

DENTINO
JURNAL KEDOKTERAN GIGI
Vol VI. No 1. Maret 2021

**EFFECT OF SALBUTAMOL SULFAT EXPOSURE TO THE SURFACE
ROUGHNESS OF BIOACTIVE RESIN**

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ABSTRACT

Bioactive composite resin is the newest restorative resin material which has good mechanical and aesthetic properties. In the oral cavity, the restoration is degraded due to exposure to acids, one of which is exposure to asthma drugs. Properties of composite resins that can be affected by degradation include surface roughness. This study aims to analyze salbutamol sulfate exposure to the surface roughness of bioactive resins. The research method used was pure experimental design with post test-only with control design. The study used 39 specimens of bioactive resin (8 mm in diameter and 2 mm in thickness), divided into 3 treatment groups, namely the 400µg salbutamol sulfate exposure group, the 800µg salbutamol sulfate exposure group and the artificial saliva control group with treatment every 24 hours for 7 days, subsequently the specimens are tested with the surface roughness of the composite resin using a surface roughness tester. The highest surface roughness value was found in the 800µg group ($8.23 \pm 0.98 \mu\text{m}$), followed by 400 µg group ($5.43 \pm 1.16 \mu\text{m}$) and the lowest in the artificial saliva group ($2.63 \pm 0.82 \mu\text{m}$). There were significant differences in all treatment groups. The exposure of salbutamol sulfate affects the surface roughness of the bioactive composite resin, a higher number of exposure doses indicates a higher surface roughness value.

Keywords: bioactive composite resins, salbutamol sulfate, surface roughness

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INTRODUCTION

Asthma is defined as a chronic inflammation of the respiratory tract characterized by a history of respiratory symptoms, such as wheezing, breathlessness, chest tightness, and coughing that can vary over time and in intensity.¹ Genetics has been shown to be a predisposition factor, but environmental interactions with genetic and host factors contribute to the prevalence of asthma.^{2,3} Asthma affects people from all age groups and has a negative impact on patients, families and communities.^{4,5} The prevalence of asthma according to the World Health Organization, an estimated 235 million people worldwide have asthma and the death rate is more than 80% in developing countries.^{4,6} In Indonesia, the prevalence of asthma was 2.4% with the recurrence proportion of 57.5% in 2018. Based on

the results of the Basic Health Research (Riskesdas) in Indonesia in 2013, it was found that the prevalence of asthma in Indonesia was 4.5% and South Kalimantan was in the order of 5 of 33 provinces with a prevalence of 6.4%.⁷

Management of asthma is pharmacological therapy. Treatments can be classified into medication taken via the inhaled route and treatment taken via the systemic route.^{7,8} The administration of asthma drugs by inhale route has gained importance in recent decades and more widely used due to it is offers several significant advantages over systemic routes.⁹ Asthma drugs via inhalation made drug concentration directly delivered into the lungs therefore drug inhalation is typically associated with minimal systemic side effects and high pulmonary efficacy that cause bronchospasm than if the drug is given

systemically.^{9,10} One of typical example of inhaled drugs is β_2 agonist class of drugs, namely salbutamol. ⁹ The dose per day can be given at 400 μ g, which is the average daily dose for people with asthma and the maximum daily dose is 800 μ g.^{11,12} Salbutamol sulfate is a group of β_2 adrenergic (short acting) agonists which is useful as the most effective bronchodilator with minimal side effects in asthma therapy and high aqueous solubility.⁹ Several studies stated that chronic treatment via inhaled route using salbutamol sulfate may affect oral cavity condition, mouth or throat irritation, reducing salivary flow and lowering salivary pH which makes patients more susceptible to caries.¹³ Salbutamol sulfate also has an effect on the surface of the restoration material, increasing discoloration and surface roughness caused by the formation of matrix pellicles which may cause the oral cavity to become acidic.^{13,14,15} A roughened surface may cause adhesion of bacteria to restorative material.¹⁵ Therefore, restorative materials must be well finished and polished to provide ideal surface characteristics and esthetics.¹² The increased surface roughness of the composite resin restorations leads to biofilm accumulation, thereby increasing the risk of secondary caries and periodontal disease.¹⁶

One of restorative materials used by dentists and is still being developed to date is composite resin. The latest advancement of the type of composite resin is bioactive composite resin.^{17,18} Bioactive composite resin is a restoration material that contains matrix ionic resin and has bioactive fillers that resemble the physical and chemical properties of teeth.^{19,20} Bioactive composite resin has main components which are generally almost the same as other types of composite resins consisting of organic, non-organic and other additional compounds. The organic component is a resin matrix in the form of a mixture of diurethane and other methacrylate modified polyacrylic acid, contains no bis-GMA, bisphenol-A and BPA derivatives. The organic phase is a filler with a percentage of 56% of the total weight consisting of amorphous silica and sodium fluoride. In addition, this composite resin has other components such as monomer bis (2-(Methacryloyloxy) Ethyl) phosphate, color pigments and dual cure system that allow polymerization mechanisms by visible light activation or chemically.²⁰ This restorative material has low wear properties, high resistance to fractures, and good polymerization process.¹⁶

Restorative material must have good resistance while in the oral cavity, the oral cavity is considered to be harsh environment for resin

restoration.²¹ A further effect that can occur in resin restorations is the degradation of the resin composite matrix which can occur through several mechanisms. The first is that the microstructure of the resin may change therefore subsequently pores are formed in the resin. The second mechanism is the diffusion of water into the resin restoration, causing the resin to become swelling, which in turn will degrade the composite resin.²² Chemical degradation of composite resins can be caused by the hydrolysis process, which is a chemical process that disrupts the covalent bonds between polymers due to the entry of water molecules between polymer bonds.²³ Water diffuses into the composite resin, reacts with the silane coupling agent, causing damage to the resin matrix bonds and filler particles, resulting in degradation that changes the microstructure of the composite resin by forming pores. The filler particles located on the surface of the composite resin can be detached to form a degradation product and causes an increase in surface roughness in composite resins.^{24,25}

Composite resin properties that can be affected by degradation of the composite resin are include in surface roughness. Degradation can be affected by acid exposure for a long time, organic matrix degradation and exposure of the organic filaments, subsequently lead to increase of surface softening and roughness and continuous for the decrease in restoration durability.²⁶

Asthma drugs affect oral cavity and restorative materials. However, there is no study evaluated the effect of asthma drugs to the surface roughness of bioactive resin. This study aims to analyze the effect of salbutamol sulfate exposure on the surface roughness of bioactive resins.

MATERIAL AND METHODS

The study has passed the ethical clearance test published by the Faculty of Dentistry, Lampung Mangkurat University No.113 / KEPKG-FKGULM / EC / IV / 2020. The specimens were fabricated with bioactive composite resin (Activa™ Bioactive Restorative, Pulpdent), with 3 treatment groups and each group consisted of 13 specimens. A total of thirty-nine specimens with 8 mm diameter and 2mm thickness based on ISO 4049 (2000) were prepared using plastic mold. The mold was placed on the top of glass slab and filled with bioactive resin until a slight excess and condensed with composite filling instrument. Matrix strip are placed on the surface and covered with glass slide on the top and gently pressed to obtain a smooth surface and to remove the excess material. All specimens were light-activated with a light cure LED unit for 20 s with an irradiation

intensity of 800mW/cm^2 , subsequently stored in incubator for 24 h at 37°C . After the periods, the specimens were exposed for 7 days at 37°C in salbutamol sulfate 400 μg (SS400), 800 μg (SS800), and immersion of artificial saliva. The specimen was removed from the incubator and subsequently ready to exposed to salbutamol sulfate. Salbutamol sulfate exposure was carried out in an acrylic box measuring length 5 cm, width 5 cm and height 5 cm therefore the drugs was concentrated and does not spread due to the influence of the wind. The specimen was placed in the center of the inner wall of the acrylic box and then fixed using double sided tape. Before being exposed, the salbutamol sulfate inhaler was shaken until the ingredients were completely mixed. The inhaler is positioned upright and the inhaler funnel is directed towards the specimen which has been placed on the inner wall of the acrylic box. The distance between the specimen and the inhaler funnel is about 5 cm and subsequently the inhaler is pressed so that it releases 100 μg of salbutamol sulfate aerosol. In SS400, there were 4 sprays (400 μg) which is the average number of daily doses used by asthma patient and for SS800 there were 8 sprays (800 μg) which is the maximum daily dose of asthma patients.¹¹ After being exposed to salbutamol sulfate, the specimens were immersed in the artificial saliva and stored in the incubator at 37°C . This procedure was carried out on each specimen in SS400 and SS800 and then repeated every 24 hours for 7 days.¹³ Artificial saliva group as a control group was not exposed to salbutamol sulfate and was only immersed in artificial saliva for 7 days. All specimens were stored in artificial saliva for 24 h at 37°C to simulate clinical conditions before measurements. Artificial saliva was prepared by mixing KCl (0.4 g/l), NaCl (0.4 g/l), $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ (0.906 g/l), $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ (0.690 g/l), $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ (0.005 g/l) and urea (1 g/l).¹³ Artificial saliva is replaced every day during the research process, subsequently the final surface roughness was measured and then reduced by the initial surface roughness value therefore the surface roughness value was obtained and entered into the data analysis.^{13,27} Parametric analysis was using the One Way Anova hypothesis test with a confidence level of 95% ($\alpha = 0.05$) and continued using the Post Hoc Bonferroni test to determine the value of significance

RESULTS

The mean value of surface roughness of the bioactive composite resin are presented in table 1.

Tabel 1. Mean and standard deviations bioactive composite resin

Group	Mean \pm SD (μm)	a
SS400	5.43 ± 1.16^A	bbr
SS800	8.23 ± 0.98^B	evia
saliva	2.63 ± 0.82^C	tion

- SS400 = composite resin specimens exposed to 400 μg of salbutamol sulfate
- SS800 = composite resin specimens exposed to 800 μg of salbutamol sulfate
- saliva = composite resin specimen immersed only in artificial saliva

The different superscript character in each variable shows the differences for each group ($p < 0.05$).

Based on table 1, it is shown that the highest mean surface roughness value was in the group of bioactive resin specimens exposed to 800 μg ($8.23 \pm 0.98\mu\text{m}$), while the lowest mean surface roughness value was in the group of bioactive resin specimens which was only immersed in artificial saliva ($2.63 \pm 0.82\mu\text{m}$). The mean surface roughness value in the group of bioactive resin specimen exposed to 400 μg salbutamol sulfate ($5.43 \pm 1.16\mu\text{m}$) was higher than the group of bioactive resin specimens which was only immersed in artificial saliva. There were significant differences in the surface roughness value among all of treatment group.

DISCUSSION

Composite resins are now increasingly developing towards the concept of aesthetic dentistry. In the development of clinical dentistry, a new type of bioactive composite resin was introduced globally in 2013. Bioactive composite resin has main components that are generally almost the same as other types of composite resins

consisting of organic, non-organic and other additional compounds.²⁰ Composite resin restoration will not be visible if the color and surface roughness is similar to the surrounding enamel surface therefore the surface of restoration have to polished. The organic matrix structure and filler characteristics have a direct influence on surface roughness. The failure of composites is mainly due to the different behavior of the resin matrix and the type and percentage of fillers in the composite resin.^{26,28} Despite the many improvements in composite resin materials, clinicians still consider the long-term durability of the restorations. Composite resin degradation is a process that also involves factor such as absorption of liquids and acid condition.²⁶ Material degradation can be associated with continuous contact with acidic conditions in the oral cavity, changes in pH in the oral cavity to acidity by the use of asthma medications for a long time.¹³ Composite resin when placed in acidic conditions releases monomers in a shorter time than when placed in water. Molecules with acidic pH diffuse into the composite resulting in microcracking which subsequently enhances absorption and retention in the monomer matrix. The mechanism continues to increase in the distance between polymer chains, resulting in a soft matrix which causes more damage.²⁶ This statement may explain the result from this study, as the dose increases from 400 µg to 800 µg there is a significant increase in surface roughness, whereas the control group immersed only in saliva showed the lowest surface roughness. This research is supported by previous studies using composite resin and glass ionomer cement.¹³ There were reported that acidic conditions show a tendency to degrade glass ionomer cements, modified polyacid composite resins, and composite resins.²⁹ Like composite resin and GIC, bioactive composite resin may also absorb water and chemicals from the oral environment, which may affect surface roughness as observed in this study. Asthma drug inhalers can produce some side effects, which are considered acidic due to their low pH and high titration acidity, can act as extrinsic agents for tooth erosion and restorative material, especially if consumed frequently.¹² Inhaler nebule has an active ingredient which contains a $(C_{13}H_{21}NO_3)_2 \cdot H_2SO_4$ sulfate group, it may affect the surfaces of the composite resin by forming a pellicle matrix that provides an acidic environment, subsequently promoting demineralization, increasing surface roughness and discoloration.¹³ This formulation is used regularly and over a long period of time, particularly by children and adults with chronic

disease, and can be an example of a potentially erosive restorative agent. These findings are in agreement with previous study stated that there was a significant increase in roughness after the use of acidic drugs. Acid medium produces surface changes in resin restorative materials.^{13,30}

Increasing surface roughness can be related to titratable acidity. The possible acidity mechanism in the degradation of the composite resin can be explained by the radical hydrolysis of the ester present in the dimethacrylate monomer, which is contain in bioactive resin composite.^{29,30}

The present study exhibits the lowest value of surface roughness obtained in the control group. This is due to the 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. These finding is in line with research conducted by Ibtisyaroh et al (2018) which showed that the longer the immersing time for the composite resin, the higher the water absorption that occurred.³¹ Immersion of composite resin will absorb water due to the matrix monomer contains polar groups that are easily attracted by water molecules to form hydrogen bonds. Water absorption will induce degradation in the composite resin. Water molecules will diffuse into the polymer chain by weakening the polymer chain and releasing matrix monomers. Water molecules also cause degradation of the filler surface and the silane coupling agent through a hydrolysis reaction. This causes the bond between the filler and the matrix to be unstable.^{13,32} This also results in reduced mechanical resistance of the resin when surface degradation occurs, resulting in a rough surface of the restoration material.

With the limitation of this study, the use of salbutamol sulfat or antiasthmatic drug as an inhaler, it is applied as a pressurized and metered-dose aerosol unit for oral inhalation, it also contains a microcrystalline suspension of sulfate group. This substance covers the teeth and dental restoration during inhalation and may remain as a residue after inhalation. Thus, patients using inhalers and nebulizers should be advised to taking care of oral hygiene and have their oral status checked regularly. Generally, it is advisable to wash the mouth immediately after using the inhaler.¹³

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