Critical Review Form
Therapy

Microstream Capnography Improves Patient Monitoring During Moderate Sedation: A Randomized, Controlled Trial, *Pediatrics* 2006;117:e1170-e1178

Objective: **To investigate "whether electronically monitoring respiratory activity reduces the incidence of arterial oxygen desaturation in pediatric patients undergoing moderate sedation for gastrointestinal endoscopy" . (p. e1171)**

Methods: **Prospective double-blinded, randomized trial at the Children's Hospital Boston GI endoscopy clinic from December 2003 to November 2004. Inclusion criteria included all consenting patients (ages 6 months to 19 years) scheduled to undergo EGD or colonoscopy with American Society of Anesthesiologist Class 1 (healthy) or 2 (single controlled disease). Exclusion criteria included ASA Class 3 to 5, general anesthesia, emergency procedure, known seizure disorder, use of mind altering or chronic pain medications.**

Subjects were randomized by independent observers to intervention (signal endoscopy nurse if capnogram alveolar hypoventilation > 15 seconds) or central (signal endoscopy nurse if > 60 seconds flat capnogram). The endoscopy RNs then repositioned the patient's head and/or stimulated them to breathe deeply. The primary outcome was oxygen desaturation defined as < 95% for > 5 seconds. Secondary outcomes included endoscopy-RN documentation of abnormal ventilation, termination of the procedure for patient safety reasons, or need for bag-mask ventilation or sedation reversal or seizure.

Gastroenterologists and endoscopy-RNs were blinded to the patient assignment and the capnography data. The independent observers were a research nurse and a research assistant. Each had five practice patients not included in the data analysis in addition to bi-weekly silent observation of one another's data collection to assess inter-rater reliability. The endoscopy RN recorded adverse events including hypoventilation, bradycardia, hypotension, vomiting aspiration or seizures. Sedation level was graded using the Ramsey Scale and documented every five-minutes by the endoscopy RN. A size appropriate nasal cannula including a continuous CO_2 sampling device (Smart Mac-Line O_2 $ETCO_2$ Oridion Medical Inc) was used. Sedation regimens followed institutional protocols with fentanyl (max dose: 5 µg/kg) and midazolam (max dose: 0.3mg/kg) IV.

In addition to univariate analysis with 2-sided Fisher's exact test for proportions and Mann-Whitney U for continuous variables, the investigators performed a multiple logistic regression analysis to adjust for any unequally distributed prognostic variables. Assuming an adverse event rate of 12%, a sample of 174 would provide 90% power to detect a five-fold reduction in need for an intervention compared with the control group (4% vs. 20%).

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?**	
1.	Were patients randomized?	Yes. "Independent observers randomly assigned patients to study arms by opening pre-generated, sequentially numbered, opaque sealed envelopes. The randomization scheme was permuted by blocks of 2, 4, 6, and 8, stratified by procedure type (esophagogastroduodenoscopy [EGD] or colonoscopy)'. (p. e1173).
2.	Was randomization concealed (blinded)?	Yes. " Investigators, patients, endoscopy unit staff (RNs and technicians), and endoscopists were blinded to study arm assignments" (p. e1173).
3.	Were patients analyzed in the groups to which they were randomized?	Yes. "We conducted an intention-to-treat analysis". (p. e1173).
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. "Intervention and control patients did not differ significantly in baseline characteristics or procedural times (Table 1)". (p. e1175).
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?**	
1.	Were patients aware of group allocation?	No.
2.	Were clinicians aware of group allocation?	No.

3.	Were outcome assessors aware of group allocation?	No, the endoscopy RNs who recorded the presence of adverse events were blinded to group assignment and therefore unaware of group allocation.
4.	Was follow-up complete?	This was a cross-sectional analysis at one point in time so there was no follow-up and no subjects were lost to data analysis.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	• Sample size 163 patients (131 EGD's, 21 colonoscopy, 11 EGD + colonoscopy) after 16 subjects refused to participate. 83 were randomized to the intervention and 80 to control (CONSORT diagram, Fig 2 p. e1175). • No adverse events occurred during the study period including no bag-mask ventilation, sedation reversal, cardiovascular, instability, or seizure. • Endoscopy RNs documented poor ventilation during five (3%) procedures and no episodes of apnea although 29 (18%) had at least one episode of oxygen saturation <95% for > 5 seconds. • Patients who experienced de-saturation did so a mean of 3.4 minutes after capnograms first depicted hypoventilation. • Patients in the intervention arm were significantly less likely to have an intra-procedural de-saturation (11% vs. 24%, $p < 0.03$). • Greater than 15 seconds of alveolar hypoventilation was rated in 58% of patients. • Two variables were associated with desaturation episodes: detection of apnea or disordered breathing by the endoscopy RN and hypoventilation noted by the RN. Logistic regression modeling adjusting for these two confounding variables still demonstrated a benefit for capnometry (OR 0.17, 95% CI 0.04 – 0.71, p = 0.15) (Table 2, p. e1176).
2.	How precise was the estimate of the treatment effect?	Very few CI's are reported so uncertain. The logistic regression OR 95% CI does not cross one.

III.	How can I apply the results to patient care (answer the questions posed below)?	
1.	Were the study patients similar to my patient?	No. These were very healthy pediatric patients in an endoscopy suite. In fact, emergent procedures were excluded. Therefore, future trials will need to demonstrate that routine incorporation of end-tidal CO_2 monitoring in emergency care settings reduce hypoxic and adverse event rates with procedural sedation.
2.	Were all clinically important outcomes considered?	No. " Our primary outcome measure is not intended to be a surrogate for significant adverse events but rather represents a point at which the operating environment in our endoscopy unit is altered by staff concern for patient safety". (p. e1177). Future trials will need to assess patient and sedating personnel satisfaction and appropriate interpretation of end-tidal CO_2 monitoring.
3.	Are the likely treatment benefits worth the potential harm and costs?	"Clinicians will often intervene to stimulate patient respiration if a pulse oximeter detects minor arterial desaturation, a relatively late sign of suboptimal ventilation. Acting even earlier by adopting a "new cockpit dial," such as capnography, may be warranted and valuable in avoiding significant morbidity and mortality". (p. e1177)

Limitations:

1) **No reference to or inclusion of all the elements of the CONSORT statement for RCT's.**

2) **Small sample size at single institution with no adverse events detected during the study period. Is capnography important solely to detect hypoxia early if the large majority of cases have no hypoxia-sequelae? How would capnography work in less academic environments or non-endoscopy sites like the ED (external validity)?**

3) **No CI's reported for proportions.**

4) **Sedation used only fentanyl/versed so uncertain extrapolation to safer, more routine ED sedation practice in 2010 (ketamine, propofol).**

Bottom Line:

Single-center pediatric endoscopy-based randomized, controlled study suggesting that capnography independently improves detection of alveolar hypoventilation and reduces arterial oxygen desaturations during moderate sedation.