Depth of neuromuscular blockade is not related to expiratory transpulmonary pressure and respiratory mechanics, in moderate to severe ARDS patients. A prospective cohort study.

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Introduction :

Neuromuscular blockade (NMB) is proposed in patients with moderate to severe acute respiratory distress syndrome (ARDS), and especially for those who, after optimization of the ventilatory parameters, the protective ventilation strategy is not feasible under sedation alone. The supposed benefit of these muscle relaxants could be partly linked to their effects on respiratory mechanics by reducing ventilation-related injuries (VILI), especially the so called atelectrauma. Although its monitoring is recommended in clinical practice, data about the depth of the NMB necessary for an effective relaxation of the thoracic and diaphragmatic muscles and, therefore, the reduction of the chest wall elastance, are scarce. We made hypothesis that complete versus partial NMB may modify respiratory mechanics and its partitioning.

Method :

We conducted a prospective study to compare the respiratory mechanics of patients with moderate to severe ARDS according to the depth of NMB, using a esophageal pressure catheter (NutriVent®, Sidam, made in Italy) for transpulmonary pressure (P_L) assessment, and using the facial train of four (TOF) for neuromuscular blockage monitoring. The esophageal balloon was calibrated according to the method described recently to estimate the individual target volume assumed to be more adequate. Each patient was analyzed at two different times: deep NMB (TOF = 0) and intermediate to light NMB (TOF > 0). Between these two measurements, the mechanical ventilation parameters were identical. The primary endpoint was the proportion of patients with expiratory transpulmonary pressure ($P_L$exp) greater than or equal to 0 according to the level of NMB, in order to assess the risk of dependant-region atelectasis and alveolar opening-closing lesion (atelectrauma). Secondary objectives included: the impact of the depth of NMB on other respiratory mechanics partition parameters, and the variability of results depending on the type of esophageal balloon calibration.

Results :

Over the period from February 2020 to February 2022, 33 patients were analyzed. At baseline, the median PaO_2/FiO_2 ratio was 88 mmHg [67–115], plateau pressure 24 cmH2O [22–25], external PEEP 10 cmH2O [8–12], for a tidal volume set at 6 mL/kg of predictive body weight. The patients were paralyzed with continuous infusion of cisatracurium. The duration of mechanical ventilation at the time of the measurements was 3 days [2–7]. Almost all ARDS was of pulmonary origin (97%) with a predominance of SARS-CoV2 pneumonia (76%). The proportion of patients with a positive $P_L$exp at condition TOF = 0 compared to condition TOF > 0 was not statistically different: 97% versus 88% (p = 0.25) (Fig 1). The depth of NMB did not modify the pulmonary dynamic stress: the inspiratory transpulmonary pressure based on ratio of elastances ($P_L$insp, EB) was identical in the two groups ($P_L$insp, EB = 17.6 cmH20 [15.4 – 21.1] at TOF = 0 versus 17.4 cmH_20 [15.4 – 20.3] at TOF > 0; p = 0.28) (Table 1). Individualized balloon calibration resulted in a median volume of 2 mL [1–2]. When considering a standard balloon volume of 4 mL as currently recommended, only 55% of patients had a positive $P_L$exp, versus 97% with balloon volume of 2 mL (p<0.001).

Conclusion :

Within a population of mainly pulmonary ARDS and ventilated with intermediate PEEP level (10 cmH20), the risk of atelectrauma (estimated here as negative PLexp) seems limited, and appears independent of the level of NMB, as assessed by facial TOF. In the limits of our sample size, these physiologically results raised the question of the benefit of complete versus partial NMB in terms of respiratory mechanics, without being able to extrapolate the results to other ARDS phenotypes or to the overall effect of muscle relaxants on all the duration of their use (estimate here punctual, and early in ARDS course evolution). These results also raise concerns about the ability of facial TOF to assess muscle relaxation of the chest wall, and the method of optimal balloon volume calibration of esophageal catheter to monitor transpulmonary pressure with accuracy.

Figure 1 :

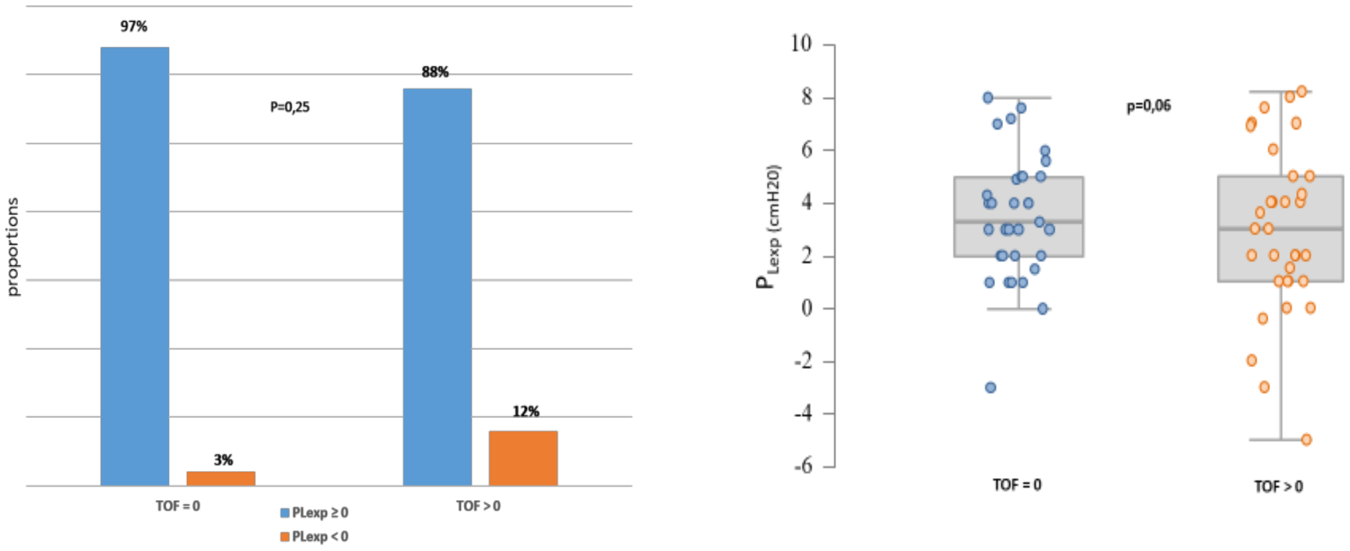

Table1 :

	TOF = 0	TOF > 0	p value
Primary outcome			
$P_{Lexp} \geq 0$ cmH2O, (n) (%)	32 (97)	29 (88)	0,25
Secondary end-points			
Pes_{exp} (cmH2O)	8 [5 – 9,5]	7 [5 – 10]	0,16
Pes_{insp} (cmH2O)	10 [8,2 – 13]	10 [8 – 13]	0,12
P_{Lexp} (cmH2O)	3,3 [2 – 5]	3 [1 – 5]	0,06
P_{Linsp} (EB) (cmH2O)	17,6 [15,4 – 21,1]	17,4 [15,4 – 20,3]	0,28
E_{CW} (cmH2O/L)	7 [5,7 – 9,5]	7 [5,3 – 10,8]	0,36
E_L/E_{RS}	0,77 [0,7 – 0,85]	0,75 [0,67 – 0,85]	0,60

Definitions :

P_{Lexp} : expiratory transpulmonary pressure

P_{Linsp}(EB) : inspiratory transpulmonary pressure based on ratio of elastances

Pes_{exp} : expiratory esophageal pressure

Pes_{insp} : inspiratory esophageal pressure

E_{CW} : chest wall elastance

E_L/E_{RS} : lung elastance/respiratory system elastance