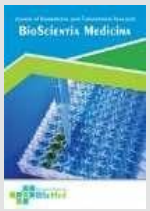
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Comparison of the Effectiveness between Povidone-Iodine and Bleomycin as Pleurodesis Agents in Patients with Malignant Pleural Effusion at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

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ARTICLE INFO

Keywords:
Bleomycin
Malignant pleural effusion
Pleurodesis agent
Povidone-iodine

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

https://doi.org/10.37275/bsm.v7i3.802

A B S T R A C T

Background: Malignant pleural effusion (MPE) is a clinical problem in which fluid accumulates in the pleural cavity. This condition is generally caused by malignancy. Pleurodesis is a medical procedure in the form of fusion of the visceral and parietal pleura in order to prevent the recurrence of pleural effusion. Pleurodesis has the risk of causing chronic inflammation, which will trigger excessive attachment between the visceral and parietal pleura. Of course, an intervention is needed to reduce the risk of inflammation, one of which is by using a pleurodesis agent, which has an anti-inflammatory effect. This study aimed to compare the efficacy of povidone-iodine compared to bleomycin as a pleurodesis agent in malignant pleural effusion patients at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. **Methods:** Prospective cohort study, where as many as 46 research subjects participated in this study and were grouped into groups that received povidone-iodine and bleomycin. The success of pleurodesis agents was assessed by the production of WSD. Data analysis was carried out using SPSS univariate and bivariate. **Results:** The results of the study showed that there was no statistical difference between the 10% povidone-iodine agent and the bleomycin agent, where p>0.05. However, in the 10% povidone-iodine group, the success rate was 100%, while in the bleomycin group, the success rate was 82.6%. **Conclusion:** There was no significant difference in the efficacy of povidone-iodine as a pleurodesis agent compared to bleomycin in patients with malignant pleural effusion at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

1. Introduction

Malignant pleural effusion (MPE) is a clinical problem in which fluid accumulates in the pleural cavity. This condition is generally caused by malignancy. A study shows that about 50-65% of this condition is caused by malignancy or metastasis of cancer. In men, MPE is generally caused by metastases from lung carcinoma, and in women, MPE is generally caused by metastases from breast carcinoma. Pleurodesis is a medical procedure in the form of fusion of the visceral and parietal pleura in order to prevent the recurrence of pleural effusion. Pleurodesis has the risk of causing chronic inflammation, which will trigger excessive attachment between the visceral and parietal pleura. Of course, an intervention is needed to reduce the risk of inflammation, one of which is by using a pleurodesis agent, which has an anti-inflammatory effect.[1-4]

Bleomycin is a pleurodesis agent that is quite often used, where this agent is useful as an anti-cancer and anti-inflammatory. Currently, injectable bleomycin is increasingly difficult to obtain, and its use is still limited. The price is so expensive how to obtain and use using the protocol. This procedure is quite strict,

and this procedure is carried out in an operating room, and requires an intensive care room if complications occur. The success rate of this pleurodesis agent is 79.1%, with a failure rate of around 20.9%. Povidone iodine is a topical antiseptic with a mechanism of action that inhibits the function of cytosolic enzymes, thereby inhibiting local inflammation and adhesions in the visceral and parietal pleura. This pleurodesis agent has been proven effective as a pleurodesis agent. The effectiveness rate of this pleurodesis agent is 76.0%, with a failure rate of 24.0%.[5-8] This study aimed to compare the efficacy of povidone-iodine compared to bleomycin as a pleurodesis agent in malignant pleural effusion patients at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

2. Methods

The research design is a prospective cohort observational study. A total of 46 research subjects participated in this study, where the research subjects met the inclusion criteria. The inclusion criteria in this study were patients with a diagnosis of malignant pleural effusion who would undergo a pleurodesis process at the cardiothoracic surgery division of Dr. Hasan Sadikin General Hospital Bandung from January 1st, 2022, to December 31st, 2022, patients who had a clinical respiratory rate <30x/minute, minimal pleural fluid < 100 cc/24 hours and lung expansion. Research subjects must sign informed consent as consent to participate in this study. This research was approved by the medical and health research ethics committee at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, Number: HK.02.03/X.4.1.3/15287/2018. The research subjects were grouped into 2 groups, namely group 1: research subjects receiving a pleurodesis agent in the form of 10% povidone-iodine and group 2: research subjects receiving a pleurodesis agent in the form of bleomycin.

The success of using pleurodesis agents is assessed by assessing the production of WSD, where if the WSD production is <100 cc/24 hours, it is considered successful, and if the WSD production is more than 100 cc/24 hours, then it is considered a failure. Pleurodesis was carried out based on standard operating procedures (SOP)/clinical practice guidelines (CPG) of the Medical Committee of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. Namely: Pleurodesis using sclerosant materials (10% povidone-iodine and bleomycin) in patients who have a thoracostomy catheter/tube installed, clamped thoracic catheter, disinfected the skin around the catheter with 10% povidone-iodine, followed by 70% alcohol, instilled pleural cavity with 2% lidocaine 5 ampoules through a catheter for pleurodesis using 10% povidone-iodine and bleomycin, the chest tube was clamped for 2 hours, then observations were made while the chest tube was clamped, the effect of pain was assessed using the visual analogue scale (VAS) rating scale which was categorized as no pain (No pain) 0-1, mild pain (mild) 1-2, moderate pain (moderate) 3-4, severe pain (severe) 4-6, and very severe pain (very severe) 6-10, then after flowing again, WSD is assessed for production during the first 24 hours, removed if production is <100 mL/24 hours and lung expansion has occurred (from chest X-ray). Various variable confounders such as age, gender, primary tumor type, albumin, and Karnofsky score were matched. Data analysis was carried out using SPSS software version 25 for Windows. Univariate analysis was performed to present the frequency distribution of each data variable test. Bivariate analysis was performed to compare the success of WSD production between 10% povidone-iodine and bleomycin treatments, with a p-value <0.05.

3. Results

Table 1 presents the characteristics of the research subjects. The results showed that the age of the study subjects was homogeneous between the 10% povidone-iodine and bleomycin groups (p>0.05). The sex of the study subjects between the 10% povidone-iodine and bleomycin groups was homogeneous (p>0.05). Primary tumor-causing effusion pleural malignancy between the povidone-iodine 10% and bleomycin groups was homogeneous (p>0.05). As well

as serum albumin between the 10% povidone-iodine and bleomycin groups were homogeneous (p>0.05).

Table 1. Characteristics of research subjects.

Characteristics	Povidone iodine 10% (n (%)) n=23	Bleomycin (n (%)) n=23	p-value*
Age (years)			0,729
Mean ± SD	46,43 ± 13,249	47,96 ± 16,205	
range	16-73	13-73	
Gender			1,000
Male	5 (21,74)	5 (21,74)	
Female	18 (78,26)	18 (78,26)	
Primary tumor			0,972
Ca lung	3 (13,04)	5 (21,74)	
Ca mammae	11 (47,83)	9 (39,13)	
Ca ovarium	2 (8,70)	2 (8,70)	
Other types	7 (30,43)	7 (30,43)	
Albumin serum (g/dL)			0,063
Mean ± SD	2,866 ± 0,613669	2,7695 ± 0,61676	
range	1,43-4	1,3-4	

*Homogeneity test, p<0,05.

Table 2 presents a comparison of the success of pleurodesis agents povidone iodine 10% and bleomycin on WSD production. The results of the study showed that there was no statistical difference between the 10% povidone-iodine agent and the bleomycin agent, where p>0.05. However, in the 10% povidone-iodine group, the success rate was 100%, while in the bleomycin group, the success rate was 82.6%.

Table 2. Comparison of pleurodesis success rates povidone iodine 10% and bleomycin.

Success	Povidone iodine 10%	Bleomycin	p-value*
Succeed	23	19	0,109
Not successful	0	4	

*Fisher exact test, p<0,05.

4. Discussion

Several studies have shown a higher success rate of povidone-iodine than bleomycin. The success rate range for povidone-iodine is around 70-100%, and for bleomycin is 60-89%. Neither the success rate of povidone-iodine was higher nor vice versa. There was no significant difference.[9-12] One of the successes of pleurodesis is determined by the type of sclerosant

used. Various substances have been reported to have been used as pleurodesis agents, including talc, oxytetracycline, quinacrine, bleomycin, mitomycin, and povidone-iodine. The ideal sclerosant is one that has a high molecular weight and polarity, low local elimination, and rapid systemic elimination with minimal side effects. The mechanism of action of povidone-iodine as a pleurodesis agent is thought to be related to its oxidative effect, which can induce an inflammatory process. There is also speculation because of its cytotoxic effect on tumor cells.[13,14]

Povidone iodine is a topical antiseptic, a type of iodine disinfectant, which directly causes in vivo protein denaturation and bacterial deposition, and subsequently results in the death of pathogenic microorganisms.[15] Therefore, it is effective in disinfection and sterilization. It can kill viruses, bacteria, spores, fungi, and protozoa with low toxicity to humans. The povidone-iodine aqueous solution has strong pharmacological activity against *Staphylococcus aureus, Neisseria gonorrhoeae, Pseudomonas aeruginosa,* syphilis, hepatitis B virus, HIV, and Trichomonas vaginalis. Povidone iodine (iodophor) or povidone acts as an iodine carrier. Iodine is considered the active component that mediates the action of microbicides. When released from the complex, free iodine (I2) penetrates the cell walls of microorganisms rapidly and has lethal effects, resulting from disruption of structure and synthesis of proteins and nucleic acids. In addition, free iodine interferes with the function of cytosolic enzymes involved in the respiratory chain, causing cell denaturation.[16] Povidone iodine also acts as a sclerosant and causes local inflammation. The mechanism of action of povidone-iodine for pleurodesis is still being debated but is thought to be related to the low pH of povidone-iodine or the oxidative effect of cytokines that induce the inflammatory process.[17] Another mechanism elicited by povidone-iodine is the production of fibroblast growth hormone (bFGF-β), which causes the formation of fibrin adhesions and fibrosis in the visceral and parietal pleura. Inflammatory reactions in mesothelial cells will release various mediators derived from cytokines, such as interleukin 8 (IL-8) and monocyte chemoattractant protein (MCP-1), vascular endothelial growth factor (VEGF), growth factor derived from platelet-derived growth factor (PDGF) and basic fibroblast growth factor (bFGF), transforming growth factor (TGF-β), and other mediators cause local irritation of the pleura.[18]

5. Conclusion

There was no significant difference in the efficacy of povidone-iodine as a pleurodesis agent compared to bleomycin in patients with malignant pleural effusion at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

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