Tolerability of Broncho-Alveolar Lavage in Ventilated Patients with Acute Lung Injury

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Abstract: Broncho-alveolar lavage (BAL) is an important diagnostic tool in many areas of thoracic medicine. On the intensive care unit (ICU), BAL is often required for a variety of indications, including assessment of possible ventilator-associated pneumonia (VAP). Recent data suggest BAL may be superior to less invasive techniques in the assessment of VAP. Older studies have highlighted potential concerns over the safety of BAL in ICU patients but this has not been confirmed in more recent studies in patients with acute respiratory distress syndrome (ARDS). This prospective cohort study aimed to clarify the tolerability of BAL in 162 ventilated ICU patients with ARDS and possible VAP.

BAL was tolerated very well with only 2 patients (1.2%) demonstrating a mild desaturation (fall of 6% in oxygen saturation) due to 1 episode of bronchospasm and secretion retention respectively which were resolved quickly. No major complications or deaths occurred and BAL samples were obtained for microbial analysis in all patients. We conclude BAL is well tolerated in carefully selected and prepared ventilated ICU patients with ARDS in whom VAP is being considered. Further large scale controlled studies comparing BAL to less invasive techniques are indicated in this cohort.

Keywords: Broncho-alveolar lavage, acute respiratory distress syndrome, safety, acute lung injury, intensive care.

INTRODUCTION

Broncho-alveolar lavage (BAL) is an essential diagnostic tool in many areas of thoracic medicine including the assessment of lung infection, parenchymal disease, neoplastic disease, airways disease and as a research tool. On the intensive care unit (ICU), BAL is often required in the assessment of infiltrative lung disease especially in evaluation for possible ventilator-associated pneumonia (VAP) [1]. Ventilator-associated pneumonia (VAP) has a significant morbidity and mortality as well as the healthcare costs and implications of prolonged hospitalisation. In one observational study, mortality due to VAP was calculated at 33-50%, prolonging hospital admission by 7-9 days and occurring in 20-30% of patient after 48 hours in ICU on a ventilator [2,3]. VAP can also be difficult to diagnose due to the myriad non-infective causes of chest radiograph (CXR) infiltrates in ventilated ICU patients, tissue being the gold standard method of diagnosis which is often not possible [4,5].

Due to the difficulty getting histology, BAL has been evaluated as an alternative technique in the diagnosis of VAP as well the less invasive techniques such as endotracheal aspirates (ETA). Studies conflict as to what is the superior diagnostic technique in VAP. There are 5 randomised controlled trials. Fagon *et al*. demonstrated the superiority of BAL over noninvasive strategies in 413 patients in a multicentre randomised study demonstrating reduced mortality, organ failure and antibiotic use (but not diagnostic yield), using non-quantitative ETA [6]. The following 4 randomised studies have not supported these findings. Sanchez-Nieto *et al*. found no difference in a single centre study of 51 patients between BAL and quantitative ETA in mortality, duration of ICU stay and period of ventilation, although more frequent antibiotic changes occurred in the BAL group [7]. Sole Violan *et al*. detected no difference in ICU stay or period of ventilation but BAL resulted in more frequent de-escalation of antibiotic therapy in a single centre study of 91 patients, although the BAL group included no-BAL techniques [8]. Ruiz *et al*. noted no difference in mortality, length of stay and period of ventilation in a single centre study of 76 antibiotic-naïve patients [9]. The recent Canadian Critical Care Trials Group multi-centre randomised controlled trial of 740 patients found no advantage for BAL over ETA in mortality or antibiotic use [10]. A variety of non-randomised studies have also evaluated BAL in VAP. We have previously reported the utility of quantitative BAL over endotracheal aspirates in VAP with superior diagnostic yield, more frequent impact on antibiotic therapy (usually de-escalation) and greater diagnostic sensitivity [11].

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There are conflicting studies regarding the safety of BAL in ventilated ICU patients with ARDS. According to recent updated national guidelines from the British Thoracic Society [12], BAL can be of utility in the diagnosis of VAP when appropriate precautions are taken, even in acute respiratory distress syndrome (ARDS), the most extreme form of acute lung injury [13]. However, during BAL in a non-ventilated patient, the standard 5.7mm bronchoscope only occupies 10-15 % of the tracheal cross-sectional area whereas in the intubated patient, it occupies 66% of a 7mm endotracheal tube (ETT) and 40% of a 9mm ETT. Therefore, some desaturation during BAL is expected. Moreover, there are also previous reports of acute changes in haemodynamic status, significant desaturation and even cardiac arrest [14]. Other studies have demonstrated safety of BAL in ARDS [15, 16].

The aim of this prospective cohort study aimed to evaluate the tolerability of BAL in 162 ventilated ICU patients with ARDS and possible VAP undergoing BAL in ICU to obtain microbiological samples.

METHODS

The Southmead Hospital Ethics Committee approved this single centre prospective study which was conducted in a 800 bedded teaching hospital in South West England, United Kingdom with a single centre 8 bedded ICU receiving particularly medical (respiratory, cardiac, renal and haematological) and surgical (urology, general surgery, orthopaedic, vascular surgery) patients. 162 ventilated patients with ARDS in the Intensive Care Unit (ICU) according to the 1994 consensus definition [17] were bronchoscoped in the ICU with BAL between 2003 and 2007. Patients were not recruited more than once. Patients were ventilated for at least 48 hours, antibiotic naïve or off antibiotics for at least 72 hours. BAL was undertaken with authorisation from the responsible intensive care physician and next of kin.

Inclusion criteria were unexplained infiltrative lung disease where VAP was a diagnostic possibility. Exclusion criteria included acute myocardial infarction, unstable angina or life-threatening cardiac arrhythmias, worsening asthma or status asthmaticus, severe pulmonary hypertension, coagulopathy and bleeding diatheses (platelets < 50 or INR > 1.4), severe uraemia, lung abscess and severe debilitation.

VAP was defined by the presence of new/progressive CXR infiltrates without other obvious cause in patients mechanically ventilated for > 4 days in the ICU, and at least two of: temperature ≥ 38 or ≤ 35^{o}C, white cell count ≥ 12 or ≤ 4 x 10^{9}/l, purulent tracheobronchial secretions, with increasing oxygen requirements, computed tomography (CT) evidence of a rapidly cavitating infiltrate, positive pleural fluid culture and/or histological evidence of neutrophilic alveolitis, bronchiolitis and consolidation [9].

All BAL procedures were performed as previously described by one respiratory physician (AM) [16]. Patients were pre-oxygenated with 100% oxygen and sedated with/without paralysis prior to BAL. During BAL, continuous oximetry, haemodynamic monitoring and ECG recording was undertaken for 4 hours. 100% oxygen was administered post-BAL as necessary. Demographic data, ICU severity scores (APACHE2, APACHE3 and SAPS2) and oxygenation index were collected. Patients were monitored for 4 hours post-BAL for complications. The minimum ETT diameter was 8mm (maximum 9mm).

Basic statistical analysis was performed using GraphPad Prism version 5 software (San Diego, California) to determine the data were normal using a normality test and then calculate mean and standard error for ICU severity scores, mean age.

RESULTS

All 162 patients were enrolled and included in the study. Baseline demographic data, ICU severity scores and oxygenation index for the 162 patients are shown in Table **1**. Baseline scores indicated a degree of physiological perturbation and impairment of oxygenation as to be expected in a cohort of ventilated patients in ICU with possible lung-related sepsis. There was a male preponderance (56%).

Table 1: Summarising Baseline Demographic, ICU Severity Score Data

Parameter	Number
Number in study	162
Age (mean)	60.9
Male (%)	90 (56)
APACHE2 (mean, se)	19.7 (0.69)
SAPS2 (mean, se)	45.1 (1.26)
APACHE3 (mean, se)	72.5 (2.3)
Oxygenation index (PaO2:FiO2) (kPa)	18.9 (6.01)

There was no BAL-attributable mortality and no major complications occurred in relation to BAL. Two

minor complications occurred (see Table **2**): 2 minor episodes of desaturation (fall in SpO2 of 6%) occurred both at 2 hours post-BAL, ie) a minor complication rate of 1.2%. The complications were due to 1 episode of bronchospasm requiring nebulised bronchodilators and 1 episode of secretion retention requiring suctioning. No associated significant haemodynamic alterations occurred. BAL samples for quantitative microbiological analysis were obtained in all cases. In 98.8% of patients (160), BAL was performed without complication.

Table 2: Summarising Frequency of Complications Due to BAL Experienced

Complications	Number (%)
Mortality/major complications	0 (0)
Minor complications	2 (1.2)*
No complications	160 (98.8)

*Desaturated > 6% at 2hours due to secretion retention and bronchospasm.

DISCUSSION

BAL is an essential diagnostic tool in the investigation of infiltrative lung disease and has diagnostic utility in VAP [1, 11, 12]. Although some earlier studies are conflicting with regard to safety issues in ARDS [14, 15, 17], our study supports Steinberg *et al*. and Medford *et al*. [15, 16] that bronchoscopy with BAL in ventilated ARDS patients in intensive care (even with extreme hypoxaemia as above) is safe provided essential precautions are taken. Essential precautions are summarised in Table **3** but include strict patient selection (please see methods for exclusion criteria) and haemodynamic stability of the patient prior to BAL, pre-oxygenation, an ETT of sufficient diameter (at least 8mm) and adequate sedation/paralysis with appropriate oxygenation and monitoring post-BAL, especially in the first 2 hours.

This single centre prospective study suggests that with careful patient selection, BAL can be performed safely in patients with ARDS and yield samples for quantitative microbiological analysis. Whilst there is a move to less invasive techniques such as non-bronchoscopic lavage [18], we feel there will continue to be a place for bronchoscopy in ICU and this study adds to the data suggesting that this technique can be performed and is well tolerated in this patient group. Further studies are required to further compare semi-quantitative less invasive techniques with BAL in this patient group to give further clarity on diagnostic approach.

CONTRIBUTORSHIP STATEMENT

ARM performed the practical procedures, ABM and ARM were involved in conceiving the study, the analysis and the manuscript.

Table 3: Summarising Recommended Essential Precautions Before Undertaking BAL

Essential precautions	Detail
Patient selection	General: No severe debilitation
	Cardiovascular: No recent myocardial infarction, unstable angina, life-threatening cardiac arrhythmias
	Respiratory: No unstable asthma, lung abscess, severe pulmonary hypertension
	Haematological: No coagulopathy, bleeding diatheses (platelets < 50 or INR > 1.4)
	Renal: No severe uraemia
Haemodynamically Stable	Heart rate < 110, systolic blood pressure >90, oxygen saturation <85% or respiratory rate >30, stable Glasgow Coma Scale
Pre-oxygenation	100% oxygen administered for 1-2 minutes prior to BAL
Adequate ETT	ETT (or tracheostomy tube) size 8-9mm
Adequate sedation/paralysis	Sedation with/without paralysis at discretion of supervising Consultant Intensivist before/during BAL to minimise physiological disturbance
Intra-BAL and Post-BAL care	During BAL and for the next 4 hours: Supplemental oxygenation to keep saturations within target range, other monitoring including resp rate, heart rate, intra-arterial blood pressure and ECG monitoring

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