Intravenous Steroid Use In The Prevention of Postoperative Cognitive Dysfunction

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Abstract

Postoperative cognitive dysfunction (POCD) is described as anesthesia's silent side effect, occurring in nearly 10% of patients 65 years and older. Evidence suggests a link between POCD and the release of inflammatory cytokines during surgery, including but not limited to, the peripheral inflammatory markers, interleukin-1Beta (IL-1B) and tumor necrosis factor-a (TNF-a). Intravenous steroids have been shown to decrease the release of these inflammatory biomarkers. A systemic review of the literature was conducted evaluating the use of prophylactic intravenous steroids in reducing the incidence of POCD. A general knowledge base deficit existed amongst the AdventHealth University (AHU) Student Registered Nurse Anesthetists (SRNAs) regarding POCD. To address the problem, an Educational PowerPoint presentation was developed with the objective to increase the knowledge base of 22 AHU SRNAs. An identical 10 question multiple-choice pre-test and posttest was administered to assess baseline knowledge and effectiveness of the presentation. Statistical analysis was performed on the mean pre-test and posttest scores which determine the students' knowledge base on the anesthetic implications of POCD significantly increased after the administration of a 30 minute educational PowerPoint. The statistical analysis revealed scores increased on average from the pre-test to posttest by nearly 45%.

Keywords: Postoperative cognitive dysfunction, dexamethasone, IL-1B, IL-6, TNF-alpha, S100B protein

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Introduction

Unintended Postoperative Cognitive Dysfunction (POCD), defined as a transient disturbance affecting patients of any age, more common in older populations after general anesthesia, is an impairment of thought processes that includes difficulty with memory, attention and concentration. It's occurrence is associated with significant morbidity and mortality (Rundshagen, 2014; Cosmo, Sessa, Fiorini, & Congedo, 2015). In reviewing the literature on this disorder, it is evident that delirium and POCD are often reported as being part of the same continuum of postoperative cognitive impairment, but they are two different entities. In particular, POCD becomes an impairment of thought processes, including memory, attention, and concentration issues effecting daily life and can last upwards of a year (Cosmo, et al., 2015). According to Androsova, Krause, Winterer, & Schneider (2015), the incidence of POCD ranges from 8.9%- 46.1% depending on the type of surgery. Androsova et al., 2015, also noted the link between POCD and postoperative complications, including longer hospital stays and the greater need for financial assistance.

Advances in medical management over the last century have made extensive surgeries in older populations with multiple comorbidities possible (Rundshagen, 2014). Most cases of POCD begin 7 days after surgery and can affect patients for up to one year postoperatively (Brown, 2016). Evidence shows that an inflammatory response is involved in the occurrence of POCD. Pro-inflammatory cytokines, TNF-a, IL-1B, interleukin-6 (IL-6) and interleukin-8 (IL-8), neuronal injury marker and C-reactive protein (CRP) are shown in correlation with POCD

(Androsova et al., 2015). According to Glumac et.al., (2017), there is beneficial effects of dexamethasone against the systemic inflammatory response induced by surgery.

As SRNAs, the incidence of POCD should be considered and thought out thoroughly for every patient greater than 65. Teaching and gaining knowledge on POCD and the interventions to provide better outcomes for the growing elderly population is imperative to reduce its incidence. The goal of this Scholarly Project was to increase the knowledge base of AHU SRNAs in their familiarity with POCD and the potential use of steroids, specifically Decadron, in decreasing the incidence. This Scholarly Project helped the SRNAs currently enrolled at AHU to understand POCD, its associated biomarkers and the potential interventions to reduce its incidence.

Project Questions

Two Scholarly Project questions were developed to assist in the systematic review of the literature. Question one is focused on addressing the clinical problem and guided our literature review, and the second addressed the educational intervention.

PICO: In patients >65 years of age undergoing surgical procedures (P), how does the administration of intravenous steroids (I) influence postoperative cognitive dysfunction (O) within the perioperative period (T)?

PICO: In Adventist University, Student Registered Nurse Anesthetists' (P), does a 30-minute (T) Educational PowerPoint Presentation regarding intravenous steroid use and their impact on patients with POCD (I) results in an increase in knowledge base (O)?

Literature Review and Synthesis

As the population continues to age and new medical developments make surgery at advanced ages increasingly possible, it is estimated that 40% of surgical procedures in the United

States (US) are performed on patients aged 65 and older (Androsova, Krause, Winterer & Schneider, 2015). Considerable evidence shows older adults have a higher possibility of developing POCD. Varying with the type of surgery, the incidence of POCD in patients aged 65 and older ranges from 8.9% to 46.1% (Androsova, Krause, Winterer & Schneider, 2015; Sorrell, 2014). This estimation makes it imperative for those administering anesthesia to older adults to understand POCD's characteristics, its incidence and unfavorable outcomes.

It is evident that delirium and POCD are often reported as being part of the same continuum of postoperative cognitive impairment, but they are two different entities. *Delirium* is an acute change in cognition that develops in the immediate postoperative period with marked fluctuation in attention and orientation, often with either agitation or lethargy. Cognitive changes with POCD are much more subtle (Lili, Zhiyong & Jianjun, 2013).

Cognitive changes during POCD are often transient, but sometimes long-term cognitive changes occur. POCD is associated with higher morbidity and mortality, increased incidence of postoperative complications, longer duration of hospital stay, greater utilization of social financial assistance and earlier retirement (Rundshagen, 2014). Thus, making even routine surgeries potentially life changing for the elderly population. Even though statistically, POCD has a high incidence rate, little is known about how to prevent or treat POCD.

POCD can range from mild to severe and last for weeks to months, with a small minority of patients experiencing permanent decline (Lili, Zhiyong & Jianjun, 2013). POCD symptoms often leads to anxiety, disturbance of the sleep–wake cycle, and depression. Other symptoms that may extend over a long period of time include memory loss, reduced ability to concentrate or process information, and difficulty handling everyday tasks. These cognitive changes may

lead to significant functional impairments, including loss of independence and decreased quality of life (Brown & Deiner, 2016).

The incidence of POCD is difficult to evaluate, as research studies have not used consistent methodologies (Peng, Xu & Ouyang, 2013). These inconsistencies begin with the basic definition of POCD, continuing with the neurocognitive tests to evaluate for POCD and finally, the time frame of associated signs and symptoms. A meta-analysis by Needman, Webb and Bryden (2017), suggested the incidence of POCD of patients who underwent coronary artery bypass graft (CABG) surgery to be 33% to 60% at 1 week postoperatively and declined to 4% to 20% at 3 months. For non-cardiac surgery, research suggested that approximately 10% to 20% of older adults' experience POCD symptoms 3 months postoperatively, although some studies showed rates as high as 50% at hospital discharge and 30% at 3 months after discharge (Rundshagen, 2014; Brown & Deiner, 2016).

Although the specific etiology of POCD following surgery is still unknown, it's believed to be multifactorial in nature. One factor being closely evaluated in the literature is the link between POCD and the bodies inflammatory response to surgical trauma. In a study by Lili, Zhiyong & Jianjun (2013), serum levels of IL-6, S100B protein, TNF-a and CRP levels were elevated in those experiencing POCD after surgery. However, several other researchers were only able to link IL-6 and S100B protein to POCD (Peng, Xu & Ouyang, 2013). The presence of these biomarkers indicated a systemic inflammation had occurred throughout the body with significant clinical implications to follow (Valentin., et al, 2016).

Serum levels of IL-6 are a sensitive marker of tissue damage. IL-6 levels increases' in response to surgical stimuli with the maximal level directly related to the duration of surgery. IL-6 is also directly related to the appearance of endotoxins (Androsova, Krause, Winterer &

Schneider, 2015. Endotoxin (lipopolysaccharide (LPS)) activates complement and cytokines and is an important cause of the systemic inflammatory response. In addition, IL-6 causes acute reactions in the liver, acts as an endogenous pyrogen, and stimulates the secretion of polymorphonuclear leukocyte elastase (PMNE). PMNE has been implicated in sepsis and acute respiratory distress syndrome (Peng, Xu & Ouyang, 2013).

S100B is a calcium-binding protein usually found in astrocytes. Its biological half-life is approximately 30min. Persistently increased levels of S100B indicate continuous release of this protein from damaged tissue (Androsova, Krause, Winterer & Schneider, 2015). Elevated serum levels of S100B have been reported to correlate with neurological deterioration after cardiac surgery and with poor likelihood of survival after hypoxia. Serum protein S100 is also a recognized marker of traumatic brain injury and with blood-brain barrier dysfunction in the absence of apparent brain injury (Peng, Xu & Ouyang, 2013).

The cytokine TNF-a is a pleotropic polypeptide that plays a significant role in brain immune and inflammatory activities (Androsova, Krause, Winterer & Schneider, 2015). "TNF-a is produced in the brain in response to various pathological processes such as infectious agents [e.g., human immunodeficiency virus (HIV) and malaria], ischemia, and trauma" (Peng, Xu & Ouyang, 2013). TNF-alpha mRNA is rapidly produced in response to brain ischemia within one hour, reaches a peak at six to12-hour post ischemia, and subsides 1-2 days later. TNF-a mRNA expression corresponds in a temporal fashion to other cytokines such as IL-6, cytokine-induced neutrophil chemoattractant (KC), and IL-1 and precedes the infiltration of inflammatory cells into the injured zone (Androsova, Krause, Winterer & Schneider, 2015). TNF-a is present early in neuronal cells in and around the ischemic tissue, yet at later time points, the peptide is found in macrophages in the infarcted tissue. TNF-a has been demonstrated to cause expression of pro-

adhesive molecules on the endothelium, which results in leukocyte accumulation, adherence, and migration from capillaries into the brain (Peng, Xu & Ouyang, 2013). Furthermore, TNF-a activates glial cells, thereby regulating tissue remodeling, gliosis, and scar formation. Thus, evidence is emerging in support of a role for TNF-a in injury induced by infectious, immune, toxic, traumatic, and ischemic stimuli. TNF-a promotes inflammation by stimulation of capillary endothelial cell pro-inflammatory responses and thereby provides leukocyte adhesion and infiltration into the ischemic brain (Androsova, Krause, Winterer & Schneider, 2015).

If inflammation plays a role in the multifactorial pathogenesis of POCD, suppression of the inflammatory response by corticosteroids might help reduce the incidence or severity of POCD (Needham, Webb & Bryden, 2017). The evidence generated so far suggested that agents that suppression of IL-6, S100B and TNF-a's production or actions would reduce leukocyte infiltration into ischemic brain regions and thereby diminish the extent of tissue loss (Qiao, Feng, Zhao, Yan, Zhang & Zhao, 2015). Dexamethasone is a potent synthetic glucocorticoid with a long duration of action. Prophylactic use of this intravenous (IV) steroid, or other IV steroids could, in theory, suppress the inflammatory response to surgery and its detrimental cascade, ultimately leading to a decrease in POCD (Glumac, Kardum, Sodic, Supe-Domic & Karanovic, 2017).

Two studies conducted on the use of IV Dexamethasone prior to the initiation of general anesthesia, indicated the group which received IV Dexamethasone compared to the placebo group, had statistically significant decreases in systemic levels of IL-6 and S100B protein. The same significance levels were also determined to correlate with better scores on the neurological assessments conducted by the researcher. The evidence suggests a correlation with the levels of the inflammatory biomarkers and the development of POCD. In the same respect, it also

suggests, prophylactic use of IV dexamethasone contributed to decreased levels of IL-6 and the S100B protein, and therefore reduced the incidence of POCD (Glumac, Kardum, Sodic, Supe-Domic & Karanovic, 2017; Valentin, et. al., 2016).

The current student nurse anesthesia curriculum at AHU mildly touches on POCD, its risk factors or preventative measures. Little is discussed about the anesthetic implications, perioperative care and complications when encountering a patient with an increased risk for developing POCD. Learning the ideal perioperative anesthesia management is essential when working with those identified at risk and all patients 65 and older. Current knowledge of the definition of POCD, its incidence rates, as well as the most appropriate anesthetic management would help provide the safest anesthetic possible to decrease the incidence of POCD, ultimately improving patient outcomes.

Contribution and Dissemination/Justification

With POCD lasting a few days to years, it decreases the patient's quality of life while also increasing surgical morbidity and mortality, especially patients over 65 years of age (Peng et al., 2013). A thorough review and synthesis of the literature was conducted on POCD and the biomarkers connected to clarify evidence-based practice modalities, such as the use of intravenous steroid use for decreasing the incidence of POCD in the patient population >65 years. An Educational PowerPoint presentation with the goal of helping ADU SRNAs understand what POCD is, the biomarkers linked to POCD and the use of intravenous steroids to reduce its prevalence was developed. As Critical Care prepared Registered Nurses, SRNAs have a base understanding of intravenous steroids and how they work. The Educational PowerPoint presentation was presented on October 25, 2018 as assigned by AHU faculty. The efficacy of the

presentation was demonstrated by an increase in mean posttest scores as compared to pre-test scores.

Project Aims

The aim of this scholarly project was to enhance the SRNAs knowledge base regarding POCD, its link to inflammatory biomarkers and the use of IV steroids, such as Decadron to prevent the release of these inflammatory biomarkers, ultimately reducing the incidence of POCD in patients >65 years. This was evidenced by an increase in mean posttest scores compared to mean pre-test scores. The scholarly project was presented to the currently enrolled SRNAs at ADU in the Fall of 2018. The independent variable in this study was the Educational PowerPoint Presentation, and the dependent variable was the difference between pre-test and posttest scores.

Project Methods

This Scholarly Project was quantitative in design. Approval or exemption from the IRB and SRC was obtained, the investigators then proceed with the Scholarly Project. A 30 minute Educational PowerPoint Presentation was administered during the Fall 2018 at AHU to the 2019 cohort (sample size 22). Inclusion criteria consisted of being in the AHU NAP cohort class 2019, and a signed informed consent. Exclusion criteria was as follows: not being present for the presentation, refusal to sign the informed consent, and being late to class. If a student arrived late and missed the pre-test, they would stay for the presentation, but were excluded from the Scholarly Project.

Prior to the pre-test the participants voluntarily signed an informed consent. The results published are public, but no self-identifiers were disclosed. Contact information for the investigators was listed in case further questions arose. The participants took a 10 question

multiple-choice pre-test on the topic presented, followed by sitting for the Educational PowerPoint Presentation. After the presentation, an identical posttest was given and returned to the investigators prior to the participants leaving.

Both pre-test and posttest only contained answers to the multiple-choice questions and no personal identifiers. Scores and tests were kept anonymous using envelopes and a numbering system, inhibiting the use of any personal identifiers. Once the project was completed, the test results were deleted from all personal computer sources. The tests were taken to one of the investigator's house and locked for protection. The data was entered in one of the investigator's personal computers with password protection for storage and evaluation. The results were then placed into a Microsoft Excel Spreadsheet; the results were analyzed using a simple paired t-test to look for a difference between the mean pre-test and posttest scores. The measurable outcome of this project was an increased knowledge base of POCD, biomarkers released and the use of intravenous steroids, as evidenced by an increase in mean posttest scores compared to mean pre-test scores.

Timeline

The timeline of this project was laid out in the syllabus of MSNA690. Trimester one had deadlines for forming a research topic, obtaining an academic mentor and chair along with formulating a Scholarly Project proposal. The Scholarly Project investigators were responsible for doing CITI modules to be compliant with the IRB by May 30, 2018. The ADU/IRB/SRC application form was submitted by July 16, 2018. The estimated date for the presentation of this Scholarly Project was the fall of 2018 during the class period for MSNA 504 Clinical Conference course. The exact presentation date was October 25, 2018. Data collection was initiated on that day, starting with a pre-test prior to the presentation. Post-implementation data

was collected immediately after the presentation. Dissemination will be completed during Spring 2019 with a poster presentation.

Data Collection Plan

Prior to the Educational PowerPoint, the investigators provided an envelope to the SRNAs which contained a 10 question multiple-choice pre-test to take on the material being presented and was collected by the investigators prior to the Educational PowerPoint Presentation. After the Educational PowerPoint Presentation, an identical posttest was administered to the participants.

Once the participants had finished the posttest they were asked to turn them back in. The test was directly handed to one of the two scholarly project investigators by each participant. Both the pre-test and posttest were counted to assure that all students participating completed and returned both tests. The participants were not required to write their names on the test as the test scores were kept de-identified. The test was graded, and the scores transcribed into a Microsoft Excel spread sheet for analysis.

Evaluation Plan

Data was transcribed into a Microsoft Excel spreadsheet and the Scholarly Project investigators pursued statistical analysis assistance through the aid of Dr. Roy Lukman, statistician at AHU. This data spreadsheet was sent to Dr. Roy Lukman in a timely manner, approximately within three weeks of the data collection date. The data was analyzed through the computer program SPSS. Using a simple paired t-test analysis, the data was examined for a difference between the mean pre-test and mean posttest scores. The Scholarly Project investigators determined the SRNAs who received the Educational PowerPoint presentation on POCD, the biomarkers released, and the use of intravenous steroid use increased their knowledge

base on the topic as evidence by improvement in mean posttest scores. The scholarly Project investigators provided project findings in the form of a research paper and post presentation.

Results/Findings

The pre-test was used to demonstrate the student's initial knowledge base of the subject. The results were obtained by utilizing a paired t-test. The posttest revealed that the students' knowledge base on the anesthetic implications of POCD significantly increased after the administration of a 30 minute educational PowerPoint. The results of the pre-test showed the participants scored an average of 43.18%, with a standard deviation of 30.61% and a standard error mean of 6.53%. The results of the posttest revealed an average score of 89.09% with a standard deviation of 11.09%, and a standard error mean of 2.36%.

The results of the Paired t-test analysis showed a standard deviation between the pre-test and posttest of 34.18% with a standard error mean of 7.29%. The t value obtained was -6.300 with a p value <0.001. The statistical analysis supports that there was a significant level of knowledge base increase following the administration of the educational presentation. Scores increased on average from the pre-test to posttest by nearly 45%, which surpassed the researcher's expectations based on current limitations. Full values and table is included in Appendix C.

Limitations/Conclusions

The Educational PowerPoint presentation was limited to a class period with the pre-test and posttest administering on the same day. This made it difficult to truly assess knowledge base and retention. Another limitation of this study was the Educational PowerPoint, it was presented to a small, convenient, homogeneous sample of 22 AHU NAP participants. The ability to add

more SRNAs from different schools would have provided a stronger Scholarly Project by allowing for a larger, more heterogeneous sample.

Despite these limitations, the investigators concluded that the 30 minute Educational PowerPoint presentation did in fact, significantly increased the participants' knowledge base on this topic. Scores improved from the pre-test to posttest by 45%. The results were validated by a p value less than 0.001. It was evident to the investigators there was a deficit knowledge base on the anesthetic implications of POCD based on the pre-test scores.

The participants overwhelmingly surpassed expectation on the posttest. The investigators set forth a goal to improve knowledge on posttests by 10 percent, when in fact, overall scores increased by greater than 40%. The investigators attribute this meaningful increase in knowledge base to the fact that participants were exposed to their knowledge base deficit in the pre-test so they were more focused when the presenters covered the topic.

The results of this project supported the need to continue to further educate SRNAs. This study showed students were very receptive to the information and significantly increased their knowledge base. The future effects of this increased knowledge base cannot be directly determined via the data collected, but it is reasonable to assume, the students are better informed on the subject to clinically manage patients at risk for POCD. The investigators hope this information will indirectly reduce morbidity and mortality related to POCD in the at risk population of patients greater than 65 years of age.

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Appendix A

ADU NAP CAPSTONE PROJECT – INFORMED CONSENT

This is a Capstone Project called *Intravenous Steroid Use in The Prevention of Postoperative Cognitive Dysfunction.* This project is being supervised by a NAP faculty member. We would like to invite you to participate in this project. The main purpose of this form is to provide information about the project, so you can make an informed decision about whether you like to participate.

WHAT IS THE PROJECT ABOUT?

The purpose of this project is to increase the knowledge base of ADU SRNAs, as it pertains to Postoperative Cognitive Dysfunction (POCD), it's link to inflammatory biomarkers released during surgery, and the prophylactic use of intravenous (IV) steroids to reduce its incidence.

WHAT DOES PARTICIPATION IN THIS PROJECT INVOLVE?

If you decide to participate in this project, you will be asked to complete an anonymous pre-test, attend a classroom presentation, and then complete an anonymous posttest. The assessment will address the base knowledge and understanding of POCD, its link to inflammatory biomarkers and the use of IV steroids to reduce the release of the associated biomarkers. Your participation by attendance at the presentation and completion of the pre-test and posttest is anticipated to take approximately 45 minutes.

WHY ARE YOU BEING ASKED TO PARTICIPATE?

You have been invited to participate as part of a convenience sample of students currently enrolled in the NAP at ADU. Your participation in this study is voluntary. You may choose to not to participate. The decision to participate or not participate in this research study is completely up to you. If you choose not to participate your refusal to participate in this research study will involve no penalty or loss of benefits to you. If you choose to participate, you can change your mind later and withdraw your consent and discontinue participation from this study at any time. If you chose to withdraw informed the PI of your wishes.

WHAT ARE THE RISKS INVOLVED IN THIS PROJECT?

Although no project is completely risk-free, we don't anticipate that you will be harmed or distressed by participating in this project.

ARE THERE ANY BENEFITS TO PARTICIPATION?

We don't expect any direct benefits to you from participation in this project. The possible indirect benefit of participation in the project is the opportunity to gain additional knowledge about POCD and the benefit of using of IV steroids in reducing its incidence in patients aged 65 and older.

HOW WILL THE INVESTIGATORS PROTECT PARTICIPANTS' CONFIDENTIALITY?

The results of the project will be published, but your name or identity will not be revealed. To maintain confidentiality of assessments, the investigators will conduct this project in such a way to ensure that information is submitted without participants' identification. All pre-test and posttest will de-identified and will be anonymously collected. The data will be transferred to a Microsoft Excel sheet on the project presenter's password locked computer. After the final poster presentation, all data will be deleted from the scholarly project presenter's computer and permanently destroyed. Thus, the investigators will not have access to any participants' identities.

WILL IT COST ANYTHING OR WILL I GET PAID TO PARTICIPATE IN THE PROJECT?

Your participation will cost approximately 45 minutes of your time, but will require no monetary cost on your part. You will not be paid to participate.

VOLUNTARY CONSENT

By signing this form, you are saying that you have read this form, you understand the risks and benefits of this project, and you know what you are being asked to do. The investigators will be happy to answer any questions you have about the project. If you have any questions, If you have concerns about the project process or the investigators, please contact the Nurse Anesthesia Program at (407) 303-9331.

_____ **Date** _____

Participant Signature/ Participant Name (PRINTED LEGIBLY)

_____ **Participant**

Appendix B

Questionnaire

1. What defines Postoperative Cognitive Dysfunction (POCD)? Select all that apply.
    a. Permanent neurological damage

   b. Impairment of thought process, including memory, attention and concentration issues.
   c. Can affect ones daily living up to one year
   d. Is the same as delirium

2. What portion of the population does POCD effect the most?
   a. Children 2-12years
   b. Geriatric, age 65 and older
   c. Those with underlying mental disorders
   d. Those undergoing combined regional and general anesthesia

3. What are the biomarkers linked to POCD? Select all that apply.
   a. Tumor Necrosis Factor-alpha (TNF-a)
   b. Interleukin 6 (IL-6)
   c. Protein S100B
   d. C-reactive Protein (CRP)
   e. All the above

4. What class of drugs decrease the release of inflammatory cytokines?
   a. Beta Blockers
   b. Sodium Channel Blockers
   c. Steroids
   d. Cephalosporin's

5. Continuous release of S100-B into the blood stream indicates?
   a. Presence of damaged tissue
   b. Correlation to neurological deterioration
   c. Traumatic brain injury
   d. Blood-brain barrier dysfunction
   e. All the above

6. TNF-a is released following injury induced by infectious, immune, toxic, traumatic, and ischemic stimuli?
   a. False
   b. True

7. POCD is associated with? Select all that apply
   a. Increased morbidity and mortality
   b. Increased financial burden
   c. Increased dexterity
   d. Ataxia

8. Intravenous Decadron should be withheld from geriatric population aged 65 years and older.
   a. True
   b. False

9. What is the mechanism of action of Decadron?
    a. Inhibits Calcium absorption
    b. Promotes insulin release
    c. Inhibits prostaglandin and pro-inflammatory cytokines
    d. Inhibits the activation of the RASS system

10. POCD has a definitive cause and prevention protocol?
    a. True
    b. False

Appendix C

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre-Test %	43.1818	22	30.61067	6.52622
	Post-Test %	89.0909	22	11.08800	2.36397

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Pre-Test % - Post-Test %	-45.90909	34.17867	7.28692	-61.06307	-30.75512	-6.300	21	.000

The paired samples t-test was conducted to analyze the data. The obtained t value (-6.300) is associated with a $p<0.001$, which is statistically significant. It can be concluded that the average percentage scored increased significantly between pre-test and posttest and the PowerPoint presentation was effective in increasing the participants knowledge base.

Appendix D

Intravenous Steroid Use In The Prevention of Postoperative Cognitive Dysfunction

Lisa Hruby, RN, BSN, SRNA
Ashley Richichi, RN, BSN, SRNA
Project Mentor: Abigail Evans, MSNA, CRNA
Project Chair: Steven Fowler, DNP, CRNA

Objectives

- Define what is Post Operative Cognitive Dysfunction (POCD)
- Identify the difference between Cognitive Dysfunction and Delirium
- Understand the physiology behind POCD
- Understand the role of anesthesia in cognitive dysfunction
- Identify ways to reduce cognitive dysfunction
- The role of dexamethasone in attenuating POCD

Case Study

First case of the day is 67 year old male, presenting for removal of a lipoma on his lower back. Patient has a medical history of hyperlipidemia and controlled hypertension. Surgical history includes, total knee replacement, appendectomy, tonsillectomy, and cervical fusion. Patient currently bikes 5 miles a day and is an active participant at his local YMCA.

The CRNA plans general anesthesia, prone position. The patient did not receive versed in pre-op, a routine induction was completed without any complications. Patient was positioned and surgery was underway. Surgical time was 35 minutes long, patient was flipped back supine and extubated uneventfully without any complications. Patient got a total of 50 mcg of fentanyl on intubation and Ofirmev 1gm IV and 4mg Ondansteron. An injection of local anesthetic was given by the surgeon at the incision site at the end of surgery.

Case Study Cont.

Patient was taken to PACU comfortable and without any issues. Patient was alert and oriented at discharge from PACU, ambulating and without any pain. Patient was discharged home a few hours later.

Patient started to have bizarre behavior 5 days after surgery as described by his wife, they followed up with their primary care provider who stated it was delirium from surgery. Patient continued on the next 6 months with cognitive changes that effected his work and family life.

PICO Question

- In patients > 65 years of age undergoing surgical procedures (P), how does the administration of intravenous steroids (I) influence postoperative cognitive dysfunction (O) within the perioperative period (T)?
- In Adventist University, Student Registered Nurse Anesthetists' (P), does a 30-minute (T) Educational PowerPoint Presentation regarding intravenous steroid use and their impact on preventing POCD (I) result in an increased knowledge base (O)?

Definition

- Cognitive dysfunction is the loss of intellectual functions such as thinking, remembering, and reasoning of sufficient severity to interfere with daily functioning.
- Patients with cognitive dysfunction have trouble with verbal recall, basic arithmetic, and concentration.

What symptoms will you see?

- Change in mental status characterized by a reduced awareness of the environment and a disturbance in attention
- Hypoactive, hyperactive, or mixed psychomotor behaviors
- Disorientation or temporary memory dysfunction.
- **Impairment of thought process, including memory, attention and concentration issues.**

Delirium vs. POCD

- These are often reported as being part of the same continuum
- Both have multifactorial pathogenesis but differ in numerous ways
- **Delirium**
  - Well defined and acute onset in cognition that develops in the immediate postoperative period with marked fluctuation in attention and orientation, often with either agitation or lethargy.
  - Usually characterized as either hyperactive, hypoactive or mixed type
- **POCD**
  - Subtler, with potential to lead to long-term cognitive changes, with a small minority of patients experiencing permanent decline
  - Usually occurs within the first three days after anesthesia, not in the immediate postoperative phase

DELRIUM	POCD
➢ Medical-underlying neurologic disorder ➢ Medication-pharmaceutical related ➢ Medication Withdrawal	➢ Not related to emergence and no underlying issue prior to surgery
➢ Not related to Emergence Delirium which is usually seen in pediatrics	➢ Impaired memory
➢ Hallucinations	➢ Decreased ability to perform tasks
➢ Abnormal State of Consciousness ➢ Hyperactive ➢ Hypoactive ➢ Mixed	➢ Decreased psychomotor dexterity skills
➢ Cognitive Deficits seen from post-op to weeks out	➢ Symptoms appear from 3 days post-op to months post-operatively
➢ Reversible, only if underlying condition is treatable	➢ **Can affect ones daily living up to one year**

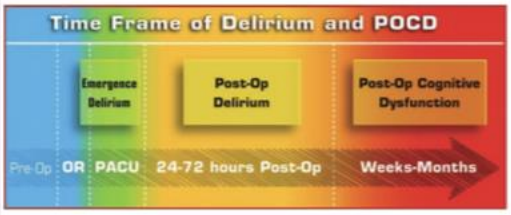


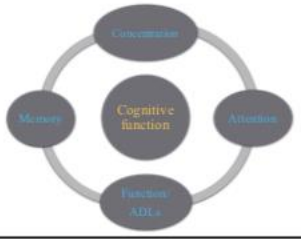
Photo credit to: http://anesthesiology.pubs.asahq.org/article.aspx?articleid=1923038

Comparing Delirium and POCD

Features	Delirium	POCD
Debut	Hours to days	Weeks to months
Onset	Acute	Subtle
Duration	Days to weeks	Weeks to months
Attention	Impaired	Impaired
Consciousness	Altered	Normal
Reversibility	Usually	Usually, but can be long lasting

(Kvenk, L., & Rasmussen, L. S., 2010).

Standardized Understanding



The Problem

- Sequelae of POCD
  - **Increased morbidity and mortality**
  - Prolonged hospitalization
  - Necessitates long-term care
  - Loss of functional ability
  - **Increased financial burden**

Pre-existing Conditions

- Who has a higher risk of developing POCD?
  - **Geriatric (age >65)**
  - Cerebral Vascular Disease
  - Peripheral Vascular Disease
  - ETOH Abuse
  - History of Intraoperative Complications
  - History of Post-Operative Complications

Non-Anesthesia POCD Triggers

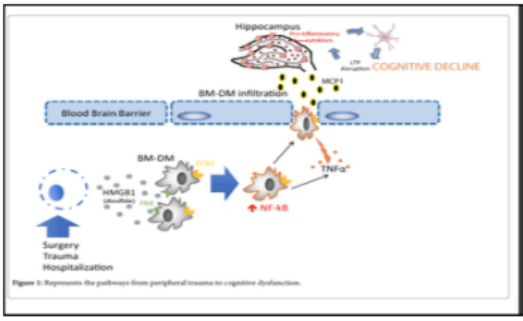
- Major surgery > Minor Surgery
- Type of Surgery: Cardiac and Orthopedic
- Old >Young
- ASA Class 3 and 4 > 1 and 2
- Education Level
- Hx of CVA
- Pre-existing MCI
- Length of Surgery

Anesthesia Triggers

- Hyperventilation
  - Pre-Frontal Dysfunction
- Residual Inhalation Agents
- Residual IV Drugs
  - Opioids
  - Propofol
  - NMB
- Hyper-metabolic state during surgery
- Post Traumatic Stress Disorder (PTSD)

Neuro Physiology

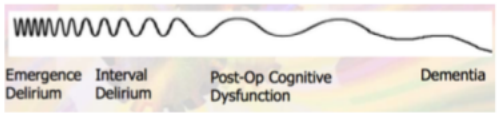
- Inflammatory Cytokines which are released as a result of injury to the CNS
  - **Interleukin 6(IL-6) and IL-1β**
    - Found in the plasma (crosses BBB)
    - Cause of Neuronal Apoptosis
  - **Tumor Necrosis Factor alpha (TNF-a)**
    - Inflammatory Cytokine
    - Released into plasma as a result of acute cerebral injury
    - Released in the presence of Inhalation agents
- **Protein S-100β**
  - Acidic Calcium Binding Protein
  - Considered a Bio-Marker for acute brain injury



Neuro Physiology

- Integrity of the Blood-Barrier is compromised by the release of cytokines
- Macrophages enter the hippocampus leading to memory impairment.
- POCD
  - Neuro Markers
    - Beta-Amyloid Protein
    - Tau Protein
      - Modulates stability if axonal microtubules

Spectrum of Cognitive Disorders



Literature Review

- 40% of surgical procedures in the United States (US) are performed on patients aged 65 and older. Varying with the type of surgery, the **incidence of POCD in patients aged 65 and older ranges from 8.9% to 46.1%**
- **POCD is associated with higher mortality, increased incidence of postoperative complications, longer duration of hospital stay, greater utilization of social financial assistance**
- Researchers found the body has an inflammatory response to perioperative stress, which may contribute to POCD via disruption of the blood-brain barrier (BBB)
- Although the specific etiology of POCD following surgery is still unknown, it's believed to be multifactorial in nature. One factor being closely evaluated in the literature is the link between POCD and the bodies inflammatory response to surgical trauma.

(Androsova, Krause, Winterer & Schneider, 2015)

Literature Review Cont.

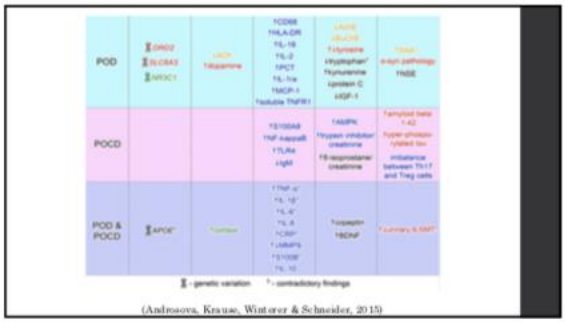
- In the study Androsova et. al. (2015), S100B is a calcium-binding protein usually found in astrocytes. Its biological half-life is approximately 30min. Persistently increased levels of S100B indicate continuous release of this protein from damaged tissue and is an indicator of neuronal injury
- **Continuous release of S100-B into the blood stream indicates:**
  - **Presence of damaged tissue**
  - **Correlation to neurological deterioration**
  - **Traumatic brain injury**
  - **Blood-brain barrier dysfunction**
- Serum levels of IL-6 are a sensitive marker of tissue damage. IL-6 levels increase in response to surgical stimuli, with the maximal level directly related to the duration of surgery. IL-6 is also directly related to the appearance of endotoxins
- In a study by Lili, Zhiyong & Jianjun (2013), they also found **serum levels of IL-6, S100B protein, TNF-a and CRP levels were elevated in those experiencing POCD after surgery**

Literature Review Cont.

- TNF-a is present early in neuronal cells in and around the ischemic tissue, yet at later time points, the peptide is found in macrophages in the infarcted tissue. TNF-a has been demonstrated to cause expression of pro-adhesive molecules on the endothelium, which results in leukocyte accumulation, adherence, and migration from capillaries into the brain (Peng, Xu & Ouyang, 2013).
- **TNF-a is released following injury to by infectious, immune, toxic, traumatic, and ischemic stimuli** (Peng, Xu & Ouyang, 2013).
- Furthermore, TNF-a activates glial cells, thereby regulating tissue remodeling, gliosis, and scar formation. Thus, evidence is emerging in support of a role for TNF-a in injury induced by infectious, immune, toxic, traumatic, and ischemic stimuli. TNF-a promotes inflammation by stimulation of capillary endothelial cell pro-inflammatory responses and thereby provides leukocyte adhesion and infiltration into the ischemic brain (Androsova, Krause, Winterer & Schneider, 2015).

Literature Review Cont.

- A study completed by Needham, Webb & Bryden, 2017, considered if inflammation plays a role in the multifactorial pathogenesis of POCD, suppression of the inflammatory response by corticosteroids might help reduce the incidence or severity of POCD.
- The evidence generated so far suggests that agents that suppression of IL-6, S100B and TNF-a's production or actions would reduce leukocyte infiltration into ischemic brain regions and thereby diminish the extent of tissue loss (Qiao, Feng, Zhao, Yan, Zhang & Zhao, 2015).
- Dexamethasone is a potent synthetic glucocorticoid with a long duration of action. Prophylactic use of this intravenous (IV) steroid, or other IV steroids could, in theory, suppress the inflammatory response to surgery and its detrimental cascade, ultimately leading to a decrease in POCD (Glumac, Kardum, Sodic, Supe-Domic & Kannovic, 2017).

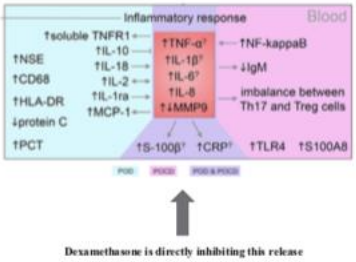


Could some drugs be protective?

- Two studies conducted on the use of IV Dexamethasone
- The two studies by, Glumac, Kardum, Sodic, Supe-Domic & Karanovic, 2017; Valentin, et. al., 2016.
  - Compared a group of individuals which received IV Dexamethasone compared to the placebo group. The group that was administered Dexamethasone had significantly lower systemic levels of IL-6 and S100B protein.
  - The same group who received Dexamethasone (8mg) also correlated with better scores on the neurological assessments.
  - Evidence suggest that the correlation with the levels of the inflammatory biomarkers and the development of POCD
  - It also suggest that prophylactic use of IV Dexamethasone contributed to decreased levels of IL-6 and the S100B protein, therefore reducing the incidence of POCD

The Use of Dexamethasone

- Dexamethasone is commonly used in the perioperative setting by anesthesia providers for their antiemetic properties (4 mg) and its ability to reduce airway swelling (8-10 mg)
- **Dexamethasone inhibits prostaglandins and pro-inflammatory cytokines** and can decrease undesirable neuropsychological adverse events such as POCD.
- **The administration of Dexamethasone directly inhibits the release of inflammatory cytokines**



Dexamethasone is directly inhibiting this release

Anesthesia: What is your plan?

- Detailed history of drugs patient is taking
- Detection of sensory of perceptual deficits
  - Keep patient informed and oriented
- Evaluation of medical problems
  - Reassure the patient and family
- Don't withhold your dexamethasone secondary to age

Research Also Showed

- Inhaled Anesthetics can worsen the likelihood of POCD
- Desflurane shows smallest percentage of POCD, especially in patients elderly patients
- Sevoflurane appears cause increased levels of IL-1β, IL-6, and TNF-α
- Inhalation Anesthesia with Sevoflurane leads to increased POCD in patients > 60yr old

So Where Are We Now?

- There is currently minimal clinical evidence linking surgery or anesthesia to incident POCD.
- Rigorous clinical research is needed to resolve the controversy whether anesthesia or surgery is likely to cause persistent neurological decline or to precipitate POCD
- However, evidence is proving the use of prophylactic IV Dexamethasone for prevention of POCD.
- Currently, POCD has NO definitive cause or prevention protocol

Summary

- POCD is variable in definition, but affects a significant number of patients (up to 40%)
- May be associated with increased cost and functional decline
- Awareness of risk factors and measures to avoid those that are preventable may benefit the patient.
- Considering the use of prophylactic Dexamethasone could decrease the chances of your patient developing POCD.
- Remember to tailor your anesthetic to each individual patient and not fall into course of routine.

References

References