Effect of 120 minutes of high pressure-volume and low pressure-volume mechanical ventilation on plasmatic markers of systemic inflammation in horses during general anaesthesia

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INTRODUCTION

Mechanical ventilation (MV) may trigger some pulmonary inflammatory response in absence of pre-existing lung disease[1]. Conventional ventilation may also enhance systemic inflammatory response after major surgical procedure[2].

AIM

To investigate SYSTEMIC changes in equine pro-inflammatory mediators (IL-6, TNF-α, ELT, MPO) after 60 min of conventional mechanical ventilation in anaesthetized horses undergoing surgery.

METHODS

Animals: 34 client-owned ASA I-II horses (9.8±5.4 years, 510±88 kg) undergoing elective soft tissue or orthopaedic surgery.

Anaesthesia: Premedication with acepromazine (0.1 mg.kg^{-1}, IM) followed by xylazine (0.6 mg.kg^{-1}, IV) 10 minutes prior to induction with ketamine (2.2 mg.kg^{-1}, IV) and midazolam (0.06 mg.kg^{-1}, IV). Partial intravenous anaesthesia was used for maintenance of anaesthesia: isoflurane in 70% O2 and 30% air; ketamine and midazolam CRIs (1 and 0.02 mg.kg.h^{-1}, respectively, discontinued 20 min prior to recovery).
Surgical procedure started 25 min after induction and lasted a minimum of 45 min.
Antibiotics and NSAIDs were given on the morning of the surgery.

Mechanical Ventilation : Intermittent positive pressure ventilation was started 10 min after induction, using a volume-target, time-cycled ventilator (Drager AVE ventilator, Drager Medical) used in continuous mandatory ventilation mode. Horses were randomly allocated to 4 groups:

- Low pressure-volume: PIP 15 cmH_2O, V_T≤ 10ml.kg^{-1}, in DORSAL (15D, n=5) or LATERAL (L15, n=11) recumbency.
- High pressure-volume: PIP 30 cmH_2O, V_T>10 ml.kg^{-1}, in DORSAL (30D, n=9), or LATERAL (L30, n=9) recumbency.

I:E ratio was set between 1:2 and 1:3. Respiratory rate 8 ± 3 breath per min (Min: 4 - Max: 15) to achieve the PIP and V_T.

Measurements:

- Peripheral arterial blood gas analysis every 20 min (AVL Compact 3 blood gas analyser). Horses were excluded if PaCO2 was < 30 or >60 mmHg, and if PaO2 < 80 mmHg.
- Peripheral venous blood samples (EDTA, jugular vein) immediately before the start at of MV (T0, n=34), after 60 min (T1, n=34) and 120 min (T2, n=12) were immediately centrifuged and the plasma was stored within 30 min at -20°C. IL-6, TNF-α, ELT and MPO measured with equine specific ELISA.

Statistical analysis:

- A linear mixed model with a 1st-order autoregressive structure was used on normalized data (significance: p<0.05)
- Fixed effects: time, recumbency, PIP and their 2x2 interactions. Main effects: anti-inflammatory drugs and antibiotics. Covariate: weight. Random effects: horse and repeated measures within horses.

RESULTS

- **Plasma concentrations of ELT and MPO significantly decreased at T1. Plasma concentration of TNF-α significantly deceased at both T1 and T2. These changed were not linked to PIP, recumbency or their 2-by-2 interactions. Plasma concentration of IL-6 was not significantly different either at T1 or T2 (fig 1-3).**
- **V_T significantly varied with PIP and recumbency; RR and $PaCO_2$ significantly varied with PIP; minute volume significantly varied with recumbency (table I).**
- **No correlation with anti-inflammatory drug and antibiotic therapies was found.**

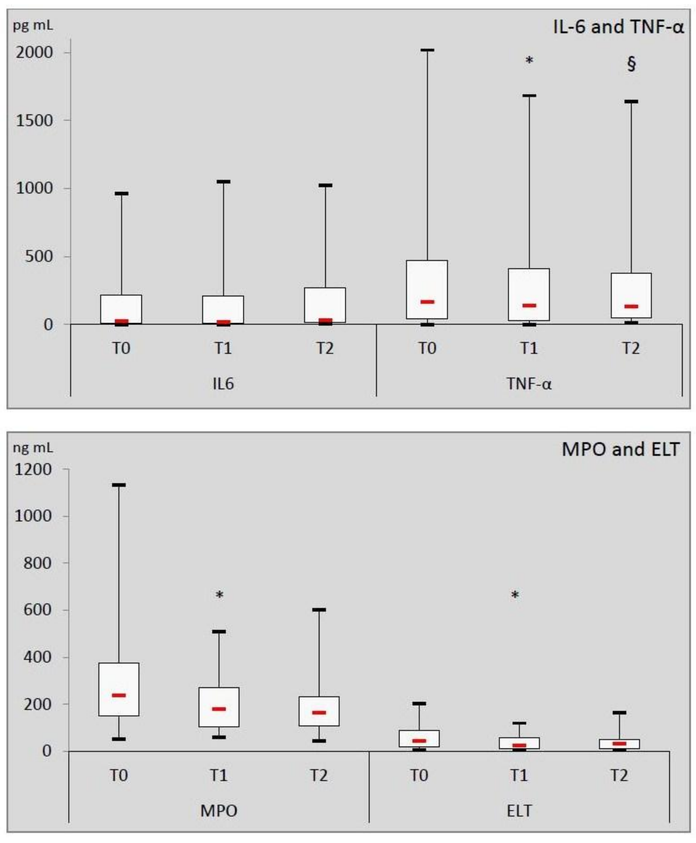

Figure 1: Plasma concentrations of equine IL-6, TNF-α , MPO and ELT at T0 (n=34), T1 (n=34) and T2 (n=12). *: Significantly different from T0 (p<0.05), §: Significantly different from T0 (p<0.05).

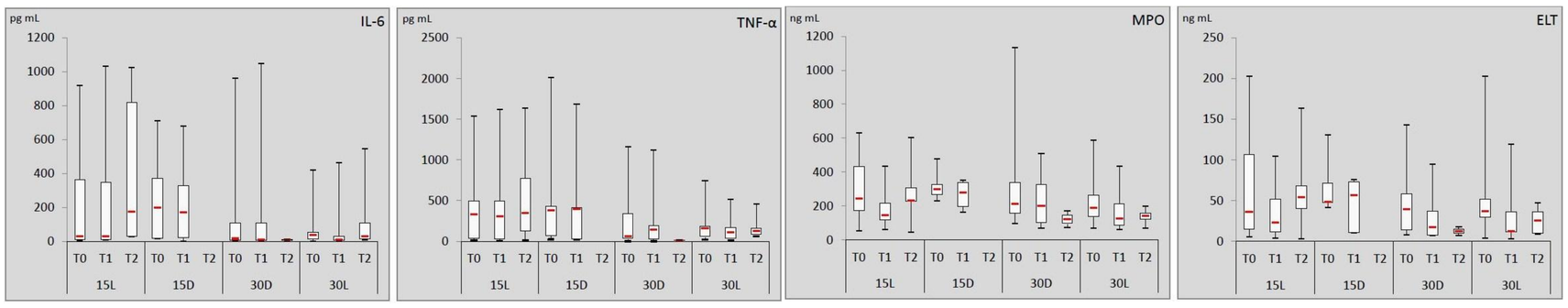

Figure 2:Plasma concentrations of equine IL-6, TNF-α , MPO and ELT at T0, T1 and T2 in 15L (T0=11, T1=11, T2=5), 15D(T0=5, T1=5, T2=0), 30D (T0=9, T1=9, T2=2)and 30L (T0=9, T1=9, T2=5).

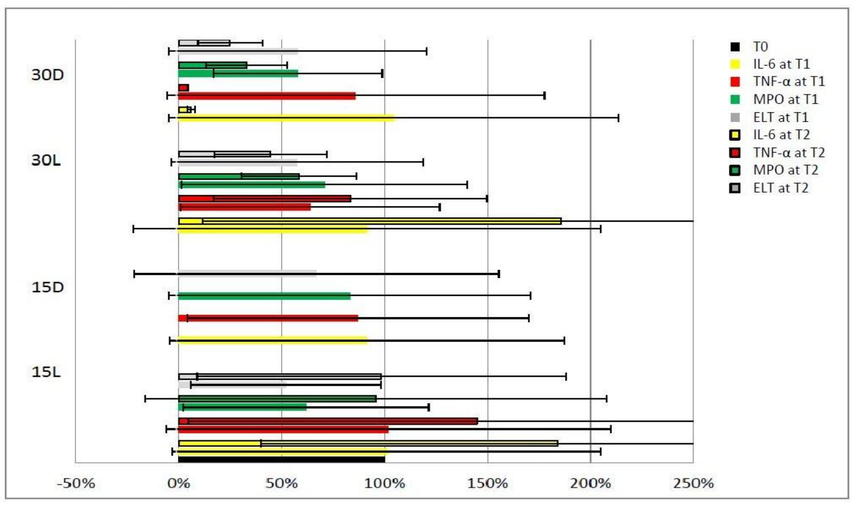

Figure 3: Percent change in plasma equine IL-6, TNF-α, MPO and ELT concentrations in 15L, 15D, 30D and 30L at T1 and T2. Results are expressed as relative values (%) of T0.

Group		15D	30D	15L	30L
RR (breaths/minute)	T0	10.2 ± 3.2†‡	5.9 ± 1.3	9.4 ± 2.6†‡	5.2 ± 0.8
	T1	11.3 ± 2.3†‡	5.3 ± 0.7	10.1 ± 2.5†‡	5.1 ± 0.5
	T2	np	5.1 ± 0.2	11.5 ± 3.1†‡	4.7 ± 0.5
VT (ml/kg)	T0	9.2 ± 2.3$^{\dagger\ddagger\text{¤}}$	16.6 ± 2.8$^{\ddagger\text{¤}\#}$	8 ± 1.8$^{\dagger\ddagger\#}$	14.2 ± 2.3$^{\dagger\text{¤}\#}$
	T1	8.5 ± 2$^{\dagger\ddagger\text{¤}}$	16.6 ± 2$^{\ddagger\text{¤}\#}$	8 ± 1.8$^{\dagger\ddagger\#}$	15.4 ± 2.8$^{\dagger\text{¤}\#}$
	T2	np	17.4 ± 2.2$^{\ddagger\text{¤}}$	7.9 ± 2.3†‡	15.5 ± 3.6$^{\dagger\text{¤}}$
Minute Volume (RR x VT)	T0	94.4 ± 36.4$^{\ddagger\text{¤}}$	96.1 ± 20.6$^{\ddagger\text{¤}}$	73.4 ± 19.9	72.2 ± 13
	T1	93.7 ± 19.3$^{\ddagger\text{¤}}$	86 ± 8.5$^{\ddagger\text{¤}}$	80.1 ± 22.6	77.3 ± 14.9
	T2	np	89.1 ± 8.4$^{\ddagger\text{¤}}$	87.4 ± 21.5	72.1 ± 15.8
PaO_2 (mmHg)	T0	np	np	np	np
	T1	170.7± 65	215.2 ± 130.3	232.5 ± 70.4	241.3 ± 48.5
	T2	np	102.9 ± 25.4	253.6 ± 84.4	222.3 ± 51.4
$PaCO_2$ (mmHg)	T0	np	np	np	np
	T1	53.5 ± 5.8	39.1 ± 3.2	51.1 ± 7.5	39.2 ± 7.2
	T2	np	37.7 ± 1.6	50.5 ± 12.2	36.1 ± 6.1

Table I: Intraoperative respiratory and pulmonary variables at T0, T1 and T2 in 15L, 15D, 30D and 30L at T1 (mean±standard deviation, †significantly different (p<0.05) from 30D; ‡significantly different (p<0.05) from 30L; ¤significantly different (p<0.05) from 15L; #significantly different (p<0.05) from 15D;

CONCLUSIONS

None of the protocols tested in this study were associated with a systemic increase of equine pro-inflammatory mediators (IL-6, TNF-α, ELT, MPO) after 120 minutes of mechanical ventilation.
The use of drugs with anti-inflammatory properties may have contributed to the overall decreased systemic inflammatory mediator concentration, despite MV and surgery.
Pulmonary inflammation, undetectable systemically, cannot be excluded, as suggested recently[3].

Abbreviations:
15L: low pressure-volume ventilation in lateral recumbency; 15D: low pressure-volume ventilation in dorsal recumbency; 30D: high pressure-volume ventilation in dorsal recumbency; 30L: high pressure-volume ventilation in lateral recumbency;
IL: Interleukin; TNF: Tumor Necrosis Factor, MPO: Myeloperoxidase, ELT: Elastase, MV: Mechanical Ventilation, PIP: Peak Inspiratory Pressure, T0: at the start of mechanical ventilation; T1: after 60 minutes of mechanical ventilation; T2. after 120 minutes of MV; V_T: Tidal Volume; RR: respiratory rate; PaO_2 = arterial partial pressure of oxygen; $PaCO_2$ = arterial partial pressure of carbon dioxide.

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References:
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