

Bon Secours Richmond
Pharmacy & Therapeutics Committees
Addition of Dye to Tube Feedings
7/2002

Recommendations: MEC approved

- The clinical focus should be on prevention of aspiration rather than identification.
- Methylene blue will be removed from the Pyxis stations.
- Glucose oxidase testing of tracheal secretions is not recommended as it lacks specificity.

Blue Food Dye (FD&C Blue No.1) may be added to the enteral formula of high-risk aspiration tube fed patients as a marker for aspiration per physician orders only for the first 48 hours of the tube feeding administration.

PROCEDURE

1. Tru Blu – 1ml-vial packets are available from pharmacy per physician orders to be added to tube feeding in increments of 1ml per liter of prescribed tube feeding for a time period of 48 hr only for observation of possible patient aspiration.
2. Pharmacy will enter orders for blue food dye with stop dates of 48 hours after the initiation date and time.
3. Nursing staff should administer the following practices for safe administration of tube feeding in the high risk aspiration patient:
 - * Head of bed must be elevated to 30-45 degrees for patients on enteral feedings.
 - *Gastric residuals should be checked prior to feeding for NG and G tubes.
 - *Tube feedings should be held if gastric residuals are greater than 100-150ccs or according to the physician's orders.
 - *Tube placement should be checked if aspiration is suspected.
4. If secretions suctioned from the patient's trachea are blue tinged the MD should be called and the tube feedings stopped.

Findings:

- The incidence of aspiration is high in enterally fed ICU patient, up to 30%, because of supine positioning, decreased gastric motility from illness or drugs, and altered mental status or other mechanisms of altered airway protective reflexes.
- No data is available to justify the use of dyes in detection of aspiration. Use of dye was started before studies were done.
- **FD&C Blue No.1**
 - Inexpensive
 - Non-absorbable in healthy patients
 - *Never tested in critically ill humans where gut permeability is increased.*
 - Available in sterile unit of use vials 2% 5ml (100 mg), 2.5% 4ml (100 mg)
 - *No studies assuring its sensitivity or safety.*
 - No consensus guidelines are available regarding the volume of dye to add to feedings, a few drops to 5 ml/250 ml.
 - Dye use precedes studies demonstrating poor sensitivity. No gold standard test is available to define aspiration.
 - Dye method has not been proven a sensitive test to detect aspiration when testing endotracheal aspirates, 3 human and one animal study have demonstrated a lack of sensitivity.
 - Liu: 0% (0/150) dye positive, 12% (18/150) glucose oxidase positive, 1 patient with clinical presentation of aspiration
 - Potts: 15 patients receiving enteral feedings in which 33% (5/15) demonstrating clinical aspiration (T >=37.8, HR >=100 BMP, WBC > 10,000, and >=1 sign of respiratory deterioration): 27% tested dye positive and 87% tested glucose oxidase positive.

	Glucose Oxidase (>=20 mg/dl)	Blue Dye
Tube Feed patients	16% (30/189 samples), 8% (16/189) exclude those samples containing blood	2.6% (5/189 samples)
Presumptive Aspiration: (Either glucose oxidase or dye positive) 53% (8/15 patients- 18 specimens)	83% (15/18 samples)	28% (5/18 samples)

Clinical Significant Aspiration 33% (5/15 patients)	87% (13/15 samples)	27% (4/15 samples)
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- Montejo-Gonzalez: 38 mechanically ventilated adults: < 1% (4/448) dye positive, 32% (143/448) glucose oxidase positive (> 20 mg/dl)
- Animal studies show that endotracheal administered blue dye appeared on the surface of the lung in 12 seconds and that retrieval of aspirated gastric contents with endotracheal suctioning was unlikely. Positive airway pressure and negative intrapleural pressure present during mechanical ventilation favor distal transit of intratracheal fluids. Thus, the assumption that aspirated blue dye would preferentially remain in the large airways accessible to suction catheters was flawed. A second large animal study (Metheny) found poor utility for blue-dye method in aspiration detection.

Swallowing Studies:

- Thompson-Henry: Aspiration was detected in five out of five cases by fiber optic endoscopic evaluation of swallowing or by modified barium swallow study. None were detected by suctioning after semisolid food dyed blue.
- Brady: 20 consecutive simultaneous modified Evans blue dye study (MEBD) and videofluoroscopic swallow study patients were completed on patients with tracheostomies at an acute rehabilitation hospital. MEBD showed a 50% false-negative error for trace aspiration when compared to the gold standard VFSS and 0% false-negative for greater than trace aspiration. In the modified Evans blue dye test the patient ingest food and liquids that have been dyed blue. The test is positive for aspiration when blue food or liquid is suctioned through the tracheostomy.
- In 1993 the use of blue dye was discouraged due to safety concerns.
- ASPEN, 1998 noted that dye had not been adequately tested and warned of unknown effects of long-term use.

Toxicity

- Intratracheally administered dyes (bromophenol blue) increase lung epithelial permeability, consistent with injurious effects.
- Amount of dye added to enteral feedings before toxicity has ranged from 5 drops per 500 ml of fluid to 20- to 100 ml of dye to feedings.
- Time from addition of dye to onset of patient discoloration varied from hours to 18 days.
- *Mitochondrial O₂ consumption is decrease by 65% at dye concentrations of 0.1 mg/ml and virtually eliminated at 0.8 mg/ml.*
- Serum appears blue-green at dye concentrations of 0.1-0.2 mg/ml, within levels those know to poison the mitochondria.
- *Toxicity features are consistent with poisoning by mitochondrial toxins (uncoupling of mitochondrial respiration): inhibits oxidative phosphorylation, blocks adenine nucleotide transport resulting in diminished adenosine triphosphate (ATP) production: lactic acidosis, altered mental status, hypotension, hyperthermia, shock, and rapid death.*
 - Signs and symptoms noted in case reports include: discoloration of urine, skin, serum and other body fluids, hypotension, profound metabolic acidosis, and MI. Cyanosis has been noted despite adequate arterial oxygenation.
- Absorbed dye may have adverse effects on the intestinal wall and mucosa associated lymphoid tissue function
- Absorption is increased in conditions associated with increased gut permeability: sepsis, severe burns, trauma, hemorrhagic shock, cardiac bypass, major vascular surgery, AAA repair, NSAID use, renal failure, celiac sprue, IBD, cystic fibrosis.
- Contamination:
 - Pseudomonas aeruginosa was isolated from respiratory secretions of 20 mechanically ventilated patients, of which 19 had been administered nasogastric tube feedings. P. Aeruginosa was isolated from a multiple-use bottle of blue food dye use in the ICU to tint the tube feedings.
- Chemistry and Pharmacology
 - Created through chemical reactions with coal tar products. Some countries do not allow its use due to carcinogenicity and toxicity.
 - Molecular weight 793 daltons.
 - FDA current limit for intake is 12.5 mg/kg per day in the healthy people.
- Lab test interference
 - Interferes with and gives inaccurate occult blood test and gastric pH test
- **Methylene blue**
 - may cause hemolytic anemia, hyperbilirubinemia, Heinz body formation and is expensive.
 - Well absorbed by GI tract and excreted in urine and bile.
 - Contraindications:
 - Glucose 6 phosphate dehydrogenase deficiency
 - Severe renal insufficiency
 - Adverse effects
 - Nausea, vomiting, diarrhea, gastritis, dysuria, painful micturition
 - Test interference:
 - false positive for blood in stool and gastric fluid (80% false + interference) unless <=1.5 ml/liter
 - colorimetric pH papers may be unreadable
 - High dose inhibits mitochondrial function.
 - Falsely low pulse oximetry readings may result with IV use.
- **Glucose oxidase method**

A single positive reading is not as significant as are almost continuously positive readings, especially when they are 90 mg/dl or more when tube feedings with glucose concentrations of > 300 mg/dl are used. Due to differing glucose concentrations of enteral products clinicians will need to look for changing patterns for glucose concentrations in tracheal secretions. Some authors recommend using enteral formulas with high glucose concentrations (200-300 mg/dl). A sputum trap is needed to collect the sample.

- Kinsey: 15 enterally fed and 15 non-enterally fed intubated patients concluded glucose method is unlikely to be useful in determining aspiration. Samples were ultrafiltered before analysis. Mean tracheal secretion glucose concentrations were 66 ± 54 mg/dl non-enteral feed and 105 ± 70 mg/dl enteral feed. No correlation between BS and tracheal secretion glucose concentrations.
- Winterbauer: 20 critical ill patients enterally fed versus control group of 50 patients not enterally fed (6 diabetic and 12 with pulmonary infection).
 - Conclusion: *Deterioration of respiratory status was associated with virtually continuous aspiration and glucose content of ≥130 mg/dl for > 50% of samples.*
 - Control group 46/50 negative for glucose (≥25 mg/dl)
 - Enterally fed group: 38% (123/323) samples positive
 - Aspiration patterns
 - 14 patients without clinically significant aspiration
 - no glucose after 80% of feedings
 - 25-90 mg/dl for 19% of feedings
 - ≥130 mg/dl for 1% of feedings
 - 6 patients with clinically significant aspiration (some combination of tachypnea, tachycardia, fever, hypoxemia, and new infiltrate on chest x-ray, no other obvious explanation, and the syndrome resolved coincident with discontinuation of the feeding.)
 - no glucose 5% of feedings
 - 25-90 mg/dl for 38% of time
 - ≥130 mg/dl for 57% of feedings
- Metheny: 62 acutely ill adults with artificial airways
 - Conclusion: It appears appropriate to use glucose oxidase reagent strip to estimate glucose concentrations in tracheobronchial fluid. Personal Communication: *Dr Metheny does not recommend glucose oxidase testing as further studies, to be published, have shown it does not demonstrate specificity.*
 - The high correlation between the lab assay and glucose oxidase strips indicates that it is reasonable to use the glucose oxidase strips at the bedside for testing.
 - Serum glucose was not shown to impact the tracheal glucose.

	Comparison Methods		Correlation
	Comparison of two methods to determine tracheobronchial glucose from 75 samples	Glucose Oxidase strip 24.2 ± 46 (range 0-255)	Laboratory Assay 21.6 ± 42 (range 0-297)
Tracheal glucose versus Capillary Blood Sugar from 66 samples drawn within 5 minutes of trach sample	Capillary Blood Glucose (range 55-381)		Poor Correlation r=0.12 P=0.36
Comparison of two methods to determine glucose content of 22 enteral formulas	Glucose Oxidase Strip 188.6 ± 157	Laboratory Assay 259 ± 206	R= 0.95 P < 0.01

- Elpern: 31 tracheally intubated patients, similar glucose patterns in enterally fed and non enterally fed patients: 38% (208/540) and 30% (11/373) with a similar range of glucose values.
- Blood in respiratory secretions is associated with false positive tests
- Use of distilled water or normal saline during suctioning is to be avoided as dilution of the trach sample occurs.
- Acetylcysteine may interfere with test

Glucose Content of Tube Feeding Formulas	
Osmolite	202
Osmolite HN	49
Isocal	44
Isocal HN	152
Pulmocare	62

- Methods to minimize the potential for aspiration
 - Up to 30% of critically ill patients receiving enteral nutrition experience clinically significant aspiration of their feedings with evidence of respiratory deterioration.
 - Document correct tube placement (pH testing, x ray documentation)
 - Auscultation is ineffective in determining the placement of Nasogastric tube or Nasointestinal tubes
 - Mark tube when correct placement is achieved to monitor for tube migration.
 - Elevation of head of bed to 30 degrees (incidence of aspiration 4 x higher in supine position)
 - Duodenal or jejunal feedings
 - Gastric motility agents (metoclopramide, erythromycin)
 - Checking residual every four to eight hours with continuous feedings and immediately before bolus feedings.
 - Hold enteral feeding when gastric residuals are > 150 ml.
 - Start feedings at a slower rate and increase slowly.
 - Intubated patients intra-cuff pressure at 20-25 cm water (18-20 mmHG)
- Signs of aspiration
 - Tachypnea, tachycardia, fever, hypoxemia, new infiltrated on chest x-ray

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