Effects of the pneumoperitoneum and Trendelenburg position on respiratory mechanics in the rats by the end-inflation occlusion method

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Abstract:

PURPOSE: To describe the consequences of the cranial displacement of the diaphgram occurring during pneumoperitoneum (Pnp) and/or Trendelenburg (Tnd) position on respiratory mechanics. Possible addictive effects and the changes of the viscoelastic respiratory system resistance were studied, which were not extensively described before.

METHODS: The end-inflation occlusion method was applied on eight rats. It allows us to determine mechanical parameters such as respiratory system static elastance, the ohmic resistance due to frictional forces in the airways, and the additional viscoelastic impedance due to tissues deformation. Measurements during mechanical ventilation were taken in controls (supine position), after 20–25° head-down tilting (Tnd), after abdominal air insufflation up to 12 mmHg abdominal pressure in the supine position (Pnp), and combining Tnd + Pnp. Tnd and Pnp modalities were similar to those commonly applied during surgical procedures in humans.

RESULTS: We confirmed the previously described detrimental effects on respiratory mechanics due to the diaphgram displacement during both Pnp and Tnd. The increment in the total resistive pressure dissipation was found to depend primarily on the effects on the viscoelastic characteristics of the respiratory system. Data suggesting greater effects of Pnp compared to those of Tnd were obtained.

CONCLUSION: The cranial displacement of the diaphgram occurring as a consequence of Pnp and/or Tnd, for example during laparoscopic surgical procedures, causes an increment of respiratory system elastance and viscoelastic resistance. The analysis of addictive effects show that these are more likely to occur when Pnp + Tnd are compared to isolated Tnd rather than to isolated Pnp.

Key words:

Pneumoperitoneum, rat, respiratory mechanics, trendelenburg position

The effects of the cranial displacement of the diaphragm on respiratory mechanics have been mainly attributed to the reduction of functional residual capacity.[1-3] Several studies have been published dealing with this subject, in which measurements were taken during positive pressure ventilation and imposition of the pneumoperitoneum (Pnp) and/or Trendelenburg position (Tnd). However, no systematic study has been published in which the effects of Pnp and/or Tnd on the viscoelastic behaviour of the respiratory system were studied. The end-inflation occlusion method, widely applied both in humans[4-6] and in experimental animals[7-9] to study respiratory mechanics, allows us to measure the airway resistance and the respiratory system elastance together with the additional viscoelastic pressure drop that follows the arrest of a constant-flow inflation. This drop has been mainly attributed to respiratory system tissues stress relaxation,[5,6,8,9] and the inflation pressure dissipation due to viscoelastic phenomena has been described as a determinant component of

the total inspiratory work breathing.[4-6,8,9] Hence, the measurement of the viscoelastic pressure drop after constant flow inflation allows us to study and quantify the highest component of the total resistive pressure dissipation.

Moreover, most previously published reports described the effects on respiratory mechanics of Pnp *per se*,[2,10-16] or of Tnd *per se*,[1,16,17] with respect to controls. The addictive consequences of Tnd superimposed on an existing Pnp with respect to Pnp alone have also been studied,[12,14-16] while a systematic analysis of results that compare the effects of Pnp + Tnd with Tnd alone is lacking. This is probably because commonly adopted surgical procedures do not allow us to study a surgical time in which isolated Tnd is present in comparison with a successive condition in which Tnd + Pnp are contemporaneously applied. In a sole report,[16] Pnp was induced both in supine and Trendelenburg positions, but the data describing the possible addictive effects of Pnp on a pre-existing Tnd were not analysed.

Thus, in this report measurements are described of respiratory mechanics in the rats obtained by the end-inflation occlusion method to study:

(a) the separate effects of Pnp or Tnd on the respiratory mechanics, and in particular on the viscoelastic characteristics of the respiratory system;

(b) the possible addictive effects which may ensue when Pnp and Tnd are contemporaneously applied. The analysis describes both the effects of Tnd added to a pre-existing Pnp, and the data obtained during isolated Tnd in comparison with the condition in which Pnp + Tnd are applied.

Methods

Animals

The experiments were carried out on eight Wistar albino rats of both sexes (mean weight 327 ± 26 g., four males).

The animals were housed and treated in accordance with the Italian law on animal experimentation (L. 116/92) and with the European Council (EC) provision 86/609/EEC, which received the World Medical Association Declaration of Helsinki.

Experimental procedure

Rats were anesthetized with 50 mg /100 g i.p. chloralose and laid on a heated operating table. After a tracheostomy, a small polyethylene cannula (2 mm i.d., 5 cm long) was inserted through an incision in the second tracheal ring and firmly secured in place.

Positive pressure ventilation with a 10 ml/kg tidal volume and a 60 per min breathing frequency (PEEP 3 cm H_2O) (Rodent Ventilator 7025, Basile, Italy) was begun, and constantly maintained throughout the experiment (apart from the short time necessary to measure respiratory mechanics, see below).

Limb ECG probes were placed, and the rats were paralyzed (*cis*-atracurium 1 mg/100 g i.p.). Positive pressure ventilation was maintained for 5 min, and respiratory mechanics were then measured using the end-inflation occlusion method.

The ventilator was disconnected, PEEP was discontinued, and the tracheal cannula was connected to a constant flow pump (SP 2000 Series Syringe Pump SP210iw, World Precision Instruments, USA) set to deliver a tidal volume (V_T) of 3 ml with a square wave flow (F) of 4 ml/s. The time for the rise and the fall of the flow was approximately 30 ms. The pump setting was carefully checked by directly taking measurements before beginning the experiments. For each inflation, the time that the ventilator remained disconnected was about 10–15 s, so that determinant arterial blood gas changes were avoided.[18]

The lateral tracheal pressure proximal to the tracheal cannula was monitored (142 pc 01d, Honeywell, USA) and continuously recorded (1326 Econo Recorder, Biorad, Italy). Because of abrupt changes in diameters were not present in the circuit, errors in flow resistance measurements, such as those previously reported,[19] were avoided. The frequency response of the transducer and the pressure measuring system was tested by sinusoidal forcing and found to be flat up to 20 Hz. In accordance with the literature,[6,7] this frequency response

was adequate to avoid mechanical artefacts in the pressure signal records.

The entire experimental procedure lasted less than 1 h. Data in the literature indicate that mechanical ventilation parameters here adopted are not injurious to the respiratory system for at least 1 h,[8,9] so that the results we obtained are not affected by mechanical ventilation-linked respiratory system injury.

Respiratory mechanics parameters measurements were obtained as below described in the following conditions: (a) in control conditions (supine position) after 5 min of mechanical ventilation; (b) some minutes after the imposition of Tnd (about 20–25° head-down tilt); (c) some minutes after Pnp induction and Tnd resolution (supine position); and (d) some minutes after Tnd restoring while Pnp was maintained.

Pnp was induced by a small bore needle (22G) inserted through the abdominal wall and air insufflation up to a pressure of about 12 mmHg. At the end of the experiments, the animals were killed by a lethal i.p. injection (Tanax® 0.3 ml/kg).

Data calculation

The end-inflation occlusion method was utilized to determine the parameters of respiratory mechanics: the static elastic pressure of the respiratory system ($P_{el,rs}$) and the sudden Newtonian resistive pressure drop at flow interruption ($P_{min,rs}$) were measured on adequately magnified tracings [Figure 1]. $P_{min,rs}$ was calculated as the difference between $P_{dyn,max}$, the maximum value of pressure at end inflation, and P_1, the pressure value immediately after flow interruption [Figure 1]. The sum of $P_{min,rs}$ and of the slower, nearly exponential, pressure drop following flow interruption due to respiratory system viscoelastic behaviour, i.e. stress relaxation,[5,6,8,9] is named $P_{max,rs}$ [Figure 1]. Our tracings allowed to identify P_1 [Figure 1], which separates the pressure drop due to the frictional forces developed in the movement of airflow in the airway ($P_{min,rs}$) from the following nearly exponential viscoelastic pressure drop which represents the effects of stress relaxation.
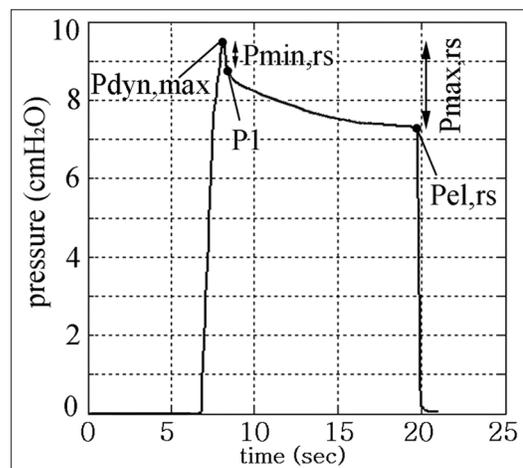
Figure 1: Example of tracing recorded upon constant flow inflation arrest. The maximum pressure achieved at end inflation ($P_{dyn,max}$), the pressure drop due to frictional forces in the airway ($P_{min,rs}$), and the overall resistive pressure drop ($P_{max,rs}$), including $P_{min,rs}$ and the nearly exponential pressure dissipation due to viscoelasticity, are shown. P_1: pressure value immediately after flow arrest.

To avoid a viscoelastic pressure component in $P_{min, rs}$, P_1 values were identified by extrapolating the pressure tracings to the time the flow stopped.[20]

The mean pressure data obtained from two to three inflations for each rat were used to calculate the respiratory system static elastance ($E_{st,rs} = P_{el,rs}/V_T$) and the ohmic inspiratory resistance to airflow offered by the airways and the movement of respiratory system tissues ($R_{min,rs} = P_{min,rs}/F$). The overall inspiratory pressure drop ($P_{max,rs}$) measurement allowed us to calculate $R_{max,rs} = P_{max,rs}/F$, which includes the ohmic airways resistance and the viscoelastic component here named $R_{visc,rs} = (P_{max,rs} - P_{min,rs})/F$.

The equipment resistance, including the tracheal cannula and the standard three-way stopcock, was measured separately at a flow rate of 4 ml/s and amounted to 0.0575 cm H_2O ml^{-1} s^{-1} (R_{eq}). All inflations were performed at a fixed flow rate of 4 ml/s, and R_{eq} was subtracted from the results, which thus represent intrinsic values.

Statistics
The mean values of the measured and calculated respiratory system mechanics parameters obtained in the four tested experimental conditions (see above) were calculated and statistically compared each other. A nonparametric text (Wilcoxon) was applied because of the rather small sample size. Data are expressed as mean ± SD ($n = 8$).

Results

The mean values of respiratory mechanics parameters measured and calculated in the four above-described experimental conditions (see Materials and methods) are depicted in Tables 1 and 2. In Table 3, the corresponding mean values of the heart rate are reported.

We found no significant changes of $R_{min,rs}$ mean values with respect to controls either as an effect of Pnp or of Tnd, while an addictive effect was observed when Pnp and Tnd were contemporaneously applied. Both $R_{max,rs}$ and $R_{visc,rs}$ mean values resulted to increase with respect to controls as an effect of both Pnp and Tnd, and an addictive effect was also confirmed. $E_{st,rs}$ mean values also exhibit significant increment as an effect of both Pnp and Tnd. This increment resulted statistically significant when Tnd + Pnp were applied also.

In addition, we analysed the respiratory mechanics parameters' changes due to Tnd + Pnp with respect to Pnp or Tnd alone. We found that the imposition of Tnd on a pre-existing Pnp did not cause significant changes in $R_{min,rs}$, $R_{max,rs}$, and $E_{st,rs}$. On the other hand, the comparison of the mean values obtained during isolated Tnd with those observed during Pnp + Tnd revealed significant increments in $R_{min,rs}$, $R_{visc,rs}$, and $R_{max,rs}$, leaving again unaltered $E_{st,rs}$.

Discussion

Experimental procedure
Modelling the respiratory system as consisting of two distinct compartments, the end-inflation occlusion method has been widely used to study respiratory mechanics in experimental animals[7-9] and in humans.[4-6]

Ideally, the inflation flow should stop instantaneously, but this is practically impossible to achieve. However, a procedure has been proposed to correct for this technical limitation.[20] In this procedure, pressure tracings are manually extrapolated to account for the time that is necessary to completely halt the inspiratory flow, thereby minimizing the error.[7-9] This procedure was employed to analyse the inflation pressure tracings in the current study and, similarly to what previously reported,[7,8] the corrections were almost negligible.

Table 1: Respiratory mechanics parameters: Comparison with supine position

	$E_{st,rs}$ (cm H_2O/ml)	$R_{min,rs}$ (cm H_2O/ml s^{-1})	$R_{visc,rs}$ (cm H_2O/ml s^{-1})	$R_{max,rs}$ (cm H_2O/ml s^{-1})
Supine	2.1 ± 0.17	0.13 ± 0.085	0.49 ± 0.11	0.62 ± 0.17
Tnd	2.4 ± 0.23	0.16 ± 0.025	0.59 ± 0.28	0.76 ± 0.085
	$P = 0.0156$		$P = 0.0155$	$P = 0.0234$
Pnp	2.3 ± 0.28	0.17 ± 0.028	0.7 ± 0.14	0.88 ± 0.14
	$P = 0.065$		$P = 0.0078$	$P = 0.0156$
Pnp + Tnd	2.5 ± 0.34	0.24 ± 0.085	0.78 ± 0.28	1.02 ± 0.2
	$P = 0.0156$	$P = 0.0234$	$P = 0.0077$	$P = 0.0078$

Mean values (±SD, $n = 8$) of the respiratory system mechanical parameters measured in controls condition (supine), after Trendelenburg 20–25° head-down tilt (TND), after pneumoperitoneum induction with air insufflation up to abdominal pressure 12 mmHg, supine (PNP), and combining Pnp and Tnd. $E_{st,rs}$: static respiratory system elastance. $R_{min,rs}$: ohmic resistance due to frictional forces in the airway. $R_{visc,rs}$: additional viscoelastic resistance due to stress relaxation. $R_{max,rs}$: total respiratory system resistance. *P* values in comparison with supine

Table 2: Respiratory mechanics parameters: comparison with coupled pneumoperitoneum and trendelenburg position

	$E_{st,rs}$ (cm H_2O/ml)	$R_{min,rs}$ (cm H_2O/ml s^{-1})	$R_{visc,rs}$ (cm H_2O/ml s^{-1})	$R_{max,rs}$ (cm H_2O/ml s^{-1})
Tnd	2.4 ± 0.23	0.16 ± 0.026	0.59 ± 0.28	0.76 ± 0.085
		$P = 0.0391$	$P = 0.079$	$P = 0.0234$
Pnp	2.3 ± 0.28	0.17 ± 0.028	0.7 ± 0.14	0.88 ± 0.14
			$P = 0.0313$	
Pnp + Tnd	2.5 ± 0.34	0.24 ± 0.085	0.78 ± 0.28	1.02 ± 0.2

Mean values (±SD, $n = 8$) of the respiratory system mechanical parameters measured after Trendelenburg 20–25° head down tilt (TND), after pneumoperitoneum induction with air insufflation up to abdominal pressure 12 mmHg, supine (Pnp), and combining Pnp and Tnd. $E_{st,rs}$: Static respiratory system elastance. $R_{min,rs}$: Ohmic resistance due to frictional forces in the airway. $R_{visc,rs}$: Additional viscoelastic resistance due to stress relaxation. $R_{max,rs}$: Total respiratory system resistance. *P* values in comparison with Pnp + Tnd

Table 3: Mean values of the heart rate during experimental time

Heart rate (b/min)			
Supine	Tnd	Pnp	Tnd + Pnp
381 ± 42	374 ± 40	348 ± 31	350 ± 42

Mean data (±SD, *n* = 8) are shown in different experimental conditions [see Table 1]. No significant difference was detected among data

It is not possible to exclude that some stress relaxation-related phenomena might occur during inflation, thereby affecting the subsequent $P_{min,rs}$. Nevertheless, any related effect would be predicted to be minor, due to the short duration of inflation compared with the stress-relaxation time-course [Figure 1].

The mechanical ventilation settings used in these experiments were the same as those described as "noninjurious" in the literature.[8,9] In particular, "noninjurious" ventilation lasting one hour has been shown to induce no alterations of respiratory system mechanics.[8,9] The results here reported, therefore, were not influenced by the injurious effects that longer term mechanical ventilation *per se* might exert.

The mean heart rate values reported in Table 2 suggest that the conditions of the animals during the experimental procedure were generally stable. Moreover, although no significant change was found, a trend toward heart rate reduction due to abdominal hypertension was seen, likely because of vagal reflex activity.

The mean values of respiratory system mechanics parameters here reported are comprised in the range of those previously measured by the same technique in rats by various authors working in different laboratories.[7-9,21]

Although present experiments were designed to reproduce the conditions occurring during surgical laparoscopic procedures, i.e. Pnp with abdominal pressure about 12 mmHg, and Tnd about 20–25° head-down, the results and the argumentations contained in the following discussion may cautiously only be extended to humans.

The effects of Tnd with respect to controls

Our data show that Tnd caused significant increments of $R_{visc,rs,}$ $R_{max,rs,}$ and $E_{st,rs,}$ while $R_{min,rs}$ increased not significantly. These results confirm those previously obtained in humans,[1,17] and the finding, although not significant, of a trend of airway resistance and respiratory system elastance increments described by Sprung *et al*.[16]

Our measurement technique for the first time allows to indicate that the previously observed increments in airway resistance are mainly due to the Tnd effects on the viscoelastic resistive pressure dissipation rather than on the ohmic component. These effects of Tnd have been mainly attributed to the induced decrement of functional residual capacity (FRC).[1]

The effects of Pnp with respect to controls

With respect to controls, the abdominal insufflation is shown to induce significant increments of $R_{max,rs,}$ $R_{visc,rs,}$ and $E_{st,rs,}$ while R_{min} is increased not significantly.

The increment in $E_{st,rs}$ has been previously described by several authors.[3,10-16] Some of them[12,14,16] also described an increment of airway resistances, but the partitioning between the ohmic and the viscoelastic components was previously performed only by Pelosi *et al*.[2] These authors studied the effects of Pnp on respiratory mechanics by the same technique presently utilized, and found the same results here described (not significant $R_{min,rs}$ changes included), but during Pnp application in the reverse Trendelenburg position in humans.

According to Pelosi *et al*.,[2] the observed increment of $E_{st,rs}$ may be due to the limited diaphragmatic excursions and stiffening of the diaphragm,[13] to the decreased lung volume,[3] and to lung distortion, induced atelectasis,[3,22] and surfactant alterations.

It is of particular interest, in our opinion, the finding that the Pnp effects on airway resistance are mainly due to the influence on the viscoelastic component. This result is in agreement with Pelosi *et al*.'s findings although in the anti-Trendelenburg position in humans.[2]

This effect of Pnp on $R_{visc,rs}$ has been attributed to lung distortion, altered surfactant function, and the possible occurrence of atelectasis,[2] but endocrinal changes might also be involved. In fact, Bloomfield *et al*.[23] demonstrated that elevated intra-abdominal pressure increases plasma renin activity and aldosterone levels. The angiotensin converting enzyme inhibitor captopril has been shown to reduce $R_{visc,rs}$,[24] while blood volume expansion was shown to increase it.[25] Hence, endocrinal changes may be involved in causing the observed $R_{visc,rs}$ increments during Pnp.

The addictive effects of Pnp + Tnd

The statistical comparison of the mean values of respiratory mechanics parameters obtained during isolated Tnd or Pnp with those observed during Pnp + Tnd reveals that the superimposition of Tnd on a pre-existing Pnp has not the same addictive effects seen when the mean values observed during isolated Tnd are compared to those measured during Pnp + Tnd, at least in rats.

The here observed lack of significant increment of $E_{st,rs}$ when data measured during Pnp are compared with those obtained during Pnp + Tnd is in agreement with the results obtained in humans,[12,14-16] and suggests that the anatomical design of the respiratory system allows a Pnp-induced reduction in lung volume which cannot be followed by further reduction when Tnd is superimposed. On the same basis, the lack of increment of $R_{min,rs}$ may be explained. As suggested by previously reported results in humans,[14,16] a trend to $R_{max,rs}$ increment was observed, which depended on the significant increase of $R_{visc,rs}$ [Table 2].

On the other hand, when the mean values observed during Tnd are compared with those obtained during Pnp + Tnd, $R_{min,rs,}$ $R_{visc,rs,}$ and $R_{max,rs}$ exhibit significant increments, and $E_{st,rs}$ constancy is maintained. These respiratory mechanics changes due to the addictive effects of Pnp + Tnd with respect to sole Tnd were never analysed before.

As a general statement, our results show that the addictive affects due to Pnp are greater than those due to Tnd. At least in the present experimental conditions, which involve abdominal pressure increment and head-down tilt of the same order of magnitude of those commonly applied during surgical procedures in humans, the gravitational effects

causing cranial diaphgram displacement due to Tnd results less effective in influencing respiratory mechanics than abdominal hypertension due to Pnp.

Confirming previous results in humans,[12,14-16] $E_{st,rs}$ seems to be not addictively influenced neither by Tnd nor by Pnp, probably due to the above-described limit in the possible reduction in rat's lung volume.

Conclusion

The present results confirm, in the rats, the effects of the cranial displacement of the diaphgram due to the abdominal hypertension and/or Trendelenburg position on the respiratory mechanics which have previously been described in the literature in humans.

Our measurement technique allowed to extend the investigation to the effects of Pnp and/or Tnd on the viscoelastic component of the respiratory mechanics, which was shown to be the determinant part of the total resistive pressure dissipation increment, and was never extensively analysed before.

At least in our experimental conditions in rats, we were able to demonstrate that Tnd does not exhibit addictive effects on $E_{st,rs}$ when superimposed on pre-existing Pnp, nor the mean values of $E_{st,rs}$ observed during isolated Tnd result significantly different from those measured during Pnp + Tnd. In contrast, addictive effects were observed on the resistive pressure dissipation. These resulted more evident when Pnp + Tnd was compared to isolated Tnd than when Tnd was superimposed on pre-existing Pnp. These results suggest a greater role of Pnp with respect to Tnd in causing the respiratory mechanics derangement during the laparoscopic surgical procedure. Future research may investigate if these conclusions may be confirmed in humans.

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