

Category :**Respiratory: ARDS**

**A105 - Mitigation of cellular apoptosis by diaphragm neurostimulation, and correlation between homovanillic acid and apoptotic markers in a moderate-ards preclinical model**

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**Introduction:**

Dopamine production and hippocampal apoptosis in ARDS subjects undergoing mechanical ventilation (MV) have not been investigated. We explored correlation between these variables, and whether a hybrid ventilatory therapy affects them.

**Methods:**

Pigs undergoing MV (volume control, PEEP 5 cmH<sub>2</sub>O, tidal volume 8 ml/kg) with moderate ARDS (PaO<sub>2</sub>/FiO<sub>2</sub> 100-200) achieved by injecting oleic acid via catheter into the pulmonary artery. Subjects were assigned to three groups (n=6 per group): lung injury (LI) with MV only (LI-MV), LI with temporary transvenous diaphragmatic neurostimulation (TTDN) every other breath (LI-TTDN50%+MV), and LI with TTDN every breath (LI-TTDN100%+MV). TTDN was delivered to achieve 15- 20% reduction in ventilator pressure-time product. The hippocampus was harvested from each subject at study end, and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay was used to stain for cellular apoptosis. TUNEL-positive percentage was determined using machine-learning software. Serum concentration of homovanillic acid at study end was analyzed. Spearman test was run to investigate any association between TUNEL percentage and homovanillic acid serum concentration. P-values <0.05 are considered statistically significant.

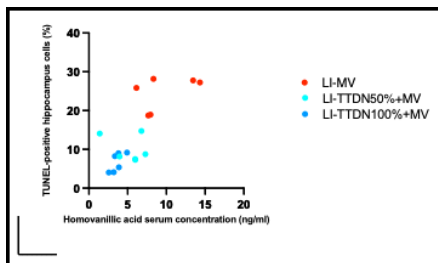
**Results:**

TUNEL-positive cell percentages were [median (IQR)]: 26 (18-27) for LI-MV, 8 (7-14) for LI-TTDN50%+MV, and 6 (4-9) for LI-TTDN100%+MV. Homovanillic acid serum concentrations (ng/ml) were: 8 (7-13) for LI-MV, 6 (3-7) for LI-TTDN50%+MV, and 3 (3-4) for LI-TTDN100%+MV. Spearman correlation test showed a positive, linear, and moderate correlation between TUNEL-positive cell percentage and homovanillic acid serum concentration, r=0.75, p=0.0003 (Figure1).

**Conclusion:**

We found a moderate correlation between the TUNEL-positive cell percentages and dopamine production in our moderate-ARDS preclinical model, and that TTDN subjects showed lower cellular apoptosis and dopamine production compared to MV only with LI.

**Image :**



*Correlation between TUNEL-positive hippocampus cells and homovanillic acid serum concentration*