Critical Review Form
Therapy

End-tidal Carbon Dioxide Monitoring during Procedural Sedation, *Acad Emerg* 2002; 9:275-80

Objectives: **"To prospectively evaluate the utility of $ETCO_2$ monitors to detect RD (respiratory depression) in patients undergoing PS (procedural sedation)" and "to determine whether the depth of sedation as perceived by the clinician can be predicted by the amount of RD detected by $ETCO_2$". (p. 276)**

Methods: **Prospective observational study of adult ED procedural sedation at Hennepin County Medical Center (Minneapolis, MN) from December 2000 – April 2001. Exclusion criteria were failure to consent. The specific procedural sedation & analgesia (PSA) regimen was at the attending physician's discretion. Every two minutes the following patient parameters were recorded: pulse oximetry, heart rate, blood pressure, respiratory rate, $ETCO_2$, and emergency physician Observer's Assessment of Alertness/Sedation scale (OAA/S). Respiratory depression (RD) was defined by either oxygen saturation < 90% for 1-minute, $ETCO_2$ > 50 mm Hg at any time or airway obstruction as noted by loss of $ETCO_2$ waveform. The primary outcome was rate of RD and was compared across different sedation regimens.**

Data were collected by a trained research assistant. At the end of the procedure the emergency physician noted any complications and whether the patient required any assisted ventilation. Spearman's rho analysis was used to test for an association between the OAA/S score and $ETCO_2$. In order to detect a 20% difference in the rate of RD between agents with χ^2 tests with an alpha of 0.05 and 80% power, 28 patients per sedative agent were required.

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?	No. This was an observational (non-randomized, not controlled) trial.
2.	Was randomization concealed (blinded)?	No – all parties knew what was being done.
3.	Were patients analyzed in the groups to which they were randomized?	Not randomized so intention-to-treat is not relevant.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No treatment and control groups.

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?	Yes – not randomized
2.	Were clinicians aware of group allocation?	Yes.
3.	Were outcome assessors aware of group allocation?	Yes, and this is particularly problematic since some clinicians may have pre-formed opinions about capnography monitoring during PSA. Since they know the study was underway and what the hypothesis and measures are, they could theoretically alter their management to make $ETCO_2$ look more or less appealing (co-intervention bias, ascertainment bias, etc.).
4.	Was follow-up complete?	No loss to follow-up was reported during cross-sectional analysis.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect? **Wash U JC TABLE 1** RD present absent Y 21 12 Sen 64 (51-74) Spec 71(61-79) PPV 64 NPV 71 N 12 29 LR+ 2.2 (1.3-3.6) LR- 0.5 (0.3-0.8) * RD = respiratory depression which was defined by a change in $ETCO_2$ by more than 10 mm Hg. **Wash U JC Table 2** Agent Total RD No RD RD Rate Metho 40 (54%) 19 21 47% Propofol 21 (28%) 4 19 19% Fent/Ver 10 (13%) 8 2 80% Etom 3 (4%) 2 1 66%	• 74 patients enrolled with mean age 38-years and 57% were male. • Bulk of procedures were fx dislocation (35%), reduction (27%) or abscess drainage (30%). • 11 patients required BVM but none > 2-minutes. Among 11 with oxygen desaturation < 90 %, five had $ETCO_2$ of < 50 mm Hg and a normal waveform yielding the Table 1 test characteristics for $ETCO_2$. • RD was noted in 33/74 (45%) including 19 (57% of those with RD) with RD. • All 11 patients requiring BVM had $ETCO_2$ defined RD (7 absent waveform, 2 $ETCO_2$ > 50, 2-pulse ox < 90%). • Investigators were unable to attain their *a priori* sample size but their results suggested (though not statistically significant) differences between PSA regimens for RD rates (Table 2). • No correlation between $ETCO_2$ and OAA/S was detected --19/33 RD patients never had an OAA/S score < 5 (they were fully awake and responsive).

2.	How precise was the estimate of the treatment effect?	Uncertain since no CI's are reported.
III.	**How can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	Yes, ED patients requiring PSA for orthopedic or abscess management. The sedating medications were somewhat atypical for 2010 EM where propofol and ketamine predominate.
2.	Were all clinically important outcomes considered?	No. The investigators did not assess patient satisfaction, procedural time, clinician acceptability, cost, or $ETCO_2$ training considerations.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain based upon this uncontrolled trial. Although the results suggest an association with the surrogate number of desaturation, numerous examples show the scientific pathway of convincing observational trials later disproven by RCT's (emphysema, naloxone for spinal injury, etc.).

Limitations

1) **Observational trial requiring RCT confirmation.**

2) **Potential incorporation bias in the primary outcome of respiratory depression since 2/3 criteria to diagnose RD involve the $ETCO_2$ and the primary outcome is being used to establish the merits of $ETCO_2$.**

3) **Under-powered for the secondary outcome of sedating regimen comparison.**

4) **No CI's are reported to assess precision.**

5) **Surrogate outcome measure (RD) used rather than patient and clinician important (though rare) adverse event.**

6) **Atypical, rarely used sedation scale. Why did the investigators not report (or at least discuss) the more commonly used Ramsey scale?**

7) **Single center with limited external validity.**

Bottom Line

Very small single-center ED-based observational study suggesting that $ETCO_2$ may augment or replace pulse oximetry to monitor procedural sedation patients. $ETCO_2$ is not correlated with one metric of sedation intensity (OAA/S). Future controlled trials should assess sufficiently large sample sizes in heterogeneous settings using measures of RD not subject to incorporation bias and assessing patient/clinician outcomes of interest before $ETCO_2$ monitoring should be labeled a procedural sedation standard-of-care.