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Research Article

The effect of salbutamol sulfate exposures on the amount of fluoride ion, calcium ion and aluminum ion release from GIC

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ABSTRACT

Background: Asthma is a chronic inflammatory disease of the respiratory tract. The most commonly used for asthma treatment is the β2-agonist salbutamol sulfate. Salbutamol sulfate has a low pH so it can affect the restoration material. One of the restoration materials that is still widely used by dentists and continues to be developed is Glass Ionomer Cement (GIC). In a low pH environment, GIC can release fluoride ions, calcium ions and aluminum ions.

Objective: To analyze the effect of salbutamol sulfate exposures on the amount of fluoride ions, calcium ions and aluminum ions release from GIC.

Method: This study used true experimental and post-test only with control group design that used 21 GIC samples with diameter of 5 mm with 2 mm thickness divided into 3 groups, i.e. the group exposed to 400 µg, 800 µg salbutamol sulfate and artificial saliva as control group with repeated treatments every 24 hours for 7 days. The measurement of the amount of fluoride ions release by using a pH meter, meanwhile calcium ions and aluminum ions release using the titration method.

Results: One Way Anova and Post Hoc Bonferroni showed significant differences in the amount of fluoride ions release in 400 µg (3.165 ± 0.415 ppm), 800 µg (3.879 ± 0.703 ppm) and artificial saliva as control group (2.333 ± 0.412 ppm), the amount of calcium ions release in 400 µg (6.943 ± 0.836 mg/gram), 800 µg (7.114 ± 0.871 mg/gram) and the artificial saliva as control group (5.986 ± 0.430 mg/gram) and the amount of aluminum ions release in 400 µg (0,197 ± 0,089 mg), 800 µg (0,730 ± 0,034 mg) and the artificial saliva as control group (0,029 ± 0,023 mg).

Conclusion: There is an effect of salbutamol sulfate exposures on the amount of fluoride ions, calcium ions and aluminum ions release from GIC.

Keywords: Glass Ionomer Cement (GIC), Salbutamol sulfate, The amount of aluminum ions release, The amount of calcium ions release, The amount of fluoride ions release.

INTRODUCTION

Asthma is a chronic inflammatory disease of the respiratory tract characterized by a history of respiratory symptoms i.e. wheezing, shortness of breath, chest tightness, and coughing.[1] Asthma is a serious health problem because it affects all age groups and has a negative impact on society.[2.] In the treatment of asthma medication, the most widely used drug is the β2 agonist drug namely salbutamol sulfate.[3] Salbutamol sulfate was acidic drugs with acidity (pH) ranges from 3.4 to 5, which is caused by the presence of sulphate groups contained in it.[4] The general dose used by people with asthma is 400 μg which is the average number of daily doses of asthmatics and the maximum number of daily doses is 800 μg.[5]

One of the restoration materials that is still widely used by dentists and continues to be developed is Glass Ionomer Cement (GIC). GIC material consists of GIC powder which is a calcium fluoroaluminosilicate glass which dissolves in acidic liquid containing silicate (SiO_2), aluminum oxide (Al_2O_3), aluminum fluoride (AlF_3), calcium fluoride (CaF_2), sodium fluoride (NaF) and aluminum

phosphate ($AlPO_4$) and GIC liquid which is a liquid from polyacrylic acid with a concentration of 40-50%. In a low pH environment, GIC can release more fluoride ions.[6] Ions which are also released from GIC in a low pH environment are calcium ions and aluminum ions.[7] If the GIC is not protected from conditions that can cause dissolution of calcium ions, then it can weaken GIC which includes a decrease in physical properties,in surface hardness and in mechanical properties which is a decrease in compressive strength.[8,9,10]

Based on the description above, the researcher aim to discover the effect of salbutamol sulfate exposures on the amount of fluoride ions, calcium ions and aluminum ions release from GIC. This research is expected to provide scientific information to the public about the effect of salbutamol sulfate exposures on the amount of fluoride ions, calcium ions and aluminum ions release from GIC and can be considered in the use of GIC restoration for asthmatics.

MATERIALS AND METHOD

The study of the effect of salbutamol sulfate exposures on the amount of fluoride ions, calcium ions and aluminum ions release from GIC began by making a research permit and ethical clearance issued by the Faculty of Dentistry, Lambung Mangkurat University No.143 / KEPKG-FKGULM / EC / I / 2019. This research is true experimental research with Post Test Only with Control Group Design. The sampling technique was carried out by simple random sampling consisting of 3 treatment groups, namely the GIC sample group exposed to 400 μg salbutamol sulfate, the GIC sample group exposed to 800 μg salbutamol sulfate and the GIC sample group which was only immersed in artificial saliva. Calculation of the number of samples using a numerical analytic formula > 2 unpaired groups and the number of each group is 7 samples.[11]

Making GIC samples begins with the process of mixing powder and liquid GIC (1: 1) on a glass lab that has been coated with a paper pad. GIC is inserted into a 5 mm diameter mold and 2 mm thickness based on (ISO) 9917-1: 2003 and covered with a celluloid strip so that the GIC surface is flat. After the GIC setting, the sample is removed from the mold and the excess GIC can be reduced using a scalpel.

The object of the study was divided into three groups, that is the group 1 and group 2 which were the treatment groups and group 3 which was the control group. The sample is removed from the incubator and the sample is exposed to salbutamol sulfate. The exposure of salbutamol sulfate was carried out in an acrylic box with 5 cm long, 5 cm wide and 5 cm high to be concentrated and not to be diffused due to the exposure of the air. The sample is placed in the middle of the inner wall of the acrylic box and then fixed using double sided tape.

Before being exposed, the salbutamol sulfate inhaler is shaken first until the ingredients are completely mixed. Subsequently, the inhaler is set upright and the inhaler funnel is directed towards the sample that has been placed on the inner wall of the acrylic box. The distance between the sample and the inhaler funnel is about 5 cm and then the inhaler is pressed so that it releases 100 μg of aerosol salbutamol sulfate. In group 1, there were 4 sprays (400 μg) which were the average number of daily doses used by asthmatics and and for group 2 with the total of 8 sprays (800 μg) which were the maximum number of daily doses of asthmatics.[5] After the exposure to salbutamol sulfate, the sample was immersed back into artificial saliva inside the incubator at 37°C. This procedure is carried out on each sample in group 1 and group 2 and then repeated every 24 hours for 7 days.[12]

Group 3 which is the control group was not exposed to salbutamol sulfate and only immersed in artificial saliva for 7 days. All research samples were stored in incubators with 37°C. Artificial saliva is replaced every day during the research process.[12,13]

The fluoride ion release measurement was conducted by grinding the sample using mortar until it is smooth and put into a beaker to be diluted with 10 ml of distilled water and 10 ml of sodium fluoride buffer. Followed by immersing the electrode into the sample solution for 3 minutes using a pH meter tool (Lutron pH-208, Taiwan). The data obtained from this study is the data from the group without exposure to salbutamol sulfate and without immersion of artificial saliva (baseline) minus by the results of group data which were exposed to salbutamol sulfate so that the results were obtained, namely the amount of fluoride ions release from GIC.

The amount of calcium ion release measurement was done by grinding the sample using mortar until smooth and put in a 250 ml beaker, then adding 100 ml distilled water and 3 drops of red methyl indicator into the solution and heated to boil. The solution of NH_4-oxalate 0.75 grams was added to 12.5 ml of distilled water and then slowly put into a beaker and heated at a temperature of 70-80°C for 15 minutes. Subsequently, 3 drops of ammonia solution (1: 1) are inserted while stirring slowly and the solution is left in heated condition for 1 hour. The precipitate is filtered using filter paper and washed deposits using distilled water until free from oxalate. The filter paper is perforated using a stirrer and the sediment is rinsed with a solution of sulfuric acid (1: 8) into another erlenmeyer. Filter paper is washed with hot distilled water to a volume of 50 ml then the solution is titrated with $KMnO_4$ 0.1 N

until the color turns pink. Later on, the data was calculated using the formula of:

Ca Weight Calculation :

0.7056 x vol. $KMnO_4$ x 2.8 mg CaO

The amount of aluminum ion release measurement was done by grinding the sample using a mortar until smooth and put in a 250 ml beaker, then add 100 ml of distilled water, 10 ml of distilled water is taken into the erlenmeyer. 10 ml of HCl 0.1 M solution was added to distilled water, then 3 drops of pp were added. The next step is titration with NaOH 0.1 N. Later on, the data was calculated using the formula of:

Al weight calculation :

$$\frac{78\ (V_{HCL}.\ M_{HCl} - V_{NaOH}.\ M_{NaOH})}{35}$$

Parametric analysis was using the One Way Anova hypothesis test with a confidence level of 95% (α = 0.05) and continued using the Post Hoc Bonferroni test to determine the value of significance.

RESULTS

Based on the study, the results of statistical tests found that all groups were normally distributed and homogeneous ($p > 0.05$). The results of the research on the release of fluoride ions are obtained by the average values listed as follows:

Table 1: Table of Mean and Standard Deviations of the Amount of Fluoride Ion Release

Groups	*Mean* (ppm) ± SD
400 μg	3.165 ± 0.415
800 μg	3.879 ± 0.703
Artificial Saliva	2.334 ± 0.412

Based on table 1., it can be concluded that the average amount of fluoride ion release is highest in the GIC sample group exposed to 800 μg of salbutamol sulfate (3.879 ± 0.703) while the lowest number of fluoride ion releases is in the GIC sample group which is only immersed in artificial saliva (2.334 ± 0.412).

Table 2: Significance Value of The Amount of Fluoride Ion Release

	400 μg	800 μg	Artificial Saliva
400 μg	-	0.063	0.026*
800 μg	-	-	0.000*
Artificial Saliva	-	-	-

* = there is a significance value ($p<0.05$)

Based on the research that has been done, the average value of the amount of calcium ions released is as follows:

Table 3: Table of Mean & Standard deviations of the Amount of Calcium Ion Release

Groups	*Mean* (mg/gram) ± SD
400 μg	6.943 ± 0.836
800 μg	7.114 ± 0.871
Artificial Saliva	5.986 ± 0.430

According to table 3. it can be seen that the highest average number of calcium ion releases is in the GIC sample group exposed to 800 μg salbutamol sulfate while the lowest average number of calcium ion releases is in the GIC sample group which is only immersed in artificial saliva.

Table 4: Significance Value of The Amount of Calcium Ion Release

	400 μg	800 μg	Artificial Saliva
400 μg	-	1.000	0.079
800 μg	-	-	0.032*
Artificial Saliva	-	-	-

* = there is a significance value ($p<0.05$)

In addition to fluoride ions and calcium ions, based on research that has been done, the average value of the amount of aluminum ions released is as follows:

Table 5: Table of Mean and Standart Deviations of The Amount of Aluminum Ion Release

Groups	*Mean* (ppm) ± SD
400 μg	0,197 ± 0,089
800 μg	0,730 ± 0,034
Artificial Saliva	0,029 ± 0,023

Based on table 5., it can be concluded that the average amount of aluminum ion release is highest in the GIC sample group exposed to 800 μg of salbutamol sulfate (0,730 ± 0,034) while the lowest number of fluoride ion releases is in the GIC sample group which is only immersed in artificial saliva (0,029 ± 0,023).

Table 6: Significance Value of The Amount of Aluminum Ion Release

	400 μg	800 μg	Artificial Saliva
400 μg	-	0.000*	0.000*
800 μg	-	-	0.000*
Saliva Buatan	-	-	-

* = there is a significance value ($p<0.05$)

DISCUSSION

Based on the research, the release of fluoride ions, calcium ions and aluminum ions in the GIC sample group exposed to 800 μg of salbutamol sulphate has a higher average amount of release of fluoride ions, calcium ions and aluminum ions than the GIC sample group exposed to 400 μg salbutamol sulfate. This is due to the GIC sample group exposed to 800 μg of salbutamol sulfate has a more acidic condition than the GIC sample group exposed to 400 μg of salbutamol sulfate. This result is in accordance with the study of Hassan et al (2012) and Septishelya et al (2016) which states that the release of fluoride ions, calcium ions and aluminum ions from GIC restoration materials will be higher when the pH is lower.[6,7]

The release of fluoride ions, calcium ions and aluminum ions in the GIC sample group exposed to 400 μg and 800 μg of salbutamol sulfate due to the acidic of salbutamol sulfate. Salbutamol sulfate is acidic drugs with acidity (pH) ranges from 3.4 to 5, which is caused by the presence of sulfate groups contained in it.[4] H_2SO_4 compounds in salbutamol sulfate made ionization reactions which can affect the acidic condition, this is due to the decomposition of H^+ and SO_4^{2-}.[14] ions. When hydrogen ions (H^+) from acids (low pH) diffuse, the H^+ ions will be exposed to the outer surface of the glass particles which are still smooth.[6,15] Based on the research by Taqa et al (2016), there is a positive relationship between the amount of fluoride ions released with the acidic environment, which is the higher level of release of fluorides are in the acidic environment.[16] The release of fluoride ions in GIC depends on the degradation of the GIC surface by low pH. Surface degradation in GIC occurs when the polycarboxylate salt group binds to H^+ is broken, then forming a single bond.[10]

Various studies have shown that conventional GIC can release fluoride ions. This is because conventional GIC consists of ion-leachable aluminofluoro-silicate, polyacrylate acid and tartaric acid.[16,17] The release of fluoride ions occurs because fluoride ions are located freely (unbound) in the matrix GIC.[7] Acid-base reactions are the main arrangement of conventional GIC and is the main factor responsible for the release of fluoride ions.[16] Acid-base reactions occur when fluroaminosilicate glass and polycarboxylic acid are combined so that glass particles break and marked by the release of Ca^{2+} (calcium) ions, Al^{3+} (aluminum) and ions F^- (fluoride) which functions to build a matrix as an ion, salt and gel. At first, calcium polyacrylate will be formed as a matrix which is then followed by the formation of polyacrylate aluminum and setting occurs in the GIC.[6,18,19]

Like other metal ions (calcium and fluoride ions), GIC also releases aluminum ions in the surrounding solution media shortly after setting.[20] Just like fluoride ions, aluminum ions also have antibacterial and anticariogenic properties which can increase the effects of fluoride when released by GIC. Aluminum forms complex compounds with fluoride and can reduced amount of free fluoride. Aluminum in the GIC can be released into the surrounding media solution when in contact with liquids, the amount of aluminum released will reduce the GIC maturation, in this case the aluminum ions covering the cement surface will be released while the aluminum trapped in the matrix will still be there.[20] Aluminum is included in the glass component from GIC in the form of Al_2O_3 to produce alkaline properties in glass and allow glass to play a role in the reaction of acid-base settings.[21]

When hydrogen ions (H^+) from acids (low pH) diffuse, the H^+ ions will be exposed to the outer surface of the glass particles which are still smooth and will cause cations on the glass surface such as Ca^{2+}, Na^+ and Al^{3+} which previously bind to polyacrylate acid will be released and come out from GIC so that small pores form on the glass surface.[6,15,22] This statement accordance with the study of Hassan et al. (2012) and Fitriyana et al. (2014) which states that calcium ions and aluminum ions can be released from GIC if they are in a low pH environment.[7,10] The reaction of calcium ion and aluminum ions release occurs during the hydrogel phase. In this reaction, the calcium ions release faster and react with the polyacrilic acid chain to form a cross bond. Calcium ions are easier to bind to carboxyl acid groups than aluminum ions because calcium ions are not strongly bound in the glass structure.[17,22,23,24]

The amount of fluoride ions, calcium ions and aluminum ions release in the GIC sample group which was only immersed in artificial saliva had a lower mean than the release of fluoride ions, calcium ions and aluminum in the GIC sample group exposed to 400 μg and 800 μg of salbutamol sulfate. This is because in this control group was only immersed in artificial saliva without exposure to salbutamol sulfate or the influence of other substances contained in the inhaler. Artificial saliva has a lower pH of 6.7 while for pH

salbutamol sulfate is 3.4 - 5 which means that salbutamol sulfate has a more acidic than the pH of artificial saliva.[4,23,25,26,27,28] Based on the results of this study, it can be concluded that there is an effect of salbutamol sulfate exposures to the amount of release of fluoride ions, calcium ions and aluminum ions from GIC.

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