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ORIGINAL ARTICLE

BIOGLUE: A REVIEW OF THE USE OF THIS NEW SURGICAL ADHESIVE IN THORACIC SURGERY

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Background: Alveolar air leaks and broncho-pleural fistulae after thoracic surgical procedures contribute significantly to hospital morbidity and mortality. BioGlue has offered the thoracic surgeon an alternative to the products presently used to reduce the incidence of these complications. This retrospective study reviews our experience with this new adhesive.

Methods: Forty patients upon whom BioGlue was used were identified through operation records. Pre-, intra- and postoperative data were collected to establish use, indications and outcome.

Results: The predominant underlying pathology was malignancy. In 32 patients BioGlue was used during the primary procedure while in the remaining eight, persistent air- or lymph-leak led to a further procedure requiring the use of glue. The indications for BioGlue use were alveolar air leak (36), broncho-pleural fistula (2) and lymph leak (2). There was one death. In 35 out of 36 patients with alveolar air leak, BioGlue controlled the leak at the site of application.

Conclusions: Our results in this particular patient group indicate that BioGlue is a reliable adjunct in the reduction of alveolar air leaks. Although further studies are necessary to establish the role of BioGlue in thoracic surgery in comparison to other sealants, these initial results are promising.

Key words: BioGlue, surgical adhesive, thoracic surgery.

INTRODUCTION

Alveolar air leaks and broncho-pleural fistulae after thoracic surgical procedures represent major complications and contribute significantly to morbidity and mortality. Consequences are longer pleural drainage and hospital stay and hence increased costs.[1–4] Inadequate postoperative pain control and persistent air leaks have been identified as the most common causes of delayed discharge from hospital.[5]

Prolonged air leaks, lasting 7 days or more, are reported to occur in up to 15% of patients[6] and may require further intervention such as the placement of additional intercostals drains, pleurodesis or re-thoracotomy.[7,8]

Several strategies have been employed with variable success to reduce the incidence of and to treat prolonged alveolar air leaks following thoracic surgery. These include the use of adhesives such as fibrin glue, gelatin-resorcinol-formaldehyde glue and more recently, a synthetic surgical lung sealant.[9–11] BioGlue (CryoLife International Inc, Kennesaw, GA) is a new surgical adhesive that is used in a number of surgical specialties and a small number of experimental studies have been published evaluating the use of this new adhesive in thoracic surgery.

BioGlue consists of a 10% glutaraldehyde and 45% bovine serum albumin solution; it is applied with a reusable, sterile, double-barrelled gun, loaded with a prefilled dual cartridge attached to a single nozzle where mixing of the two components occurs during delivery. The exposure of the bovine albumin, extracellular matrix and cell surfaces to the glutaraldehyde component causes their lysine molecules to bind to each other, creating a strong scaffold. Polymerization starts to occur immediately and 65% of its final binding power is achieved within 2 min and the maximum power is obtained within 3 min, regardless of the surrounding temperature. The cost of a 5 mL cartridge is approximately $US250 and in our experience one cartridge is sufficient for almost all procedures.

At the time of initiation of this retrospective study, a Medline search revealed that there are so far only experimental studies or case reports that evaluate the role of this new adhesive in thoracic surgery, particularly for the control of alveolar air leaks.[12,13] We believe this study to be the first to review clinical experience with BioGlue in a series of patients in thoracic surgery.

In Australia, the Therapeutic Goods Administration (Canberra, ACT) approved the use of BioGlue in thoracic surgery and indeed in all other surgical specialties in February 2001. Prior to this, permission for its use was obtained on an individual basis (individual patient use (IPU)).

METHODS

With this retrospective study we reviewed our initial experience with the use of BioGlue for the control of alveolar air leaks in a series of 36 patients undergoing thoracic surgical procedures. We also present four cases in which BioGlue was used for other purposes (e.g. control of broncho-pleural fistulae (two) and lymph leaks (two)).

Patients were identified by our operative records. Data collected included: gender, age, comorbidities, indications for surgery, procedures performed, postoperative course and complications. The period of the study was from September 1998 to March 2001. During the same time a total of 645 thoracic surgical procedures were carried out, which highlights the selective use of BioGlue during this initial evaluation phase. The decision to use

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BioGlue was made by the surgeon at the time of operation after conventional attempts (e.g. lung sutures or staples) had failed to control the leak sufficiently.

Of the 36 patients with alveolar air leak, 27 were male and nine female (age range 1 month to 83 years). The predominant underlying pathology leading to operation was malignancy of either lung (16) or pleura (one) as shown in Table 1. A past history of chronic obstructive pulmonary disease or significant smoking (greater 20 pack-years) was present in 25 patients, one patient had cystic fibrosis.

The surgical procedures carried out are illustrated in Table 2 and included partial lung resection in the form of lobectomy (10) or wedge/segment resection (eight).

In two patients BioGlue was used in an attempt to treat a persistent lymph leak. One patient, a 19-year-old female, had a haemangio-lymphoma. The other patient, a 73-year-old male, was diagnosed with advanced lung cancer with chest wall involvement who developed the lymph leak after lobectomy with chest wall resection.

Of the two patients with broncho-pleural fistulae, a 56-year-old male underwent pneumonectomy for advanced bronchogenic carcinoma. BioGlue was applied to the bronchial stump after sutures failed to control a large air leak. The other patient, a male aged 54 years, had developed a chronic (more than 12 months) fistula following pleuro-pneumonectomy for advanced mesothelioma. An attempt was made to seal this fistula with BioGlue bronchoscopically via a Swan–Ganz catheter.

Table 1. Pathology leading to operation (n = 36)

Malignancy	
Pulmonary	16
Pleural	1
Chronic obstructive lung disease/emphysema	4
Pneumothorax (recurrent or persistent despite drainage)	7
Benign lung tumour	1
Lung abscess	1
Metastatic thymoma	1
Empyema	1
Congenital cystic adenomatoid malformation of right lower lobe	1
Lung injury during OHS	3

OHS, open heart surgery.

Table 2. Surgical procedure (n = 36)

Lobectomy	10
Pleurodesis	6
Segment/wedge resection	8
Lung volume reduction surgery	4
Repair of inadvertent lung injury during OHS	3
Drainage of pleural effusion	2
Pleural biopsy	1
Lung biopsy	1
Excision of mediastinal tumour	1

OHS, open heart surgery.

RESULTS

Patient group treated for alveolar air leaks

In 30 patients BioGlue was utilized during a primary procedure. In the remaining six, persistent air leak after a primary operation without the use of BioGlue required a further intervention in which BioGlue was used. The mean time from primary procedure to re-intervention was 7.7 days (range 1–21 days). The mean duration of pleural drainage with intercostals catheters was 4 days and the mean hospital stay 10 days (range 1–78 days).

There was one death. Two patients required reintervention for persistent alveolar air leak following the use of BioGlue. The first patient, a 59-year-old man, with severe chronic obstructive pulmonary disease had persistent air leaks after bilateral lung volume reduction surgery and was returned to the operating room on the second postoperative day. Multiple alveolar air leaks were identified on both sides, including leaks from staple lines where BioGlue had been applied during the primary procedure. Despite revision and further application of BioGlue the air leaks continued.

The patient subsequently developed empyema and died from respiratory failure on the 19th postoperative day. This case was also the only case in our series in which BioGlue failed to seal an alveolar air leak.

One further patient required reintervention for continuing air leak. This patient was initially planned for bilateral lung volume reduction surgery. During the primary procedure BioGlue was used on the right side for air leak from the posterior part of the staple line of the right *upper* lobe. The procedure on the left had to be abandoned because of severe adhesions. Postoperatively there was large air leakage from the right side and the patient was returned to the operating room on the fourth postoperative day. A tear in the right *lower* lobe was identified, distant from the staple line where BioGlue had been applied during the initial operation and this was sealed with fibrin glue on this occasion. However, the air leak persisted and a further operation was necessary on the 11th postoperative day. The air leak was found at the site of fibrin glue application and was finally sealed with BioGlue. Three days later the intercostal catheter was successfully removed.

In addition to the above-mentioned patient who subsequently died, there was one further patient who developed empyema postoperatively after right upper lobectomy for pulmonary malignancy. This 69-year-old man was discharged with an intercostal catheter with a Heimlich valve on postoperative day 13 and 1 month later this was removed uneventfully.

Two patients developed pneumonia postoperatively. One of these was treated with i.v. antibiotics for 5 days and was discharged on day 14. The other patient, a 55-year-old woman was discharged on day 7 after an initially uneventful recovery from right upper lobectomy for malignancy. However, she was admitted to and subsequently transferred from a peripheral hospital 1 week after discharge with severe bilateral bronchopneumonia. This was complicated by septic shock and the patient required intubation and inotropic support. This patient eventually made a good recovery after a prolonged and complicated course and was discharged 3 months after readmission.

Three patients required drainage of a pleural effusion. One of those had a recollection after initial thoracotomy for decortication and drainage of an empyema and this was evacuated during a rethoracotomy on postoperative day 9. The other two patients had an intercostal catheter insertion and a needle aspiration, respectively, during which haemoserous fluid was drained.

Patients treated for lymph leak

The patient with haemangio-lymphoma initially underwent video assisted thoracoscopy for pleurodesis but went on to have open drainage of a chylothorax with application of BioGlue to the major leak. Despite that, lymph leakage continued and subsequently pleurectomy was performed 3 months after the first operation. A specimen of BioGlue was sent for histological examination during this procedure and revealed colloid-like eosinophilic material with a small number of macrophages without significant inflammatory reaction. The patient continued to have recurrent chylothoraces and eventually underwent radiotherapy.

The second patient underwent lobectomy with partial resection of ribs 1–4. This patient postoperatively developed significant lymph-leakage and was taken back to the operating room on the 7th postoperative day. BioGlue was applied to the site of leakage. Four days after the procedure, the intercostal catheter was removed without further evidence of recurrence.

Patients with broncho-pleural fistula

One of these two patients underwent pneumonectomy for lung malignancy and during the initial operation a large air leak was present at the oversewn stump. BioGlue was applied with satisfactory result intraoperatively. On the 2nd postoperative day his intercostal catheter was uneventfully removed.

The other patient was 12 months post pleuro-pneumonectomy and had developed a chronic broncho-pleural fistula. Eventually an attempt was made to seal the leak with the application of BioGlue via a Swan–Ganz catheter during bronchoscopy. This, however, was unsuccessful and the leak continued.

DISCUSSION

Persistent air leaks after thoracic procedures remain an important issue despite numerous strategies used to reduce the incidence of this complication. Surgical adhesives have been used for a number of years. New products continue to appear and their usefulness requires evaluation. BioGlue has been utilized in various surgical specialties and is regarded as safe for use in humans.[14]At our institution BioGlue was introduced in 1998 and in this series we reviewed our initial experience.

Our results indicate that BioGlue is a useful adjunct in the treatment or prevention of alveolar air leaks following thoracic procedures. As mentioned in the introduction, the use of BioGlue has been very selective in that we only used BioGlue after standard, well tried conservative measures were deemed unsuccessful.

In 35 out of 36 patients alveolar air leaks were controlled at the site of application of BioGlue. To reliably assess the duration of postoperative air leak we used the duration of pleural drainage with intercostal catheters. With this we aimed to overestimate rather than underestimate the duration of air leakage as patients records seemed to be unreliable in terms of last documented air leak.

Wain *et al*.[15] found no significant difference in the duration of pleural drainage in their series comparing patients with and without the use of surgical lung sealant. This mean duration was similar to the one observed in our series. They did, however, find a significantly shorter mean time from skin closure to last observed air leak in the group treated with surgical lung sealant. Similar results have been reported by Porte *et al*.,[11] reviewing the same product. In both of these published studies there was no significant difference in the mean hospital stay between treatment groups and controls.

Fleisher *et al*.[16] revealed no significant difference between patients treated with fibrin glue and a control in terms of mean air leak duration, chest tube drainage and hospitalization. Our figures seem to compare favourably with this report. The occurrence of adverse events such as empyema, pneumonia and pleural effusions was similar in this study to the reports by these authors.

The small number of patients in whom BioGlue was used for broncho-pleural fistulae and lymph leakage limits conclusions about the place of BioGlue for these conditions.

We realize that our series can only be a preliminary review and that the effect of BioGlue on duration of air leakage and hospitalization will need to be evaluated in a randomized trial, similar to the ones undertaken by Wain *et al*. and Porte *et al*. for surgical lung sealant.[11,15] Our patient group may not be entirely representative as BioGlue was used firstly for patients where other means of dealing with air leaks had been unsuccessful or secondly for patients who already had persistent leak after the initial procedure. Technical refinements with the application of BioGlue may expand its indications and successful outcomes. In patients with broncho-pleural fistulae, the gluing of biological patch material over the bronchial stump may be beneficial.[13]

In conclusion, all our surgeons regarded BioGlue as a useful adjunct when dealing with air leaks especially for the emphysematous lung. Preparations for a randomized trial are being made to evaluate the influence of BioGlue on the duration of air leak, pleural drainage and hospital stay compared with that of a control group.

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