

## **Increased tidal volume variability as a marker of opioid-induced respiratory depression in children**

\*J Mark Ansermino, MBBCh, MMed, MSc, FFA(SA) †Sean J Barbour, BSc (Hon)), \*Christine A Vandebek, BBA, MBA.

\*Department of Anesthesiology, British Columbia's Children's Hospital and University of British Columbia.

**Introduction.** During opioid administration, decreasing respiratory rate is typically used as a predictor of respiratory depression. Prior to opioid-induced apnea, progressively irregular breathing patterns have been noticed. We hypothesize that opioid administration to children will increase tidal volume variability ( $TV_{var}$ ) and that this will be a better predictor of respiratory depression than a decrease in respiratory rate.

**Methods.** We recruited 32 children aged 2 to 8 years scheduled to undergo surgery. During spontaneous ventilation, flow rates and respiratory rates were continuously recorded while remifentanyl was infused at stepwise increasing doses each lasting 10 minutes. The infusion was continued until the patient showed signs of respiratory depression. Flow data from each dose was used to calculate tidal volumes, from which  $TV_{var}$  was calculated. The respiratory rate and  $TV_{var}$  during the last ( $D_{last}$ ), second to last ( $D_{-2}$ ) and third to last ( $D_{-3}$ ), administered doses were compared to those during baseline (fourth to last dose). We chose a threshold of  $TV_{var}$  increase and compared it to a decrease in respiratory rate below 10 breaths/minute as predictors of respiratory depression.

**Results.** Compared to baseline, the  $TV_{var}$  increased by 336% and 668% during  $D_{-2}$  and  $D_{last}$  respectively, whereas respiratory rate decreased by 14.3%, 31.7% and 55.5% during  $D_{-3}$ ,  $D_{-2}$  and  $D_{last}$  respectively. A threshold increase in  $TV_{var}$  of 150% over baseline correctly predicted respiratory depression in 41% of patients, compared to a drop in respiratory rate correctly predicting 22% of patients.

**Conclusions.**  $TV_{var}$  increases as children approach opioid-induced respiratory depression. This is a more useful predictor of respiratory depression than a fall in respiratory rate because the  $TV_{var}$  increase is 10 times the drop in respiratory rate, a  $TV_{var}$  increase correctly predicts respiratory depression twice as often as decreased respiratory rate, and  $TV_{var}$  is independent of age related alterations in physiologic respiratory rates.