 kV, weight rate of Ca and P in 30  $\mu\text{m}^2$  was gauged.

**Table 1.** pH of Experimental and Control Groups

Group	pH*
Control	6.89±0.02
Children's Tylenol <sup>®</sup> suspension	5.40±0.11
Brufen syrup for children	4.20±0.00
Children's Tylenol <sup>®</sup> tablet	4.15±0.00

All values are mean±standard deviation.

\*p < 0.05, by Kruskal-Wallis test.

**Table 2.** Microhardness Change of Enamel Surface according to the Periods of 3, 5, and 8 Days Respectively (Unit: VHV)

Group	N	VHN before	VHN after			VHN difference rate (%)
			3 day**	5 day**	8 day**	
Control	20	317.01±24.48	319.31±22.28	320.71±21.27	320.93±20.85	1.24±2.67
Children's Tylenol <sup>®</sup> suspension	20	316.28±19.62	303.98±22.01	278.33±20.69	260.66±22.16	-17.59±8.63
Brufen syrup for children	20	318.11±18.79	299.56±17.58	283.06±23.72	258.33±24.13	-18.79±6.59
Children's Tylenol <sup>®</sup> tablet	20	317.69±15.89	291.99±21.64	255.99±15.93	242.01±14.31	-23.82±6.54

All values are mean±standard deviation.

VHN: Vickers hardness number.

\*\*p < 0.01, by Kruskal-Wallis test.

#### 6) Observation and analysis of scanning electron microscope (SEM)

Dried pieces were carbon-taped to stub and coated as 150 nm, using Ion sputter (E-1030; Hitachi). With SEM (S-4700, Hitachi), under 15 kV, they were magnified as 5,000 times to observe.

#### 7) Statistical analysis

To compare the differences of before, after 3-day, after 5-day, and after 8-day, Nonparametric Kruskal-Wallis test and SPSS version 22.0 (IBM Co., Armonk, NY, USA) as statistics data analysis program were used. Statistical markedness was evaluated in the significant level of 0.05.

## Results

### 1. Measurement of acidity of antipyretic · analgesic medicines for children

Average acidity of 3 kinds of experimental group was pH 4.59±0.57: the lowest figure, pH 4.15±0.00 of Children's Tylenol<sup>®</sup> tablet; 4.20±0.00 of Brufen syrup for children syrup; and finally, the highest one, pH 5.40±0.11 of Children's Tylenol<sup>®</sup> suspension; pH 6.89±0.02, that of distilled water of control group (Table 1).

### 2. Measurement of enamel surface microhardness on deciduous tooth

Before the process, there was no significant difference among every group (p > 0.01), but after 3, 5, and 8 days, each group indicated marked one (p < 0.01). Pre-post difference result of control and experimental groups were as follows: Children's Tylenol<sup>®</sup> tablet was 23.82±6.54%; Brufen syrup for children syrup, 18.79±6.59%; Children's

Tylenol® suspension, 17.59±8.63% in decrease in order; in contrast, control group 1.24±2.67% in increase (Table 2).

3. Quantitative analysis of calcium (Ca) and phosphorus (P) on deciduous tooth

In the experimental group, the amount of Ca in deciduous teeth's enamel was diminished as time went by; thus, after 3 days, there were significant differences in each group (p < 0.05; Table 3). Meanwhile, P also steadily was lost, but it had no meaningful differences (p > 0.05; Table 4).

4. Observation and analysis of scanning electron microscope (SEM) on deciduous tooth

The enamel surface of deciduous teeth immersed in distilled water was flat and smooth; it underwent no changes after 3, 5, and 8 days (Fig. 1, A1 ~ 3).

With regard to the experimental groups, the enamel surfaces of deciduous teeth immersed for 3 days were shaped as prism by acid in Children's Tylenol® suspension and Brufen syrup for children (Fig. 1, B1, C1), whereas the ones immersed in Children's Tylenol® tablet had minute crack and damaged surface (Fig. 1, D1).

Those immersed in Children's Tylenol® suspension for 5 days presented more prism and rougher surface (Fig. 1, B2), and those immersed in Brufen syrup for children syrup showed porosity in softening enamel's crystals (Fig. 1, C2). The last one's cracks were deepened and its crystals were crumbled (Fig. 1, D2).

Finally, fine cracks and narrow fissures appeared in the enamel's surface immersed in Children's Tylenol® suspension for 8 days (Fig. 1, B3), and Brufen syrup for children formed cracks and harshen the surface by melting it (Fig. 1, C3). In similar way, Children's Tylenol® tablet made deep cracks in the middle of general collapse and severe ruggedness of surface (Fig. 1, D3).

Discussion

Naturally, various factors affect dental erosion, but according to the experiment of West et al.<sup>15)</sup> acids cause erosion of enamel and that higher the temperature and the longer hours aggravates erosion of enamel.

Relating to the causes, this paper measured acidity of antipyretic·analgesic medicines for children. Which is

Table 3. Calcium Analysis of Enamel Surface according to the Period of 3, 5, and 8 Days by Using EDX (Weight %)

Group	N	Before	After			Difference rate (%)
			3 day	5 day	8 day*	
Control (D/W)	3	28.00±8.04	24.48±1.88	26.74±1.87	29.72±2.26	6.14±27.29
Children's Tylenol® suspension	3	30.73±1.18	19.58±3.01	17.58±1.60	9.40±4.28	-69.41±15.17
Brufen syrup for children	3	29.23±2.33	28.64±1.05	26.55±1.62	13.06±2.64	-55.32±6.87
Children's Tylenol® tablet	3	35.49±4.64	27.36±3.84	23.58±1.57	14.13±5.09	-60.19±9.02

All values are mean±standard deviation.

EDX: dispersive X-ray spectroscopy.

\*p < 0.05, by Kruskal-Wallis test.

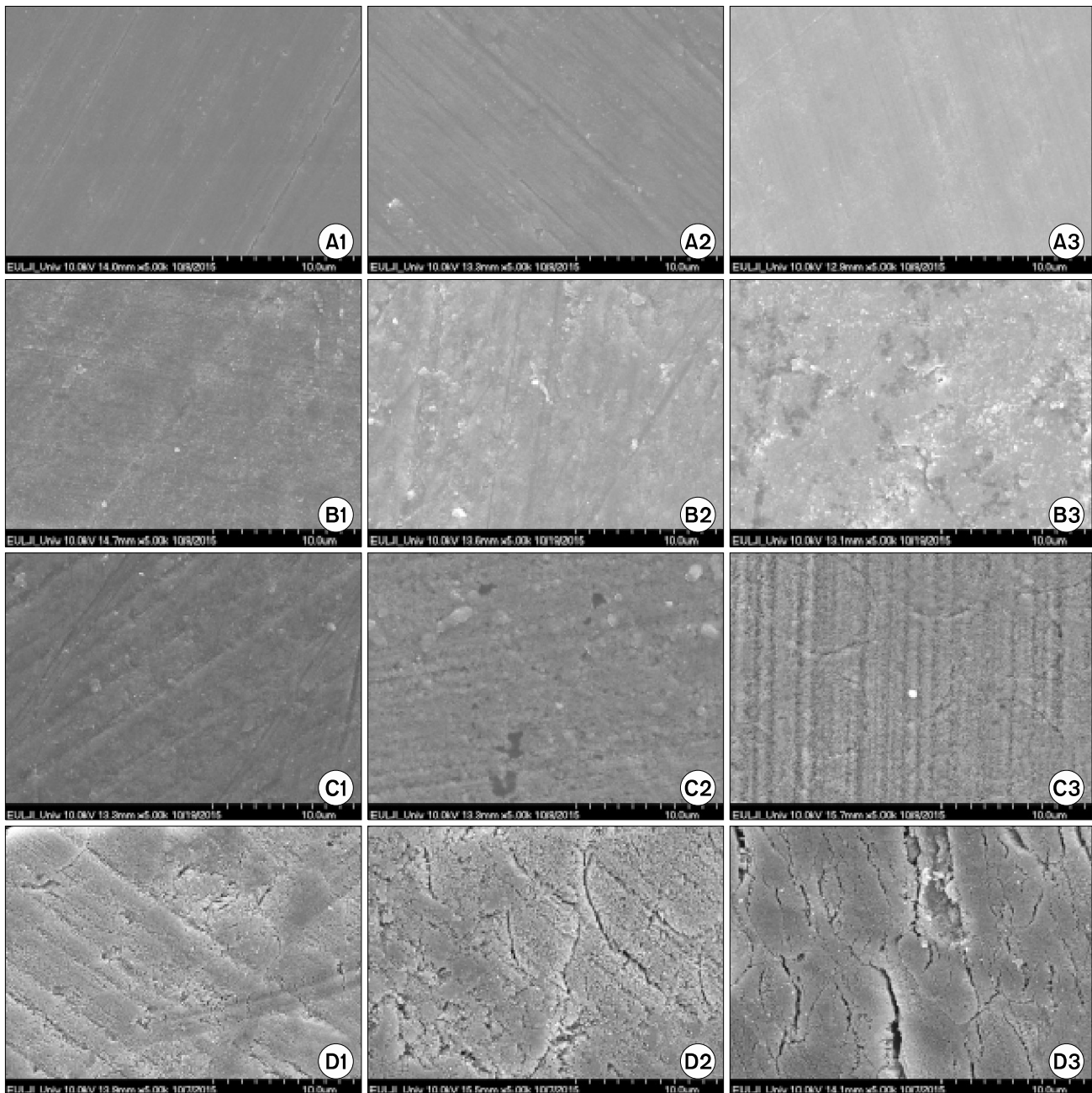
Table 4. P Analysis of Enamel Surface according to the Period of 3, 5, and 8 Days by Using EDX (Weight %)

Group	N	Before	After			Difference rate (%)
			3 day	5 day	8 day	
Control (D/W)	3	15.98±2.28	14.10±2.08	14.65±0.68	15.56±0.16	-2.63±14.55
Children's Tylenol® suspension	3	15.51±1.55	12.36±1.27	9.50±3.34	7.63±2.70	-50.81±17.02
Brufen syrup for children	3	16.14±0.96	15.92±0.20	13.76±1.00	9.29±2.50	-42.44±14.82
Children's Tylenol® tablet	3	17.29±2.05	14.11±2.95	13.16±0.88	10.48±3.56	-39.39±17.64

All values are mean±standard deviation.

EDX: dispersive X-ray spectroscopy.

\*p < 0.05, by Kruskal-Wallis test.



**Fig. 1.** Scanning electron microscope image of enamel surface after having treated in medication and distilled water for 3, 5, and 8 days ( $\times 5,000$ ). (A) Control, (B) Children's Tylenol<sup>®</sup> suspension, (C) Brufen syrup for children, (D) Children's Tylenol<sup>®</sup> tablet. 1: 3 days, 2: 5 days, 3: 8 days.

similar as average acidity of domestic 15 kinds drugs as pH  $4.70 \pm 0.94$ <sup>12)</sup>, and that of 8 kinds of syrups, pH  $4.73 \pm 0.63$ <sup>16)</sup>. Therefore, antipyretic·analgesic medicines for children used in this experiment may affect teeth erosion due to its lower acidity.

Besides, the microhardness on the surface detector mea-

sured teeth's hardness to survey degree of erosion of deciduous teeth's enamel surface. In pre-treatment, there were no meaningful differences, but there were after 3, 5, and 8 day treatment. Lim et al.<sup>16)</sup> research said average decrease rate of enamel's surface microhardness reported  $15.83 \pm 6.72\%$  in 8 kinds of children's syrups for 5 days with pH circu-

lation model. Likewise, this study acquired similar result, its decrease rate of  $14.15 \pm 11.46\%$  in the process of soaking for 5 days. Despite using circulation treatment considering remineralization of saliva, statistically marked hardness decrease indicated damage of deciduous teeth's enamel. Among various researches<sup>17,18)</sup> associated with reduction ratio of surface fine hardness caused by low pH, according to Lee et al.<sup>17)</sup>, the experiment on enamel's hardness immersing in 4 kinds of orange juices with average pH 4.0 for 10 minutes was lowered by 7.2 ~ 11.2%. Moreover, according to the paper on deciduous teeth immersed in acidic beverages<sup>18)</sup>, erosion was accelerated in that span of time; it was immersed in coke for 5 minutes, its enamel of deciduous teeth surface microhardness decreased by 16.90%, and after 120 minutes, 45.71%. Therefore, it is expected that lower pH and more dose can elevate erosion hazard of deciduous teeth; however, in the case of control group, enamel's average hardness was boosted by 1.23%, for its surface would be remineralized by distilled water.

The quantitative analysis of Ca and P using EDX is the following: Ca and P in the experimental group was lowered in that span of time set. The research related with Ca of enamel, for example, Nankar et al.<sup>19)</sup> assessed possibility of dental caries and erosion by quantifying Ca's solubility with 5 kinds of syrups in Pune, India. For 1 min., 10 min., and 8 hours, they mixed enamel powder with syrups, and the longer it immersed in, the more calcium was dissolved. On the other hand, there were no relations between dissolution and acidity of minerals. As for this paper, Children's Tylenol<sup>®</sup> suspension with the highest pH has the highest mineral solubility, Ca as  $69.41 \pm 15.17$  weight%, P as  $50.81 \pm 17.02$  weight %. It might be linked to molecular chelation, removing molecules from structures by surrounding metals like Ca, regardless of medium's pH, molecular chelation.

Meanwhile, in case of SEM analysis to learn enamel's surface change as time goes by, lower pH render enamel's surface more harmed and rougher than its control group. Coarse prism was noticeable in its surface, and specifically, Children's Tylenol<sup>®</sup> tablet has deep cracks in surface across the board. Tupalli et al.<sup>20)</sup> evaluated erosion inducing ability of deciduous teeth caused by 10 kinds of syrups with SEM. When they were in multi-vitamin with

pH 4.5 for 1 minute, bumps like pole-shape appeared in enamel surface, and in antibiotic syrup with pH 6.4 for 10 minutes, corroded prism by acid was formed. Reportedly, there were holes like crater in enamel in antiepileptic syrup with pH 6.9 for 1 minute. This result would be similar to that of this paper, assessment of erosion inducing ability of deciduous teeth with SEM by observing harmed surface.

Through the above, children's syrup with lower pH can erosion teeth enamel surface, and loss of Ca and P may lead dental caries. Therefore, using children's syrup requires oral hygiene including brushing teeth. And it is considered that the pharmaceutical company should notice the probability of tooth erosion on direction for the use of medicine so that children who took those medicines can improve their oral hygiene.

## Summary

The purpose of this study was to learn possibility of teeth erosion by applying 3 kinds of over-the-counter drugs, especially antipyretic·analgesic medicines for children and comparing·analyzing surface and hardness change of deciduous teeth in that span of time, using SEM and EDX. In pre-treatment, there were no significant difference among every group ( $p > 0.01$ ), but there were after 3, 5, and 8 day treatment ( $p < 0.01$ ). In the quantitative analysis with EDX, the amount of Ca in deciduous teeth's enamel was diminished after 8 days; there were significant differences in each group ( $p < 0.05$ ) while the experimental group with P had no meaningful differences ( $p > 0.05$ ). As to surface observation with SEM, medicine with the lowest pH, or Children's Tylenol<sup>®</sup> tablet has the roughest surface, Brufen syrup for children syrup, Children's Tylenol<sup>®</sup> suspension, and lastly distilled water in order.

New study implicates fever reducers with lower pH can erosion teeth's enamel and loss of Ca and P may lead dental caries. Therefore, using children's syrup requires oral hygiene including brushing teeth.

## 요약

어린이 해열·진통제 중 안전상비의약품 3종을 유치에 적용하여 시간 경과에 따른 유치의 표면과 경도변화를 SEM

과 EDX로 비교·분석하여 부식 가능성을 알아보고자 본 연구를 시행하여 다음과 같은 결과를 얻었다. 유치 법랑질 표면미세경도 측정 결과, 처리 전은 모든 군에서 유의한 차이가 나타나지 않았으나( $p > 0.01$ ), 3일, 5일, 8일 경과 후 각 군 간에서는 유의한 차이를 나타냈다( $p < 0.01$ ). EDX를 이용하여 Ca과 P의 정량분석 결과, 유치 법랑질 기질 내 Ca은 8일 경과 후 각 군 간에서는 유의한 차이가 나타났고( $p < 0.05$ ), P은 모든 군에서 유의한 차이가 나타나지 않았다( $p > 0.05$ ). SEM을 이용하여 유치 표면을 관찰한 결과, pH가 가장 낮은 어린이용 타이레놀 정이 표면 거칠기가 가장 심한 것으로 관찰되었고, 다음으로 어린이 부루펜 시럽, 어린이 타이레놀 현탁액, 증류수 순이었다.

이상의 연구 결과를 통해 pH가 낮은 어린이 해열·진통제는 법랑질 표면에 치아 부식을 일으킬 수 있는 가능성이 있고, Ca과 P의 소실은 치아우식증에 이환될 수도 있다. 따라서 어린이 해열·진통제 투약 시 유·아동은 칫솔질과 같은 구강위생관리가 필요하다고 생각된다. 또한 제약회사에서는 이러한 약품들을 복용한 유·아동들이 구강위생조치를 할 수 있도록 약품 내 주의사항 안내서에 치아부식 가능성을 고지해야 할 것으로 생각된다.

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