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Paralysis has no effect on chest wall and respiratory system mechanics of mechanically ventilated, sedated patients

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Abstract *Objective:* To evaluate the separate effects of sedation and paralysis on chest wall and respiratory system mechanics of mechanically ventilated, critically ill patients.
Setting: ICU of the University "La Sapienza" Hospital, Rome.
Patients and participants: 13 critically ill patients were enrolled in this study. All were affected by disease involving both lungs and chest wall mechanics (ARDS in 4 patients, closed chest trauma without flail chest in 4 patients, cardiogenic pulmonary oedema with fluidic overload in 5 patients).
Measurements and results: Respiratory system and chest wall mechanics were evaluated during constant flow controlled mechanical ventilation in basal conditions (i.e. with the patients under apnoic sedation) and after paralysis with pancuronium bromide. In details, we simultaneously recorded airflow, tracheal pressure, esophageal pressure and tidal volume; with the end-inspiratory and end-expiratory airway occlusion technique we could evaluate respiratory system and chest wall elastance and resistances. Lung mechanics was evaluated by subtracting chest wall from respiratory system data. All data obtained in basal conditions (with the patients sedated with thiopental or propofol) and after muscle paralysis were compared using the Student's *t* test for paired data. The administration of pancuronium bromide to sedated patients induced a complete muscle paralysis without producing significant modification both to the viscoelastic and to the resistive parameters of chest wall and respiratory system.
Conclusions: This study demonstrates the lack of additive effects of muscle paralysis in mechanically ventilated, sedated patients. Also in view of the possible side effects of muscle paralysis, our results question the usefulness of generalyzed administration of neuromuscular blocking drugs in mechanically ventilated patients.

Key words Muscle relaxants · Sedation · Respiratory system mechanics · Chest wall mechanics · Mechanical ventilation

Introduction

Mechanically ventilated, critically ill ICU patients are often sedated to obtain both anxiety reduction and ventilator adaptation during complete ventilatory support [1].

Moreover, patients affected by diseases considered at risk for barotrauma, commonly receive not only sedatives but also muscle relaxants, assuming that the addition of paralysis can reduce the resistive load represented by chest wall viscoelastic characteristics [2].

It is surprising that, in face of a so commonly diffuse procedure, no experimental evidence supports the benefit of muscle paralysis on respiratory system mechanics of sedated patients, above all in view of the increasing amount of studies describing prolonged paralysis [3–6] or persistent muscle weakness [7–15] in critically ill patients receiving muscle relaxant infusions in ICU. The aim of this study was to evaluate the effects of muscle paralysis on respiratory system and chest wall mechanics of ICU patients mechanically ventilated during propofol or sodium thiopental (TPS) sedation.

Patients and methods

Thirteen consecutive patients affected by diseases involving both lungs and chest wall (9M, 4F), whose mean age was 54±19 years ($\bar{X}$+SD), requiring mechanical ventilation for acute respiratory failure, were enrolled in this study, after obtaining informed consent from the patients legal guardian. This protocol was approved by our Institutional Ethics Committee. Major patients data are exposed in Table 1.

When this study was performed all patients had been admitted in our ICU since 2–4 days for pathologies involving both lungs and chest wall (ARDS in 4 patients, closed chest trauma without flail chest in 4 patients, cardiogenic pulmonary oedema with fluidic overload in 5 patients).

All patients were tracheally intubated via the nasal route (8–8.5 mm ID) and mechanically ventilated (Servo 900 C Solna – Sweden) in control mode with the following setting: Vt 10 ml/kg; I:E 1:2; Respiratory rate 12–14/min; FIO_2 0.5; PEEP 5 cmH_2O; square wave.

Six patients were sedated with propofol (continuous infusion at 5–8 mg/kg/h after a 1 mg/kg bolus dose) while 7, in which head trauma was present, were sedated with sodium thiopental (continuous infusion at 1.5 mg/kg/h). With these doses all patients were heavily sedated (Ramsay score V class) and well adapted to the machine, without spontaneous triggering activity. In all patients, airflow was measured with a n° 2 heated pneumotachograph (Metabo, Switzerland), connected to a differential pressure transducer (MP 45, Validyne, CA) and mounted between the y-piece of the ventilator circuit and the patient connectors. Airway pressure was measured at tracheal level by a pressure transducer (Bently Trantec, Irvine, CA) connected to a 1.5 mm ID multiple lateral holes catheter inserted into the tracheal tube. The catheter tip was positioned at 2 cm from the carinal end of the tube, as described in a previous paper [16]. Volume was obtained by integration of the flow signal (Gould Integrator, France). Esophageal pressure was measured with a thin latex balloon (8 cm long, 2.5 cm in circunference) sealed over a 2 mm ID polyethylene catheter connected to a pressure transducer (Bentley Trantec, Irvine, CA). The balloon catheter was introduced into the lower third of the esophagus and filled with 1 ml of air. The correct position of the esophageal balloon was checked before the experiment with an occlusion test [17], i.e. comparing the negative pressure deflections of Peso and Paw during inspiratory efforts made against an occluded airway. As with the airway occluded no significant change in lung volume can occur, the change in transpulmonary pressure is zero and the esophageal balloon records changes in Peso nearly equivalent to the simultaneously recorded Paw changes.

Table 1 Main patient data (*ARDS* adult respiratory distress syndrome; *COPD* chronic obstructive pulmonary disease; *CPO, F.O.* cardiogenic oedema in patients with fluidic overload, *TPS* sodic thiopentone)

Patient	Sex	Age	Diagnosis	Sedation	Outcome
1	M	20	Trauma, ARDS	TPS	D
2	M	42	Trauma, ARDS	TPS	S
3	M	52	Trauma, COPD	TPS	S
4	M	28	Trauma	TPS	S
5	F	29	Trauma	TPS	S
6	M	76	Trauma, ARDS	TPS	D
7	F	52	Trauma, COPD	TPS	S
8	F	70	CPO, F.O.	Propofol	D
9	M	78	CPO, F.O.	Propofol	D
10	M	62	CPO, F.O.	Propofol	D
11	M	66	CPO, F.O.	Propofol	S
12	F	58	CPO, F.O.	Propofol	S
13	M	70	Trauma, COPD	Propofol	D

All signals were recorded with a four channel Roche polygraph at 12.5 mm/s speed. During the experiment we continuously monitored, for patient supervision, the electrocardiogram, heart rate, systemic arterial pressure, right atrial pressure; pulse oximetry (Ohmeda Biox, France) was used monitor SaO_2.

Muscle paralysis was confirmed with a peripheral nerve stimulator using ulnar surface electrodes (Lifetech Inc., Houston, Tx): the ulnar nerve was stimulated at the wrist using a tetanic stimulation (50 Hz for 5 s).

The patients were studied in supine position; during the whole procedure a physician not involved in the study was present to take care of the patients.

Measurements were initially obtained in basal condition (apnoic sedation without paralysis): the inspiration hold buttons of the ventilator were used to obtain a 3 s end-inspiratory and end-expiratory airway occlusion [16]. All corrections for the occlusion time of the scissor valves were made according to Kochi et al. [18].

End-inspiratory airway occlusion was followed on airway pressure tracings by a drop from peak inspiratory pressure (Pmax) to the elastic recoil pressure of the respiratory system (Pelrs or P2): this pressure drop was, as previously described [19], biphasic and a pressure value at the end of the initial rapid drop was observed (P1).

The ohmic resistance of the respiratory system (RRS min), was calculated as $(Pmax-P1)/\dot{V}i$. No correction for endotracheal tube (ET) resistance was necessary as airway pressure was measured two cm below the ET distal end [16].

The total resistance of the respiratory system (RRS max), including RRS min plus the additional respiratory impedance generated by stress relaxation and time constant inhomogeneities, was calculated as $(Pmax-P2)/\dot{V}i$.

End-expiratory airway occlusion was kept for 3 s obtaining a plateau: the difference between end-inspiratory and end-expiratory occlusion airway pressure was divided by the expired tidal volume to calculate the elastance of the respiratory system (Ers), keeping in account auto PEEP, when present.

As previously described by D'Angelo and coll. in normal subjects [20], end-inspiratory airway occlusion was not followed by a biphasic Peso decay, exhibiting only a slow decay to a plateau (P2eso), representing the elastic recoil pressure of the chest-wall (Pel cw). The end inspiratory airway occlusion manoeuvre was repeated three times at 15 s intervals, observing superposable values of Pmax eso and P2eso in the individual breaths. Accordingly superposable values of derived variables (chest-wall resistance and compliance) were obtained.

The resistance of the chest-wall (R cw) (mainly representing viscoelastic resistance) was calculated as $(Pmax\,eso-P2\,eso)/\dot{V}i$. [20].

The difference between end-inspiratory and end-expiratory plateau esophageal pressure was divided by the expired tidal volume to obtain the chest-wall elastance.

Lung elastance was obtained by subtracting chest wall elastance from respiratory system elastance.

The patients, who had never received muscle relaxants, were then paralyzed with pancuronium bromide (0.1 mg/kg i.v.). After 8 min from the end of the injection the complete absence of neuromuscular response was controlled with ulnar skin electrode stimulation (tetanic stimulation), and measurements were repeated with the above described procedure.

To reduce the effect of circuit compliance we used a 60 cm inspiratory segment, avoiding the use of water traps and Heat and Moisture Exchanger during the study procedure: circuit compliance was 0.3 ml/cm H_2O.

The values of RRSmin, RRSmax, ΔRRS, Ers, Ecw, El obtained during apnoic sedation and during apnoic sedation plus paralysis have been compared using the Student's *t* test for paired data; *p* values <0.05 were considered as statistically significant.

Results

Average data of respiratory system, chest wall and lung mechanics under basal conditions (apnoic sedation) and after paralysis are summarized in Table 2.

We did not notice significant modifications of the observed variables after pancuronium administration either in the group of patients sedated with propofol or in the group with thiopentone: in other terms, the addition of paralysis to sedation did not cause modifications of the viscoelastic and resistive variables of the chest wall (Fig. 1).

As no modification of lung mechanics was observed after pancuronium administration, respiratory system mechanics (that represent the sum of chest wall and lung mechanics) were also unmodified. Finally we did not observe, during the experiment, significant modifications of the haemodynamic variables and blood gases after the addition of paralysis to apnoic sedation.

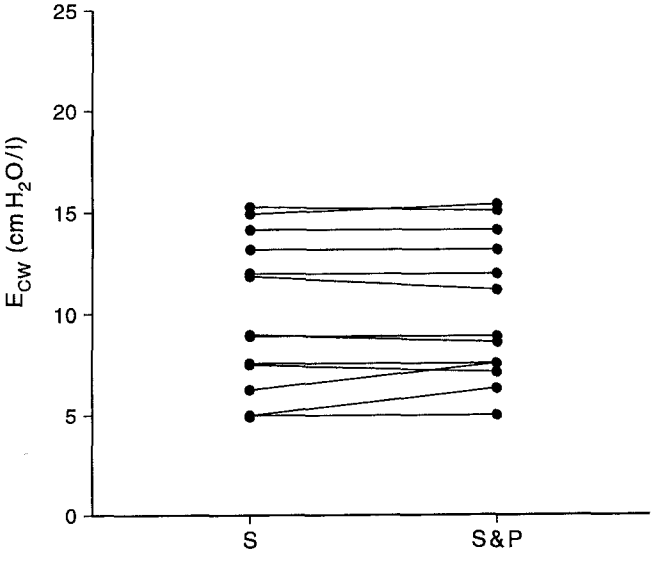

Fig. 1 Modifications of the individual chest wall elastance (*Ecw*) values in 13 patients mechanically ventilated. *S* sedation; *S and P* sedation plus paralysis

Table 2 Modifications of the respiratory system, chest wall and lung mechanics before and after paralysis in 13 mechanically ventilated, sedated patients. (*Ers, El, Ecw* elastance of the respiratory system; lungs and chest wall respectively, *Rcw* resistance of the chest wall, *RRS* max total resistance of the respiratory system; *RRS* min minimal resistance of the respiratory system)

	Apnoic sedation	Sedation + Paralysis
Ers (cmH_2O/l)	24.9 ± 11	24.7 ± 10.9
Ecw (cmH_2O/l)	10.6 ± 3.1	10.7 ± 2.9
El (cmH_2O/l)	14.2 ± 9.5	14.3 ± 9.1
Rcw (cmH_2O/l/s)	1.9 ± 0.5	2 ± 0.9
RRS max (cmH_2O/l/s)	12.5 ± 4.3	11.9 ± 3
RRS min (cmH_2O/l/s)	6.6 ± 2.9	6.6 ± 2.8
ΔRRS (cmH_2O/l/s)	5.7 ± 1.9	5.2 ± 1.7

Discussion

Patients affected by acute respiratory failure of parenchymal origin are commonly treated in ICU with mechanical ventilation. As respiratory drive is commonly increased in these conditions, they usually receive deep sedation to obtain optimum adaptation to the ventilator. Moreover, muscle relaxants are often prescribed [2], assuming that paralysis can reduce the increase in airway pressure directly related to the viscoelastic resistance of the chest wall. Although poorly based on experimental data, this use is quite common and at least in the USA [1, 2], it appears to have expanded considerably during the past 5 years. At this purpose, Hansen-Flaschen et al. report a more than 3 fold increase of neuromuscular blocking drug administration in their 700 beds adult ICU comparing 1989 with the first 6 months of 1992 [21].

In view of this diffuse therapeutic approach and of the dramatic increase of literature reports of life-threatening complications directly or indirectly related to prolonged muscle relaxants administration in ICU, we were surprised by the low number of experimental studies dedicated to the evaluation of the additional effects produced by muscle paralysis on respiratory system and chest wall mechanics of sedated mechanically ventilated patients.

We therefore analyzed this aspect in a consecutive group of mechanically ventilated patients; our results showed lack of detectable effects on chest wall, lung and respiratory system mechanics of pancuronium administration at doses able to provide complete neuromuscular blockade in sedated patients.

These results are consistent with the data recently reported by Putensen and coll., analyzing the static pres-

sure/volume curve of the whole respiratory system in pigs [22] and to data obtained in normal humans [23].

This is an important point, as many severe complications have been reported in critically ill patients receiving muscle relaxants for periods longer than 2 days, with the aim of "simplifying" the mechanical ventilatory support or decreasing the airway pressure.

Both retrospective [3, 10] and prospective [6–8] studies have demonstrated that a large percentage of patients show muscular weakness after prolonged administration of pancuronium or vecuronium. This is particularly common in patients affected by renal failure, sepsis, status asthmaticus or in patients concomitantly receiving steroids.

We chose propofol and sodium thiopentone to sedate our patients, because these drugs are widely used in our ICU, above all for associated head and chest trauma patients, and both rapidly induce a deep level of apnoic sedation. Although the same level of apnoic sedation can be easily obtained with other drugs as opiates-benzodiazepines association, and we commonly perform reliable respiratory mechanics measurements also with this kind of sedation, our results must be strictly considered specific to the type of sedation used in this study.

Another aspect was the evaluation of chest wall resistance in humans during pathologic conditions.

Contrary to cats [24] and dogs [25], and according to the results reported with the same technique by D'Angelo in healthy human subjects [20], in this study the chest wall of humans affected by thoracic diseases did not show clear evidence of a flow resistive component, as suggested by the constant absence of an immediate Peso drop following the end-inspiratory flow occlusion in all the recorded breaths. However, great caution is necessary when interpreting esophageal pressure tracings that can present important artifacts due to the inertial behaviour of the signal acquisition system.

In conclusion this study questions the usefulness of generalyzed neuromuscular blocking drugs administered to sedated patients for the purpose of increasing chest wall and respiratory system compliance; probably in a large part of ICU patients an optimal ventilator adaptation with reduced values of airway pressure can be achieved with apnoic sedation alone, avoiding the risk of major complications described after prolonged pancuronium or vecuronium administration: in other terms a better use of sedatives could probably reduce the need for prolonged muscle paralysis in a large part of the mechanically ventilated ICU patients.

However, it is important to keep into consideration that paralysis may be still needed in some patients with catastrophic respiratory failure who present a residual respiratory center activity despite profound sedation, only as a "last resource" strategy to obtain the abolition of spontaneous breathing activity and an optimal adaptation to the ventilator.

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