ID: 245

TITLE: CEREBRAL OXYGENATION AND HEMODYNAMIC PARAMETERS DURING PRESSURE-CONTROLLED VS VOLUME-TARGETED VENTILATION IN EXTREMELY PREMATURE INFANTS.

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CONTENT:

Despite the advances in the non-invasive respiratory support conventional mechanical ventilation (CMV) remains an important therapy in the management of newborns with severe respiratory failure. It has been reported that volume-targeted CMV may be superior to pressure-controlled CMV in the neonate resulting in reduced risk of death or bronchopulmonary dysplasia, however it is not a standard of care in all neonatal units yet and its physiological effects are not fully understood. Hence, this study was aimed at determining the effects of volume-targeted mechanical ventilation on cerebral oxygenation and hemodynamic parameters of extremely premature infants.

A prospective crossover study was conducted at the Department of Neonatology, Poznań University of Medical Sciences in 2017-2018. 20 infants born before 28 weeks of gestation requiring mechanical ventilation were enrolled. Each newborn was ventilated for 3 hours with pressure controlled-assist/control (PC-A/C) ventilation, followed by 3-hours of PC-A/C volume guarantee (VG) ventilation. During both periods cerebral oxygenation (StO2) was assessed using near-infrared spectroscopy (NIRS) and hemodynamic parameters: cardiac output (CO), stroke volume (SV), cardiac index (CI), stroke volume variation (SVV), index of contractility (ICON) were measured using electrical velocimetry (EV).

The average birth weight in the study group was 848 g and the average gestational age was 25.7 weeks. During PC-A/C VG ventilation minute expiratory volume (MVE) was more stable (SD 0.02 vs 0.05 p<0.001) and mean airway pressure (MAP) was lower (8.4 vs 8.7 cmH20, p<0.01), than during pressure-controlled mode. There was no statistically significant difference between mean values of StO2 (80 vs 81%, ns), but the variability of StO2 assessed by comparison of its standard deviation was statistically significantly lower during PC-A/C VG ventilation (SD 1.4 vs 1.9, p<0.01). No statistically significant differences were found for hemodynamic parameters (eg. CO 0.25 vs 0.24 L/min, ns; SV 1.6 vs 1.7ml, ns; SVV 15 vs 14.5%, ns), but there was a trend towards less variable values of heart rate during the PC-A/C VG ventilation (SD 1.8 vs 2.3, p<0.09).

It has been shown that hemodynamic parameters are stable and cerebral oxygenation is less variable during PC-A/C VG ventilation as compared to the pressure-controlled mode. This may be due to less fluctuations in carbon dioxide levels in the blood and more stable cerebral blood flow. Obtained results confirm beneficial cardiorespiratory and cerebral effects of volume-VOLUME targeted ventilation in extremely premature infants.

COI: None declared
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**TITLE:** BIOLOGICAL INTERACTIONS BETWEEN A NEW SYNTHETIC SURFACTANT (CHF5633) AND SECRETORY PHOSPHOLIPASE A2 SYSTEM

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**CONTENT:**

Secretory phospholipase A2 is the enzyme responsible for the hydrolysis of phospholipids at the sn-2 position and the first step of the inflammatory cascade. sPLA2 activity has been directly correlated to mortality and other major outcomes in ARDS (both in adults and children). (1,2) sPLA2 is also directly correlated to oxygenation, need for ventilatory support and lung compliance in preterm babies with RDS and in those with pneumonia or sepsis. (3) Inflammatory acute lung injury models have demonstrated the importance of sPLA2 in their pathogenesis and the possible interest of a strategy involving a sPLA2-resistant surfactant or surfactant protection against sPLA2. (4)

We aimed to explore the biological interactions between sPLA2 and CHF5633 synthetic surfactant and to verify that CHF5633 is at least as effective as poractant-alfa in sPLA2 inhibition. Jurkat cells were differentiated in macrophage-like cells and stimulated with azacitidine, INF-gamma and LPS. sPLA2-IIA (lung subtype of the enzyme) mRNA expression and protein concentration were measured with RQ-PCR and ELISA, respectively. Enzyme activity was assayed as previously published. (5) CHF5633 and poractant-alfa inhibition of sPLA2-IIA was tested at 0-75-150-300-1500 µg/ml for 24h. Single phospholipids, DOPG and POPG (poractant-alfa and CHF5633 components, respectively) and DPPC at 20, 20 and 320 µg/ml, respectively, were also tested. TNFalpha, IL-1Beta, GM-CSF, IL-6, and IL-8 were also assayed.

Both poractant-alfa and CHF5633 significantly reduced sPLA2-IIA content in a dose-dependent manner in cultured Jurkat cells (Figure). CHF5633 and poractant-alfa did not significantly affect any cytokine amount at any dose. POPG seems slightly weaker than DOPG in inhibiting the TNFalpha-induced expression of sPLA2-IIA. In fact, POPG (at 20 µg/ml) significantly reduced TNFalpha expression (DPPC as control 1.6 ± 0.1 vs. POPG 0.5 ± 0.2, rel. exp.; p=0.03) but with no visible effect on sPLA2-IIA at gene and enzyme-amount levels. No phospholipid significantly affected any cytokine amount.

Both poractant-alfa and CHF5633 reduced sPLA2-IIA in a dose-dependent manner. Cytokine amounts were not affected by neither surfactants. These data cannot exclude a stronger effect of surfactants in other human cells or in complex in vivo systems, through a paracrine effect.

COI: N. Pelizzi and F. Salomone are Chiesi Farmaceutici employees. Chiesi Farmaceutici supplied its own products (poractant alfa and CHF5633) without limitations to the study. Apart of this, the authors declare no other conflict of interests.