Comparison of Blue Dye Visualization and Glucose Oxidase Test Strip Methods for Detecting Pulmonary Aspiration of Enteral Feedings in Intubated Adults*


Study objective: To compare the relative utility of blue dye visualization with a glucose oxidase test strip method for detecting aspiration of enteral feedings.

Design: Tracheally intubated adults were prospectively monitored for aspiration of enteral feedings.

Setting: Intensive care units of two community hospitals in Michigan.

Interventions: None.

Patients: The experimental group consisted of 15 patients receiving enteral feedings. The control group included 14 patients not enterally fed.

Measurements and results: Blue food coloring was added to feeding formulas to obtain a visible blue color. At 8-h intervals, tracheal secretions were examined for blue discoloration, followed by measurement of glucose concentration using a calibrated glucose meter. Clinically significant aspiration was defined to require the following: (1) a bloodless positive glucose reading (≥20 mg/dl); (2) one or more signs of systemic inflammation; and (3) one or more signs of respiratory deterioration. Eight (53 percent) of 15 patients in the experimental group experienced at least one episode of presumptive aspiration as defined by either a bloodless positive glucose reading or visible blue discoloration of tracheal secretions. Clinically significant aspiration occurred in 5 (33 percent) of 15 patients in whom bloodless glucose readings were positive in 13 (19 percent) of 67 samples; among patients not developing this complication, glucose was found in only 3 (5 percent) of 60 samples; (p=0.005). Inspecting tracheal secretions for blue dye usually failed to detect aspiration episodes identifiable by the glucose oxidase test strip method (relative sensitivity, 13 percent). Blue dye visualization performed no better among patients developing clinically significant aspiration (relative sensitivity, 15 percent). Patients who developed clinically significant aspiration received more of their enteral feedings in the supine position than patients without this complication (89 percent vs 21 percent; **p<0.001**).

Conclusions: Inspecting tracheal secretions for blue discoloration failed to detect most episodes of enteral feeding aspiration. Glucose oxidase test strip methods should replace blue dye visualization for detecting aspiration of enteral feedings in intubated adults.

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Materials and Methods

Patients

Tracheally intubated adults admitted to the intensive care units of two community teaching hospitals in central lower Michigan were prospectively monitored for aspiration of enteral feedings between October 1990 and April 1991. Patients were excluded if they were younger than 18 years old or if informed consent could not be obtained. Oral intake was not permitted during the study period, thereby eliminating the mouth as a direct source of glucose detected in respiratory secretions. Direct tracheal suctioning of these intubated patients for specimen collection ensured that glucose concentrations were measured only for secretions located in the respiratory tract. The study population consisted of 15 experimental group patients receiving enteral feedings and 14 control group patients not receiving enteral nutrition. Analysis of control group specimens enabled estimation of the frequency of measurable glucose concentrations in tracheal secretions in the absence of enteral feedings as a source of glucose. Five patients initially enrolled in the control group crossed over to the experimental group at the initiation of enteral feedings.

Decisions regarding tube placement and all aspects of enteral nutrition were made by each patient's personal physician without influence by the investigators. Data collection was terminated on death or extubation. Informed consent was obtained from all patients or their representatives. The study protocol was approved by the human research committees at Michigan State University (East Lansing, Mich.), E. W. Sparrow Hospital, and Ingham Medical Center (Lansing, Mich.).

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**Definitions and Rationale of Methods to Detect Enteral Feeding Aspiration**

Adding blue dye to enteral formulas and inspecting respiratory secretions for blue discoloration to detect enteral feeding aspiration is a common but subjective test requiring a visual interpretation. The utility of this method is unknown. Using glucose oxidase test strips and an automated glucose meter to measure glucose concentration in respiratory secretions is an objective method for detecting enteral feeding aspiration not requiring interpretation. The subjective nature of the blue dye visualization method and in the absence of published data comparing this method with glucose oxidase test strip methods for detecting enteral feeding aspiration, we initially separated aspiration events into two categories, presumptive aspiration and objective aspiration.

We defined a *positive glucose reading* as a tracheal secretion specimen having a glucose concentration ≥20 mg/dl, measured using an automated glucose meter (AccuCheck IIM; Boehringer Mannheim Corporation, Indianapolis, Ind). *Presumptive aspiration* was defined as having occurred when tracheal secretions showed either a positive glucose reading (without visible blood) or observable blue discoloration. This definition allowed the two methods to be compared in their ability to detect aspiration events.

**Objective aspiration** was defined as a bloodless, positive glucose reading regardless of blue discoloration of tracheal aspiration secretions. *Clinically significant aspiration* was defined as the occurrence of objective aspiration combined with one or more signs of systemic inflammation (temperature ≥37.8°C; heart rate ≥100 beats/min; leukocyte count ≥10,000/cu mm), and one or more signs of respiratory deterioration (respirations ≥20/min; new pulmonary infiltrate; increase in quantity or purulence of secretions [≥25 leukocytes and <10 squamous epithelial cells per 10X field]; worsening hypoxia [PaO₂ <60 mm Hg with a FIO₂ >0.50]). Patient position was considered upright when the head of the bed was raised ≥30° from the horizontal.

**Instruments**

Blue food coloring (FD&C Blue No. 1, FD&C Red No. 40; McCormick & Co, Inc, Hunt Valley, Md) was added to feeding formulas to achieve a visible blue color according to the standard protocols of the participating hospitals. At 9-h intervals and whenever an acute aspiration event was suspected, a nurse-investigator suctioned tracheal secretions into a transparent suction trap (Sherwood Medical, St Louis, Mo) and examined the specimen for blue discoloration against a white background under full room lighting. Any visible evidence of blood in the tracheal secretions was also noted. To prevent observation bias, results of visual inspection were immediately recorded. Each specimen was then reacted with a glucose oxidase test strip (Chemstrip bG, Boehringer Mannheim Corporation) and the glucose concentration measured using a glucose meter (AccuCheck IIM). At the time of sampling, vital signs, patient position, and gastric residual volume were recorded. Other data collected included arterial blood gas results, leukocyte counts, and evidence of purulent tracheal secretions. Chest roentgenograms performed during the study were compared with roentgenograms done within 48 h of enrollment to identify new pulmonary infiltrates. Physician providers in this study had access to the results of visual inspection for blue discoloration but not results of glucose testing.

**Glucose Concentrations of Enteral Formulas**

To determine the sensitivity of the glucose oxidase test system for detecting contamination of tracheal secretions with enteral formulas, the glucose concentrations of four commercial formulas were tested (Osmolyte, Osmolyte HN, Ensure, and Jevity; Ross Laboratories, Columbus, Ohio). An average 67.5 ± 13 μl blue food coloring was added to each 100 ml undiluted formula to obtain a prominent and visibly uniform blue color for each commercial product, matching the blue color intensity of the standard enteral formulas of the participating hospitals. Serial twofold dilutions of each formula were then prepared using 0.9 percent sodium chloride. Equal aliquots of formula were randomly selected and tested in a blinded manner. The presence or absence of blue discoloration was recorded first, followed by determination of glucose concentration using a glucose oxidase test strip and a calibrated glucose meter (AccuCheck IIM) according to the manufacturer’s protocol for determining the glucose concentration of capillary blood specimens.

**Quality Control**

Accuracy of glucose readings during the study was confirmed by visual comparison of the color of each reacted test strip against the manufacturer’s color standards and by calibration of the meter at least monthly. No discrepancies were observed between visual inspection results and automated reading of the test strips.

**Statistics**

Differences between means were analyzed using the two-tailed Student’s t test. Differences between discrete variables were analyzed using χ² with Yates’ correction when appropriate. Significance of differences between proportions was determined using a one-tailed Z test. Significance was set at p<0.05.

**Results**

**Glucose Concentration of Enteral Formulas**

Results of inspection for blue discoloration and mean glucose concentrations for each dilution of enteral formula are presented in Table 1. In three of the four formulas tested, visible blue discoloration was
Table 2—Characteristics of Study Patients

<table>
<thead>
<tr>
<th>Item</th>
<th>Control Group</th>
<th>Experimental Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients*</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Men</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Women</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Total samples (n = 306)</td>
<td>117</td>
<td>189</td>
</tr>
<tr>
<td>Mean age ± SD, yr†</td>
<td>58 ± 20</td>
<td>66 ± 17</td>
</tr>
<tr>
<td>Mean LOS ± SD, days†</td>
<td>25 ± 13</td>
<td>31 ± 31</td>
</tr>
</tbody>
</table>

*Includes five patients who crossed over from the control group to the experimental group at the initiation of enteral feedings.
†p<0.05.
‡LOS = length of stay.

maintained through the 1:16 dilution. The presence of visible blue discoloration correlated with a glucose reading ≥20 mg/dl in 18 (94 percent) of 19 samples positive by either method. Therefore, a glucose reading ≥20 mg/dl was considered sufficient to detect aspiration of enteral feedings comprising 1/16th (v/v) of accessible tracheal secretions.

Study Patients

Characteristics of the study patients are presented in Table 2. In general, experimental group patients were significantly older and were hospitalized longer.

Control Group Patients

Of the 117 control group samples, glucose results were positive in 21 (18 percent). Nineteen (90 percent) of these 21 positive glucose readings were associated with visible evidence of blood. Hence, a positive glucose result not explainable by contamination of the specimen with blood was seen in only two (1.7 percent) of 117 control specimens. While blue dye was not detected in any control group sample, it is noteworthy that no mechanism was available to blind nurse-investigators to knowledge regarding the group assignment of individual patients.

Experimental Group Patients

Of the 189 experimental group samples, glucose readings were positive in 30 (16 percent), while blue dye was present in only five (2.6 percent). Fourteen (47 percent) of the 30 glucose-positive samples had visible evidence of blood. Thus, a positive glucose result not explainable by contamination with blood was seen in 16 (8 percent) experimental group samples.

Eight (53 percent) of 15 patients in the experimental group experienced at least one episode of presumptive aspiration. Of the 18 experimental group specimens demonstrating either a bloodless positive glucose reading or visible blue discoloration, glucose readings were positive in 15 (83 percent) while blue dye was detectable in only five (28 percent; p<0.001).

Clinically Significant Aspiration

Clinically significant aspiration occurred in five (33 percent) of 15 enterally fed patients. First biochemical evidence of aspiration using glucose oxidase test strips preceded the onset of clinically significant aspiration by an average of 10.4 ± 4.7 h (mean ± SD). Experimental group patients who went on to develop clinically significant aspiration had biochemical evidence of aspiration nearly four times more frequently (13 [19 percent] of 67 bloodless specimens) than those who did not develop this complication (3 [5 percent] of 60 bloodless specimens; p = 0.005).

Since inspection for blue discoloration in tracheal secretions detected comparatively few of the aspiration episodes revealed by glucose measurements, we applied the criteria for presumptive aspiration to patients with clinically significant aspiration to determine whether blue dye performed any better in detecting aspiration in this subgroup. The findings were similar to those for all experimental group patients. Of the 15 samples of this subgroup that were positive either by blue dye or glucose criteria, positive glucose readings were obtained in 13 (87 percent) of 15 samples, while blue discoloration was visualized in only four (27 percent) of 15 samples (p<0.001).

Test Performance Determinations

Comparing the relative utility of blue dye visualization with the glucose oxidase test strip method for detecting pulmonary aspiration of enteral feedings is complicated by the lack of an objective and broadly accepted “gold standard” test. Based on the results shown in Table 1 and given that the glucose oxidase test strip protocol is an objective method for detecting contamination of tracheal secretions with enteral formulas, we assumed that positive glucose readings (bloodless tracheal specimens with glucose concentrations ≥20 mg/dl) would have a 100 percent sensitivity and specificity in detecting aspiration of enteral feedings sufficient to comprise 1/16 (v/v) of accessible tracheal secretions.

Table 3—Relative Utility of Blue Dye Visualization for Detecting Aspiration of Enteral Feedings*

<table>
<thead>
<tr>
<th></th>
<th>All Experimental Group Patients (n = 15)</th>
<th>Experimental Group Patients Developing Clinically Significant Aspiration (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>97</td>
<td>96</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>89</td>
<td>83</td>
</tr>
</tbody>
</table>

*Compared with glucose oxidase test strip method.
Using a positive glucose result as objective evidence of aspiration, we then calculated the relative sensitivity, specificity, and predictive values of using blue dye to detect aspiration of enteral feedings (Table 3). Values were calculated separately for the entire experimental group and the subgroup that developed clinically significant aspiration. These data revealed that the blue dye visualization method failed to detect the vast majority of aspiration episodes recognized by glucose testing. The blue dye visualization method highly agreed with glucose testing results only when the latter were negative.

**Body Position and Frequency of Aspiration**

We also evaluated the relationship between body position and development of clinically significant aspiration in enteraly fed patients. Among the five experimental group patients who developed clinically significant aspiration, body position was noted to be supine at the time of collection of 79 (98 percent) of 81 specimens. Body position was not specified at the time of collection of the remaining 17 specimens in this subgroup. In contrast, only 19 (21 percent) of 91 specimens obtained in the ten experimental group patients who did not develop clinically significant aspiration were associated with feeding in the supine position (p<0.001).

**Discussion**

In this study, blue dye visualization was much less sensitive than the glucose oxidase test strip method for detecting pulmonary aspiration of enteral feedings in critically ill, intubated adults. The insensitivity of the blue dye visualization method was not limited to trivial and asymptomatic aspiration events, as this test performed no better in detecting episodes of clinically significant aspiration. Our monitoring protocol using glucose oxidase test strips was a simple and objective method for detecting aspiration of enteral feedings at an early stage when prompt intervention may have helped to minimize or prevent clinical deterioration.

Aspiration of oropharyngeal secretions is common despite cuffed and properly inflated endotracheal tubes. In mechanically ventilated patients, aspiration of oropharyngeal secretions colonized with Gram-negative bacteria contributes significantly to the development of nosocomial pneumonia. Upper airway and gastric colonization are exceedingly common, occurring regardless of gastric pH in patients receiving enteral nutrition. Up to 30 percent of critically ill patients receiving enteral nutrition experience clinically significant aspiration of their feedings with evidence of respiratory deterioration. Aspiration of enteral feedings is often initially inapparent and is a potentially life-threatening event.

A traditional method of monitoring for enteral feeding aspiration has been the addition of blue dye to enteral formulas with visual inspection of tracheal secretions for blue discoloration. While this method has been previously used widely to detect aspiration, to our knowledge, there have been no well-controlled studies evaluating its accuracy. Previous investigators using blue dye to detect feeding formula aspiration reported blue discoloration in tracheal secretions in 0 to 4 percent of patients. These authors attributed the low rate of aspiration to use of small-caliber feeding tubes and conscientious nursing care. Consistent with these studies, we identified blue discoloration in only 5 (2.6 percent) of 189 experimental group samples.

Testing for glucose in tracheal secretions has been proposed as a more sensitive monitoring method for detecting enteral feeding aspiration. Winterbauer and colleagues identified glucose in 38 percent of tracheal secretions sampled, with 19 of 20 intubated patients experiencing at least one episode of enteral feeding aspiration and 30 percent developing clinically significant aspiration. More recently, Kingston and coworkers reported 50 percent of samples positive for glucose in patients receiving enteral nutrition. In 5 (21 percent) of 24 patients, feeding formula aspiration was identified by detection of glucose in bloodless tracheal secretions. Our findings are consistent with these two studies, with presumptive aspiration seen in approximately one half of our patients and clinically significant aspiration in one third.

To our knowledge, no previously published study has directly compared glucose testing and blue dye visualization of tracheal secretions for the detection of enteral feeding aspiration events.

While inspection for blue discoloration was inferior to glucose determinations for detection of enteral feeding aspiration episodes, we considered the possibility that bloodless samples that were positive for glucose but negative for blue discoloration may have represented trivial episodes of aspiration that were of no significance in predicting clinically significant aspiration. However, when inspection for blue discoloration was evaluated in patients who went on to develop clinically significant aspiration, the sensitivity, specificity, and predictive values remained essentially unchanged (Table 3). In light of these findings, it is possible that previously reported low rates of enteral feeding aspiration using blue dye visualization methods were due in part to insensitivity of the monitoring instrument used.

Leakage of blood into respiratory secretions may cause false-positive glucose readings as observed in 19 (90 percent) of the 21 glucose-positive control group samples in our study. Only 2 of 117 samples of the control group could not be explained by the presence of visible blood. This was likely due to small amounts of occult blood within the samples. In two previous studies using glucose oxidase test strips, no sample was positive in the absence of visible blood.
ever, both studies were uncontrolled, making it possible that a small fraction of the events attributed to aspiration were actually due to the presence of apparent blood in the secretions. Hence, in the absence of obvious contamination of respiratory secretions with blood, aspiration of enteral feedings appears to be reliably detectable using glucose oxidase test strips.

Early detection of enteral feeding aspiration may help prevent subsequent morbidity and mortality. In this study, an average 10.4 ± 4.7-h delay occurred between initial biochemical evidence of aspiration using glucose oxidase test strips and the development of clinically significant aspiration. This delay represented an opportunity for physician intervention to prevent or minimize complications. Since we did not actively intervene in patient care at any point during this study, we could not determine if early detection and intervention reduce nosocomial pneumonia resulting from aspiration of enteral feedings. This possibility requires further investigation.

Patients who experienced clinically significant aspiration in this study were fed almost exclusively in the supine position, while those fed most of the time with the head of the bed elevated at least 30° did not develop this complication. Elevating the head of the bed has been proposed to prevent enteral feeding aspiration, yet its usefulness has never been conclusively proved.5,13,17 Our results strongly support the recommendation that the head of the bed remain elevated at least 30° in patients receiving enteral nutrition. However, further investigation is needed to determine if feeding in the upright position has independent benefit in reducing aspiration pneumonia in enterally fed patients.

This study illuminated a number of important issues around risks for and detection of aspiration of enteral feedings in patients with artificial airways. However, the relatively small number of study patients and the lack of investigator control over feeding tube selection, placement, and enteral nutrition management prevented conclusions to be reached about the potential contribution of these factors to the development of aspiration pneumonia.

Despite these limitations, the results of this study allow us to generate some specific recommendations for health professionals. Since aspiration of enteral feedings is a common event occurring in many critically ill, intubated adults, the health care team should remain vigilant for inapparent episodes of aspiration (using glucose oxidase test strips) and early signs of clinically significant aspiration. Whenever possible, the head of the bed should remain elevated at least 30° in patients receiving enteral nutrition. Further, we conclude that the addition of blue dye to enteral formulas with inspection of tracheal secretions for blue discoloration is inadequate for the detection of enteral feeding aspiration and should be replaced by glucose oxidase test strip methods in these patients. Detecting glucose in tracheal secretions of these enterally fed patients should be seen as a potential warning sign of impending clinically significant aspiration, with adjustment of feedings or other interventions instituted as appropriate.

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REFERENCES
3 Elpern EH, Jacobs ER, Bone RC. Incidence of aspiration in tracheally intubated adults. Heart Lung 1987; 16:527-31
12 Jacobs S, Chang RWS, Lee B, Bartlett FW. Continuous enteral feeding: a major cause of pneumonia among ventilated intensive care unit patients. JPEN 1990; 14:353-56
14 Sands WA. Incidence of pulmonary aspiration in intubated patients receiving enteral nutrition through wide- and narrow-bore nasogastric feeding tubes. Heart Lung 1991; 20:75-80