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Adverse Outcomes of Mild Hypocapnia During General Anesthesia: An Evidence-Based

Education Module

A DNP Project Presented to the Faculty of the Nicole Wertheim College of Nursing and Health Sciences Florida International University

> In partial fulfillment of the requirements For the Degree of Doctor of Nursing Practice

> > By

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ABSTRACT

Title: Adverse Outcomes of Mild Hypocapnia During General Anesthesia: An Evidence-Based Education Module

Impact Statement: Promoting normocapnia practices by maintaining EtCO2 levels of 40 mmHg or above during general anesthesia will ultimately enhance mortality rates and patient outcomes *Background*: There are few research articles on low intraoperative end-tidal carbon dioxide (EtCO₂) levels in postoperative mortality. This study examines the correlation between intraoperative EtCO₂, length of hospital stay (LOS), and mortality in individuals receiving general anesthesia.

Objective: The relevance of this project is to improve surgical patient outcomes by decreasing mortality and length of hospital stay. At the end of this project, anesthesia providers will see strong evidence for the application of normocapnia (EtCO₂ levels of 40 mmHg or above) during the intraoperative management of patients undergoing surgical procedures under general anesthesia.

Methods: A systematic search utilized Ovid, Medical Literature Analysis and Retrieval System Online (MEDLINE), Cumulative Index to Nursing and Allied Health Literature (CINAHL), and ProQuest. A pretest survey assessed the providers' initial knowledge and attitudes regarding intraoperative EtCO₂. This step was followed by a PowerPoint presentation and a post-test survey.

Results: The examination of nine research studies was determined to be credible. During general anesthesia (GA), the included studies focused on patient results with intraoperative EtCO₂ levels ranging from 30-35 mmHg to 40 mmHg or higher.

Discussion: Most patients with $EtCO_2$ less than 35 mmHg experienced a hospital length of stay of more than six days compared to individuals with $EtCO_2$ greater than 35 mmHg. Moreover, decreased $EtCO_2$ is related to adverse outcomes regardless of blood pressure, representing a state of compensation for decreased cardiac output, by raising peripheral vascular resistance while maintaining blood pressure.

Conclusion: Several studies established that normocapnia is beneficial and should be considered a routine intervention during GA. Hypocapnia and the hyperventilation necessary to create it are detrimental. Additionally, increased mortality and LOS are proven unfavorable

consequences of low EtCO₂. Mild hypercapnia can improve oxygen supply by improving tissue perfusion, increasing carbon dioxide levels, and vasodilation.

Keywords: Normocapnia; hypocapnia; end-tidal concentration, EtCO₂; intraoperative, Postoperative, Mortality, Outcomes.

I. INTRODUCTION

Problem Identification

End-tidal carbon dioxide concentrations (EtCO₂) between 30-35 mmHg have traditionally sustained mild hypocapnia during general anesthesia.^{4,6} Studies in general surgery have identified a correlation between low EtCO₂ (less than 35 mmHg) and unsatisfactory postoperative outcomes, such as increased in-hospital mortality and an extended postoperative length of hospital stay.⁴

Furthermore, comprehensive research of over 4,000 patients undergoing general anesthesia for abdominal surgery discovered that decreased intraoperative EtCO₂ was associated with a 2.2-fold rise in postoperative 90-day mortality.⁴ Moreover, investigations involving older patients undergoing non-cardiac surgery revealed that the length and degree of intraoperative hypocapnia attributed to the severity of postoperative delirium.⁷ According to multiple publications, mild hypercapnia (EtCO₂ readings of 40 mmHg or greater) is advantageous and should be standard anesthetic management.^{3,4,6} This project aims to enhance patient outcomes with the standardization of intraoperative EtCO₂ concentrations of 40 mmHg or higher during general anesthesia.

Background

Capnography is the noninvasive quantification of carbon dioxide (CO_2) partial pressure in exhaled breath displayed as CO_2 concentration over time. The CO_2 waveform, referred to as a capnogram, depicts CO_2 attention and time.¹ Capnography generates factual data about ventilation, perfusion, and metabolism. In Europe in the 1970s and the United States in the 1980s, capnography became a core element of anesthesia practice.¹ Capnography is currently the gold standard for monitoring EtCO₂ levels in individuals undergoing general anesthesia.^{1,4} EtCO₂ is a beneficial and precise measure for determining the partial pressure of arterial carbon dioxide (PaCO₂) in mechanically ventilated patients. By altering patient factors, providers modify the respiratory rate and ventilator tidal volume to achieve the desired EtCO₂.⁸ During general anesthesia, mild hypocapnia (EtCO₂ between 30-35 mmHg) due to hyperventilation is relatively evident in clinical practice, affecting approximately 70% of clients. The assumption that hypocapnia is safer and superior to hypercapnia may explain its widespread occurrence.²⁻⁴ Mild hypocapnia inhibits the return of spontaneous breathing efforts, decreasing muscle relaxant use and higher doses of anesthetics. Hypocapnia, on the other hand, can have negative physiological implications that result in undesirable outcomes in patients.²⁻⁴

Scope of the Problem

Two assumptive mechanisms facilitate the correlation between decreased intraoperative EtCO₂ levels and increased postoperative mortality. According to one hypothesis, low EtCO₂ demonstrates hypocapnia, which has negative consequences such as hypotension caused by peripheral vasodilation, cerebral vasoconstriction, decreased tissue perfusion, arrhythmia, hypercoagulability, pulmonary cellular impairment, increased intrapulmonary shunt, and cognitive decline.²⁻⁴

Hypocapnia could also be due to an elevated PaCO₂- EtCO₂ gradient, implying pathological circumstances such as diminished pulmonary blood flow, increased ventilation/perfusion ratio (V/Q) mismatch, increased shunting rates, hemodynamic instability, and a higher alveolar dead space. With prolonged physiologic dead space, shunt perfusion, decreased cardiac output, and a reduced V/Q ratio, the PaCO₂- EtCO₂ gradient can rise to variable degrees.²⁻⁴

The PaCO₂- EtCO₂ gradient increases in various pathologic conditions such as asthma, COPD, and acute respiratory disease. Intraoperative measurement of a PaCO₂- EtCO₂ difference of more than 8-10 mmHg indicates increased mortality in trauma patients and poor prognosis in sepsis patients.^{3,4} In hemodynamically stabilized individuals, a PaCO₂- EtCO₂ gradient of 2-5 mmHg is considered normal.³ Additionally, hypocapnia may indicate a reduced cardiac output and pulmonary blood flow when ventilation is unchanged throughout the surgery.⁴

Knowledge Gaps

Researchers discovered several knowledge gaps during the research process. First, there were unknown or unmeasured confounders. These included probable reasons for anesthesiologists to strive for a particular EtCO₂ level and insufficient data sources regarding anesthetic depth, ventilation parameters, hypothermia, and smoking habits.⁴ Second, the influence of the PaCO₂- EtCO₂ gradient on 90-day mortality used the first intraoperatively recorded PaCO₂ level, but it did not consider the effect of modifications over time in either the PaCO₂ level or the PaCO₂- EtCO₂ gradient.⁴

Further research is necessary to determine if low EtCO₂ is attributable to hyperventilation-induced hypocapnia or if it is due to a widening PaCO₂- EtCO₂ gradient.^{4,9} However, other interpretations other than EtCO₂ on the causative pathway are also plausible. It is questionable whether lowering EtCO₂ levels would affect mortality because EtCO₂ could indicate physiologic instability instead of being a modulator of mortality.⁹

Proposal Solution

Mild hypocapnia is considered an independent risk factor for a lengthier hospitalization and can result in adverse outcomes. There is a statistically significant relationship between

normocapnia and reduced length of stay.²⁻⁴ Normocapnia can have favorable effects such as lung protection, increased tissue perfusion, cardiac index, and decreased postoperative surgical site infection. Furthermore, mild respiratory acidosis protects against organ injury, and aiming for a lower-than-average PaCO₂ may be detrimental.^{3,4}

Mild hypercapnia can promote oxygen delivery by increasing tissue perfusion due to higher carbon dioxide levels and vasodilation. Higher CO₂ levels increase oxygen off-loading due to the shift of the oxyhemoglobin dissociation curve to the right. Moreover, mild hypercapnia improves pulmonary function in patients with respiratory distress syndrome.^{3,4} Several studies have found that normocapnia was desirable and should be a standard intervention during general anesthesia.²⁻⁴

Conclusion

The notion of keeping EtCO₂ levels between 30 and 35mmHg is scientifically unsound. Hypocapnia and the hyperventilation necessary to create it are detrimental. Additionally, increased mortality and LOS are proven unfavorable consequences of low EtCO₂. Mild hypercapnia can improve oxygen supply by improving tissue perfusion, thus increasing carbon dioxide levels and vasodilation.³⁻⁵ Higher CO₂ levels enhance oxygen off-loading because the oxyhemoglobin dissociation curve shifts to the right. In addition, moderate hypercapnia promotes pulmonary function in individuals suffering from respiratory distress syndrome. Several investigations have discovered that normocapnia is favorable and should be considered a standard intervention during general anesthesia.²⁻⁵

II. PICO QUESTION/ PURPOSE

Population (P): Surgical patients

Intervention (I): Maintaining normocapnia intraoperatively

Comparison (C): Current practice of mild hypocapnia

Outcomes (O): Improved patient outcomes and mortality rates

Primary DNP Project Goal

End-tidal carbon dioxide (EtCO₂) monitoring is an effective and reliable method for detecting arterial carbon dioxide partial pressure (PaCO₂) in ventilated patients during surgery. EtCO₂ measurement employs capnography, producing relevant carbon dioxide ventilation, perfusion, and metabolism information.¹

In current clinical practice at the immersion site, mild hypocapnia (EtCO₂ between 30-35 mmHg) via hyperventilation is relatively common under general anesthesia. Hypocapnia's ubiquitous occurrence justifies the notion that it is safer than or at least suitable compared to hypercapnia.²⁻⁴ Mild hypocapnia impedes the resumption of spontaneous breathing attempts, resulting in decreased muscle relaxant and anesthetic drug use. Mild hypocapnia, however, can have deleterious physiological consequences in patients, resulting in unfavorable results.²⁻⁴

The project's general objective is to raise awareness about the advantages of normocapnia (EtCO₂ levels of 40 mmHg or above). Normocapnia lowers the risk of mortality and shortens the duration of hospitalization.²⁻⁵ Additionally, normocapnia has many benefits, including pulmonary protection, enhanced tissue perfusion, and a reduced cardiac index, which can help prevent postoperative sequelae. In addition, mild respiratory acidosis protects organs from harm.³⁻⁵ A well-defined gap exists between the evidence-based goal of normocapnia versus the existing anesthesia practice of mild hypocapnia.

Goals and Outcomes

The SMART model serves as a framework for creating assessment objectives and outcomes. In order to bridge the gap between current practice and the project objective, goals

should be specific, measurable, attainable, relevant, and time-bound (SMART).¹⁰ The relevance of this project is to improve surgical patient outcomes by decreasing mortality and length of hospital stay. At the end of this project, anesthesia providers will adopt the application of normocapnia during the intraoperative management of patients undergoing surgical procedures under general anesthesia.

III. DEFINITION OF TERMS

Normocapnia

Normocapnia is a normal PaCO₂ range of 35 to 45mmHg.¹¹

Hypocapnia

Hypocapnia, also known as hypocarbia, reduces alveolar and blood CO_2 levels below the standard range of 35 mmHg.³

Intraoperative

The intraoperative phase begins when the patient is admitted into the operating theatre, continues with the administration of anesthesia, and ends with the completion of surgery.¹²

Postoperative

The postoperative period begins when the client is transferred to the post-anesthesia care unit

(PACU) and concludes when they are transferred to a surgical unit or released from the

hospital.12

Mortality

Mortality is death within a specific period attributable to a preceding surgery.¹³

IV. METHODOLOGY

Eligibility Criteria

Articles were selected using the inclusion and exclusion criteria to clarify the objectives. Studies for the inclusion criteria were full text, published over the last two decades, and written in English. Individuals over 18 years old were selected.^{2,4,6} The participants were categorized into two groups depending on the average EtCO₂ value under general anesthesia. The hypocapnia group was less than 35 mmHg, while the normocapnia group was above 35 mmHg.²⁻⁴ Exempted participants included those who perished during surgery, had surgery assisted by laparoscopy or a robot, were missing EtCO₂ data, one-lung ventilation,³ or had undergone reoperation.²

Additional patient information included age, height, weight, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) categorization, and comorbidities.^{2,3} The intraoperative variables retrieved were the procedure's length, anesthesia duration, peak inspiratory pressure (PIP), and EtCO₂, which were documented in the anesthesia records every 15 minutes.² During surgery, hemodynamic information such as central venous pressure (CVP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate were collected every 5 minutes. Laboratory measurements, including PaCO₂ from arterial blood gas analysis, were obtained every hour throughout the surgery.²

The database sources utilized for the study originated from library resources and services at Florida International University. The following search keywords were selected using the proper Boolean operators and search symbols depending on the clinical inquiry: EtCO₂, end-tidal concentration, hypocapnia, normocapnia, and intraoperative and mortality outcomes.

Information Sources

PubMed, Ovid, MEDLINE, CINAHL, and ProQuest were database systems used for the research. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guided the literature review further.

Search Strategies

The preliminary search resulted in 1,025 articles. CINAHL and MEDLINE both yielded 720 articles. Articles published within the last ten years and written in English certified the most pertinent and recent articles. The search produced 386 publications for MEDLINE and 244 journals for CINAHL. The remaining 630 articles were retrieved and forwarded to the citation database Covidence for analysis. There were 96 duplicate articles eliminated, leaving 534 articles for additional critique. Reports that did not fulfill the inclusion criteria became disqualified.

Setting and Participants

Nurse anesthetists practicing at the immersion site will be selected to participate in the project. The data-collecting approach utilized for evaluating the project will be in the form of a questionnaire. This analysis is appealing because it is inexpensive, non-threatening, and supports anonymity. Furthermore, data from a large sample of participants may be acquired.¹⁰ The individuals selected will be anesthesia providers at the immersion site. Two surveys will be distributed to the respondents before and after the educational intervention discussing mild hypocapnia versus normocapnia. Outcomes will evaluate the distinctions in the participants' understanding of the advantages and disadvantages of mild hypocapnia and normocapnia. Qualtrics will be employed to develop the surveys and analyze the findings.

Description of Approach and Project Procedures

A detailed evaluation will determine the opportunity and relevance of the project to all stakeholders. The SWOT analysis technique will examine the internal and external qualities and vulnerabilities to the program's success.

A team of expert stakeholders will be appointed to provide educational intervention and guide the project's development process. The anesthesia providers will participate in a questionnaire to measure their knowledge of the advantages and disadvantages of mild hypocapnia and normocapnia. The participants will be presented with evidence-based knowledge regarding appropriate EtCO₂ intraoperative management to prevent postoperative complications. Educational materials will be dispersed by email in a PowerPoint presentation and factsheets throughout the anesthesia lounge.

Protection of Human Subjects

Qualtrics, a HIPAA-compliant online survey platform, will be used to get consent from participants. Surrogate identification will recognize the individuals. The project will not include personal information. Data storage will be in a password-protected electronic database that will solely be available to the primary researcher.

Data Collection

Demographic data include education, gender, ethnic background, and racial group. Furthermore, respondents will estimate the length of time of anesthesia practice and the specialty of preference. Participants will complete a survey containing ten multiple-choice questions following the educational intervention. Responses from Qualtrics will compare the anesthesia providers' knowledge before and after the academic session. The entire project will occur over a month to allow anesthesia personnel to learn about the adverse effects of hypocapnia.

Data Management and Analysis Plan

An electronic platform will store the data. This platform's password will be known only to the principal investigator. In this research, there will be no direct identities. Pre- and postquestionnaire results will determine the efficacy of the educational intervention.

V. RESULTS

Study Characteristics

The six research articles selected for this review examined three chief concepts from the topic in question. The first concept discussed in 4 publications concluded the standardization of EtCO₂ during GA to be equal to or greater than 40 mmHg.²⁻⁵ The second concept discussed by the three articles was the increased inpatient and outpatient mortality rate in the postoperative phase. Lastly, the third concept examined the increased level of hospital stay of more than six days after GA.²⁻⁴

Results of individual studies

The level IV study by Way and Hill⁵ aims to discredit the current anesthesia practice of maintaining mild hypocapnia with EtCO₂ levels between 30 and 35 mmHg. Furthermore, an evaluation occurred between low cardiac output states and EtCO₂. The authors conducted a literature review using keywords: general anesthesia, intraoperative, hypocarbia, hypocapnia, and hyperventilation.⁵ However, the study found no peer-reviewed reports detailing the overt advantages of mild hypocapnia during GA. Despite a lack of peer-reviewed research, the practice of mild hypocapnia is evident in clinical settings. Additionally, the findings indicated that the normocapnic group outperformed the hypocapnic group in cognitive function.⁵

Dong et al.² conducted a comparative study that used data from 4,781 individuals who had abdominal surgical operations over nine years. The association investigated low EtCO₂ and

90-day mortality. The overall 90-day mortality rate was 1.2 percent (55 of 4,710), as opposed to 2.2 percent (30 of 1,374) in the low EtCO₂ group (< 35 mmHg) and 0.8 percent (25 of 3,336) in the standard EtCO₂ group.⁴ Unlike the hypocapnic group, the normocapnic and mild hypercapnic groups were not associated with increased 90-day mortality. Inpatient hospital mortality was 1.3 percent (61 of 4,710) overall, 2.3 percent (32 of 1,374) in the low EtCO₂ group, and 0.9 percent (29 of 3,336) in the regular EtCO₂ group.⁴ Additionally, individuals with low EtCO₂ were more likely to experience higher in-hospital mortality than patients with normal ETCO₂. The temporal and cumulative effects of low EtCO₂ (35 mmHg) were higher inpatient mortality. Conversely, an increase in PaCO₂- EtCO₂ gradient lead to higher 90-day mortality.⁴

Akkerman et al.³ performed a Level I random control trial involving 317,445 eligible participants. Statistical analysis used medians with interquartile ranges (IQR) for continuous data collection and frequencies and percentages for categorical variables. The Kolmogorov-Smirnov test assessed the normalcy of constant variables in advance. The Kruskal-Wallis test compared variances in baseline characteristics, mean arterial pressures, and ventilation parameters between the primary cohort and the subgroups.⁶ The time-weighted average and area under each patient's curve (TWA-AUC) were calculated from minute-level EtCO₂ data, employing a fitted cubic spline curve for all four criteria.⁶

Akkerman et al.³ completed individual analyses for the whole cohort and subgroups. A P value of 0.05 was deemed statistically relevant. The TWA-AUC average is plotted every quarter of the year for all four EtCO₂ criteria. The data revealed a prolonged duration over the 45-mmHg threshold.⁶ The median (IQR) EtCO₂ level was plotted over time and showed a slight rise from 33 mmHg in 2008 to 35 mmHg (P < 0.001) in 2016. Patients with a greater median EtCO₂ were in a lower ASA class, had a higher BMI, and were younger males on average.⁶ Patients with a

greater median $EtCO_2$ had a more insufficient median respiratory minute ventilation (RMV). Patients with an intermediate $EtCO_2$ (between 29 and 41 mmHg) had the most prolonged surgery and general anesthesia.⁶

Dony et al.⁴ performed a level 1 RCT involving 5,317 surgical patients. On average, patients were 51 years old, 42% were female, with an ASA classification of II, and 23% were over 65. The average LOS was 6.2 days. 37% of the participants (n = 1994) remained hospitalized for over six days. The study revealed that 66% of patients maintained an EtCO₂ of less than 35 mmHg.³ The average EtCO₂ level was 32.9 mmHg for the total population. In the hypocapnic group, more elderly patients and women were present (P < .001). At 30 days, mortality rates were 84 out of 3,554 (2.4 percent) in the hypocapnic group versus 15 out of 1763 (0.9 percent) in the normocapnic and mild hypercapnic groups.³

A retrospective study performed by Park et al.⁵ included a level I RCT trial involving 727 patients. The hypocapnia group's average $EtCO_2$ was 33.3 mmHg compared to 36.5 mmHg in the normocapnia group (p < 0.001). Even though the normocapnic group had a higher body weight than the hypocapnic group, the BMI was similar between the two groups. The normocapnic group had significantly greater SBP, CVP, and PIP values.²

VI. DISCUSSION

Summary of the Evidence

Way and Hill⁵ discuss the benefits of maintaining mild hypercapnia, except in specific scenarios that involve elevated intracranial pressure (ICP) or diaphragmatic muscle dysfunction. Moreover, hypercapnic respiratory acidosis can render reversing nondepolarizing neuromuscular blocking drugs, such as neostigmine, more challenging.⁵ Decreased EtCO₂ is related to adverse

outcomes regardless of blood pressure, representing a state compensating for decreased cardiac output by raising peripheral vascular resistance while maintaining blood pressure.⁴

The PaCO₂- EtCO₂ gradient rises in various pathologic situations, including asthma, chronic obstructive pulmonary disease, and acute respiratory failure. Intraoperative measurement of a PaCO₂- EtCO₂ differential of more than 8-10 mmHg worsens mortality in trauma patients and predicts grim outcomes in sepsis patients.³⁻⁵ A PaCO₂- EtCO₂ gradient of 2-5 mmHg is typical in hemodynamically stable individuals.³ Furthermore, hypocapnia may decrease cardiac output and pulmonary blood circulation while ventilation remains constant throughout the surgery.⁴

Citation and Theme of the article	Design/ Method	Sample/Setting	Major Variables Studied and Their Definitions	Measurem ent and Data Analysis	Findings/Resul ts	Conclusions Mogire 19
Dong L, Takeda C, Yamazaki H, et al. Intraoperative end- tidal carbon dioxide and postoperative mortality in major abdominal surgery: A historical cohort study	Retrospe ctive single- center historical cohort study	- Major abdominal surgery: n=4,781 - Under 18 years: n=7 -Regional anesthesia: n=2 -Eligible for inclusion criteria: n=4,772 -Exclusion criteria: Missing EtCO ₂ data- n=4; OLV- n=50	Minimum vs. maximum EtCO ₂ concentration	Kyoto- IMPACT database.	Of the 4,710 patients, 1,374 (29%) had reduced EtCO ₂ , and 55 (1.2%) perished within 90 days of surgery.	An increase in 90-day mortality had a mean intraoperative EtCO ₂ of 35 mmHg.
Akkermans A, van Waes JAR, Thompson A, et al. An observational study of end-tidal carbon dioxide trends in general anesthesia	Retrospe ctive, multicen tre, observati onal study	-General cohort: n=245,725 -Intracranial and carotid artery surgery: n=12,527 -Laparoscopic surgery: n=44,507 -Robotic laparoscopic surgery: n=12,977 -COPD: n=1709	EtCO ₂ thresholds: < 28, <35, <45, and > 45 mmHg	The Kruskal- Wallis test investigate d variability and random -effect multivariab le logistic regression frameworks	The time- weighted average area- under-the-curve (TWA-AUC) and median EtCO ₂ showed only a minor increase in EtCO ₂ .	The study discovered significant inter- hospital and inter- provider variations in EtCO ₂ throughout the period, implying a wide range of EtCO ₂ tolerance or a lack of evidence to substantiate a particular target range.
Mutch WAC, El- Gabalawy R, Girling L, Kilborn K, Jacobsohn E. End-Tidal Hypocapnia Under Anesthesia Predicts Postoperative Delirium	ENGAG ES- Canada study. Hypothe sis study.	N=101 Sociodemograph ics; preop cognitive functioning; Preop psychiatric characteristics; preop patient morbidity; surgical characteristics; Delirium	The effects of hemodynamic variability, EtCO ₂ concentrations , and anesthetic agents on the incidence of POD	Bivariate and linear regression structures	POD severity correlated with cognitive dysfunction, age, depression, anxiety, and intraoperative EtCO ₂ .	POD was linked to intraoperative ventilatory management, evidenced by low EtCO ₂ levels. These results imply that maintaining intraoperative normocapnia may benefit patients at risk of POD.
Dony P, Dramaix M, Boogaerts JG. Hypocapnia measured by end- tidal carbon dioxide tension during anesthesia is associated with an increased 30-day mortality rate	Retrospe ctive, observati onal study	-Patients and perioperative variables in both EtCO ₂ groups: n=5317. - EtCO ₂ (20-34 mmHg): n=3554 - EtCO ₂ (35-49 mmHg): n=1763	-Patient mortality in the 30 days after surgery -LOS	Logistic regression models	Hypocapnia occurred in 66% of the patients. The 30-day mortality rate in the low EtCO ₂ group was 84 of 3554 (2.4%) vs. 15 of 1763 (0.9%) in the normocapnia group. In the low ETCO ₂	Low EtCO ₂ levels during anesthesia are related to increased postoperative mortality and length of stay. These findings highlight the significance of avoiding hypocapnia during anesthesia

					group, 35% of patients received hospitalization for more than six days, compared to 30% in the normocapnia group	to enhance surgical outcomes.
Lee J-H, Kang P-Y, Jang Y-E, Kim E-H, Kim J-T, Kim H-S. A pharmacodynamic model of respiratory rate and end-tidal carbon dioxide values during anesthesia in children	Retrospe ctive study	N= 56 Ages: 1 month to 6 years), not taking a chronic (> 7 days) antiepileptic drug. Exclusion criteria were increased intracranial pressure, moyamoya disease, or other conditions that affect PaCO ₂	The correlation between respiratory rate and EtCO ₂ during mechanical ventilation in general anesthesia patients	A pharmacod ynamic model with NONMEM (nonlinear mixed- effects modeling) software	The RR needed to achieve an EtCO ₂ of 35 mmHg (50 percent reduction of highest EtCO ₂ [40 mmHg] to lowest EtCO ₂ [30 mmHg]) in patients taking an antiepileptic drug was approximately five times lower than in non- users	The adjusted RR required setting the EtCO ₂ between 35 and 40 mmHg, while mechanical ventilation under general anesthesia was much lower in patients taking antiepileptic drugs than in patients not.
Park J-H, Lee H-M, Kang CM, et al. Correlation of Intraoperative End- Tidal Carbon Dioxide Concentration on Postoperative Hospital Stay in Patients Undergoing Pylorus-Preserving Pancreaticoduodene ctomy	Retrospe ctive study	N=727 Hypocapnia group: n=384 Normocapnia group: n=343)	Hypocapnia group (< 35mmHg) vs. normocapnia group (> 35 mmHg)	IBM SPSS Statistics software for statistical analysis	The hypocapnia group had a considerably longer median LOS than the normocapnia group (22 days vs. 18 days). They did not vary in terms of postoperative mortality	In patients undergoing pylorus- preserving pancreaticoduode nectomy, decreased levels of intraoperative EtCO ₂ during general anesthesia were correlated with a higher LOS.
Zavhorodnia VA, Androshchuk OI, Kharchenko TH, Kudii LI, Kovalenko SO. Hemodynamic effects of hyperventilation on healthy men with different levels of autonomic tone	Retrospe ctive study	N=77 males aged 18–23 years Sympathicotonic (I, n = 22) Normotonic (II, n = 30) Parasympathicot onic ones (III, n = 25)	Sympathicoto nic, normotonic, and parasympathic otonic	Fisher's F- test through the ANOVA process	PetCO ₂ was higher in parasympathicot onic participants (41.3 mmHg) than in normotonic (39.5 mmHg) and sympathicotonic (39.3 mmHg)	The duration of the R-R interval decreased in normotonic individuals. The heart index increased in all groups, while general peripheral resistance decreased primarily in normotonic and parasympathicoto nic individuals
Lee SM, Missirlis PI. Low intraoperative end- tidal carbon	Observat ional study- RCT	N/A	Low EtCO ₂ alarm pre-set at 35 mmHg.	N/A	It is still uncertain whether establishing	There is a link between low EtCO ₂ and death, though this could

dioxide: a promising target to improve outcomes or a marker of physiologic instability					EtCO ₂ at an increased target would decrease mortality or other factors such as decreased ventilation vs. cardiac output	be due to confounding variables
Way M, Hill GE. Intraoperative End- Tidal Carbon Dioxide Concentrations: What Is the Target?	N/A	N/A	Normocapnic group, hypocapnic group, and hypercapnic group	N/A	Higher-than- targeted EtCO ₂ levels enhance patient outcomes and are related to lower postoperative complications	Mild hypercapnia with EtCO ₂ values of 40 mmHg or higher is advantageous and should become the standard of practice
Petran J, Ansems K, Rossaint R, et al. Effects of hypercapnia versus normocapnia during general anesthesia on outcomes: A systematic review and meta-analysis	Parallel- arm RCT	N=1,794 Hypercapnia group: n=901 Normocapnia group: n=893	Normocapnia vs. hypercapnia	Random- effects meta- analysis	The hypercapnia group had a reduced duration of endotracheal intubation	The results show no evidence of a beneficial effect of increased CO ₂ partial pressure levels during general anesthesia.

Participant Demographics

Pre-test participants' demographics and experience are demonstrated in Tables 1 and 2.

Table 1. Demographics

Demographics	N (%)
Total Participants	5 (100%)
Gender	
Male	4 (80 %)
Female	1 (20 %)
Ethnicity	
Caucasian	2 (40 %)
Latino	3 (60 %)
Medical Profession	
DNP	4 (80%)

MSN	1 (20%)
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Table 2. Experience

Experience	
< 1 year	0
1 to 5 years	2
6 to 10 years	2
10+ years	1

The study included a total of 5 participants. 20% (n=5) of the participants were females, and 80% (n=4) were males. The participants in this study stemmed from two ethnic groups, Caucasians (40%) and Latinos (60%). All of those who participated are CRNAs. 80% have their Doctorate in Nursing Practice, and 20% have their Master of Science in Nursing. Individuals were questioned about their length of time practicing, which were as follows: those 1 to 5 years (n=2, 40%), 6 to 10 years (n=2, 40%), and over 10 years (n=1, 20%).

Pre-test Results Summary

This section provides information on the participants' knowledge of intraoperative EtCO₂. 60% of participants comprehended that an EtCO₂ level greater than 40 mmHg resulted in unsatisfactory postoperative outcomes. However, 75% of respondents incorrectly believed that an EtCO₂ level higher than 40 mmHg resulted in pulmonary impairment. None of the participants thought that an EtCO₂ level of less than 35 mmHg increased pulmonary shunting. Only one participant recognized that hypocapnia does not cause vasodilation. Furthermore, 0% of those surveyed believed that an EtCO₂ level greater than 40 mmHg promotes improved pulmonary function in people with respiratory distress syndrome.

Post-test participants' demographics and experience are demonstrated in Table 3 and Table 4.

Table 3. Demographics

Demographics	N (%)
Total Participants	4 (100%)
Gender	
Male	3 (75 %)
Female	1 (25 %)
Ethnicity Caucasian	1 (25 %)
Latino	3 (75 %)
Medical Profession	
DNP	3 (75%)
MSN	1 (25%)

Table 4. Demographics

Experience	
< 1 year	0
1 to 5 years	2
6 to 10 years	1
10+ years	1

Post-test Demographics

The post-test study had four participants. 25% (n=1) of the participants were female, while 75% (n=3) were male. This study's participants included two ethnicities: Caucasians (40%) and Latinos (60%). All of those who took part are CRNAs. 75% have a Doctorate in Nursing Practice, and 25% have a Master of Science in Nursing. Individuals' years of practice were as follows: 1 to 5 years (n=2, 50%), 6 to 10 years (n=1, 25%), and more than 10 years (n=1, 25%).

Post-test Results Summary

Following the pre-test, participants viewed an educational PowerPoint presentation that provided additional information about this study. After the educational presentation, participants

completed a post-test questionnaire. The post-test questionnaire assessed their knowledge after they had completed the pre-test. The respondents were more knowledgeable about intraoperative EtCO₂. There was a 50% increase in participants understanding that EtCO₂ > 40 mmHg resulted in increased tissue perfusion. More than 75% of participants understood that an EtCO₂ of 35 mmHg caused increased pulmonary shunting.

Furthermore, 100% of respondents agreed that EtCO₂ levels greater than 40 mmHg increased tissue perfusion. There was a 50% increase in participants who believed hemorrhage was the primary cause of death in trauma patients exposed to low levels of EtCO₂. Finally, 50% of those polled believed that an EtCO₂ concentration greater than 40mmHg promotes improved pulmonary function in people suffering from respiratory distress syndrome.

	Pre-	Post-	Difference
	Test	Test	
Mild hypocapnia, which includes end-tidal carbon dioxide concentrations (EtCO ₂) between:	100%	75%	25%
What level of EtCO ₂ has unsatisfactory postoperative outcomes? (mmHg)		75%	50%
What are the effects of $EtCO_2$ level > 40 mmHg?	0%	75%	75%
What are the effects of $EtCO_2$ level < 35 mmHg?		100%	100%
True or False: Most patients with $EtCO_2 < 35$ mmHg experienced a hospital length of stay of more than six days_compared to individuals with $EtCO_2 > 35$ mmHg.		75%	25%
Which of these options is NOT a consequence of hypocapnia?	87.5%	100%	12.5 %

Pre and Post-Test Questions and Results

What is normocapnia linked to?	50%	75%	25%
What is the primary cause of death in trauma patients exposed to decreased levels of EtCO ₂ ?	50%	100%	50%
Which EtCO ₂ concentration promotes enhanced pulmonary functioning in individuals suffering from respiratory distress syndrome?	0%	50%	50%
causes an increase in oxygen affinity for hemoglobin, resulting in the onset of hypoxia.	100%	100%	0 %

VII. IMPLICATIONS FOR ADVANCED NURSING PRACTICE

Mild hypocapnia causes microvascular spasms, oxygen deficiency, and energy decline in body cells. Moreover, health deterioration induced by hyperdynamic instability and stress may persist for a considerable time.¹⁴ Low EtCO₂ levels cause vegetative-vascular dystonia, ischemic heart disease, hypertension, osteochondrosis, insomnia, migraines, and constipation. Furthermore, low EtCO₂ has adverse outcomes such as higher mortality and LOS. Normocapnia can improve oxygen delivery by increasing tissue perfusion due to elevated EtCO₂ levels and vasodilation.³⁻⁵ Increasing awareness about EtCO₂ concentrations among anesthesia providers will drastically improve the surgical outcomes of patients postoperatively.

Promoting normocapnia practices by maintaining EtCO₂ levels of 40 mmHg or above during general anesthesia will ultimately enhance mortality rates and patient outcomes.²⁻⁵ Also, this project has the potential to create awareness among other anesthesia practitioners nationwide, resulting in a favorable shift in practice. Assessing factors that might affect the process or impede the project's capacity to attain its objectives and outcomes is imperative. The program may face risks such as anesthesia professionals' negative attitudes regarding normocapnia due to the deviation from the established mild hypercapnia practice. The emphasis on evidence-based initiatives should increase compliance, especially by the leadership team.

Limitations

There are unmeasured or unknown variables. These include potential motives for anesthesia providers to strive for a specific EtCO₂ level and a lack of data sources on ventilation settings, anesthetic depth, smoking practices, and hypothermia.⁴ Moreover, whether low EtCO₂ is related to hyperventilation-induced hypocapnia or an increase in PaCO₂- EtCO₂ gradient is unclear.^{4,9} Weaknesses in the project might include inaccurate data collection, biased anesthesia providers hesitant to adapt to evidence-based research, and patients unwilling to engage in the follow-up phase.

Consequences of Problem

Hypocapnia produces oxygen insufficiency, microvascular spasms, and body cells' energy depletion. Under normal circumstances, the decline of health caused by stress and hyperdynamic instability might endure.¹⁴ The CO₂ concentration in such cases is 20–40% lower than average.¹⁴ Additionally, the reduction in carbon dioxide content in the blood causes a rise in oxygen affinity for hemoglobin resulting in the onset of hypoxia and its subsequent ramifications.¹⁴

Most patients with EtCO₂ less than 35 mmHg experienced a hospital length of stay of more than six days compared to individuals with EtCO₂ greater than 35 mmHg.^{2,3} Hypocapnia is substantially related to mortality in trauma literature. One study revealed that hemorrhage was the primary cause of death in individuals exposed to decreased levels of EtCO₂. 14/31 deaths (45%) occurred in the hypocapnia group in a random controlled trial compared to 7/25 deaths (28%) in the normocapnia group.⁹

VIII. CONCLUSION OF THE LITERATURE REVIEW

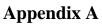
Among the 4 participants in the educational intervention, 75% (n = 3) demonstrated gained knowledge on the effects of EtCO₂> 40 mmHg, while 25% (n = 2) showed no change. Furthermore, 75% (n = 3) of the participants associated the EtCO₂level with unsatisfactory postoperative outcomes. The outcomes were positive. All four participants (n = 4) demonstrated an improved understanding of the effects of intraoperative EtCO₂hypocapnia and normocapnia. More research is needed to develop, educate, train, and potentially change current practice standards.

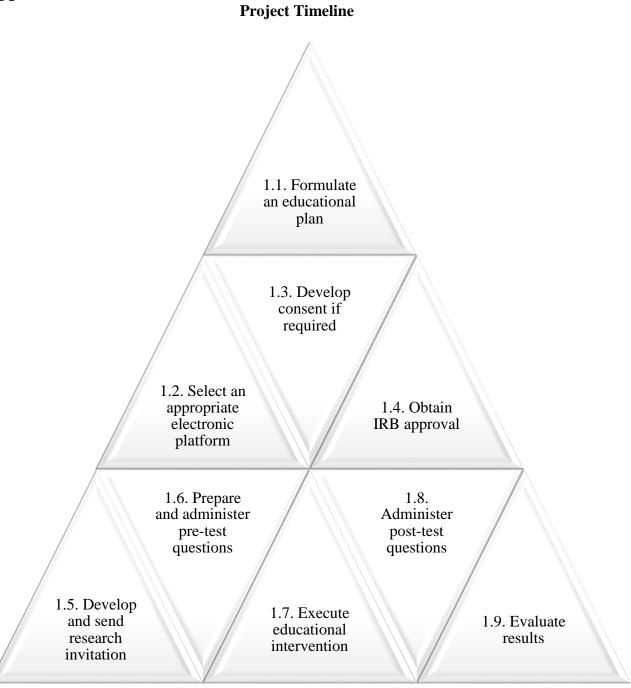
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X. APPENDIX





Appendix B



Miami Beach Anesthesiology Associates, Inc.

Mount Sinai Medical Center • Division of Anesthesia

S. Howard Wittels MD

Hector Davila MSS. MD Executive Dire Guillermo Garcia MD Vice Chairma

Rick Hasty MD

Sebastian Baquero MD Christopher Bauer MD

Vicente Behrens MD

Jayanand D'Mello MD Research Coordinator

Laura Foster MD

Pablo Fumero MD Pedro Garcia MD

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Jason Hovos DO Residency Program Co-Assistant Director

Flor Marin MD

Gerald Rosen MD Residency Program Director

Jason Wigley MD Residency Program Co-Assistant Director

Alexander Volsky MD Jennifer Wright MD

J.P. Mato DNP, CRNA CRNA Director & SRNA Coordinator

Paula Schultz DNP, CRNA **OB-Chief CRNA**

February 1, 2022

Dr. Vicente Gonzalez, DNP, CRNA, APRN Assistant Professor Department of Nurse Anesthesiology Florida International University

Dr. Gonzalez,

Thank you for inviting Mount Sinai Medical Center to participate in Doctor of Nursing Practice (DNP) project conducted by Christine Mogire entitled "Adverse Outcomes of Mild Hypocapnia During General Anesthesia: An Educational Module" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthesiology at Florida International University. I have given the student permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best outcomes for patients by selecting interventions supported by the evidence. This proposed quality improvement project seeks to investigate and synthesize the latest evidence.

We understand that participation in the study is voluntary and carries no overt risk. All Division of Anesthesia providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password encrypted digital cloud, and only be accessible to the investigators of this study: Christine Mogire and Dr. Gonzalez.

Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. Christine Mogire will behave professionally, follow standards of care, and not impede hospital performance. We support the participation of our Division of Anesthesia providers in this project and look forward to working with you.

Respectfully,

Mar-

Jampierre (J.P.) Mato, DNP, CRNA, APRN **Executive CRNA Director** SRNA Coordinator/Supervisor Electronic Mail: Jampierre@bellsouth.net Mobile Phone: 954-668-6080

> 4300 Alton Road, Suite 2454, Miami Beach, FL 33140 Office (305) 674-2742 • Facsimile (305) 674-9723

Appendix C



Office of Research Integrity Research Compliance, MARC 414

Christine Mogire

A

April 6, 2022

"Adverse Outcomes of Mild Hypocapnia During General Anesthesia: An evidence-based education module"

IRB-22-0130 111491 04/06/22

or

As a requirement of IRB Exemption you are required to:

- 1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
- 2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.

discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb

EJ

Appendix D



CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT

"DNP Project Proposal: Adverse Outcomes of Mild Hypocapnia During General Anesthesia: An evidence-based education module."

SUMMARY INFORMATION

Things you should know about this study:

- **<u>Purpose</u>**: Educational module to improve health care provider knowledge on intraoperative end-tidal carbon dioxide (EtCO₂) concentrations that benefit positive patient outcomes.
- **<u>Procedures</u>**: If you choose to participate, you will be asked to complete a pre-test watch a voice PowerPoint, and then a post-test
- **<u>Duration</u>**: This will take about a total of 20 minutes total.
- **<u>Risks</u>**: The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.
- **<u>Benefits</u>**: The main benefit to you from this research is to enhance patient outcomes with the standardization of intraoperative EtCO₂concentrations of 40 mmHg or higher during general anesthesia.
- <u>Alternatives</u>: No known alternatives are available to you other than not participating in this study.
- <u>**Participation**</u>: Taking part in this research project is voluntary.

Please carefully read the entire document before agreeing to participate.

PURPOSE OF THE PROJECT

You are being asked to be in a quality improvement project. This project aims to improve healthcare provider knowledge of intraoperative EtCO₂concentrations that benefit positive patient outcomes.

DURATION OF THE PROJECT

Your participation will require about 20 minutes of your time. If you decide to participate, you will be 1 of 10 participants.

PROCEDURES

If you agree to be in the project, we will ask you to do the following things:

If you agree to be in the study, we will ask you to do the following things:

1. Complete an online 10-question pre-test survey via Qualtrics, an Online survey product for which the URL link is provided

2. Review the educational PowerPoint Module lasting 10 minutes via Qualtrics, an Online survey product for which the URL link is provided.

3. Complete the online 10-question post-test survey via Qualtrics, an Online survey product for which the URL link is provided.

RISKS AND/OR DISCOMFORTS

The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as expected in any type of educational intervention, which may include mild emotional stress or mild physical discomfort from sitting on a chair for an extended period.

BENEFITS

The following benefits may be associated with your participation in this project: Enhanced patient outcomes, with the standardization of intraoperative EtCO₂concentrations of 40 mmHg or higher during general anesthesia.

The program's overall objective is to increase the quality of healthcare delivery and improve healthcare outcomes for our patients.

ALTERNATIVES

There are no known alternatives available to you other than not participating in this project. However, if you would like to receive the educational material given to the participants in this project, it will be provided at no cost.

CONFIDENTIALITY

The records of this project will be kept private and protected to the fullest extent provided by law. If we might publish any sort of report, we will not include any information that will make it possible to identify you as a participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this research project is voluntary.

COMPENSATION & COSTS

You have no cost or payment to receive health education and/or participate in this project.

RIGHT TO DECLINE OR WITHDRAW

Your participation in this project is voluntary. You are free to participate in the project or withdraw your consent during the project. Your withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove you without your consent when they feel it is in their best interest.

RESEARCHER CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Christine Mogire at 302-252-6404 at Cmogi001@fiu.edu

IRB CONTACT INFORMATION

If you would like to talk with someone about your rights about being a subject in this project or about ethical issues with this project, you may contact the FIU Office of Research Integrity by phone at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT

I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions about this study, and they have been answered for me. By clicking on the "

Appendix E



Pre-test and Post-test Questionnaire

INTRODUCTION

The primary aim of this QI project is to improve healthcare provider knowledge of intraoperative end-tidal carbon dioxide (EtCO₂) concentrations that are beneficial for positive patient outcomes.

Please answer the question below to the best of your ability. The questions are either in multiple-choice or true/false format and are meant to measure knowledge and perceptions on intraoperative EtCO₂ concentrations.

PERSONAL INFORMATION

1.	Gender: Male	Female	Other

Age Range (circle): (25-30), (30-35), (35-40), (40-45), (45-50), (50-55), (55-60), (60-65), (65-70)

3. Ethnicity: Hispanic Caucasian African American Asian Other_____

- 4. Position/Title: _____
- 5. Level of Education: Certificate Bachelors Masters Doctorate Other
- 6. How many years have you been an anesthesia provider? (circle)

1-5 years 6-10 years Over 10 years

QUESTIONNAIRE

- 1. Mild hypocapnia, which includes end-tidal carbon dioxide concentrations (EtCO₂) between _____ mmHg, has been utilized traditionally during general anesthesia.
 - a. 25-30
 - b. 30-35
 - c. 35-40
 - d. 40-45

2. What level of EtCO₂ has unsatisfactory postoperative outcomes? (mmHg)

- a. <35
- b. 36
- c. >40
- d. None of the above

3. What are the effects of EtCO₂ level > 40 mmHg?

- a. Pulmonary cellular impairment
- b. Hypotension
- c. Hypercoagulability
- d. Increased tissue perfusion

4. What are the effects of EtCO₂ level < 35 mmHg?

- a. Increased pulmonary shunting
- b. Increased tissue perfusion
- c. Decreased cardiac index
- d. Decreased postoperative infection

5. True or False: Most patients with EtCO₂ < 35 mmHg experienced a hospital length of stay of more than six days_compared to individuals with EtCO₂ > 35 mmHg.

- a. True
- b. False

6. Which of these options is <u>NOT</u> a consequence of hypocapnia?

- a. Microvascular spasm
- b. Energy depletion in body cells
- c. Oxygen insufficiency

d. Vasodilation

7. What is normocapnia linked to? (Select 2)

- a. Lower risk of mortality
- b. Higher risk of mortality
- c. Shorter duration of hospital stay
- d. Longer duration of hospital stay

8. What is the primary cause of death in trauma patients exposed to decreased levels of EtCO₂?

- a. Pulmonary embolism
- b. Stroke
- c. Hemorrhage
- d. Myocardial infarction

9. Which EtCO₂ concentration promotes enhanced pulmonary functioning in

individuals suffering from respiratory distress syndrome?

- a. <35
- b. 36
- c. >40
- d. None of the above

10. _____ causes an increase in oxygen affinity for hemoglobin, resulting in the onset of

hypoxia.

- a. Hypercapnia
- b. Hypocapnia
- c. Hyperthermia
- d. Acidosis

APPENDIX F



