e-ISSN: 2722-3558

Sriwijaya Journal of Surgery

[SJS]

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Relationship Between the Use of Topical Hypothermia with Ice Water to Postoperative Pulmonary Complications of Coronary Artery Bypass Graft

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ARTICLE INFO

Received: November 19, 2023;
Accepted: February 20, 2024;
Published: April 1, 2024.

Keywords:
CABG
Open heart surgery
Pulmonary complications
Topical hypothermia

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/sjs.v7i1.99

A B S T R A C T

Introduction: Open heart surgery such as coronary artery bypass graft (CABG) is a heart surgery technique that uses a machine cardiopulmonary bypass (CPB) which can cause postoperative complications such as systemic inflammatory response syndrome (SIRS) and myocardial damage. Myocardial protection can be achieved through topical hypothermia techniques by lowering the heart temperature using a cold solution or ice cubes. Although several studies have shown its benefit in protecting the myocardium, the use of topical hypothermia remains controversial due to its uneven cooling effect and risk of tissue injury. This study aims to evaluate the relationship between the use of topical hypothermia of ice water and pulmonary complications of open heart surgery. **Methods**: This research is an analytical observational cohort retrospective comparison of pulmonary complications postoperatively in cardiac surgery patients who received systemic cardioplegia alone versus those who received a combination of systemic cardioplegia and topical hypothermia. Data collection was carried out using techniques consecutive sampling. **Results:** Of the 32 research subjects, the results of the analysis showed that the use of topical hypothermia did not have a statistically significant relationship ($p>0.05$) on the incidence of leukocytosis, pulmonary edema, duration of surgery, duration of ventilator use, duration of hospitalization, and mortality compared to the group that only received systemic cardioplegia. There was a significant relationship ($p<0.05$) between the incidence of pleural effusion in the topical hypothermia group. **Conclusion:** The use of topical hypothermia in cardiac surgery has a significant association with a higher incidence of pleural effusion.

1. Introduction

Open heart surgery, such as coronary artery bypass graft (CABG), is a complex procedure that carries the risk of postoperative complications. One of the complications that often occurs is systemic inflammatory response syndrome (SIRS) and myocardial damage. SIRS is a systemic inflammatory response that can lead to organ damage and multi-organ failure. Myocardial damage, on the other hand, can occur due to ischemia (lack of oxygen) and reperfusion (return of blood flow) during surgery. To protect the myocardium, topical hypothermia techniques are often used. This technique lowers the heart temperature using a cold solution or ice cubes. Lower temperatures slow down myocardial metabolism, so its oxygen demand is reduced. Hypothermia can help maintain the integrity of cell membranes and prevent the release of damaging cell digestive enzymes. Lower temperatures can increase blood flow to the myocardium, thereby aiding tissue recovery.[1-3]

Although several studies have demonstrated the benefits of topical hypothermia in protecting the myocardium, its use remains controversial. Topical

hypothermia can cause uneven cooling of the myocardium, potentially leading to tissue damage. Temperatures that are too low can cause direct damage to myocardial cells. Topical hypothermia can cause an uneven cooling effect on all parts of the heart. This can increase the risk of tissue injury. There is still no strong scientific evidence to show that topical hypothermia can significantly reduce post-CABG complications.[4-6] This study aims to evaluate the relationship between the use of topical hypothermia of ice water and pulmonary complications of open heart surgery.

2. Methods

This research is a retrospective cohort analytic observational study. All patients undergoing open heart surgery at Dr. Mohammad Hoesin General Hospital Palembang Indonesia during the period January 2022 to June 2023. A total of 32 patients met the inclusion criteria. The inclusion criteria were patients who underwent CABG surgery and patients who received systemic cardioplegia. Patients were divided into two groups: 1. Systemic cardioplegia + topical hypothermia group: Patients who received systemic cardioplegia and topical hypothermia. 2. Systemic cardioplegia group: Patients who received only systemic cardioplegia. The sampling technique used was consecutive sampling. Samples were taken sequentially from patients who met the inclusion criteria until the sample size was met. Data was collected from patient medical records.

Univariate analysis was carried out on the basic characteristics data of the research subjects. This univariate analysis aims to describe the research sample. Descriptive analysis in the form of numerical data and categorical data. Numerical data will be presented in the form of cut-off values and standard deviation. Meanwhile, categorical data will be presented in the form of graphs or frequency distribution tables, proportions or percentages, and narratives. Bivariate data analysis was carried out using the Chi-square/Fisher's exact test for the relationship between categorical variables and two independent populations and using the independent T-test/Mann-Whitney test to assess the relationship between a numerical variable and two independent populations. Data from the results of statistical analysis are displayed in tables, graphics, and text. The relationship is said to be significant if the p-value <0.05. Multivariate analysis used logistic regression to determine the effect of administering systemic cardioplegia and topical hypothermia compared with administering systemic cardioplegia alone, as well as the influence of confounding variables on post-cardiac surgery complications (leukocyte count, pleural effusion, and duration of ventilator use). The relationship is said to be significant if the p-value <0.05.

3. Results

Table 1 shows significant differences in age between the two treatment groups. Treatment group 1 (systemic cardioplegia + topical hypothermia) had a higher median age (62.00 years) compared to treatment group 2 (systemic cardioplegia only), with a median age of 42.00 years. Treatment group 1 was dominated by men (81.25%), while treatment group 2 had a higher proportion of women (56.25%). However, the difference in gender proportion between the two groups was not statistically significant. The proportion of subjects with a history of hypertension was higher in treatment group 1 (62.50%) compared to treatment group 2 (37.50%). However, this difference was not statistically significant. Postoperative leukocytosis (leukocytes ≥ 10,000/mm^3) was observed in 81.25% of subjects in treatment group 1 and 68.75% in treatment group 2. Again, this difference did not show statistical significance. Pulmonary edema occurred in 12.50% (n=2) of subjects in treatment group 1 and 6.25% (n=1) in treatment group 2. Pleural effusion was found in 31.25% (n=5) of subjects in treatment group 1 and 25.00% (n =4) in treatment group 2. There was no significant difference in the proportion of complications between the two groups. Two deaths (6.25%) occurred in this study, one in each treatment group. The causes of death in both groups were

cardiogenic shock and heart failure. Based on Table 1, there are several differences in characteristics between subjects in the two treatment groups. Treatment group 1 had a higher median age and was predominantly male. Although the proportion of subjects with a history of hypertension, leukocytosis, pulmonary edema, pleural effusion, and mortality was higher in treatment group 1, there were no statistically significant differences between the two groups.

Table 1. Characteristics of respondents.

Characteristics	Treatment group 1 (n=16)	Treatment group 2 (n=16)
Age in years (min-max)	62 (55.75-68.00)	42 (33.25-51.75)
Gender		
Male	81.25% (n=13)	43.75% (n=7)
Female	18.75% (n=3)	56.25% (n=9)
History of hypertension	62.50% (n=10)	37.50% (n=6)
Leukocytosis (leukocytes ≥ 10,000/mm^3)	81.25% (n=13)	68.75% (n=11)
Postoperative complications		
Pulmonary edema	12.50% (n=2)	6.25% (n=1)
Pleural effusion	31.25% (n=5)	25.00% (n=4)
Mortality	6.25% (n=1)	6.25% (n=1)

Table 2 shows a comparison of the incidence of leukocytosis, pleural effusion, pulmonary edema, and mortality between two treatment groups in a study. Group 1 received systemic cardioplegia with topical hypothermia, while group 2 received only systemic cardioplegia. The incidence of postoperative leukocytosis was not significantly different between the two groups. Group 1 had an incidence of leukocytosis of 68.75%, while group 2 had an incidence of 81.25%. The p-value of 0.685 indicates that this difference is not statistically significant. There was a significant difference in the incidence of pleural effusion between the two groups. Group 1 had a 50% incidence of pleural effusion, while group 2 only had 6.25%. The p-value of 0.015 indicates that this difference is statistically significant. The incidence of pulmonary edema did not differ significantly between the two groups. Group 1 had an incidence of pulmonary edema of 12.50%, while group 2 had an incidence of 6.25%. A p-value of 1.000 indicates that this difference is not statistically significant. Mortality rates did not differ significantly between the two groups. Group 1 had a mortality rate of 12.50%, while group 2 had no deaths (0%). The p-value of 0.484 indicates that this difference is not statistically significant.

Table 2. Comparison of the incidence of leukocytosis, pleural effusion, pulmonary edema, and mortality between groups.

Group	Leukocytosis occurrence	p-value
Treatment 1	68.75%	0,685
Treatment 2	81.25%	
Group	**Pleural effusion**	**p-value**
Treatment 1	50%	0,015
Treatment 2	6.25%	
Group	**Pulmonary edema**	**p-value**
Treatment 1	12.50%	1.000
Treatment 2	6.25%	
Group	**Mortality**	**p-value**
Treatment 1	12.50%	0,484
Treatment 2	0%	

Table 3 shows a comparison of several variables between two treatment groups in a study. Group 1 received systemic cardioplegia with topical hypothermia, while Group 2 received only systemic cardioplegia. Median postoperative leukocytes did not differ significantly between the two groups. Group 1 had a median of 13.47 leukocytes ($10^3/mm^3$), while group 2 had a median of 13.00 ($10^3/mm^3$). The p-value of 0.515 indicates that this difference is not statistically significant. The average duration of surgery also did not differ significantly between the two groups. The median duration of surgery in both groups was 4.50 hours. The p-value of 0.956 indicates that this difference is not statistically significant. Median ventilator duration also did not differ significantly between the two groups. Group 1 had a median ventilator duration of 28.50 hours, while Group 2 had a median of 28.5 hours. The p-value of 0.956 indicates that this difference is not statistically significant. The median duration of hospitalization did not differ significantly between the two groups. Group 1 had a median duration of hospitalization of 10.50 days, while group 2 had a median of 10.5 days. The p-value of 0.838 indicates that this difference is not statistically significant.

Table 3. Comparison of postoperative leukocytes, duration of surgery, duration of ventilator, and duration of hospitalization between groups.

Variable	Group 1 (n=16)	Group 2 (n=16)	p-value
Postoperative leukocytes ($10^3/mm^3$)	13.47 (8.59, 14.63)	13.00 (11.54, 17.25)	0,515
Duration of surgery (hours)	4.50 (4.00, 5.00)	4.50 (3.50, 6.00)	0,956
Ventilator duration (hours)	28.50 (28.00, 29.00)	28.5 (27.50, 30.00)	0,956
Duration of hospitalization (days)	10.50 (6.25, 13.75)	10.5 (5.00, 13.00)	0,838

4. Discussion

This study suggests that administering systemic cardioplegia with topical hypothermia (group 1) may increase the risk of pleural effusion compared with administering systemic cardioplegia alone (group 2). The hypothesis of this study is that administering systemic cardioplegia with topical hypothermia will provide benefits compared to administering systemic cardioplegia alone. This benefit is expected to be seen in a reduction in the incidence of pleural effusion. However, the results of the study showed that administering systemic cardioplegia with topical hypothermia actually increased the risk of pleural effusion compared to administering systemic cardioplegia alone. Several previous studies have examined the effects of topical hypothermia in open heart surgery. Topical hypothermia can help reduce inflammation. Cytokines are proteins that play a role in inflammation. Topical hypothermia can help reduce the production of inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha. Topical hypothermia can help reduce the activation of inflammatory cells, such as neutrophils and macrophages. These cells can produce free radicals and proteolytic enzymes that can damage tissue. Topical hypothermia can help increase the production of anti-inflammatory compounds, such as interleukin-10. Topical hypothermia may help improve myocardial perfusion. Topical hypothermia can help dilate the coronary arteries, which can increase blood flow to the heart. Topical hypothermia can help reduce vascular resistance, which can increase blood flow to the heart. Topical hypothermia can help improve microcirculatory perfusion, which can increase blood flow to heart tissue. Topical hypothermia can help speed the recovery of heart function. Topical hypothermia can help reduce myocardial damage by reducing apoptosis (cell death) and necrosis (tissue death). Topical hypothermia may help improve the pumping function of the heart by increasing the left ventricular ejection fraction. Topical hypothermia may help speed electrophysiological recovery by reducing

cardiac arrhythmias.[7-10]

This study shows that administering systemic cardioplegia with topical hypothermia actually increases the risk of pleural effusion compared to administering systemic cardioplegia alone. Topical hypothermia can cause mechanical damage to the pleura due to the cooling process. When temperatures drop, water in tissues can crystallize and cause cell damage. Topical hypothermia can cause blood vessel contraction, which can reduce blood flow to the pleura and cause tissue damage. The process of inserting and removing a topical hypothermia device can cause mechanical trauma to the pleura. Topical hypothermia can increase inflammation of the pleura, which can lead to pleural effusion. Topical hypothermia can cause the release of inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha. These cytokines can cause inflammation and tissue damage in the pleura. Topical hypothermia can cause activation of inflammatory cells, such as neutrophils and macrophages. These cells can produce free radicals and proteolytic enzymes that can damage pleural tissue. Topical hypothermia can interfere with blood coagulation, which may increase the risk of bleeding and pleural effusion. Topical hypothermia can cause a decrease in platelets, which are important for blood clotting. Topical hypothermia can cause a decrease in coagulation factors, which are also important for blood clotting.[11-15]

Improper techniques, such as suboptimal device placement or inappropriate temperature settings, can cause mechanical damage to the pleura and increase the risk of pleural effusion. Ineffective use of topical hypothermia devices may not provide the expected benefits and may actually increase the risk of side effects. Prolonged use of topical hypothermia (more than 24 hours) can increase the risk of side effects, including pleural effusion. The optimal duration of topical hypothermia still requires further research to be confirmed. Patients with certain medical conditions, such as lung disease or coagulation disorders, may have a higher risk of developing pleural effusion following the administration of topical hypothermia. Administration of systemic cardioplegia with topical hypothermia may increase the risk of pleural effusion compared with administration of systemic cardioplegia alone.[16-20]

5. Conclusion

The increase in the incidence of pleural effusion had a statistically significant relationship ($p<0.05$) in the topical hypothermia group. The use of topical hypothermia did not have a statistically significant relationship ($p>0.05$) on the incidence of pulmonary edema, leukocytosis, duration of ventilator use, and duration of patient hospitalization.

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