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# Intramedullary epinephrine and surgical hole on femoral cortex before intramedullary K-wire and bone cement insertion resulting in lower amount of PMMA (polymethyl methacrylate) particles on rabbit's myocardium



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## ABSTRACT

**Background:** Cemented hip arthroplasty can result in devastating complication such as Bone Cement Implantation Syndrome (BCIS). BCIS consists of decreased blood pressure, decreased heart rate, a decrease of consciousness, and sudden death. This devastating condition caused by systemic circulation of polymethyl methacrylate (PMMA). Decrease heart rate caused by PMMA reaction with the heart muscle. PMMA reach heart muscle due to the increased intramedullary pressure and the opening of the intramedullary blood vessel during cementation.

**Aim:** The purpose of this study is to prove that intramedullary epinephrine and femoral hole before the insertion of bone cement and K-wire result in the lower amount of PMMA in rabbit's myocardium.

**Methods:** This research is conducted as experimental research with post-test only control group design with the subject rabbits. A total of 28 research subjects who met the inclusion criteria of the study were randomly divided into treatment and control groups. The control group

did not receive epinephrine and femoral hole treatment. Treatment group 1 received epinephrine intramedullary only, treatment group 2 received femoral hole only, and treatment group 3 received intramedullary epinephrine and femoral hole.

**Results:** Statistical analysis using parametric tests one-way ANOVA found a significant difference between treatment and control groups on the amount of rabbit's heart muscle. The amount of PMMA particle in all treatment groups are lower than the control group with a p-value of 0.000 ( $p < 0.05$ ). The amount of PMMA particle in treatment group 3 (received epinephrine and femoral hole) is lower than the control group with a p-value of 0.000 ( $p < 0.05$ ).

**Conclusion:** The conclusion of this research is intramedullary epinephrine and femoral hole making before the insertion of bone cement and K-wire result in the lower amount of PMMA particle in rabbit's myocardium

**Keyword:** Epinephrine, femoral hole, rabbit's myocardium, PMMA (*polymethyl methacrylate*)

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## INTRODUCTION

Bone Cement Implantation Syndrome (BCIS) is one of the complications of cemented hip arthroplasty. Clinical research showed that cemented arthroplasty has a better result in the clinical outcome of arthroplasty.<sup>1</sup> BCIS is one of fatal intraoperative complication in operations that use bone cement.<sup>2,3</sup> BCIS characterized by hypoxia, hypotension, cardiac arrhythmia, increase pulmonary resistance, and cardiac arrest.<sup>2,3</sup> Research by Lafont (1997) in 48 patients underwent Total Hip Replacement (THR) resulted in 1 patient (2%) with reduced systolic pressure and 8 patients (17%) with oxygen desaturation.<sup>4</sup> A study conducted by Herenbruck et al. in 2002 stated that cemented arthroplasty of the hip joint with long stem was associated with an increased incidence of BCIS.<sup>5</sup> BCIS generally occur in the action of hip joint replacement using bone cement.<sup>2</sup>

Several techniques have been proposed to reduce the risk of BCIS occurrence, but no technique has been stated to be the most superior and established as an operational standard in arthroplasty using bone cement. Based on the background of the pathophysiology of BCIS, this condition involves vasodilation of intramedullary blood vessels during the process of reaming and increased intramedullary pressure. Therefore, the researchers tried to overcome these two things in experimental animals by combining epinephrine intramedullary and surgical holes in the rabbit femur. With this technique, it is expected to provide an intramedullary pressure reduction effect and cause vasoconstriction of the blood vessels in the medulla, thus reducing the entry of PMMA particles into the systemic bloodstream of the rabbit.

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## MATERIAL AND METHODS

This study was an experimental study using a post-test only control group design with rabbit subjects. This study used 28 male rabbits, age 3-5 months weight 1.5-2 kg. Samples were taken from the population of the study subjects which met the random inclusion criteria of the study. The control group (Group 1) received bone cement and intramedullary K-wire on the right femur bone, while in the intervention group was divided into three groups:

Group 2 received intramedullary epinephrine insertion before being given bone cement and intramedullary K-wire on the right femur bone.

Group 3 received a surgical hole on the distal femur right before being given bone cement and intramedullary K-wire on the right femur bone.

Group 4 received epinephrine and a surgical hole on the distal femur right before being given bone cement and intramedullary K-wire.

Cardiac tissues were obtained after 15 minutes, then evaluated histologically for the amount of PMMA particle.

## RESULTS

The research analysis included descriptive data distribution of PMMA particles on cardiac muscle. Furthermore, the data are analyzed using SPSS for Windows version 22.0.

The average number of PMMA particles in the treatment group 1 was  $13.32 \pm 0.53$  particles per field of view, in treatment 2 was  $16.29 \pm 0.59$  particles per field of view, in treatment 3 was  $11.61 \pm 0.76$  per field of view, while in the control group was  $18.79 \pm 0.55$  per field of view.

The research variables in the treatment and control groups were tested for normality test. Shapiro-Wilk test was used as the normality test since the amount of data is 28 ( $n < 50$ ). The homogeneity test of data variant was done using Levene's test.

The inferential analysis aims to generalize the results of the study to the population. One-way ANOVA is used as the parametric test if the data is normally distributed. The Kruskal Wallis test is used if it is not a normal distribution. Assessment of test results using 95% CI and p-value on the significant margin of 0.05.

Post hoc analysis showed that treatment group 3, which is given intramedullary epinephrine and surgical hole, has a lower amount of PMMA particle compared with treatment group 1 (epinephrine) and treatment group 2 (surgical hole). This result is statistically significant with a p-value less than 0.05.

## DISCUSSION

The use of intramedullary epinephrine before bone cement and K-wire insertion may decrease the number of PMMA particles entering through intramedullary blood vessels. The process of reaming will allow PMMA particles to enter the systemic circulation through the opened blood vessels. The administration of intramedullary epinephrine provides the intraarticular vasoconstrictive effect, thereby reducing the entry of PMMA particles into the systemic circulation.<sup>6</sup> In a study conducted by Qi et al. showed that the administration of epinephrine intramedullary proved to prevent the occurrence of hypotensive reactions caused by the use of arthroplasty with bone cement.<sup>6</sup> Hypotensive reactions do not occur because epinephrine causes vasoconstriction of intramedullary blood vessels to prevent entry of PMMA particles into the systemic circulation.

Giving pressure when inserting bone cement into the intramedullary aimed to improve bone cement attachment with bone, thus stabilize the construction of implants in bone. The arthroplasty performed without the use of bone cement shows a low intramedullary pressure and less hemodynamic disturbance. The degree of embolism is closely related to the increase in intramedullary pressure.<sup>7</sup> Emboli caused by cementation during arthroplasty have a strong correlation with BCIS.<sup>2</sup>

Bone Cement Implantation Syndrome (BCIS) is one of the causes of death during surgery in patients treated with arthroplasty using bone cement. This situation begins with hypotension, hypoxemia, cardiac arrhythmia, and cardiac arrest that can occur during the cementation process.<sup>7</sup> Decreased cardiac contractility, and cardiac cascade activation of the heart may be caused by many factors including PMMA, the density of the patient's bone, and increased intramedullary pressure.<sup>7,8</sup>

The viscosity of the cement used influences the increase in pressure. This type of bone cement has a long waiting phase of approximately 5 minutes; then the working phase will increase rapidly and will harden in 1 to 2 minutes.<sup>9</sup> The use of low viscosity bone cement reduces intramedullary pressure, thereby reducing the risk of BCIS. This study used bone cement with low viscosity (Cemfix 3). This type of bone cement is used in all study groups to negate the effect of the viscosity on the intramedullary pressure produced.

The intramedullary pressure in the cementation process differs throughout the femoral intramedullary space. In a study conducted by Rothberg et al. in

2013 using cadaver femur, the highest pressure was found in the distal areas of the femur. The intramedullary pressure in the proximal femur was 461 psi (95% CI, 2-6 psi), in middle femur was 761 psi (95% CI, 5-9 psi), and in distal femur was 961 psi (95% CI, 7-10 psi).<sup>3</sup> Based on this study, researchers aimed to reduce intramedullary pressure by making a hole in the distal femur.

Drilling surgical hole in the distal femur may reduce the entry of PMMA particles into the systemic circulation, especially in the heart. The PMMA particles enter into the systemic circulation due to increased pressure on the intramedullary chambers. Increased pressure on the intramedullary space may increase the entry of PMMA particles into the systemic circulation.<sup>7</sup> Drilling a hole in the femur can reduce the pressure on the intramedullary space.<sup>8</sup>

High intramedullary pressure may be reduced by femoral opening and use of low viscosity bone cement.<sup>3</sup> In this research, a hole has been drilled in the distal femur with a distance of 0.5 cm from the lateral epicondylus of femur rabbit and size 1 mm. Due to the limitations of the tool, the intramedullary pressure is not worked. We assumed a similar pressure decrease among the treatment groups as we used rabbits with similar weight and age and similar hole size.

Several things have been done to reduce the risk of BCIS regarding surgical techniques. It includes washing of medulla (lavage), proper bleeding control, avoiding the use of prosthesis and the use of prosthesis without cement, and drilling a hole in the medulla (venting medulla).<sup>2,10</sup> Drilling a hole in the bone allows air to come out and reduce air emboli. However, it will also increase the risk of fracture.<sup>2</sup>

Some techniques have been proposed to reduce the risk of BCIS incidence, but no technique is considered the most superior and defined as standard operational standards in arthroplasty action using bone cement. Researchers try to overcome these two things in experimental animals that combine epinephrine intramedullary and the manufacture of holes in the femur of rabbits to reduce PMMA exposure in the tissue, especially the heart.

In this study, the researchers provide solutions to reduce the entry of PMMA particles reach the heart muscle by reducing intramedullary pressure and vasoconstriction of intramedullary vessels. The use of intramedullary epinephrine before bone cement and K-wire may result in intramedullary vessel injection. Preparation of the hole on the distal rabbit femur serves to reduce intramedullary pressure, thus reducing PMMA particles entry into the

systemic circulation. The combination of these two things is expected to further reduce the number of PMMA particles that enter into the systemic circulation, especially in the heart muscle.

In research conducted by Qi et al. said that the administration of epinephrine intramedullary proved to prevent the occurrence of hypotensive reactions caused by post-use arthroplasty with bone cement.<sup>6</sup> PMMA particles that enter the systemic circulation can reach the heart. Inhibition of  $Ca^{2+}$  uptake by methyl methacrylate is a dose-dependent condition. In some reports, it was said that methyl methacrylate induced cardiovascular suppression mediated by disruption of  $Ca^{2+}$  homeostasis balance.<sup>6</sup> In this study, we used the number of PMMA particles per field as the parameter of intervention success due to the dose-dependent effect caused by the interaction between PMMA particles and heart muscle.

Preparation of the distal hole of the femur may reduce the entry of PMMA particles into the systemic circulation, especially in the heart. Increased pressure on the intramedullary space may increase the entry of PMMA particles into the systemic circulation.<sup>7</sup> In a study conducted by Rothberg et al. in 2013 using cadaveric femur, the highest pressure was found in the distal areas of the femur.<sup>7</sup> Based on this study, researchers aimed to reduce intramedullary pressure by making a hole in the distal femur. Preparation of a hole in the femur may reduce the pressure on the intramedullary space.<sup>8</sup>

In this study, the group that is treated with epinephrine (Group 1) and the group that is treated with a hole in the femur (Group 2) showed a lower mean number of PMMA particles than the control group. The average difference was statistically significantly different. Groups treated with a combination of intramuscular epinephrine administration and femoral hole (Group 3) showed a lower mean number of PMMA particles than the control group. This average difference is statistically significantly different. This result suggests that a combination of epinephrine administration and femoral hole before bone cement and K-wire may result in a lower number of PMMA particles in the heart muscle than the control group.

## CONCLUSION

Intramedullary epinephrine and drilling hole on femoral cortex before intramedullary k-wire and bone cement insertion resulting in lower amount of PMMA (polymethyl methacrylate) particles on rabbit's myocardium.

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