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ACCEPTANCE

This thesis, THE RELATIONSHIP BETWEEN ENTERAL NUTRITION FORMULA COMPOSITION, FEEDING TUBE PLACEMENT SITE, AND THE START OF ENTERAL FEEDINGS ON THE DEVELOPMENT OF VENTILATOR ASSOCIATED EVENT IN AN ADULT INTENSIVE CARE UNIT, by Jessica M. Alexander was prepared under the direction of the Master's Thesis Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree Master of Science in the Byrdine F. Lewis School of Nursing and Health Professions, Georgia State University. The Master's Thesis Advisory Committee, as representatives of the faculty, certify that this thesis has met all standards of excellence and scholarship as determined by the faculty.

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ABSTRACT

THE RELATIONSHIP BETWEEN ENTERAL NUTRITION FORMULA COMPOSITION, FEEDING TUBE PLACEMENT SITE, AND THE START OF ENTERAL FEEDINGS ON THE DEVELOPMENT OF VENTILATOR ASSOCIATED EVENT IN AN ADULT INTENSIVE CARE UNIT

by

Jessica M. Alexander

**Background**: Ventilator associated pneumonia (VAP) is a major cause of morbidity, longer intensive care unit (ICU) stay, increased duration of mechanical ventilation, and increased healthcare cost in critically ill patients. Critically ill patients are at increased risk for malnutrition, which is associated with impaired immune function, impaired ventilator drive and weakened respiratory muscles. Malnutrition has been thought to increase the risk of VAP due to bacterial translocation from the gastrointestinal tract to the lungs. Previous research that has evaluated the effect of enteral nutrition on malnutrition associated with VAP has been inconsistent in part because of the subjectivity of the old definition of VAP. In 2013, the Center for Disease Control and Prevention (CDC) developed a new definition for the diagnosis of VAP, which includes three tiers of a ventilator associated event (VAE); ventilator associated condition, infection-related ventilator-associated complication, or possible or probable VAP). The purpose of this study is to retrospectively examine the relationship between enteral formula, tube-feeding placement site, time of tube feeding initiation and the incidence of VAE using this new CDC definition.

**Objective**: The aim of the study was to retrospectively examine the relationship between enteral formula, tube-feeding placement site, time of tube feeding initiation and the incidence of VAE using this new CDC definition.

**Participants/setting**: The medical records of 162 adult patients admitted to one of the ICUs (Medical ICU, Surgical ICU, Neurological ICU, Burn ICU) at Grady Memorial Hospital (GMH) in Atlanta, GA in 2013

**Main outcome measures**: Demographic and baseline medical characteristics including the type of enteral formula used (standard, immune-modulating, hydrolyzed, immune-modulating and hydrolyzed, or mixed), enteral tube feeding placement (gastric or small bowel), and timing of enteral nutrition (never fed, fed ≤48 hours after admission or fed >48 hours after admission) were collected.

**Statistical analysis**: Demographic and baseline medical characteristics were described using frequency statistics and compared by VAE status using the Mann-Whitney U and Kruskal-Wallis tests. The relationship between tube placement, enteral formula, timing of feeding and the diagnosis of a VAE was evaluated using the Chi-square test.

**Results**: In 2013, 81 patients admitted to the ICU at GMH were diagnosed with a VAE. The median age of the study population (n=162) was 50 years (range, 19 to 88 years) and the median BMI was 27.6 kg/m$^2$ (range, 13.2 to 83.2 kg/m$^2$). The majority of the population was African American (53.1%) and male (64.2%). Most patients were fed through a gastric tube (86.4%), were given an immune-modulating enteral formula (32.1%) and were fed after 48 hours of admission (44.4%). After subdividing by ICU location, 12 of 14 patients (86%) in the Medical ICU who were diagnosed with a VAE were either never fed or fed >48 hours after admission vs. 7 of 13 (54%) of patients in the

Medical ICU who were not diagnosed with a VAE (p=0.031). No other relationships between the type of feeding initiation, tube placement, and enteral formula were found by VAE status for the population or by ICU location.

**Conclusion**: Adults admitted to the Medical ICU may have a reduced risk of developing a VAE if fed within 48 hours of admission. The type of enteral formula provided and the route of administration was not associated with the diagnosis of VAE. Future prospective studies should include all critical care patients to further evaluate the effect of nutrition on VAE outcome.

# THE RELATIONSHIP BETWEEN ENTERAL NUTRITION FORMULA COMPOSITION, FEEDING TUBE PLACEMENT SITE, AND THE START OF ENTERAL FEEDINGS ON THE DEVELOPMENT OF VENTILATOR ASSOCIATED EVENT IN AN ADULT INTENSIVE CARE UNIT

by
Jessica M. Alexander

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Presented in Partial Fulfillment of Requirements for the Degree of

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TABLE OF CONTENTS

LIST OF TABLES

## ABBREVIATIONS

| | |
|---|---|
| VAP | Ventilator Associated Pneumonia |
| ICU | Intensive Care Unit |
| CDC | Centers for Disease Control and Prevention |
| VAE | Ventilator Associated Event |
| VAC | Ventilator-Associated Condition |
| IVAC | Infection-related Ventilator-Associated Complication |
| GMH | Grady Memorial Hospital |
| NNIS | National Nosocomial Infection Survey |
| NG | Nasogastric |
| NJ | Nasojejunal |
| CPIS | Clinical pulmonary infection score |
| ND | Nasoduodenal |
| GRV | Gastric Residual Volumes |
| SICU | Surgical Intensive Care Unit |
| MICU | Medical Intensive Care Unit |
| NICU | Neurosurgical Intensive Care Unit |
| BICU | Burn Intensive Care Unit |
| BMI | Body Mass Index |
| y | years |
| m | meters |

| | |
|---|---|
| kg | kilograms |
| PN | Parenteral Nutrition |
| TBI | Traumatic Brain injury |

# CHAPTER I

# THE RELATIONSHIPS AMONG ENTERAL NUTRITION FORMULA COMPOSITION, FEEDING TUBE PLACEMENT SITE, AND THE START OF ENTERAL FEEDINGS ON THE DEVELOPMENT OF A VENTILATOR ASSOCIATED EVENT IN AN ADULT INTENSIVE CARE UNIT

## Introduction

Ventilator associated pneumonia (VAP) is a major cause of morbidity, longer intensive care unit (ICU) stay, increased duration of mechanical ventilation, and increased healthcare cost in critically ill patients.[1] Critically ill patients are at increased risk for malnutrition because of stress hyper-metabolism.[2] Malnutrition is associated with impaired immune function, impaired ventilator drive, and weakened respiratory muscles, leading to prolonged ventilator dependence and increased infectious morbidity and mortality.[3,4] Malnutrition is thought to increase the risk for VAP through bacterial translocation from the gastrointestinal tract to the lungs.[2] It is important to feed critically ill patients whenever medically possible to avoid the development of malnutrition. However, this does not always happen quickly or efficiently due to the perceived fears of complications associated with enteral feeding.

The effect of enteral nutrition on malnutrition associated with VAP has been researched for many years but the literature remains inconsistent. Reasons include subjectivity and complexity of the old definition of VAP (used until 2013), lack of documentation between facilities, and pressure on physicians to have lower reported

incidences of VAP. The Centers for Disease Control and Prevention (CDC) recently developed a new definition of VAP in an attempt to address some of these issues. The new definition for diagnosis uses a combination of objective criteria and recordable data that helps in getting close to a standardized VAP definition. VAP prevention as a national patient safety goal has been proposed as one of the conditions that is non-reimbursable by Medicare and Medicaid[1], which intensifies the pressure on physicians to have lower incidences of VAP. The subjective nature of the previous definition of VAP caused large variation in diagnosis from physician to physician as well as study to study.[1] Thus, the CDC released the Ventilator Associated Event (VAE) surveillance definition in January 2013, which is based on an objective, streamlined, and potentially automatable criteria. There are three definition tiers with the VAE definition: 1) Ventilator-Associated Condition (VAC), 2) Infection- related Ventilator-Associated Complication (IVAC), and 3) Possible and Probable VAP. These different tiers build upon one another, but all VAEs are identified by using a combination of objective criteria: deterioration in respiratory status after period of stability or improvement on the ventilator, evidence of infection, or inflammation and laboratory evidence of respiratory infection.[5] In order to determine the validity of the current evidence, objective measures need to be used in future research. There is a lack of literature on the relationship between the use of enteral feedings and VAE. The literature evaluating feeding tube placement site and VAP incidence is inconsistent and there are no studies examining VAE incidence. Moreover, the relationship between the start of enteral feeding and VAP requires reexamination using the new CDC definition of VAE.

A study was conducted at Grady Memorial Hospital (Grady) in Atlanta, Georgia to retrospectively examine the relationship between type of enteral formula, tube-feeding placement site, time of tube feeding initiation (within 48 hours vs. after 48 hours) and the incidence of VAE. Grady is a Level 1 trauma center with five adult intensive care units. Outcome Data Collectors at Grady have been using the new CDC definition of VAE since January, 2013. The research hypotheses of the study were:

1. Patients who received enteral tube feedings within 48 hours of admission will have lower rates of VAE than patients who either received feedings after 48 hours or did not receive any enteral feedings.
2. Patients who receive Impact®, an immune-modulating formula, will have a lower incidence of VAE than patients receiving other formulas.
3. Patients who have a nasojejunal tube for enteral feeding will have lower incidence of VAE compared to patients with a feeding nasogastric tube.

# CHAPTER II

## Literature Review

From 1975 to 1985 the CDC conducted a nationwide study to examine if hospital acquired infections could be reduced through control programs. The CDC determined that four components of surveillance were needed: 1) feedback of infection control rates to hospital staff; 2) enforcement of preventative practices; 3) a supervising infection preventionist to collect and analyze surveillance data; and 4) the involvement of a physician or microbiologist with specialized training in infection prevention and control.[6] This was the beginning of the CDC recognizing a need for a VAP definition and an outline for the different components necessary to survey and diagnose the infection. In 1988 the National Nosocomial Infection Survey (NNIS) defined two pneumonia criteria for adults that included clinical findings with the results of laboratory tests but did not include chest x-rays.[7,8] In 2002, the new NNIS pneumonia definitions were implemented, which required chest x-ray evidence.[7] The new CDC surveillance definition uses a combination of objective criteria: deterioration in respiratory status after a period of stability or improvement on the ventilator, evidence of infection or inflammation, and laboratory evidence of respiratory infection.[8]

### *Enteral Feeding Tube Placement*

Four studies have examined the relationship between transpyloric feeding tube placement and the incidence of VAP. The study by Acosta-Escribano et al. (2010) compared nasogastric (NG) feeding tube to nasojejunal (NJ) feeding tube in patients with

traumatic brain injuries.[9] A total of 104 patients were randomized into either NG (n= 54) or NJ (n= 50) tube-feeding placement and were fed the same formula as a continuous feeding. Pneumonia was determined using the clinical pulmonary infection score (CPIS) criteria with a score higher than 6 indicating pneumonia. Almost half (n=47) of the patients developed VAP, 16 in the NJ group compared with 31 in the NG group ($p < 0.01$). Patients with traumatic brain injuries had decreased incidence of VAP when fed through a transpyloric feeding tube than when fed through a nasogastric feeding tube. Hsu et al. (2009) compared nasoduodenal (ND) and NG feeding tubes in critically ill patients.[10] A total of 121 patients were randomized to ND (n=59) and NG (n=62) feedings. In this study, VAP diagnosis required the agreement of two third-party pulmonologists reviewing radiographs using the CDC criteria. Fifteen patients (24.2%) in the NG group compared with 5 (8.5%) patients in the ND group developed VAP ($p= 0.02$). Patients in the medical ICU who were fed via an ND tube had lower incidence of VAP and better outcomes than those fed with NG tubes. Davies et al. (2012) also compared NJ and NG feedings in mechanically ventilated critically ill adults with elevated gastric residual volumes (GRV) within 72 hours of admission to the ICU.[11] A total of 180 patients were included in the study. Initially patients were fed through an NG tube, then they were randomized to either NJ feedings (n=91) or to remain on NG feedings (n=89). An intention to treat analysis was used. Twelve patients randomized to the NJ group could not receive the feeding, as the tube did not pass beyond the stomach. In addition, eight patients assigned to the NG group were switched to an NJ feeding tube due to enteral nutrition intolerance. If the development of VAP was suspected, additional data were collected and provided to an adjudication panel. The diagnosis of VAP was

confirmed if at least two of the three adjudicators met the diagnosis of VAP. Eighteen patients in the NJ group and 19 patients in the NG group developed VAP ($p = 0.94$). Switching patients to a NJ feeding tube after they exhibited delayed gastric emptying did not significantly decrease the incidence of VAP.

White et al. (2009) compared NG and post-pyloric feedings in critically ill patients.[12] A total of 104 patients were randomized with 54 in the NG group and 50 in the post-pyloric group. Four patients originally randomized to NG feeding received a post-pyloric tube due to increased GRV. Ten patients randomized to post-pyloric feeding received a NG tube due to unsuccessful placement of the post-pyloric tube. VAP was diagnosed using a CPIS score greater than 6 and the presence of fever, leukocytosis, pulmonary secretions, as well as radiographic imaging. Under the intent to treat analysis, VAP was diagnosed in five patients in the post-pyloric group and eleven in the nasogastric group ($p=0.18$). Treating patients with early post-pyloric tubes did not significantly decrease the incidence of VAP compared to early NG tubes.

These studies used varying diagnosis of VAP and had high subjectivity toward the diagnosis due to the inter-observer variability.[1] Radiography as a tool for VAP diagnosis has been highly criticized because interpretation is subjective. The new definition removes this subjectivity by eliminating the radiographic imaging as part of the diagnostic criterion. Furthermore, the results of these studies indicate that the relationship between tube-feeding placement site and the incidence of VAP is still unknown.

***Enteral Nutrition Formula and Timing of Implementation***

Very few studies have examined the effect of different enteral adult formulas on the incidence of VAP. Caparros et al. (2001) compared the effect of providing a high-

protein enteral nutrition formula with supplemental arginine, fiber, and antioxidants to a standard high-protein formula on overall nosocomial infection rates in critically ill patients.[13] The researchers did not specifically analyze data for the presence of VAP. Nevertheless, this study did not find a significant relationship between the type of formula used and rates of nosocomial infections (p= 0.3).

In a retrospective study Artinian et al. (2006) examined the effects of nutrition timing on VAP incidence in critically ill patients.[14] Early feeding was defined as feeding within the first 48 hours of mechanical ventilation with patients who were ventilated for more than 2 days. VAP diagnosis was defined as new or progressive infiltrate, consolidation, cavitation, or pleural effusion of new onset of purulent sputum or change in character of sputum, organism isolated from blood culture, isolation of pathogen from specimen obtained by tracheal aspirate, bronchial brushing or biopsy, or histopathologic diagnosis of pneumonia.[14] A total of 2,537 patients had been fed early and 1,512 were identified as having received later feedings. After controlling for baseline differences, early feeding was associated with a higher risk of VAP development. In the early feeding group, 284 patients were diagnosed with VAP compared to 143 in the later feeding group (p=0.08). Feeding tube placement was not collected in this patient population and thus could not be analyzed. It cannot be ruled out that there may have been a significant difference between early and late feeding groups and tube placement. This tube placement could have had an effect on VAP.

# CHAPTER III

## Methods

We conducted a retrospective review of medical records of patients admitted to the ICU at Grady Memorial Hospital in Atlanta, GA during 2013. There are five ICUs at Grady including two Surgical ICUs (SICUs), a Medical ICU (MICU), a Neurosurgical ICU (NICU), and a Burn ICU (BICU). Patients admitted to the SICU were greater than 18 years old and had life threatening injuries that required immediate surgical intervention. Patients admitted to the MICU were greater than 18 years old whose admitting diagnoses included organ failure, sepsis, or gastrointestinal bleeding. Patients with life threatening neurological issues such as status epilepticus, hemorrhagic or ischemic strokes were admitted to the NICU. Admissions to the BICU included both pediatric and adult patients who had sustained life-threatening burns to their skin as well as smoke inhalation injuries.

Patients who received mechanical ventilation for more than 48 hours were included in the study. Exclusion criteria included patients below the age of 18 years, previous anatomy altering upper gastrointestinal surgery, bowel obstruction, pregnancy, presence of a gastrostomy or jejunostomy tube on admission, death within 48 hours, and intubation >24 hours after admission. Patients who developed a VAE were identified using a VAE registry maintained by Grady Memorial Hospital infection preventionist. An equal number of patients, matched by ICU admission, who were not diagnosed with a VAE were randomly selected for comparison. All patient identifiers (name, birthdate,

medical record number, social security number) were removed and an individual patient identifier was assigned to protect patient privacy. The medical records were reviewed for demographic and baseline medical characteristics, including, diagnosis of VAE, admitting diagnosis, specific enteral feeding tube placement (gastric tube placement or small bowel tube placement), the timing of enteral nutrition (before or after 48 hours of admission, or never fed enterally), and type of enteral formula used (standard formula or immune-modulating formula or hydrolyzed formula or immune-modulating and hydrolyzed formula or mixed formula).

Standard enteral formulas such as Isosource®, Novasource®, and Jevity® are most commonly used to feed patients and contain intact proteins, carbohydrates, long chain triglycerides, and vitamins and minerals; some contain fiber. The formulas used in this population were Isosource®, Novasource®, Jevity® and Suplena® which is a low protein product with lower nutrient content of some vitamins and minerals. Immune modulating formulas contain one or more nutrients beyond the standard macro- and micronutrients. These additional nutrients could include arginine, glutamine, omega 3 fatty acids, antioxidants, gamma linoleic acid, nucleotides, and antioxidants.[9] The immune-modulating formulas used in this population were Impact® and Oxepa®. Hydrolyzed formula is a peptide-based formula that contains 100% enzymatically hydrolyzed (elemental) whey protein.[10] The hydrolyzed formula used in this population is Peptamen® and Peptamen Bariatric®. The immune-modulating, hydrolyzed formula contains hydrolyzed casein protein, arginine, glutamine, omega-3 fatty acids and nucleotides.[11] The immune-modulating, hydrolyzed formula used in this population was

Impact Peptide®. For the purposes of this study, any patient that received more than one category of formula were analyzed as receiving a mixed formula.

Data were recorded onto a source document and subsequently entered into a Microsoft Excel database. Demographic and baseline characteristics, feeding tube placement, and early versus late feedings were described using frequency statistics. Variables were compared by VAE status using the Mann- Whitney U test and Kruskal-Wallis analysis of variance by ranks as the data were not normally distributed even after log transformation. The difference in type of tube placement (Gastric vs. Small bowel), the type of enteral formula, the initiation of feeding and the incidence of VAE were evaluated using a Chi-square test. Data were analyzed as a total population of ICU patients and by ICU location as the severity of illness varies among the units. All statistical analyses were conducted using SPSS (version 20.0, SPSS, Inc., Chicago, IL).

# CHAPTER IV

## Results

In 2013, eighty-one patients admitted to the ICU at GMH were diagnosed with a VAE. The comparison group included 81 patients who had not been diagnosed with a VAE. The median age of the study population (n=162) was 50 years (range, 19 to 88 years) and the median admitting body mass index (BMI) was 27.6 $kg/m^2$ (range, 13.2 to 83.2 $kg/m^2$) (Table 1). Patients BMI were analyzed because previous studies have shown that a higher BMI increases the risk for infection. The majority of the population was African American (53.1%) and male (64.2%). The age of patients differed by ICU admission status (Table 2). However, no significant difference in anthropometric status was observed by ICU location. No significant differences in demographic or anthropometric characteristics were observed by VAE status (Table 3).

Table 1. Demographic and anthropometric characteristics of the total population

| Characteristics | Total Population (n=162) |
|---|---|
| Age (years)[a] | 50 (34.75, 63.25) |
| Gender (%) | |
| Male | 64.2 |
| Female | 35.8 |
| Race (%) | |
| African American | 53.1 |
| Caucasian | 34.6 |
| Hispanic | 4.3 |
| Asian | 1.9 |
| American Indian | 0.6 |
| Multiracial | 0.6 |
| Unknown | 4.9 |
| Height (m)[a] | 1.727 (1.65, 1.80) |
| Weight (kg)[a] | 82 (70, 98.2) |
| BMI ($kg/m^2$)[a] | 27.67 (23.9, 32.6) |

[a]Median (25%, 75%)

BMI - Body Mass Index, y – years, m – meters, kg – kilograms

Table 2. Demographic and anthropometric characteristics of the population by intensive care unit (ICU)

| Characteristic[a] | Neuro ICU (n = 32) | Burn ICU (n = 22) | Surgical ICU (n = 80) | Medical ICU (n = 28) | P-value |
|---|---|---|---|---|---|
| Age (y) | 57 (45, 66) | 55 (35, 64) | 43.50 (26, 57) | 53 (43, 64) | **0.001** |
| Height (m) | 1.7 (1.63, 1.77) | 1.75 (1.7, 1.8) | 1.75 (1.65, 1.8) | 1.71 (1.62, 1.77) | 0.145 |
| Weight (kg) | 83.9 (70.25, 100.52) | 80 (74.9, 98.1) | 81 (70, 92.2) | 81.3 (68.2, 103) | 0.764 |
| BMI ($kg/m^2$) | 30.1 (23.9, 30) | 27.1 (24.2, 30.9) | 26.9 (23.9, 32.1) | 26.8 (23.3, 36.4) | 0.448 |

[a]Median (25%, 75%)

ICU – intensive care unit, BMI – body mass index, y – years, m – meters, kg – kilograms

Table 3. Demographic and anthropometric characteristics by VAE status

| Characteristics[a] | VAE (n = 81) | NON-VAE (n = 81) | P-value |
|---|---|---|---|
| Age (y) | 49 (32, 64) | 51 (35, 63) | 0.482 |
| Height (m) | 1.727 (1.65, .80) | 1.727 (1.63, 1.80) | 0.691 |
| Weight (kg) | 83.9 (70.5, 100) | 80 (70, 90) | 0.434 |
| BMI ($kg/m^2$) | 27.67 (24.0, 32.8) | 27.38 (23.52, 32.17) | 0.950 |

[a]Median (25%, 75%)

VAE - ventilator associated event; BMI – body mass index, y – years, m - meters, kg – kilograms

The enteral feeding characteristics of the population are shown in Table 4. Most patients were fed through a gastric tube (86.4%), were given an immune-modulating enteral formula (32.1%), and were fed after 48 hours of admission (44.4%). The feeding tube placement, enteral formula, and time to feeding initiation characteristics by ICU status are shown in Table 5. The majority of patients in the BICU, SICU, and MICU who received a feeding tube and all NICU patients requiring enteral nutrition support were fed via gastric tube. Most of the patients fed through a small bowel tube were in the SICU. Providers in the NICU and MICU prescribed standard enteral formula for the majority of their patients. The SICU providers prescribed an immune-modulating formula more frequently while the BICU providers prescribed an immune-modulating, hydrolyzed formula more frequently. Dietitians at GMH refer to the American Society of Parenteral and Enteral Nutrition/ Society of Critical Care Medicine's guidelines for the provision

and assessment of nutrition support therapy in the adult critical ill patient when making recommendations for nutrition support in critically ill patients, which may be the reason why an immune-modulating formula was used more frequently. The majority of patients admitted to the NICU and BICU were fed within 48 hours of admission (71.9% and 36.4%, respectively) while most of the patients in the SICU and MICU were fed after 48 hours (55% and 50%, respectively).

Table 4. Enteral feeding characteristics of the total ICU population

| Characteristics | Total Population (n = 162) |
|---|---|
| Feeding Tube Placement (%) | |
| Gastric | 86.4 |
| Small bowel | 5.6 |
| Unknown | 8.0 |
| Enteral Formula (%) | |
| Standard | 27.8 |
| Immune-modulating | 32.1 |
| Hydrolyzed | 3.1 |
| Immune-modulating, hydrolyzed | 11.7 |
| Mixed formula | 8.0 |
| Unknown | 17.3 |
| Initiation of Feeding (%) | |
| Before 48 hours | 30.9 |
| After 48 hours | 44.4 |
| Never fed enterally | 22.2 |
| Unknown | 2.5 |

ICU – intensive care unit

Table 5. Enteral feeding characteristics of the population by ICU admission status

| | Neuro ICU (n = 32) | Burn ICU (n = 22) | Surgical ICU (n=80) | Medical ICU (n=28) |
|---|---|---|---|---|
| Feeding Tube Placement (%) | | | | |
| Gastric | 100 | 95.5 | 78.8 | 85.7 |
| Small bowel | 0 | 4.5 | 10 | 3.6 |
| Unknown | 0 | 0 | 11.3 | 10.7 |
| Enteral Formula (%) | | | | |
| Standard | 78.1 | 0 | 3.8 | 60.7 |
| Immune-modulating | 0 | 22.7 | 57.5 | 3.6 |
| Hydrolyzed | 3.1 | 0 | 1.3 | 10.7 |
| Immune-modulating, hydrolyzed | 3.1 | 50 | 8.8 | 0 |
| Mixed formula | 9.4 | 13.6 | 6.3 | 7.1 |
| Unknown | 6.3 | 13.6 | 22.5 | 17.9 |
| Initiation of Feeding (%) | | | | |
| Before 48 hours | 71.9 | 36.4 | 13.8 | 28.6 |
| After 48 hours | 21.9 | 31.8 | 55 | 50 |
| Never fed enterally | 6.3 | 31.8 | 27.5 | 17.9 |
| Unknown | 0 | 0 | 3.8 | 3.6 |

ICU – intensive care unit

The enteral feeding characteristics of the population by VAE status are shown in Table 6. Gastric and small bowel tube placement was similar between patients with and without a VAE. An immune-modulating or hydrolyzed formula was prescribed more frequently for patients who were not diagnosed with a VAE vs. those diagnosed. A greater number of non-VAE patients were fed before 48 hours than VAE patients (28 vs. 22, respectively). Similarly, more VAE patients were never fed enterally than non-VAE patients (21 vs. 15, respectively). However, these differences were not statistically significant.

Table 6. Enteral feeding characteristics of the population by VAE status

| | VAE (n = 81) | Non-VAE (n = 81) | P-value |
|---|---|---|---|
| Tube Placement (n) | | | |
| Gastric | 72 | 68 | 0.685 |
| Small bowel | 4 | 5 | |
| No tube/Unknown | 5 | 8 | |
| Enteral Formula (n) | | | |
| Standard | 20 | 25 | 0.223 |
| Immune-modulating | 20 | 32 | |
| Hydrolyzed | 1 | 4 | |
| Immune-modulating, hydrolyzed | 10 | 9 | |
| Mixed formula | 9 | 4 | |
| No formula/Unknown | 21 | 7 | |
| Feeding Initiation (n) | | | |
| Before 48 hours | 22 | 28 | 0.398 |
| After 48 hours | 38 | 34 | |
| Never fed enterally | 21 | 15 | |
| Unknown | 0 | 4 | |

VAE – ventilator associated event

After subdividing by ICU location, 12 of 14 patients (86%) in the MICU who were diagnosed with a VAE were either never fed enterally or fed >48 hours after admission vs. 7 of 13 (54%) patients in the MICU who were not diagnosed with a VAE

(p=0.031). No other relationships between the type of feeding initiation, tube placement, or enteral formula were found by VAE status for the population or by ICU location (Tables 7-10).

Table 7. Enteral feeding characteristics by VAE status in patients admitted to the Neuro ICU

| | VAE (n=16) | Non-VAE (n=16) | P-value |
|---|---|---|---|
| Tube Placement (n) | | | |
| Gastric | 16 | 16 | N/A[a] |
| Small bowel | 0 | 0 | |
| Enteral Formula (n) | | | |
| Standard | 11 | 14 | 0.154 |
| Immune-modulating | 0 | 0 | |
| Hydrolyzed | 0 | 1 | |
| Immune-modulating, hydrolyzed | 0 | 1 | |
| Mixed formula | 3 | 0 | |
| No formula/Unknown | 2 | 0 | |
| Feeding Initiation (n) | | | |
| Before 48 hours | 10 | 13 | 0.282 |
| After 48 hours | 4 | 3 | |
| Never fed enterally | 2 | 0 | |

[a]No statistics are computed because tube placement is a constant

ICU – intensive care unit

Table 8. Enteral feeding characteristics by VAE status in patients admitted to the Burn ICU

| | VAE (n=11) | Non-VAE (n=11) | P-value |
|---|---|---|---|
| Tube Placement (n) | | | |
| Gastric | 11 | 10 | N/A[a] |
| Small bowel | 0 | 0 | |
| Unknown/no tube | 0 | 1 | |
| Enteral Formula (n) | | | |
| Standard | 0 | 0 | 0.751 |
| Immune-modulating | 3 | 2 | |
| Hydrolyzed | 0 | 0 | |
| Immune-modulating, hydrolyzed | 5 | 6 | |
| Mixed formula | 1 | 2 | |
| Unknown/No formula | 2 | 1 | |
| Feeding Initiation (n) | | | |
| Before 48 hours | 4 | 4 | 0.276 |
| After 48 hours | 5 | 2 | |
| Never fed enterally | 2 | 5 | |

[a]No statistics are computed because tube placement is a constant

ICU – intensive care unit

Table 9. Enteral feeding characteristics by VAE status in patients admitted to the Surgical ICU

| | VAE (n=40) | Non-VAE (n=40) | P-value |
|---|---|---|---|
| Tube Placement (n) | | | |
| Gastric | 34 | 29 | 0.380 |
| Small bowel | 3 | 5 | |
| Unknown/No Tube | 3 | 6 | |
| Enteral Formula (n) | | | |
| Standard | 2 | 1 | 0.134 |
| Immune-modulating | 17 | 29 | |
| Hydrolyzed | 0 | 1 | |
| Immune-modulating, hydrolyzed | 5 | 2 | |
| Mixed formula | 4 | 1 | |
| Unknown/No tube | 12 | 6 | |
| Feeding Initiation (n) | | | |
| Before 48 hours | 6 | 5 | 0.925 |
| After 48 hours | 22 | 22 | |
| Never fed enterally | 12 | 10 | |
| Unknown | 0 | 3 | |

ICU – intensive care unit

Table 10. Enteral feeding characteristics by VAE status in patients admitted to the Medical ICU

| | VAE (n = 14) | Non-VAE (n = 14) | P-value |
|---|---|---|---|
| Tube Placement (n) | | | |
| Gastric | 11 | 13 | 0.288 |
| Small bowel | 1 | 0 | |
| Unknown | 2 | 1 | |
| Enteral Formula (n) | | | |
| Standard | 7 | 10 | 0.846 |
| Immune-modulating | 0 | 1 | |
| Hydrolyzed | 1 | 2 | |
| Immune-modulating, hydrolyzed | 0 | 0 | |
| Mixed formula | 1 | 1 | |
| Unknown/ No formula | 5 | 0 | |
| Feeding Initiation (n) | | | |
| Before 48 hours | 2 | 6 | **0.031** |
| After 48 hours | 7 | 7 | |
| Never fed enterally | 5 | 0 | |
| Unknown | 0 | 1 | |

ICU – intensive care unit

# CHAPTER V

## Discussion and Conclusions

Patients admitted to an ICU at Grady Memorial Hospital who were mechanically ventilated for >48 hours and who received a feeding tube were more likely to be fed an immune-modulating formula into their stomach. Most patients were fed >48 hours after admission. We found an association between the lack of initiation of enteral nutrition and diagnosis of a VAE in Medical ICU patients but not in any other ICU population. We found no association between feeding tube placement or the type of enteral formula used and VAE status in the total population or after subdivision by ICU location.

Current clinical guidelines recommend that enteral nutrition be started within 24 to 48 hours of admission.[3,12] Artinian et al. (2006) found that early feeding was associated with a higher risk of VAP development. We did not find that early feeding was associated with a VAE. However, Artinian et al. defined early feeding as feeding within 48 hours of mechanical ventilation in patients who were ventilated for more than 2 days and included patients that were not ventilated upon admission. In our study, patients were defined as having been fed early if they were fed within 24 to 48 hours of mechanical ventilation but patients had to be mechanically ventilated upon admission. In the Artininan et al. study, patients were not excluded if they were not intubated on admission. Therefore, patients may have received food prior to ventilation, which may have contributed to their findings. Moreover, researchers from the study speculate that their patient population was less ill suggesting that they may have been fed prior to mechanical ventilation and possibly aspirated their food. Our study excluded patients that

could feed independently and thus eliminated this possibility. In contrast, patients in our population who were admitted to the MICU and never fed using the gastrointestinal tract were more likely to have been diagnosed with a VAE.

Altintas et al. (2011) conducted a study that examined the effect of enteral vs. parenteral nutrition (PN) on outcomes of mechanically ventilated patients.[13] The primary outcome was the development of VAP. This study was a randomized control trial where nutrition support was started within 48 hours on 71 patients. Thirty patients were randomized to enteral feedings and the remaining 41 patients received PN. The researchers did not find that PN increased the risk of VAP in the medical-surgical ICU. While not statistically significant, 26.8% of the patients who received PN developed VAP compared to 16.7% of patients who received enteral nutrition. Our study did find a significant association between not receiving enteral nutrition with the diagnosis of a VAE in the MICU. This could be because the patients in the category of 'never fed enterally' included patients that received PN as well as those who received no nutrition. This association could also be present because the patients admitted to the MICU were more critically ill than the patients admitted to other ICUs. The MICU could have a disproportionate number of patients with malnutrition due to the presence of chronic disease, which means they could have impaired immune function as well as bacterial translocation from the gastrointestinal tract. The patient's malnutrition is then exacerbated once they are admitted with an acute illness and are not fed through the gastrointestinal tract.

Our results were similar to those of Capparos et al. (2001) with regard to the type of enteral formula prescribed. Approximately 60% of patients in the study received

either a standard formula or an immune-modulating formula. Capparos et al. did not find a significant relationship between the type of enteral formula and nosocomial infection, which includes VAP. However, the only two formulas used in the study were a standard high-protein formula and an immune-modulating formula. Our study also did not find a relationship between type of formula and VAE. Therefore, the type of enteral formula may not be as important as receiving optimal nutrition. Optimal nutrition is defined as meeting energy expenditure as assessed by indirect calorimetry as well as protein intake of 1.2 g/kg of preadmission weight for critically ill patients.[14] When a patient receives optimal nutrition there is a protection and a rebuilding of body protein mass. Inadequate nutrition is associated with an increased risk of complications such as infection.[14] Given that no association between the type of formula prescribed and the development of a VAE was found in our study, it is possible that providing adequate calories and protein plays a greater role in the relationship. Nutritional requirements were not determined as a part of our study but would be important to evaluate in future research.

The findings of this study regarding enteral tube placement and VAE association are consistent with the findings of White et al. (2009) and Davies et al. (2012). These studies did not find an association between VAP and feeding tube placement. However, Acosta-Escribano et al. (2010) and Hsu et al. (2009) found that patients fed into the small bowel had a lower incidence rate of VAP. Acosta-Escribano et al. examined feeding tube placement only in traumatic brain injury (TBI) patients. While some of the patients in our study had experienced TBI, this was not the primary diagnosis in the majority of the population. TBI patients are at increased risk for gastroparesis lasting 3-5 days, which increases risk for aspiration and which will sometimes necessitate a post-pyloric tube

placement.[15] Hsu et al. found that patients in the MICU had a lower incidence rate of VAP if they were fed into the small bowel. While the current study did not have similar findings, it is important to note that the majority of patients (86.4%), regardless of ICU, received a gastric tube placement. This did not allow for a true analysis on effectiveness of small bowel tube feedings on the incidence of VAE.

The primary limitation of our study is that it is retrospective. We are unable to make a determination of cause and effect between VAE and lack of feeding in the medical ICU. Furthermore, we are unable to fully evaluate the effect of gastric vs. small bowel feeding tube placement and enteral formula type since there were few patients who received a small bowel tube or formulas other than standard or immune modulating. After subdividing by ICU location, this became more problematic as there were insufficient numbers of patients to make the comparison and little diversity in terms of feeding tube placement and the type of formula used. Also, some patients' height, weight and calculated BMI were estimated. Therefore, these results should be interpreted with caution. Future research should include analysis of VAE status by BMI category (underweight, normal weight, overweight, or obese). Another limitation of the study is that patients were excluded if they were intubated after 24 hours of admission. Since we did not capture the patients that were intubated later, our results cannot be generalized to all ICU patients who are mechanically ventilated. However, by eliminating these patients, food consumed orally was not introduced and thus was not a confounding factor in the evaluation of the association between the timing of implementation, enteral formula, or feeding tube placement and a VAE. Another limitation is that nutrition intake was not compared to the patients' calorie and protein requirements. Our results may reflect

inadequate nutrition vs. the effect of feeding initiation on the development of a VAE.

Despite the limitations of our study, adults admitted to the MICU may have a reduced risk of developing a VAE if fed within 48 hours of admission. The type of enteral formula provided and the route of administration were not associated with the diagnosis of VAE. It is understandable that patients, under certain circumstances (e.g., abdominal surgery or being hemodynamically unstable), cannot be fed enterally while being mechanically ventilated. If patients in the MICU cannot be fed, the healthcare team should take extra precautions to reduce the risk of the patient having a VAE. These precautions include elevating the head of the bed, oral care with chlorhexidine, stress ulcer prophylaxis, deep venous thrombosis prophylaxis, daily assessment of sedation and spontaneous breathing, improving secretion drainage by body positioning, leakage prevention through endotracheal tube modifications, and inhibition of biofilm formation.[1] Increased awareness and preparedness with these patients can help to decrease the risk of VAE in the MICU population and improve outcomes.

Future studies should include a prospective evaluation of all critical care patients to further evaluate the effect of nutrition on VAE outcome. In order to further understand the relationship between VAE and lack of feeding in the MICU, future randomized studies need to be performed in order to determine a cause and effect relationship between feeding initiation and VAE. There should be future prospective randomized trials including all critical care patients in order to effectively evaluate small bowel vs. gastric feeding and the type of enteral formula prescribed. Future research should also include studies that match VAE and non-VAE patients by diagnosis and age.

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