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Changes in pulmonary mechanics after fiberoptic bronchoalveolar lavage in mechanically ventilated patients

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Abstract *Objective:* We prospectively assessed the impact of bronchoalveolar lavage (BAL) on respiratory mechanics in critically ill, mechanically ventilated patients. *Study design*: Mechanically ventilated patients underwent BAL of one lung segment using 5×20 ml of sterile, physiologic saline with a temperature of 25–28 °C. The fractional inspired oxygen was increased to 1.0, but ventilator settings were otherwise left unchanged. Static pulmonary compliance, pulmonary resistance, alveolar ventilation, and serial dead space were measured 60 min and 2 min before and 8, 60, and 180 min after BAL to assess the consequences of the procedure. In addition, blood gases [partial pressure of carbon dioxide in arterial blood ($PaCO_2$) and arterial oxigen tension (PaO_2)], hemodynamic variables (heart rate, systolic and diastolic blood pressure), and body temperature were recorded at the same time points.
Setting: Intensive care unit of a university hospital.

Patients: 18 consecutive critically ill, mechanically ventilated patients. *Results*: Pulmonary compliance decreased by 23 % ($p < 0.05$) and pulmonary resistance increased by 22 % ($p < 0.05$) shortly after BAL. The changes in pulmonary compliance and resistance were more than 30 % in one third of the patient population. One hour after the procedure, PaO_2 was significantly lower and $PaCO_2$ significantly higher than before the procedure. Three hours after the procedure, pulmonary resistance returned to pre-BAL values but compliance remained 10 % below baseline values ($p < 0.05$).
Conclusion: BAL in mechanically ventilated patients is associated with deterioration of pulmonary mechanics and function.

Key words BAL · Bronchoalveolar lavage · Pulmonary mechanics · Pulmonary compliance · Pulmonary resistance · Mechanical ventilation · Respiratory function · Intensive care

Introduction

Bronchoalveolar lavage (BAL) is a widely used diagnostic and therapeutic technique in clinical practice. BAL in normal volunteers is reported to be safe and does not lead to measurable changes in pulmonary function parameters [1]. Most reports on BAL in critically ill, mechanically ventilated patients indicate that is usu-ally well tolerated [2–4]. However, individual patients may suffer from serious side effects such as prolonged oxygen desaturation [2, 3, 5, 6]. In one report, in which the side effects of BAL were evaluated in 107 critically ill, ventilated patients, hypoxemia was reported in 14 cases 10 min after the procedure. Moreover, reductions in arterial oxygen tension (PaO_2) have been reported to persist in some patients for 4 h and more after the

procedure [2]. The reason for the deterioration in oxygenation after BAL may be inherent in factors such as the sedation and relaxation regimen during the procedure [1], the amount and temperature of BAL fluid used [7, 8], and the underlying disease [1]. However, BAL may also induce changes in pulmonary mechanics, details of which are lacking in the literature. We therefore studied the effects of BAL on pulmonary mechanics and function in critically ill, mechanically ventilated patients.

Materials and methods

Study population

After obtaining approval from the ethics committee at the University of Jena and informed consent from patients or next-of-kin, 18 consecutive intensive care patients undergoing mechanical ventilation were prospectively studied. Heart rate, arterial blood pressure, and body temperature were recorded continuously in all patients. Patients were hemodynamically stable without inotropic or vasopressor agents. Pressure–controlled ventilation with a positive end–expiratory pressure (PEEP) of 5 to 8 cmH_2O (median 5) was used in all cases. All patients required fiberoptic BAL for microbiologic diagnosis of a suspected nosocomial pneumonia. Patients with hemodynamic instability and patients with evidence of lobar atelectasis were excluded from the study. Patients were sedated with individual doses of fentanyl and droperidol and were paralyzed with pipecuronium (0.1 mg/kg initially and 0.015 mg/kg hourly in repeated doses) to eliminate any influence of respiratory muscle activity on pulmonary compliance (C_{tot}) during the study period.

Protocol

BAL was performed by the same physician in all patients. The fiberoptic bronchoscope (Olympus BF 10, external diameter of 5.2 mm, Olympus Optical, Tokyo, Japan), was inserted into the endotracheal tube (≥ 8.5 mm i.d.) through an adapter. During BAL, the fractional inspired oxygen concentration (FIO_2) was increased to 1.0, but ventilator settings were otherwise left unchanged. The tip of the bronchoscope was wedged into the orifice of a radiographically or bronchoscopically suspect lung segment (lower lobe segments 8–10) and five aliquots of 20 ml sterile, physiologic saline with temperatures between 25 and 28 °C were instilled and gently suctioned.

Measurements

To evaluate the mechanical properties of the lung we used a previously described [9] analyzer configuration (Hamilton Bonaduz AG, Bonaduz, Switzerland). Airway flow (F_{aw}) was measured with a Lillytype pneumotachograph (Jaeger Baby PT), which was connected to a ± 150-cmH_2O differential pressure transducer (Miro Switch, Freeport, Il., USA). The same transducer was used to measure airway pressure. The pneumotachograph was placed between the endotracheal tube and the Y-piece of the ventilator circuit. End-tidal CO_2 concentration was measured by a modified mainstream analyzer (Novametrix Model 1260, Novametrix, Wallingford, Conn., USA). The modification was done to decrease the rising time of the instrument (10–90 %) down to 40 ms. The

Table 1 Patient characteristics. Values are median (range) (*FIO₂* fractional inspired oxygen, *PaO₂* arterial oxygen tension)

Age (years)	41 (24–71)
Male/female	14/4
Weight (kg)	75 (60–100)
Reason for admission to ICU:	
Multiple trauma	10[a]
Neurosurgerical procedure	3
Abdominal surgery	3
Other	2
FIO_2 before BAL	0.4 (0.3–0.5)
PaO_2/FIO_2 (mm Hg) before BAL	260 (142–438)
Preexisting lung disease	2[b]

[a] Seven of the 10 patients with multiple trauma had evidence of thoracic trauma
[b] Two patients (2 and 7 in Table 2) had indications of a long smoking history and obstructive lung disease

dead space of the sensor head, including CO_2 analyzing cuvette, was less than 15 ml. All signals were low pass filtered with a second order Bessel filter (cut off frequency 25 Hz). Measurement signals were read into a personal computer by means of an analog-digital converter (DT2801-A, Data Translation, Marlborough, Mass., USA) at a rate of 60 samples per s and per channel. The flow signal was corrected for changes in gas composition and gas temperature. The pressure channels were calibrated by a water manometer. The F_{aw} channel was calibrated by a syringe (1550 ml), using the time integral of flow after delivering the calibration volume [10].

C_{tot}, total lung resistance (R_{tot}), serial dead space (V_{ds}), and expiratory tidal volume (V_t) were recorded by means of calculated, computerized breath-by-breath analysis. The calculation of C_{tot} and R_{tot} was performed by the least square fit method [11]. V_{ds} was estimated by numerical analysis of mixed air range from the main stream capnogram (Novametrix M1260). V_a was defined as the difference between expiratory volume and V_{ds} [10, 11]. Respiratory data sampling took place 60 (t-60) and 2 (t0) min before, and 8 (t8), 60 (t60), and 180 (t180) min after BAL. Medians of five successive breath–by–breath values were used as samples of time steps. Blood gas and hemodynamic variables were recorded 2 min before, and 8, 60, and 180 min after the procedure.

Statistical analysis

Values are expressed as the mean ± standard error of the mean (SEM). Using the Statistical Package for the Social Sciences, a repeated measures analysis of variance was used to compare the means of R_{tot}, C_{tot}, V_{ds}, and V_a at the different time points. Multiple Wilcoxon signed ranks tests were used to compare data pairs. A Bonferroni correction was applied to multiple comparisons [12]. A Spearman correlation was used to study the relationship between changes in pulmonary mechanics and changes in oxygenation.

Results

Important patient data are presented in Table 1 and changes in respiratory parameters are shown in Fig. 1. There were no significant differences in parameters be-
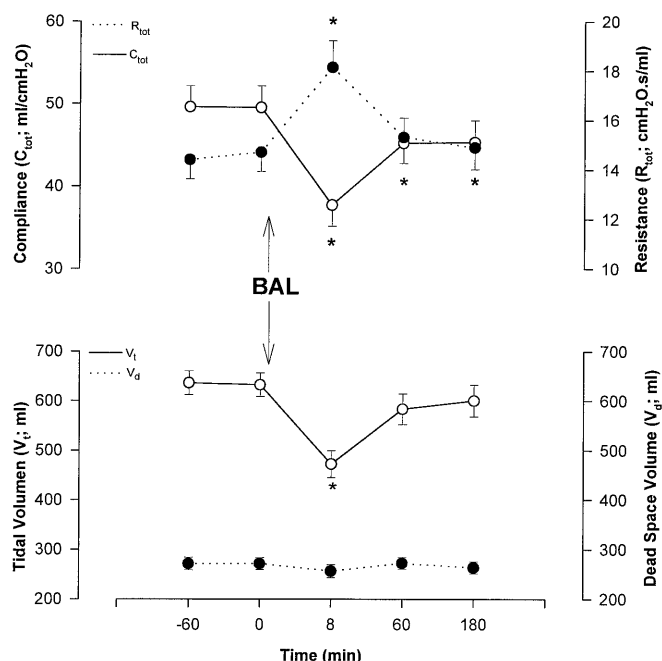
Fig. 1 Effects (mean ± SEM) of bronchoalveolar lavage BAL on total compliance C_{tot}, total resistance R_{tot}, tidal volume V_t, and dead space volume V_d are shown from 60 min before to 180 min after BAL. * $p < 0.05$ compared to –60 min

Table 2 Effects of BAL on compliance C_{tot} and resistance R_{tot} in individual patients

Patient no	C_{tot} (ml/cmH₂O)				R_{tot} (cmH₂O.s/ml)			
	t0[a]	t8	t60	t180	t0	t8	t60	t180
1	65	41	54	55	10	15.5	10	9
2	26	12	21	22	24	31	25.5	25
3	53	41	50	49	13	17	14	13
4	42	38	46	36	15	16	13	17
5	25	26	26	24	17	17	17	17
6	45	40	43	44	15	15	15	14
7	37	29	35	36	20	23	19	20
8	59	48	55	56	14	14	14	14
9	42	27	37	37	19	19	18	17
10	50	31	43	44	14	23	15	15
11	51	37	42	44	12	15	14	12
12	52	47	49	49	12	13	12	11
13	47	26	39	42	14	23	17	16
14	58	46	56	57	14	14	13	13
15	57	45	54	57	14	17	15.5	14
16	59	54	55	56	13	15	17	15
17	47	34	42	39	18	25	19	20
18	40	27	34	34	15	25	16	15

[a] t0 = before BAL, t8, t60, and t180 = 8, 60, and 180 min after BAL

Table 3 Effects of BAL on cardiorespiratory parameters (*PaCo₂* arterial carbon dioxide tension, (*HR* heart rate, *SAP, DAP* systolic and diastolic arterial blood pressure)

Time (min)	PaCO₂ (mmHg)	PaO₂ (mmHg)	HR (/min)	SAP (mmHg)	DAP (mmHg)
t0[a]	34 ± 1	109 ± 10	104 ± 5	124 ± 5	64 ± 4
BAL					
t8	44 ± 1*	(153 ± 25)[a]	106 ± 4	148 ± 7*	76 ± 4*
t60	38 ± 2*	91 ± 9*	107 ± 5	123 ± 7	66 ± 4
t180	37 ± 4	106 ± 16	107 ± 4	127 ± 6	65 ± 4

* $p < 0.05$ compared to t0
[a] $FIO_2 = 1.0$ shortly before this measurement

tween t-60 and t-0. Therefore, a steady state of pulmonary function before beginning BAL can be assumed. The BAL procedure lasted approximately 5–6 min. Pulmonary compliance decreased by 23.5 % ($p < 0.05$) 8 min after BAL and was still significantly below baseline values 60 and 180 min later. Conversely, pulmonary resistance increased by 21.8 % ($p < 0.05$) at 8 min but returned to pre-BAL values 60 min later. In six patients, pulmonary compliance decreased and pulmonary resistance increased by more than 30 %. V_a decreased significantly by almost 25 % after BAL but returned to near baseline values at the end of the observation period (t180). No changes in (V_{ds}) were observed.

Patients did not react uniformly to BAL (Table 2). In some patients pulmonary C_{tot} decreased dramatically (56 % in patient 2) whereas R_{tot} values were far less affected by BAL. In others, R_{tot} was more affected than C_{tot} (patient 18). In a few patients (patient 5, for example), neither C_{tot} nor R_{tot} values were affected or improved after BAL. Nor did the values achieved before BAL correlate with the subsequent changes in these parameters.

In accordance with the decline in alveolar ventilation, arterial CO_2 ($PaCO_2$) increased after BAL (Table 3). One hour after the procedure, $PaCO_2$ was significantly higher and PaO_2 significantly lower than at baseline (identical FIO_2). Changes in PaO_2 60 min after BAL show a stronger correlation with changes in R_{tot}

at 8 min ($r = 0.67$, $p < 0.01$) than with changes in C_{tot} at 8 min ($r = 0.48$, $p < 0.06$). Due to administration of 100 % oxygen during BAL, values obtained at 8 min do not reflect an improved gas exchange.

Except for a small but significant increase in systolic and diastolic arterial blood pressure at t-8, hemodynamic variables remained unchanged (Table 3). Only one patient experienced a sustained drop in arterial blood pressure (systolic 80 mmHg). No arrhythmias, bleeding episodes, changes in body temperature, or pneumothoraces occurred.

Discussion

Although the use of BAL has increased during the last few years, only a few studies have focused on the possi-

ble adverse effects it may have on pulmonary mechanics [2–4]. In a group of 18 critically ill, mechanically ventilated patients, we found significant deterioration in pulmonary mechanics after BAL with a small amount of saline. Immediately after completion of the procedure, pulmonary R_{tot} increased and pulmonary C_{tot} decreased as compared to baseline values. C_{tot} was still significantly below baseline values 60 and 180 min later, whereas R_{tot} returned to pre-BAL values 60 min later. The deterioration in pulmonary mechanics led to decreases in PaO_2 and increases in $PaCO_2$.

Increases in R_{tot} in response to BAL have been reported in several studies performed in spontaneously breathing subjects[7, 13]. The transient character of the obstructive ventilatory changes seen in our study is in keeping with findings in spontaneously breathing patients [4, 7, 13]. In response to BAL, one study [7] found evidence of obstructive ventilatory changes at mid-flow with an insignificant reduction in forced expiratory volume in 1 s (FEV_1) and FEV_1/FVC (forced vital capacity). Others report decreases in FVC and FEV_1 in both asthmatics and control subjects in response to BAL [14]. There are several possible mechanisms to account for the increased airway obstruction following BAL. Some of these changes are attributed to bronchoscopy as such [15, 16] and include mucosal edema of large airways caused by local trauma by the fiberoptic bronchoscope itself, and vagally mediated reflex bronchospasm, which can be prevented by atropine [17]. However, the more severe challenge to the airways caused by lavage may not be mitigated by atropine [18].

In our study population C_{tot} decreased by more than 20% immediately after BAL and was still significantly reduced 3 h later. Contrary to our results, Steinberg et al. [19] found no significant changes in static C_{tot} in patients with the acute respiratory distress syndrome (ARDS) after BAL. Their patients, however, were not paralysed. This makes estimation of C_{tot} more unreliable because of possible changes in chest wall compliance due to respiratory muscle activity [10]. Hertz et al. also found no significant changes in static compliance in mechanically ventilated patients undergoing BAL [2]. They, however, conducted a retrospective study, where postlavage variables of respiratory function were recorded in some patients only 6 h after BAL and were taken from the ventilator settings (V_t, plateau airway pressure, PEEP). This is known to produce less accurate results than the method we used, as the compliance of the ventilator and the hoses are included.

Several mechanisms could account for the changes in C_{tot} (and R_{tot}) after BAL. In addition to simple entrapment of lavage fluid, induction of inflammatory pulmonary edema and inactivation of or interference with pulmonary surfactant may represent other causes. Although induction of inflammatory pulmonary edema is less well studied, transudation of serum and serum components into the alveolar space and release of cytokines have been proposed as having a possible role in compliance reduction after BAL [20–24]. The reduction of pulmonary surfactant may also lead to alveolar atelectasis, thereby worsening C_{tot}. The influence of BAL on pulmonary surfactant has been the subject of many studies. In a primate model, Krombach et al. [25] found a reduction of phospholipids (to which surfactant belongs) in lavage fluid from 47.5 to 24.5 µg/ml after serial BALs. In healthy human volunteers, phospholipid concentration decreased from 1.09 to 0.25 µg/ml after instillation of four 60-ml aliquots of saline [26]. Preexisting reduced surfactant function in patients with ARDS may also be one reason why some studies failed to find changes in static lung compliance in response to BAL [24].

Mode of ventilation together with incongruity between bronchoscope diameter and endotracheal tube size during BAL may also predispose to changes in C_{tot}. We employed pressure controlled ventilation to maintain opening pressures and avoid alveolar collapse during the procedure. During pressure controlled ventilation, the presence of the bronchoscope inside the endotracheal tube may impair gas flow and predispose to small airway collapse and atelectasis, which is in turn reflected by a decrease in pulmonary compliance (and an increase in resistance). However, these problems occur if the bronchoscope reduces the diameter of the endotracheal tube by more than 50% [27]. In our study, maximal tube obstruction was only 37%. (We used a 5.2–mm bronchoscope in 8.5– to 9.5–mm tubes.) This suggests that the interaction between mode of ventilation and incongruity between bronchoscope diameter and endotracheal tube size is unlikely to have caused the pulmonary mechanical alterations seen in our study.

Pulmonary mechanics did not deteriorate in all of our patients. Some patients even showed slight improvement in R_{tot} and C_{tot}. This may have been due to removal of mucus from the airway. Another possible reason is that in some individuals an auto-PEEP created by the presence of the bronchoscope in the airway could have led to recruitment of atelectatic alveoli [19, 28]. Also, alterations in C_{tot} and R_{tot} before the procedure did not correlate with changes after lavage. This is keeping with a previous study in which changes in FEV_1 and FVC were comparable in both control subjects and asthmatics [14].

Among the common side effects during BAL, we also found a small increase in blood pressure shortly after the procedure. This may be related to insufficient sedation or sympathetic discharge caused by stimulation of airway receptors by the bronchoscope [28]. Although there are reports [23] of sepsis-like effects in pneumonia patients undergoing BAL, body temperature did not change and except for one patient with prolonged arterial hypotension, hemodynamic status remained stable after the procedure.

In conclusion, the results of the present study show that BAL with a moderate amount of saline can lead to significant deterioration in pulmonary mechanics. Decreases in C_{tot} were still significant several hours after the procedure. Increases in R_{tot} were transient but may have contributed to the longer lasting deterioration in oxygenation.

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