Journal of
Cardio - Thoracic Medicine

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The Effects of Glubran Glue on Alveolar Air Leak in Patients with Chronic Empyema

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ARTICLE INFO

Article type:
Original article

Article history:
Received: 25 Nov 2021
Revised: 19 Dec 2021
Accepted: 31 Dec 2021

Keywords:
Air leak
Complications
Glubran glue
Surgery

ABSTRACT

Introduction: Air leak is one of the post-surgical complications following thoracic surgeries. Studies have shown that patients with more intraoperative air leaks are at higher risk of developing prolonged postoperative air leak. Various adjuncts have been used in attempts to reduce alveolar air leaks (AAL). One of these, is the topical application of Glubran-2. This study examines the role of Glubran-2 in management of air leak in patients with chronic empyema.

Methods: This was a randomized clinical trial that included 44 patients with chronic pulmonary empyema who underwent decortication and pleurectomy. They were divided into 2 equal groups. In the first group, Glubran-2 was used for management of air leak and in another group other routine methods were used for this purpose. Patients in each group were assessed according to their age, sex, location of the lesion, cause of the lesion, air leak and duration of hospitalization. The data were analyzed using the software Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL) software.

Results: All data of the clinical features showed no significant difference among case and control group in patients with chronic empyema at baseline (P>0.05). Alveolar air leak duration and duration of hospitalization were significantly lower in the sealant group compared to the no-sealant group (P< 0.001 and P< 0.01, respectively). Prolonged AAL (PALL) was found in 5 (50.0 %) patients in the case group and 15 (83.3 %) patients in the control group for a total of 20 (50 %) patients. There was no significant difference between the two groups regarding PAAL (P= 0.77).

Conclusion: Our results support the use of Glubran-2 glue for decreasing alveolar air leak and then decreasing duration of hospitalization in the patients who underwent the thoracic surgeries.

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Introduction

Alveolar air leak is a frequent complication after lung surgery and has a rate between 48% and 75%(1).It was shown that more intraoperative air leak is associated with a longer duration of postoperative air leak (2). Inserting a chest tube is a common treatment for air leakage complications; however, it can make the patients stay more in the hospital, immobilized, and suffer more pain. Hence, controlling alveolar air leaks during the operation reduces chest tube used time, hospitalization time, and related morbidities.

Purulent effusion collection in the pleural cavity is called empyema. According to the length of the disease, empyema is categorized into acute and chronic forms. Empyema with a disease duration of more than three months is described as chronic empyema (3). Chronic empyema management includes controlling the infection and diminishing the dead area of the thoracic cavity (4). Bleeding and air leakage are some complications of the interventions on patients with chronic empyema (5).

Glubran-2 (N-butyl-2-cyanoacrylate and methacryloxy sulfolane co-monomer), is a synthetic adhesive agent used topically on tissues in open or laparoscopic surgeries (1, 6). Glubran 2 sealing is widely used; It showed biliostaticability in liver resection (7), it was an effective treatment method for branchial fistula(8), it was an efficient alternative to traditional circumcision methods (9), and also many other applications. Although some studies supported sealant's potential to decrease severity and incidence of alveolar air leakage (1, 10-12), some other did not find any decrease in the incidence of alveolar air leak and suggested further studies (6, 13). Allama et al.'s study showed Glubran 2 efficacy for air leakage on 30 patients. Glubran could significantly reduce the length of hospitalization, tube duration, and air leak duration (10). But, another study on 33 patients achieved no benefits for the length of hospitalization or development of prolonged air leak (PAL), (14).

Herein, we recruited patients with chronic empyema to investigate whether the use of glubran glue as a sealant during lung surgery would lower alveolar air leak and its complication.

Methods

This was a randomized clinical trial study carried out from January 2019 to November 2021. The ethics committee of our institution approved this research, and consent to participate in the study was obtained from each patient.

All patients underwent the lung decortication and pleurectomy with/without pulmonary resection. Entirely, resections were carried out by standard dissection and stapling techniques. 44 individuals were randomly divided into two groups. The intervention group consisted of 22 patients who had been administered synthetic tissue adhesive (Glubran-2), while the control group including 22 patients who had not been received tissue adhesive and routine methods were used for them. In patients assigned to the interventional group, 1 ml of glubran glue was sprayed on the leakage site.

After completing the procedure, the degree of air leak was graded from 1 to 4 according to the scale of Cerfolio Classification of Air Leaks (1, Forced expiratory (FE), if bubbling during forced expiration only, typically when asking the patient to cough, 2, Expiratory (E), if bubbling during Expiratory only, typically with or without coughing, 3, Inspiratory (I), if bubbling during Inspiratory only, typically with or without coughing and 4, Continuous bubbling (C), Continuous bubbling presents in the air leak chamber during both inspiration and expiration). These leaks tend to be large and are more likely to be seen in patients receiving positive-pressure ventilation (Table 1), (15).

Patients in each group were assessed according to their age, sex, location of the lesion, cause of the lesion, air leak, and duration of hospitalization. The data were analyzed using the software Statistical Package for the Social Sciences (SPSS Inc, Chicago, IL) system. Quantitative variables were analyzed using a Student's t test. Qualitative variables were evaluated with the chi- 2 test and Fisher's exact test. A P-value was considered statistically significant when it was less than 0.05.

Results

All data of the clinical features showed no significant difference among case and control group at baseline (P>0.05), (Table 2). Our results showed that 60% of our patients were in grade 1, FE who had bubbling during forced expiration only, typically when asking the patient to cough, 30% of them were in grade 2, E who had bubbling during Expiratory only and 10% of them were in grade 4,C who had continuous bubbling present in the air leak chamber during both inspiration and expiration.

The use of Glubran-2 glue reduced the duration of hospitalization in the case group (5.68 ± 1.96 days) compared to the control group (7.77 ± 2.28 days) (P-Value = 0.002). Glubran-2 glue also reduced alveolar air leaks in the case group (3.81 ± 1.13 days) comparing with the control group (6.13. 1.35 days) (P-Value = 0.0001) (Table 3). PAAL was found in 5 (50.0 %) patients in the case group and 15 (83.3 %) patients in the control group for a total of 20 (50 %) patients. There was no significant difference between the two groups regarding PAAL (P=0.77).

Discussion

Prolonged air leak is among the most severe complications of pulmonary surgery that affects 15% to 18% of patients (16). Various methods have been employed to reduce postoperative air leakage such as local application of sealants. As compared to traditional approaches of stapling or suturing alone, methods like patch, glue, or buttress can prevent the occurrence of prolonged air leak for more than 7 days (17).

Table 1: Cerfolio Classification of Air Leaks

Grade 1, FE	**During forced expiration only, typically when asking the patient to cough**
Grade 2, E	Expiratory only
Grade 3, I	Inspiratory only
Grade 4, C	Continuous bubbling present in the air leak chamber during both inspiration and expiration. These leaks tend to be large and are more likely to be seen in patients receiving positive-pressure ventilation.

Table 2: Clinical features in 2 study groups

Variable		Case N=22	Control N=22	P-value
Age (years)		56.22±10.13	58.77±10.71	**0.423**
Gender, n (%)	Male	17(77.3)	12(54.5)	**0.10**
	Female	5(22.7)	10(45.5)	
Location of the lesion, n (%)	RUL	4(21.1)	2(10.5)	**0.417**
	RML	0(0.0)	2(10.5)	
	RLL	9(47.4)	7(36.8)	
	LUL	1(5.3)	3(15.8)	
	LLL	5(26.3)	5(26.3)	
Cause of the lesion, n (%)	Primary lung cancer	2(9.1)	0(0.0)	**0.387**
	Metastatic cancer	2(9.1)	1(4.5)	
	Benign nodule/miscellaneous	18(81.8)	21(95.5)	
Procedure, n(%)	Resection	1(4.5)	0(0.0)	**0.598**
	Decurtication &Plorectomy	17(77.3)	18(81.8)	
	Decurtication &Plorectomy &Resection	4(18.2)	4(18.2)	
FEV1 = forced expiratory volume in 1 second (% predicted)		1.45±0.16	1.36±0.13	**0.055**

Different kinds of sealants have been utilized, and their efficacy has been proven in relevant literature. The appropriate sealant should be effective, safe, simple to apply, and cost-efficient. In this study, we evaluated the efficiency of Glubran-2 sealant in reducing postoperative air leakage. The results of current study showed that alveolar air leak and hospitalization duration were significantly lower in the sealant group comparing with the no-sealant group in patients with chronic empyema ($P < 0.001$ and $P < 0.01$, respectively).

In terms of the duration of postoperative air leakage, Allama et al., reported that sealant group had significantly shorter duration than control group (3 vs. 5.5 days; P: 0.001) (18). This is in line with the findings of Zaraca et al., (19) (1.6 vs. 5.04 days; P< 0.001), D'Andrilli et al., (20) (3.5 vs. 4.2 days; P: 0.01), Porte et al., (21) (33.7 vs. 63.2 hours; P: 0.013), Fabian et al., (22) (1.1 vs. 3.1 days, P: 0.005), Venuta et al., (23) (5.6 vs. 10 days; P: 0.03), and Lang et al., (24) (1.9 vs. 2.7 days; P: 0.015). Moreover, a systematic review by Tsilimigras et al., demonstrated the effect of BioGlue in reducing postoperative air leak duration (25), and Malapert et al. conducted a meta-analysis and concluded that surgical sealants substantially reduces the chances of a prolonged air leak (16). In contrast, Wong and Goldstraw reported no significant differences in air leak duration between groups (26).

Different studies yielded conflicting findings on the basis of postoperative hospital stay. Venuta et al., (23) (8 vs. 11.6 days), Allen et al., (27) (6 vs. 7 days), Anegg et al., (28) (6.2 vs. 7.7 days), and Allama et al., (18) (5 vs. 6.2 days) reported a significantly shorter stay in the treatment group. On the other hand, Malapert et al. (16) and D'Andrilli et al., (20) noted no significant differences in hospital stay between groups. The Cochrane systematic review investigated at 16 studies with 1642 randomized patients and found that sealants reduced postoperative air leaks, but that this reduction is not necessarily linked to a shorter hospital stay. Besides, they did not suggest the use of surgical sealants in a systematic manner with the goal of decreasing hospital stay (29).

Several studies showed significantly shorter chest tube duration in the treatment group. For example, Allama et al., (18) reported chest tube duration of 6.3 days for no-sealant group and 4.6 for sealant group (P: 0.009). This coincides with the results of Anegg et al., (28) (5.1 vs. 6.3 days), and Fabian et al., (22) (3.5 vs. 5 days). Also, Wong and Goldstraw (26) found that both groups had the same chest tube duration (6days). Regarding chest tube drainage, Allama et al., (18), Fabian et al., (22), and D'Andrilli et al., (20) found no significant differences between sealant and no-sealant group.

Alar et al., included 69 patients who had undergone lobectomy or bilobectomy for lung cancer in their study, and Glubran-2 was utilized in the treatment group and compared to the control group (14). According to their findings, the use of Glubran-2 after lung resection for lung cancer did not reduce the occurrence of prolonged air leak. Moreover, it had no positive impact on length of stay in hospital and hospital costs (14).

Table 3: Clinical outcomes in 2 study groups

Variable		Case N=22	Control N=22	P-value
Duration of hospitalization (Days)		5.68±1.96	7.77±2.28	**0.002**
Alveolar air leaks (AAL), (Days)		3.81±1.13	6.13±1.35	**0.0001**
Prolonged AAL (PAAL), n (%)	Negative	5(50.0)	3(16.7)	**0.77**
	Positive	5(50.0)	15(83.3)	

In an in vivo study on 55 rats, Vakalopoulos et al., (30) performed a laparotomy and established an anastomosis with four interrupted sutures, accompanied with either application of Glubran-2, Omnex, Histoacryl Flexible, or no sealant. They found that Glubran-2 had a high inflammatory response and the highest leakage rate (30). In a similar study, 26 rabbits were evaluated for sealing efficacy in experimental lung incision and partial pulmonary resection. A comparison of Glubran-2 and fibrin sealant revealed that fibrin sealant is preferable to Glubran-2 for the prevention of air leaks and bronchopleural fistulas due to superior degradability and biocompatibility (31).

Conclusion

Our results support the use of Glubran-2 glue for decreasing alveolar air leak and then decreasing duration of hospitalization in the patients who underwent the thoracic surgeries.

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