OBJECTIVE PHARMACODYNAMIC EVALUATION OF DOXAPRAM IN PRETERM INFANTS

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Background Pharmacodynamic evaluation is challenging in neonatal clinical care, and often based on subjective human interpretation of clinical signs and the available ‘snapshot’ of physiological parameters. High frequency data (≥ 1Hz) of bedside patient monitors provide the opportunity of continuous and objective drug evaluation.1 This study investigates the predictive value of continuously available vital and ventilatory parameters to evaluate doxapram therapy. Doxapram is a respiratory stimulant to avoid mechanical ventilation and adverse outcomes of hypoxemia in preterm infants.2

Methods Preterm infants admitted to a level III NICU centre who received doxapram therapy were eligible for inclusion. Stored vital and ventilatory parameters were retrospectively analysed. Multivariate analysis was performed to identify variables that influenced therapy failure (intubation or death) or success. Variables with a p value < 0.1 in univariate analysis were included in the multivariate analysis. Additionally, the ΔSpO2/FiO2-ratio was calculated by subtracting the median SpO2/FiO2-ratio 1 day after therapy from the median SpO2/FiO2-ratio 1 day before therapy.

Results The first episode of doxapram treatment was analysed in a total of 61 preterm infants with a median postnatal age at therapy start (PNA) of 3.0 weeks (IQR: 2.0–3.6). The success rate of doxapram therapy was 57%. Out of all parameters, the SpO2/FiO2-ratio showed to be the most indicative for therapy outcome. The predictive model included the ΔSpO2/FiO2-ratio, the PNA, the administration of a loading dose at start, and intubation within 24 hours before the start of doxapram (area under the curve of 0.828). The ΔSpO2/FiO2-ratio was inversely associated with therapy outcome (OR 0.26, CI 95% 0.07–0.83; p = 0.03).

Conclusion The ΔSpO2/FiO2-ratio between 1 day before and 1 day after start of the therapy is predictive of failure or success of doxapram therapy. The use of physiological data shows potential in the pharmacodynamic evaluation of doxapram therapy.