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## Improving Anesthesia Care Provider Knowledge of Analgesia in Procedures for Retinopathy of Prematurity

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**Improving Anesthesia Care Provider Knowledge of Analgesia in Procedures for  
Retinopathy of Prematurity**

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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**DEDICATION**

For my mother and grandmother, I miss you every day.

Romans 8:31 “If GOD is for us, who can be against us?” When the enemy stood before me, my GOD stood beside me. GOD, I thank you for your mercy and countless blessings.

To my husband and sons, I love you dearly, everything I do is for you. Thank you to my family, friends, and mentors who supported me throughout my journey. I love and appreciate each of you. I am truly grateful for Dr. Carla Mayorga who taught me the life skills that helped me stay the course. Lastly, my deepest gratitude to Dr. Yhovana Gordon for her dedication to my success.

## ABSTRACT

**Background:** Retinopathy of prematurity is a leading but preventable cause of blindness in children worldwide. In the United States, approximately 600 premature neonates become legally blind each year. Over 50,000 children suffer visual impairment as a result of ROP globally. Laser photocoagulation therapy is a procedure to treat ROP and improve short and long-term outcomes.<sup>1</sup> Pain management during this procedure is imperative to prevent adverse events in the neonate. An optimal analgesic agent that is safe and efficacious is needed to provide adequate analgesia.<sup>2</sup> The purpose of this review was to identify effective treatment methods to reduce pain in neonates undergoing procedures for ROP.<sup>1</sup>

**Methods:** An extensive search was performed using online electronic journal databases including CINAHL Plus with Full Text, PubMed, and Embase to identify research studies within the past 7 years that evaluated the effectiveness of intravenous fentanyl for pain management in infants undergoing ROP procedures.

**Results:** Of the articles reviewed, 5 were considered relevant for review. Research studies that evaluated the effectiveness of analgesia in the neonatal population during screening and laser photocoagulation for ROP were identified.

**Keywords:** Retinopathy of prematurity, analgesia, fentanyl, sucrose, laser photocoagulation, laser surgery

## **INTRODUCTION**

### **Problem Identification**

Retinopathy of prematurity (ROP) is a vasoproliferative disease that primarily affects the developing retinal vessels of premature neonates.<sup>1</sup> This immature retinal vasculature disorder was recognized in 1942 and initially named retrolental fibroplasia.<sup>2</sup> The pathogenesis of ROP is not well understood, but endothelial growth factor (VEGF) has been noted to play a crucial role in its development.<sup>3</sup> The retina does not have blood vessels until approximately 16 weeks gestation. Vessels then begin to branch out from the optic disc and reach the periphery of the eye one month after birth.<sup>2</sup> Abnormalities in vasculogenesis and neovascularization are caused by dysregulation of VEGF.<sup>3</sup>

Within the first few weeks of life, approximately 30% of premature infants weighing less than 1500g develop ROP. Premature infants exposed to high oxygen concentrations in confined spaces such as incubators are at higher risk for developing ROP. Methods to prevent ROP were aimed at limiting concentrations of oxygen administered to preterm infants to 40%. However, morbidity and mortality resulted when concentrations of oxygen were restricted.<sup>2</sup> Although retinal detachment and blindness may result from severe disease,<sup>1</sup> laser therapy (LT) can help prevent blindness by suppressing overproduction of VEGF in the retina. It also ablates peripheral retina ischemic areas by inducing the regression of new vessels.<sup>3</sup> Laser therapy reduces the risk of poor visual outcomes<sup>1</sup> but is well known to be a painful procedure. It involves a significant amount of pain for the neonate. Yet, evidence is lacking with regard to an analgesia protocol during laser surgery for ROP.<sup>4</sup>

## **Background**

Approximately 28,300 to 45,600 infants suffer from irreversible visual impairment due to ROP annually worldwide. Those at the highest risk of developing ROP are infants weighing 1250g or less before 31 weeks gestation at delivery.<sup>3</sup> The risk of developing ROP is significantly higher in sicker infants with low birth weights. Risk is also increased in those requiring continuous positive airway pressure (CPAP), low Apgar scores at 5 minutes, use of surfactant or erythropoietin, meningitis, sepsis, patent ductus arteriosus, abdominal distension, intraventricular hemorrhage, need for blood transfusions, or diet intolerance.<sup>2</sup>

There is no definitive current anesthetic practice, but general anesthesia or sedation can be used for laser surgery for ROP. In hospitals in the United Kingdom, the NICU intubates and sedates these neonates. This is performed in approximately 90% of cases. The rationale is to prevent the adverse respiratory events that can occur during or after laser treatment. To improve analgesia techniques necessary to manage pain in the neonate undergoing laser photocoagulation for ROP, a further evaluation of the well-defined pain responses in neonates and appropriate anesthetics is needed.<sup>5</sup>

## **Scope of the Problem**

Survival rates continue to improve for premature infants. This has led to an exponential rise in the diagnosis of retinopathy of prematurity, which has been observed in the developing world since the 1980s. However, increased immaturity in these infants that results from the advances in neonatal intensive care has led to an increased incidence of ROP. If left untreated, ROP may lead to the development of strabismus, retinal detachment, vitreous hemorrhage, myopia, vitreoretinal fibrosis, secondary angle-closure glaucoma, and is a significant cause of vision loss in premature neonates.<sup>2</sup>

Retinopathy of prematurity is a leading but preventable cause of childhood blindness worldwide.<sup>3</sup> Screening and diagnosis determine treatment options. Laser treatment is the recommended primary treatment for type 1 ROP.<sup>5</sup> Laser photocoagulation is the most effective therapy in limiting its progression but can be painful. The primary source of pain is thought to be the eyelid speculum, but pharmacological analgesic measures are often limited in preterm infants due to the vulnerability of this population.<sup>2</sup> There are limited studies of low-dose opioid therapy for analgesia in neonates undergoing laser photocoagulation for ROP. This is likely the cause of the knowledge deficit of an efficacious analgesia protocol.

### **Consequences of the Problem**

Pain contributes to instability in neonates.<sup>5</sup> Increased hemodynamic instability, apnea, and raised intracranial pressures may result from untreated pain in preterm neonates. Additionally, altered pain processing, impaired visual perceptual ability, and attention deficit disorder are some long-term consequences associated with pain. Thus, pain management in preterm neonates is of great importance.<sup>4</sup>

Several risks must be evaluated when considering laser therapy for premature infants, as many are likely to have chronic lung disease that leads to respiratory instability and other systemic consequences of their prematurity. General anesthesia and intravenous sedation can lead to respiratory depression in neonates that necessitate endotracheal intubation and ventilation. Reintubation carries its own risks and can lead to acute trauma to the mouth, larynx, pharynx, and nose while contributing to bradycardia and hypoxia.<sup>5</sup> Without establishing a protocol to effectively manage pain in neonates during laser surgery, they remain at risk for adverse effects such as bradycardia, apnea, oliguria and feeding intolerance.



## **Knowledge Gaps**

Oral sucrose is the most commonly used analgesic to reduce pain behaviors in neonates in the neonatal intensive care unit (NICU).<sup>4</sup> While oral glucose may provide comfort during painful procedures, pain control remains problematic.<sup>2</sup> Currently, differences exist in anesthetic care practices for ROP. There is a need to develop an anesthesia care plan for laser therapy for ROP. Anesthetic practices may vary due to the safety concerns and differing expertise of individual anesthesiologists, ophthalmologists, and neonatologists.<sup>5</sup>

In a survey of American ophthalmologists and neonatologists, 60% preferred intravenous sedation to general anesthesia. A significant failure rate was observed in IV sedation by neonatologists attempting to provide analgesia without the constraints of an anesthesiologist and an operating theater.<sup>1</sup> Anesthetic preference and procedure frequency may impact the choice of anaesthetic.<sup>5</sup> While general anesthesia with intubation may be superior to IV sedation because it facilitates ideal operating conditions, it predisposes these vulnerable patients to adverse reactions and the risks associated with intubation and ventilation.<sup>1</sup> The analgesia/sedation protocol used for laser therapy for ROP in a multicenter observational study in Japan, demonstrated a decrease in pain response when fentanyl was used. While research continues to identify prevention and alternative treatments for ROP, more research and evidence are needed to improve analgesia during laser therapy for ROP.<sup>4</sup>

## **Proposal Solution**

There are multiple approaches to the anesthetic management of preterm infants undergoing laser therapy.<sup>1</sup> General anesthesia or sedation with analgesia is commonly used.<sup>4</sup> However, the most effective anesthesia regimen with the lowest risk of perioperative adverse

events remains to be identified. While anesthetists and neonatologists can provide anesthesia and sedation, there is no consensus on an accepted protocol describing appropriate analgesic agents.<sup>1</sup>

Opioid therapy can be used efficaciously for analgesia in neonates undergoing laser photocoagulation for ROP without increasing the risk of respiratory depression and apnea, which can subsequently lead to intubation and mechanical ventilation. An optimal analgesic agent that is a safe and effective option for managing pain in this population is needed.<sup>4</sup> An effective alternative approach using opioid sedation is necessary to avoid volatile anesthetics and repeated anesthetic exposure which may affect neurodevelopment.<sup>1</sup>

Anesthesia providers are responsible for minimizing pain associated with procedures and surgical interventions. The efficacy of a fentanyl infusion in comparison to oral sucrose to provide optimal pain management during laser surgery for ROP should be evaluated to ensure optimal care.<sup>4</sup> This goal can be accomplished by evaluating the literature for analgesic techniques that provide effective pain management to facilitate laser surgery for ROP, which can be disseminated to improve clinical knowledge.

### **Summary of the Literature**

Anesthetic support varies greatly, and there are no specific guidelines for which type of anesthesia is preferable.<sup>6</sup> This is likely due to the limited literature that is available for anesthetic management for ROP screening and therapy.<sup>7</sup> The open label randomized trial by Sethi et al.<sup>4</sup> compared oral sucrose and a low dose fentanyl infusion. It is the first randomized controlled study with an adequate sample size to assess the effect of sucrose and fentanyl in the first 24 hours post procedure. It minimized bias by using independent clinicians to assess primary and secondary outcomes. Oral sucrose was not effective in pain reduction as evidenced by the

percentage of time the infants spent crying. Intravenous fentanyl was associated with a decreased pain response and observed to be a safe analgesic post procedure.<sup>4</sup>

To ensure that infants receive optimal intervention, safe and effective anesthesia manipulation is necessary for ROP procedures. Fentanyl sedation and general anesthesia were well tolerated without life-threatening events. Yet, the use of general anesthesia can lead to back-and-forth transfer of an infant to a higher level hospital.<sup>6</sup> Opioid analgesia avoids the risks associated with general anesthesia such as complications with postoperative extubation.<sup>8</sup> However, opioid dosing must be optimized to prevent potential oversedation, accompanying postoperative pain, and prolonged ventilation.<sup>6</sup>

While ketamine is a potent analgesic that does not require intubation, thereby preserving airway patency and respiratory function, its use is questionable due to significant movement and concerns regarding neurotoxicity.<sup>9</sup> Intravenous fentanyl is more potent, has a rapid onset of action, and penetrates the central nervous system.<sup>8</sup> Surgery was successful with fentanyl, intubation was avoided, and no serious adverse events were encountered.<sup>10</sup>

## **Methods**

### ***Eligibility Criteria***

Studies for this literature review were evaluated and chosen according to the constructed PICO question and objectives of the project. Inclusion criteria limited the search to studies published in the past 7 years, written in or translated to English, and with full-text availability. Exclusion criteria restricted the search to studies that contained the intravenous analgesic agent fentanyl. The studies were focused on procedures used in the screening and treatment of ROP. All database sources used for the research project were accessed via the online library for Florida International University (FIU). Based on the clinical question developed, keywords searched in

the appropriate Boolean operators include retinopathy of prematurity, analgesia, fentanyl, sucrose, laser photocoagulation, and laser surgery.

### ***Search Strategy***

Online databases searched include The Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus with Full Text, PubMed, and Embase. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) further guided the literature review. Assisted by the medical and health science librarians, keywords searched include: (retinopathy of prematurity OR ROP) AND (analgesia OR fentanyl) AND (laser surgery OR laser therapy OR laser photocoagulation) AND (sucrose). The initial search, using the inclusion and exclusion criteria, generated 482 articles. CINAHL yielded 264 articles, PubMed yielded 206 articles, and Embase yielded 58 articles. Randomized trials, retrospective studies, and observational studies were selected for inclusion. Duplicates articles were removed. The abstracts of 19 articles were reviewed. Of these, 5 met the criteria and were selected for a full text review.

**Table 1.** Database Search

<b>Table Database</b>	<b>Key concepts/words</b>	<b>Filters applied</b>
<b>CINAHL</b>	“Retinopathy of prematurity OR ROP” AND “analgesia OR fentanyl OR sucrose” AND “laser surgery OR laser therapy OR laser photocoagulation”	<ul style="list-style-type: none"> <li>▪ Publication date 2015-2022</li> <li>▪ Full text</li> <li>▪ English</li> </ul>
<b>PubMed</b>	“Retinopathy of prematurity OR ROP” AND “analgesia OR fentanyl OR sucrose” AND “laser surgery OR laser therapy OR laser photocoagulation”	<ul style="list-style-type: none"> <li>▪ Publication date 2015-2022</li> <li>▪ Full text</li> <li>▪ English</li> </ul>
<b>Embase</b>	“Retinopathy of prematurity OR ROP” AND “analgesia OR fentanyl OR sucrose” AND “laser surgery OR laser therapy OR laser photocoagulation”	<ul style="list-style-type: none"> <li>▪ Publication date 2015-2022</li> <li>▪ Full text</li> <li>▪ English</li> </ul>

### ***Study Selection***

By utilizing Dearholt and Dang's recommendations and practice tools for appraising research evidence, 5 studies were identified for inclusion.<sup>11</sup> Two well-designed randomized trials, an observational study, and 2 retrospective studies were selected as they identified key concepts of the of the PICO question. All of the studies used intravenous fentanyl as an analgesic agent for pain management during ROP procedures. The authors emphasized the efficacy of intravenous fentanyl in reducing pain and maintaining a good level of analgesia in infants who undergo ROP therapy.<sup>10</sup> Articles by Sethi et al. and Madathil et al. are randomized trials. Retrospective studies were conducted by Piersigilli et al. and Jiang et al. Only one observational study by Öрге et al. was used.

**Table 2.** Inclusion and Exclusion Criteria

<b>Inclusion</b>	<b>Exclusion</b>
Population: <ul style="list-style-type: none"> <li>• Infants diagnosed with ROP</li> </ul> Intervention <ul style="list-style-type: none"> <li>• Intravenous therapy</li> <li>• Fentanyl</li> <li>• Ketamine</li> <li>• Topical anesthetic</li> <li>• Sucrose</li> </ul> Outcomes: <ul style="list-style-type: none"> <li>• Decrease in pain scale scores</li> </ul> Type of study: <ul style="list-style-type: none"> <li>• Randomized trials</li> <li>• Retrospective studies</li> <li>• Observational studies</li> </ul>	Population: <ul style="list-style-type: none"> <li>• Infants with cardiac anomalies</li> </ul> Intervention: <ul style="list-style-type: none"> <li>• Intranasal fentanyl</li> <li>• Midazolam</li> </ul> Outcomes: <ul style="list-style-type: none"> <li>• Articles with results that do not contain numerical data</li> </ul> Type of study: <ul style="list-style-type: none"> <li>• Studies using human subjects</li> <li>• Studies without full texts</li> <li>• Books</li> <li>• Magazines</li> <li>• Dissertations</li> <li>• Editorials</li> </ul>

## Results

As previously noted, of the articles reviewed, five were considered relevant for review. Research studies that evaluated the effectiveness of analgesia in the neonatal population during screening and laser photocoagulation for ROP were identified. The quality and validity of each study was thoroughly evaluated. A critique of each study is provided.<sup>11</sup>

## Review

The study by Sethi et al. was an open-label parallel randomized clinical trial that ranks as Level 1 evidence. The focus of the study was explicitly stated in the title: fentanyl versus 24% oral sucrose for ROP in premature infants. The abstract neither describes each section nor includes the time frame for the study. No statistical information is presented in the introduction. The article's purpose is stated in the introduction and discusses the potential benefits of an analgesic agent that is safe and efficacious in premature infants.

The randomized trial was based on recent research and supported the need for the study. The materials and methods used include all spontaneously breathing preterm neonates. Specific exclusion criteria were met prior to enrollment. No prophylactic respiratory support was provided during the procedure. Topical anesthesia, one drop of 0.5% paracaine, was administered every 20 minutes during the procedure. An assistant was present to immobilize the neonate's head in a sniffing position to ensure airway patency. An intravenous catheter was placed before the laser therapy. The fentanyl group received a dose of 1mcg/kg/hr via infusion 15 min prior to the procedure and continued until the procedure ended. The control group received a single 2ml oral dose of 24% sucrose from the same trained staff prior to the procedure without any repetitive dosing.

Randomization was performed using computer-generated numbers to allocate the neonates into groups. The use of a computer-generated program ensures reliability and validity when randomizing neonates that meet the inclusion criteria. The nature of the intervention precluded blinding in the study, but outcome assessors were blinded to the group assignment to minimize bias. The sample size is sufficient, with 29 infants in the fentanyl group and 28 in the oral 24% sucrose group. Except for delivery mode, baseline demographic variables were comparable between the two groups. The primary outcome evaluated was the proportion of time spent crying during the procedure. Secondary outcomes included premature infant pain profile-revised (PIPP-R) scores, apnea, need for mechanical ventilation, salivary cortisol levels, urinary incontinence, and/or feeding intolerance in the first 24 hours post-procedure. PIPP-R score grades physiological indicators (heart rate and oxygenation), behavioral indicators (eye squeeze, brow bulge, and nasolabial furrow), gestational age (GA), and adjusts for gestational age. Voice and video recording were performed with a baseline behavioral state established with a video recording before the start of the procedure.

The average PIPP-R score at any time and the median proportion of time spent crying during the procedure were significantly less in the fentanyl group compared to the oral 24% sucrose group. The proportion of infants experiencing apnea during and within 24 hours after the procedure was the same between the groups. None of these infants required ambu-bagging as tactile stimulation was a sufficient intervention. Thus, low-dose fentanyl infusion was found to be safe in the first 24 hours post-procedure.

The inability to blind the intervention groups is the major limitation of the study. Additionally, salivary cortisol levels, a marker for stress, could only be obtained in 53% of the study population due to difficulty in extracting saliva. A low-dose fentanyl infusion is effective

and safe for treating pain during laser treatment for ROP. However, more studies are needed to optimize the dose of fentanyl to provide better analgesia.

The retrospective study by Piersigilli et al. evaluated the clinical charts of 13 neonates. These neonates were sedated with propofol and given an analgesic agent, fentanyl, for laser treatment of ROP. The title accurately describes what is being investigated but does not mention the population that is studied. A concise overview of each section of the study is provided in the abstract. The introduction provides statistical information on the scope of the problem. It clearly states that the study aims to evaluate the effectiveness of propofol sedation in conjunction with fentanyl analgesia to avoid intubation and mechanical ventilation during and after laser photocoagulation treatment for ROP in preterm infants.

Retrospective analysis of clinical data was performed to evaluate the effectiveness of the propofol and fentanyl protocol to avoid intubation and mechanical ventilation. Unlike the previous randomized trial, baseline ventilation status and rate of complications were used to assess the protocol's efficacy. These complications include apneic events, temperature instability, desaturations, bradycardic episodes, and changes in ventilation status. The standardized sedation flow sheet containing vital signs (temperature, heart rate, blood pressure, and oxygen saturation) in 3-minute intervals in the medical record was utilized for this purpose.

Compared to the randomized trial by Sethi et al., a laryngeal mask airway (LMA) was placed, and a flow-inflating resuscitation bag was used instead of maintaining spontaneous breaths. No topical analgesia was provided. Propofol is a short-acting hypnotic agent that lacks an analgesic effect. Therefore, a dose of 2 mg/kg of 5% propofol was administered via a peripheral line inserted prior to the procedure until sedation was achieved to a maximum dose of 4mg/kg followed by a bolus of 1 ug/kg of fentanyl. A continuous propofol infusion was initiated



at 4mg/kg/hr and increased to 6 mg/kg/hr to maintain adequate sedation. The LMA was removed, the propofol infusion was discontinued, and a blood gas analysis was performed at the end of the surgery.

No bradycardia or hypotension was observed. An increase in heart rate and a slight decrease in blood pressure were noted but remained within normal parameters for the age. Two infants presented with some episodes of oxygen desaturation and apnea, which resolved after using the oxygen and flow-inflating resuscitation bag. Two neonates required NCPAP for 2 hours to relieve apnea spells and two other infants required a bolus of 10 mg/kg caffeine to treat apnea and desaturation. While ventilatory support was used, none of the infants required endotracheal intubation and mechanical ventilation. The blood gas did not show any significant increases in carbon dioxide levels.

This study is based on a single analgesic protocol using the opioid fentanyl. A calculation of the power of the study could not be performed due to the nature of the study, which reviewed cases treated with a new anesthetic technique with comparisons made only among relevant variables. The sample size is small, with 9 male and 4 female neonates. Exclusion criteria were not discussed. Chronic lung disease was present in 11 infants, although only 1 required nasal continuous positive airway pressure (nCPAP) at the time of surgery. The type of documentation by the Neonatal Intensive Care Unit (NICU) staff is not specified as written or computer charting.

The use of propofol with fentanyl analgesia was effective in laser surgery without adverse effects. However, the use of propofol in children under the age of three is not recommended by the Food and Drug Administration (FDA). It can cause severe hypotension and propofol infusion syndrome with repeated boluses or continuous infusions greater than 24 hours. This syndrome is

characterized by myopathy, metabolic acidosis, hyperkalemia, and acute cardiac failure. A randomized study is needed to assess the safety of propofol in this population but may prove difficult because of their vulnerability.

In the retrospective, longitudinal study by Jiang et al., multiple anesthesia techniques are assessed for tolerability and efficacy during laser therapy for ROP. The article's title serves to inform what is being investigated and the population to which it is applicable. The abstract provides a brief overview of each section found in the study. The problem is not well defined in the introduction, which also fails to quantify the scope of the problem by providing statistical information. The need for the study is made evident, but research questions are not clearly identified.

A retrospective evaluation of medical records was conducted over a specified time frame. Group A consisted of infants receiving topical anesthesia with proxymetacaine. Group B consisted of infants treated with intravenous fentanyl sedation. Fentanyl was given at 2 ug/kg via a pump over 20 min prior to surgery and continuously at 2 ug/kg/hr during treatment. Group C comprised infants receiving general anesthesia with halothane inhalation and neuromuscular blockade. Intubation and mechanical ventilation were employed with groups B and C. The position of the infant's head was maintained with an assistant. NICU nurses or assistants provided stimulation to eliminate bradycardic (heart rate of 90 beats per minute or less) or apneic (cessation of respiratory activity for 20 seconds or more) episodes.

Group A contained 31 subjects, Group B had 47 subjects, and Group C contained 19 subjects. The study population was said to be heterogeneous, but inclusion and exclusion criteria were not provided. Topical tropicamide eye drops were administered three times in 20-minute

intervals in addition to proxymetacaine 0.5% given 5 minutes before and immediately before the procedure. The number of laser burns to each eye varied for each subject.

On average, ophthalmologists needed 12-16 minutes more to complete the procedure compared to groups B and C. Excessive head movement was observed in the infants in group A. An accurate baseline stability was obtained and the greatest instability was observed in group A. Four infants in this group suffered life-threatening respiratory distress or hypoxia requiring resuscitation. No difference was observed postoperatively in groups B and C. Fentanyl sedation was well tolerated and a safe analgesia modality with no occurrence of life-threatening events. Fentanyl is highly efficient, sustainable, displays satisfactory neonatal pain agitation and sedation scale (N-PASS) scores, and maintains a more stable cardiorespiratory status during and after laser treatment for ROP.

Unlike the study by Sethi et al., which utilized a PIPP-R score to evaluate pain, this study used the N-PASS every 20 minutes and cardiorespiratory index (CRI) by Haigh to assess the tolerance of fentanyl sedation. N-PASS scores include crying/irritability, behavioral state, facial expression, extremities tone, and vital signs. Vital signs were only recorded in the NICU monitoring chart every half hour during laser treatment and 2 hours following the procedure. Additionally, a radiant warmer was used, the neonate was swaddled, and a pacifier was offered. Only one other study, the last randomized trial discussed, implemented one of these interventions.

The N-PASS score was only used for the fentanyl group, making it difficult to determine differences in pain control between the groups. The retrospective nature of the study did not allow a definitive determination of causality of postoperative cardiorespiratory instability. Another shortcoming of this study is unresolved questions, including the optimal fentanyl dose to

be used that avoids possible oversedation. These questions can be addressed in a prospective study.

The research by Öрге et al. is based on an observational study. A time frame and a description of each section of the study is found in the abstract. The purpose of the article is identified to compare the complication rates of two opioids, fentanyl and morphine, for laser therapy for ROP. Evaluating the complication rates serves as the premise that fentanyl is a safe analgesic agent for this surgery.

The medical records of preterm infants undergoing laser photocoagulation for ROP by a single surgeon were reviewed. Exclusion criteria were patients who received only general anesthesia or sedation. Of the 40 medical records and 53 treatments reviewed, 42 met the inclusion criteria. A single treatment was randomly selected for infants who received multiple procedures. The study included 39 patients: 17 in the morphine group and 18 in the fentanyl group. Baseline ventilation status was obtained before surgery. The rate of complications that were documented includes apneic episodes, bradycardic episodes, temperature instability, desaturations, and changes in ventilation status during the surgery. A nurse and neonatology physician observed and recorded the sedation flow sheet. A completed NICU standardized sedation flow sheet documenting vital signs in 5-minute intervals and any complications were used just as in previous studies.

The rate of change in ventilation status following administration of anesthesia and during ROP surgery was the primary outcome. Temperature instability (measured outside of the normal range of 36.5 °C- 37.4 °C), apnea (a 20-second interval without respiratory effort), bradycardia (heart rate less than 80 beats per minute), and desaturation events (oxygen saturation less than 85%) were secondary outcomes. Fentanyl was administered at 1 mcg/kg, diluted to 2 ug/ml, and

infused over 20 minutes. The occurrence of apneic events, temperature instability, bradycardia, and worsening of ventilatory status were increased in the morphine group compared to the fentanyl group. The incidence of desaturation events was higher in the fentanyl group but did not alter ventilatory status.

Less respiratory compromise and fewer adverse events were observed with fentanyl than morphine. This leads to the conclusion that fentanyl may be a safer anesthetic agent for ROP laser surgery. However, the small sample size limits the statistical significance of comparing these two opioids and establishes the need for a prospective, randomized study to determine a true association that can inform practice guidelines. The study is further limited by its retrospective nature and low complication rates. The anxiolytic, midazolam, was not used in any other studies, and it is unclear whether its use in both groups on a case-by-case basis had any effect on the complication rates.

The open-label randomized trial by Madathil et al. was based on current research and has an experimental design that ranks as Level I evidence, answering the question of the efficacy of two interventions. The title reflects the interventions to be investigated and the population in which it is studied. An overview of each section of the study is listed in the abstract. The scope of the problem is not discussed except in the setting of a tertiary care institution where the study was conducted. Although statistical information is not provided, the problem and its implications are well defined along with the proposed interventions. The introduction clearly states the study's intent to find an optimum regimen useful for providing sedation and analgesia during laser photocoagulation.

This study contained two intervention arms. A control arm could not be included in the study design because it would be considered unethical to withhold analgesia for this procedure.

Inclusion and exclusion criteria were very specific. Allocation of the study participants into the two groups was performed by an independent investigator who generated random sequences that were serially numbered and concealed. Outcome assessors were blinded to the groups, but blinding could not be done because of the nature of the interventions.

One group received an intravenous fentanyl bolus followed by an infusion and the other group received intermittent ketamine boluses. In the first group, an intravenous fentanyl bolus of 2 ug/kg was given over 5 minutes, 15 minutes prior to the procedure, and a continuous bolus was initiated at 1 ug/kg/hr until completion of the procedure. Inadequate responses evidenced by restlessness, increased crying from baseline, facial expression suggestive of pain, and a sustained increase in heart rate greater than 24 beats from baseline allowed titration by 0.5 ug/kg/hr every 15 minutes to a maximum of 3 ug/kg/hr. In the other group, an intravenous ketamine bolus dose of 0.5 mg/kg was administered 1 minute prior to the procedure and the same dose given intermittently every 10 minutes to a maximum of 2 mg/kg (four doses) if inadequate responses were observed. Both groups received topical anesthesia with 0.5% ophthalmic paracaine drops every 20 minutes during the procedure and were swaddled. If the infant developed hemodynamic instability, bradycardia, or apnea (no respiratory effort for more than 20 seconds or of lesser duration if accompanied by bradycardia or desaturation less than 85%), subsequent doses of ketamine and fentanyl infusion were not administered.

A power analysis was conducted to determine the sample size needed for the randomized trial. Initially, of the infants screened during a specified period, 97 infants were enrolled. There were 51 infants in the fentanyl group and 46 in the ketamine group. The regimen was subsequently revised to an increased fentanyl bolus of 2 ug/kg followed by a 2 ug/kg/hr infusion to a maximum of 5 ug/kg/hr. Ketamine was increased to a bolus dose of 1 mg/kg followed by

intermittent doses of 0.5 mg/kg to a maximum of 4 mg/kg. An additional 27 infants were enrolled (14 in the ketamine group and 13 in the fentanyl group).

Adequate anesthesia was measured every 15 min by PIPP-R scores of less than 7 and the proportion of time, less than 5%, that the infant cried during the procedure (calculated by using the duration of time the infant cried divided by the total procedure time). An independent assessor analyzed the continuous voice recording of the infant to calculate this proportion. Blinded to the group allocations, two independent assessors analyzed the video recordings. A baseline video recording was done then completed every 15 minutes until the end of the procedure. In comparison to the study by Sethi et al., PIPP-R scores were taken every 10 minutes and an average was obtained.

A score of 7-12 was indicative of mild to moderate pain and a score greater than 12 indicated severe pain. Secondary outcomes include apnea, upgrade of respiratory support due to a change in mean cardiorespiratory stability score (devised by Haigh), vasoactive support or fluid boluses for hemodynamic instability, urinary retention for 12 hours that required catheterization, feeding intolerance (recurrent vomiting, abdominal tenderness, increase in abdominal girth by more than 2 cm before feeding, gastric residual of more than 50% of feed volume), hemorrhagic aspirates, bloody stools, and NICU admission for 24 hours or greater.

A greater proportion of analgesia was observed in the fentanyl group compared with the ketamine group, but both groups did not achieve adequate anesthesia. The need for supplemental oxygen during the procedure compared to post-procedure was increased for both fentanyl and ketamine. Apnea during the procedure was also increased in comparison to post-procedure for both regimens. The regimens were well tolerated and there was no difference in side effects post-procedure. Adequate analgesia was only observed in the revised regimens.

When considering limitations to the study, the sample size was sufficient but lacked complete birth and caregiving data due to the enrollment of referred infants. A majority of enrolled infants weighed 1500g or greater, making the applicability of study results to very low birth weight infants difficult. Although baseline characteristics were similar in both groups, the fentanyl group had a slight male preponderance. In the study, a robust methodology was employed, high-quality interventions were implemented, and proposed outcome measures that are clinically relevant were achieved, and results are displayed in several tables and flow diagrams.



**Table 3.** Report of Selected Studies

<b>Author(s)</b>	<b>Purpose</b>	<b>Methodology / Research Design</b>	<b>Intervention(s)/ Measures</b>	<b>Sampling/Setting</b>	<b>Primary Results</b>	<b>Relevant Conclusions</b>
<b>Sethi et al. (2019)</b>	To compare the efficacy of low dose fentanyl infusion and 24% oral sucrose in providing optimal pain relief during laser surgery for ROP	Open Label Randomized Clinical Trial Level 1	Low dose fentanyl infusion 1 mcg/kg/hr versus single oral dose of 24% sucrose; patients were spontaneously breathing	Sufficient sample size, preterm infants enrolled ( $n = 58$ ), fentanyl group ( $n = 29$ ), oral 24% sucrose group ( $n = 29$ )  Study conducted in a level 3 NICU in North India	Median proportion of time spent crying and average PIPP-R score during the procedure was significantly less in the fentanyl group compared with the oral 24% sucrose group	Low dose fentanyl (1mcg/kg/hr) infusion found to be safe and effective in reducing pain
<b>Piersigilli et al. (2019)</b>	To introduce a protocol for laser treatment of ROP to avoid intubation and minimize side effects of anesthesia and ventilation	Retrospective review, Level III	A retrospective review was performed on preterm infants affected by ROP stage III- IV who received 5% propofol at 2-4 mg/kg, then 4mg/kg/hr continuously during the procedure to a max dose of 6 mg/kg/hr and a fentanyl bolus of 1 ug/kg for the laser treatment of ROP; LMA was placed and patients were ventilated with a	Sample size among retrospective results was small ( $n = 13$ )  Study conducted in the Department of Neonatology of the Bambino Gesù Children's Hospital in Rome, Italy	Laser surgery was completed without intubation, 4/13 infants required minimal respiratory support, heart rate post procedure was elevated but within normal range, no bradycardia or hypotension	The study concluded that a good level of anesthesia and analgesia was achieved and maintained during laser photocoagulation which prevented intubation and mechanical ventilation during and after the procedure

			flow-inflating resuscitation bag			
<b>Jiang et al. (2017)</b>	To assess the efficacy and tolerability of anesthesia techniques for laser therapy in premature infants	Retrospective review, Level III	<p>A retrospective review was performed on preterm infants who received laser photocoagulation surgery for ROP</p> <p>Three groups: A received topical anesthesia with proxymetacaine, B received intravenous fentanyl sedation at a dose of 2 ug/kg via a pump over 20 min prior to surgery and continuously at 2 ug/kg/hr during the procedure, C received general anesthesia with halothane inhalation and neuromuscular blockade; group B and C were intubated and mechanically ventilated</p>	<p>Sample size among retrospective results was large (<math>n = 97</math>), topical anesthesia (<math>n = 31</math>), fentanyl (<math>n = 47</math>), general anesthesia (<math>n = 19</math>)</p> <p>Study conducted in the Department of Neonatology of the Guangdong Women and Children's Hospital in Guangzhou, China between July 2013-December 2014</p>	<p>N-PASS score used to evaluate tolerability of laser treatment was 1.8 for fentanyl indicating a satisfactory level of pain</p>	<p>Findings concluded that fentanyl is highly efficient and maintains a more stable cardiorespiratory condition during and after laser therapy</p> <p>An optimal fentanyl dose is needed to avoid possible oversedation</p>

			Radiant warmer was used, neonate was swaddled and a pacifier offered			
<b>Örge et al. (2013)</b>	To compare the complication rates of morphine and fentanyl in preterm infants undergoing laser therapy for ROP	Retrospective review, Level III	A retrospective review was performed on preterm infants who received laser treatment for ROP	<p>Sample size among retrospective results was small (<math>n = 35</math>), morphine (<math>n = 17</math>), fentanyl (<math>n = 18</math>)</p> <p>Study conducted at the NICU of Rainbow Babies and Children's Hospital, Case Western Reserve University from June 2007 to September 2010</p>	<p>Worsening of ventilation status: 5/17 (29%) for morphine group and 1/18 (6%) for fentanyl group; Temperature instability: 1/17 (6%) for morphine group and none in the fentanyl group; Incidence of apneic events: 6/17 (35%) for the morphine group and 2/18 (11%) in the fentanyl group; Incidence of bradycardic events: 7/17 (41%) for the morphine group and 5/18 (28%) in the fentanyl group; Incidence of desaturation events: 9/17 (53%) in the morphine group and 12/18 (67%) in the fentanyl group</p>	Fentanyl may be a safer form of anesthesia for ROP laser surgery as it is associated with fewer adverse events and less respiratory compromise
<b>Madathil et al., (2021)</b>	To investigate if intravenous ketamine or intravenous fentanyl can provide adequate anesthesia in	Open Label Randomized Clinical Trial Level 1	<p>Intravenous fentanyl and intravenous ketamine were studied</p> <p>Fentanyl bolus of 2 ug/kg given over 5</p>	Sufficient sample size, infants enrolled ( $n = 97$ ), fentanyl group ( $n = 51$ ), ketamine group ( $n = 46$ ) with the initial regimen	Proportion of infants with adequate anesthesia was low, 16.3% for fentanyl group and 4.5% for ketamine in the initial regimen	Fentanyl and ketamine provided adequate anesthesia in a minority of preterm infants, more studies are needed to determine

	preterm neonates undergoing laser photocoagulation for ROP		<p>minutes, 15 minutes prior to the procedure, a continuous bolus was initiated at 1 ug/kg/hr until completion of the procedure; intravenous ketamine bolus dose of 0.5 mg/kg 1 minute prior to the procedure and intermittently every 10 minutes to a maximum of 2 mg/kg (four doses)</p> <p>Both groups received topical anesthesia with 0.5% ophthalmic paracaine drops every 20 minutes during the procedure, patients were swaddled</p> <p>Revised regimen of fentanyl 2 ug/kg followed by a 2 ug/kg/hr infusion to a maximum of 5 ug/kg/hr, ketamine bolus dose of 1 mg/kg followed by intermittent doses of</p>	<p>Study steering committee recommended higher doses and consequently, additional infants were enrolled (<math>n = 27</math>), fentanyl group (<math>n = 13</math>), ketamine (<math>n = 14</math>)</p> <p>Study conducted in a day care facility of a tertiary care hospital in North India between April 16, 2018 and May 5, 2019</p>	<p>Adequate anesthesia was higher with the revised regimen, 23.1% for fentanyl group and 7.1% for ketamine</p> <p>PIPP-R scores and percentage cry duration were better</p>	adequate procedural analgesia
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			0.5 mg/kg to a maximum of 4 mg/kg			
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## Discussion

Anesthetic support varies greatly and there are no specific guidelines for which type of anesthesia is preferable.<sup>6</sup> This is likely due to the limited literature that is available for anesthetic management for ROP screening and therapy.<sup>7</sup> The open label randomized trial by Sethi et al. compared oral sucrose and a low dose fentanyl infusion. It is the first randomized controlled study with an adequate sample size to assess the effect of sucrose and fentanyl in the first 24 hours post procedure. It minimized bias by using independent clinicians to assess primary and secondary outcomes. Oral sucrose was not effective in pain reduction as evidenced by the percentage of time the infants spent crying. Intravenous fentanyl was associated with a decreased pain response and observed to be a safe analgesic post procedure.<sup>4</sup>

To ensure that infants receive optimal intervention, safe and effective anesthesia manipulation is necessary for ROP procedures. Fentanyl sedation and general anesthesia were well tolerated without life-threatening events. Yet, the use of general anesthesia can lead to back-and-forth transfer of an infant to a higher level hospital.<sup>6</sup> Opioid analgesia avoids the risks associated with general anesthesia such as complications with postoperative extubation.<sup>8</sup> However, opioid dosing must be optimized to prevent potential oversedation, accompanying postoperative pain, and prolonged ventilation.<sup>6</sup>

While ketamine is a potent analgesic that does not require intubation, thereby preserving airway patency and respiratory function, its use is questionable due to significant movement and concerns regarding neurotoxicity.<sup>9</sup> Intravenous fentanyl is more potent, has a rapid onset of action, and penetrates the central nervous system.<sup>8</sup> Surgery was successful with fentanyl, intubation was avoided, and no serious adverse events were encountered.<sup>10</sup> These evidence-based research studies lay the groundwork for the quality improvement (QI) project. An

educational module will be created based on the findings in the research studies. Using a questionnaire, the knowledge of anesthesia providers will be assessed before and after teaching an effective analgesic protocol for ROP procedures.

### **Purpose/PICO Clinical Questions/Objectives**

#### ***PICO Question or Purpose***

Population (P): Anesthesia providers

Intervention (I): Educational intervention

Comparison (C): None

Outcomes (O): Improved knowledge of analgesia in procedures for retinopathy of prematurity

There are several objectives for the literature review conducted on the topic of interest. Current research is investigated to find and compare analgesic modalities used for treating pain in infants undergoing ROP procedures. The protocols are carefully reviewed to determine an optimal anesthetic agent that minimizes adverse events. The most effective pain management protocol is identified by evaluating the research studies that utilize evidence-based practice. This anesthesia protocol, which has demonstrated improved patient outcomes, will lay the foundation for improving knowledge in anesthesia providers who provide anesthesia care for ROP.

#### ***Primary DNP Project Goal***

Retinopathy of prematurity (ROP), initially named retrolental fibroplasia, was recognized in 1942. It is a proliferative disorder that can occur in the immature retinal vasculature of premature infants.<sup>2</sup> The pathogenesis of ROP is not well understood but vascular endothelial growth factor (VEGF) is known to play an essential role in the development of ROP. Its dysregulation causes abnormalities in vasculogenesis and neovascularization. Laser therapy prevents blindness by suppressing overproduction of VEGF in the retina and helps induce the

regression of new vessels via ablation of peripheral retina ischemic areas.<sup>3</sup> ROP, if left untreated, predisposes infants to develop myopia, strabismus, vitreoretinal fibrosis, vitreous hemorrhage, secondary angle closure glaucoma, retinal detachment, and ultimately complete vision loss. As survival rates continue to improve since the 1980s due to advances in neonatal care, increased immaturity leads to a higher likelihood of developing ROP. The re-emergence of ROP is a significant cause of blindness in the developed world. Early screening and treatment are crucial in the prevention and management of this disease.<sup>2</sup>

Therapy modalities are dependent on the stage and severity of ROP. They include cryotherapy, laser photocoagulation, and vitreoretinal surgery for severe cases. Laser therapy is the treatment of choice for less severe ROP. This is because it can target tiny vessels with more precision, burning abnormal ones while leaving the surrounding tissue unaffected. These tissues are important for subsequent vascularization. As the laser makes more refined burns on the retina, the accuracy of the treatment of the vessels is improved. While this may cause pain, the use of the eyelid speculum is thought to be the primary source of pain for this population and causes infants to be unstable. Controlling pain in the preterm neonate is problematic due to their vulnerability which may limit the use of pharmacological analgesic interventions.<sup>2</sup> Uncontrolled pain can lead to hemodynamic instability, apnea, increased intracranial pressures, altered pain processing, impaired visual perceptual ability, and attention deficit disorder.<sup>4</sup>

Anesthetic care treatments include topical analgesia with or without oral sucrose, general anesthesia (GA) with intubation, and the most popular choice of intravenous sedation (IVS) and analgesia with elective ventilation.<sup>2</sup> GA and IVS can cause respiratory depression in the neonate requiring intubation and ventilation. Chronic lung disease is a systemic consequence of



prematurity and predisposes infants to respiratory compromise. Reintubation can result in acute trauma to the mouth, nose, larynx, pharynx, cause bradycardia, hypoxia, and lung injury from positive pressure ventilation. Anesthesia protocols are needed to determine analgesia that is efficacious for procedural pain during treatment for ROP. These protocols will guide anesthesia providers in utilizing optimal pharmacological agents for pain relief in this vulnerable population.<sup>5</sup> The focus of this project is to improve knowledge base among providers regarding pain management in infants who need therapy for ROP.

### **Goals and Outcomes**

The SMART acronym describes the framework utilized to guide the development of the goal objectives. According to SMART, objectives should be specific, measurable, achievable, realistic, and time-phased.<sup>12</sup>

#### ***Specific***

Anesthesia providers will increase their knowledge of a standardized evidence-based protocol for the management of anesthesia care for patients who undergo procedures for ROP.

#### ***Measurable***

The effectiveness of the ROP protocol was evaluated following analysis of a questionnaire provided to participants before and after an educational intervention. Outcomes were measured by evaluating the current knowledge of pain management for ROP procedures and comparing this to knowledge acquired post-intervention which can be applied in clinical practice. The Qualtrics online survey system software was used to create surveys and conduct data analysis.

***Achievable***

Anesthesia providers including anesthesiologists, certified registered nurse anesthetists (CRNAs), and anesthesiologist assistants (AA) were educated in appropriate anesthetic and analgesic agents for pain management in infants requiring intervention for ROP.

***Realistic***

Anesthesia providers were presented with an education module for the management of anesthesia care. The module included appropriate anesthetic and analgesic agents for procedures for ROP.

***Timely***

The educational module for anesthesia care protocols for patients undergoing intervention for ROP was completed and available to anesthesia providers within a period of 1 month. The outcome of this initiative was for anesthesia providers to have access to anesthetic protocols to minimize pain and provide optimal care for ROP procedures.

**Definition of Terms**

**Retinopathy of prematurity** – a vasoproliferative disorder of the retinal vessels which primarily affects premature infants and can lead to blindness<sup>3</sup>

**Analgesia** – is the relief from pain as achieved from the use of an analgesic agent<sup>4</sup>

**Fentanyl** – opioid analgesic agent used in the management of pain<sup>4</sup>

**Sucrose** – oral sweetener solution used in the management of pain<sup>4</sup>

**Laser Photocoagulation** – a form of corrective laser surgery for the eyes<sup>1</sup>

## **Methodology**

### ***Settings and Participants***

This project took place in hospital, which has a neonatal intensive care unit that may request anesthesia for infants affected by retinopathy of prematurity. There are several anesthesia providers including anesthesiologists, certified registered nurse anesthetists, and anesthesia assistants. Some are staff and may work full time, part time, or per diem status while others may work as contractors with a medical staffing agency. The hospital is located in Hollywood, FL with providers of diverse educational backgrounds.

### ***Description of Approach and Project Procedures***

The DNP project intervention was initiated by inviting the anesthesia providers of the designated hospital to participate in the study. A pretest/posttest design was used to assess knowledge of analgesics for procedural pain in infants requiring screening and therapy for ROP. Before the educational intervention, data was collected on educational level, years in practice, and frequency of work interaction with the population being studied. The educational intervention had a duration of approximately 45 minutes. Participants were asked to complete the posttest following completion of the intervention.

### ***Protection of Human Subjects***

The Institutional Review Board (IRB) makes the determination of any risks to potential participants. If any risk is noted, informed consent was obtained prior to the initiation of the project via Qualtrics. Participants may withdraw from the project at any time. The benefit of participation to the anesthesia providers is the improved knowledge of an anesthetic protocol that minimizes pain in the infant undergoing procedures for ROP.

### ***Data Collection***

Education was the primary demographic data to be collected. Years of practice experience and educational data were collected from the participants as educational level can vary among anesthesia providers. Anesthesiologists attend medical school, and CRNAs are registered nurses who attend anesthesia programs, which depending on the timeframe they attended school, may possess a certificate, master's, or doctoral degree. These providers may practice autonomously depending on what state they practice. However, in the state of Florida, CRNAs work under the supervision of the anesthesiologist. An AA can only work under direct supervision of the anesthesiologist. These various anesthesia providers completed pre- and posttests of the educational intervention, and the data collected was analyzed and reported.

### ***Data Management and Analysis Plan***

Data collected were stored electronically. Only the primary investigator had access to the stored data. Direct identifiers were not collected. Questionnaires obtained via Qualtrics surveys were used to compare knowledge pre and post intervention.

## **RESULTS OF QUALITY IMPROVEMENT**

### **Pretest and Posttest Sample**

After accessing the Qualtrics Online Survey System, the preintervention survey contained 5 participants. Of the 5 participants, 4 answered the demographic questions. One participant could not complete the study due to errors with question display. An evaluation of the posttest survey showed that 2 participants did not complete the survey. Thus, the preintervention sample contained 4 individuals, and the posttest sample contained 3 individuals.

Participants varied in age, gender, race, and the number of years in anesthesia practice. All the preintervention participants were female. Age of the participants ranged from 38 to 50

years old ( $n = 4$ ) with a majority of the participants being over the age of 47. The participants' race varied with African Americans serving as the largest group of participants ( $n = 2$ ). There was 1 Hispanic and 1 Caucasian participant. CRNAs were the only group who responded ( $n = 4$ ) with most CRNAs having greater than 10 years of experience ( $n = 3$ ) and 1 CRNA with 1-2 years of experience ( $n = 1$ ). Table 3 provides the complete demographic breakdown of the preintervention sample.

Three ( $n = 3$ ) of the original four participants participated in the educational module and completed the posttest survey. All of the participants were CRNAs ( $n = 3$ ; 100%) and were females ( $n = 3$ ; 100%). Of these individuals, two were between the age of 46-55 ( $n = 2$ ; 66.6%) and one was between the age of 36-45 ( $n = 1$ ; 33.3%). The data represented a range of ethnicities including Hispanic ( $n = 1$ ; 33.3%), Caucasian ( $n = 1$ ; 33.3%), and Black or African American ( $n = 1$ ; 33.3%). Additionally, the data represented individuals of various years of anesthesia practice including 1-2 years ( $n = 1$ ; 33.3%) and >10 years ( $n = 2$ ; 66.6%).

Demographics of the postintervention participants is displayed in Table 3.

**Table 4.** Demographics

<i>Demographic item</i>	<b>Pre-Intervention Demographics <math>N = 4</math></b>	<b>Post- Intervention Demographics <math>N = 3</math></b>
	Count; Percent	Count; Percent
<b>Gender</b>		
<i>Male</i>	0; 0	0; 0
<i>Female</i>	4; 100%	3; 100%
<b>Age (years)</b>		
25-35	0; 0	0; 0
36-45	1; 25%	1; 33.3%

46-55	3; 75%	2; 66.6%
<b>Race</b>		
<i>Hispanic</i>	1; 25%	1; 33.3%
<i>Caucasian</i>	1; 25%	1; 33.3%
<i>Black or African American</i>	2; 50%	1; 33.3%
<i>Asian</i>	0; 0	0; 0
<i>Other</i>	0; 0	0; 0
<b>Position/ Title</b>		
<i>Anesthesiologist (MD)</i>	0; 0	0; 0
<i>Certified Registered Nurse Anesthetist (CRNA)</i>	4; 100%	3; 100%
<i>Anesthesiologist Assistant (AA)</i>	0; 0	0; 0
<b>Level of Education</b>		
Masters	1; 25%	1, 25%
Doctorate	3; 75%	2; 75%
Other	0;0	0;0
<b>Anesthesia experience (years)</b>		
<i>1-2</i>	1; 25%	1; 33.3%
<i>2-5</i>	0;0	0;0
<i>5-10</i>	0;0	0;0
<i>&gt;10</i>	3; 75%	2; 66.6%

## Pretest Knowledge

The purpose of the pretest was to assess current knowledge about analgesia for ROP.

Four individuals took the pretest and three completed the posttest. Table 5 displays the scores and differences for both components. The pretest showed that the participants were knowledgeable on the opioid observed to be a safe analgesic ( $n = 4$ , 100%). However, it showed a lack of knowledge in an effective dose of fentanyl for sedation following a bolus dose ( $n = 2$ , 50%), the primary source of procedural pain ( $n = 2$ , 50%), and anesthesia modalities in procedures for ROP ( $n = 2$ , 50%).

Participants were asked to rate their likeliness to use fentanyl as an analgesic to manage pain in infants undergoing procedures for ROP. In the preintervention survey, the participants answered as follows: extremely unlikely ( $n = 2$ , 50%), somewhat unlikely ( $n = 1$ , 25%), and extremely likely ( $n = 1$ , 25%). When asked the likeliness to recommend fentanyl sedation as an opioid of choice for ROP treatment, participants in the postintervention survey responded as follows: neither likely nor unlikely ( $n = 3$ , 75%) and extremely unlikely ( $n = 1$ , 25%). This data is shown in Table 6.

**Table 5.** Difference in Pre- and Posttest Knowledge

Questions	Pre-test	Post-test	Difference
1. The percentage of premature infants weighing less than 1500g that develop ROP	50%	100%	+50%
2. Irreversible visual impairment due to ROP worldwide may be as high as	25%	33.3%	+8.3%
3. Risk of developing ROP is higher in	50%	66.6%	+16.6%
4. Untreated ROP may lead to	50%	66.6%	+16.6%

<i>5. Consequences of pain in infants include all of the following except</i>	50%	66.6%	+16.6%
<i>6. Long term consequences of untreated pain in infants include</i>	50%	66.6%	+16.6%
<i>7. The primary source of procedural pain is related to</i>	50%	100%	+50%
<i>8. Anesthesia modalities in procedures for ROP include</i>	50%	100%	+50%
<i>9. Sucrose is effective for pain management in procedures for ROP</i>	50%	33.3%	-16.7%
<i>10. What percentage of infants are intubated to prevent the adverse respiratory effects associated with ROP procedures</i>	25%	100%	+75%
<i>11. The opioid observed to be a safe analgesic with a rapid onset, penetrates the central nervous system and associated with a decreased pain response is</i>	100%	100%	0
<i>12. Which is true regarding a low dose fentanyl infusion for sedation</i>	75%	66.6%	-8.4%
<i>13. What is an effective dose of fentanyl for sedation following a bolus dose</i>	50%	100%	+50%



**Table 6.** Difference in Pre- and Posttest Perspective of Fentanyl as an Effective Analgesic For ROP

**14. How likely are you to use this analgesic modality to manage pain in infants undergoing procedures for ROP?**

	Pretest	Posttest	Difference
<i>Neither likely nor unlikely</i>	0	33.3%	+33.3% %
<i>Somewhat likely</i>	0	33.3%	+33.3%
<i>Extremely likely</i>	25%	33.3%	+8.3%
<i>Somewhat unlikely</i>	25%	0	-25%
<i>Extremely unlikely</i>	50%	0	-50%

**15. How likely are you to recommend fentanyl sedation as an opioid of choice for ROP treatment?**

	Pretest	Posttest	Difference
<i>Neither likely nor unlikely</i>	75%	33.3%	-41.7%
<i>Somewhat likely</i>	0	33.3%	+33.3%
<i>Extremely likely</i>	0	33.3%	+33.3%
<i>Somewhat unlikely</i>	0	0	0
<i>Extremely unlikely</i>	25%	0	-25%

**Posttest Knowledge**

Posttest scores are displayed in Table 5. After viewing the educational module, most areas showed improvement. There were a few that showed a decrease or stagnancy in knowledge. An increase in knowledge of 50% was observed in the question regarding the population affected by ROP. An increase in knowledge of 50% was also observed in the question regarding pain related to the treatment of ROP and an effective dose of fentanyl for sedation following a bolus dose. The questions regarding risks factors for developing ROP and consequences of ROP showed improvement of +16.6%. There was no change in the question regarding the opioid observed to be a safe analgesic with a rapid onset as both the pretest and

posttest showed a 100% pass rate. Thus, participants answered the question correctly before and after the educational module. An unfavorable change was observed in two questions of the survey. Sucrose as an effective intervention for pain management in procedures for ROP showed a decline by 16.7% and a low dose fentanyl infusion for sedation showed a decline by 8.4%.

The change in perspective of fentanyl as an effective analgesic for ROP is depicted in Table 6. There was a 33.3% change in the participants who were somewhat likely or neither likely nor unlikely to use fentanyl to manage pain in infants undergoing procedures for ROP. Additionally, there was an 8.3% change in those who were extremely likely to use the analgesic modality. Thus, a positive difference was demonstrated for all these responses. Similarly, the postintervention results of the likeliness to recommend fentanyl sedation as an opioid of choice for ROP treatment showed an improvement in perspectives. Participants were 33.3% extremely likely and somewhat likely to recommend fentanyl.

### **Summary of Data**

Overall, a small change in knowledge occurred as reflected in Table 5. The average score of the pretest was 67.5 and the average score of the posttest was 79.9 with an overall average improvement of 8.46. There was a 50% improvement in knowledge about the population affected by ROP, the primary source of pain related to ROP procedures, treatment modalities for ROP procedures, and an effective dose of fentanyl for sedation. The pretest and posttest showed a minor improvement in 6 questions and no change in knowledge for one of the questions. It should be noted that the latter question was answered correctly in the pretest and posttest. Lower posttest scores were observed in 2 areas including sucrose utilization for ROP procedures and a low dose fentanyl infusion, indicating a decrease in knowledge. A change in perspective towards

utilization of fentanyl as an analgesic was observed. Participants are extremely likely or somewhat likely to use and recommend fentanyl for sedation for ROP.

### **Limitations**

A significant limitation of this survey was the sample size. While the survey was distributed via email to 37 people, only 3 individuals completed the pre-intervention and post-intervention surveys. Reliability of the results would have been strengthened with a larger sample size. An additional limitation of the data is that all participants were CRNAs. Thus, the data did not represent the knowledge and attitudes of the different anesthesia providers at this site within the healthcare system. Lastly, the delivery method of this survey may have been a limitation. The self-paced nature of the educational module may have prevented completion of the survey, as the participants may not have set aside adequate time to complete it. Provision of an in-class presentation would have ensured that the participants viewed the educational module and possibly yielded more reliable data.

### **Discussion of the Results with Implications to Advanced Nursing Practice**

The most frequently used analgesic in infants is oral sucrose. The proposed mechanism for its analgesic effect is believed to be the release of endogenous opioid. It is associated with a reduction in pain behaviors in preterm and term infants for painful procedures such as venipuncture, heel lancet prick, and intramuscular injection. It is often used in conjunction with topical anesthesia to avoid intubation.<sup>4</sup> This has been proven to be inadequate for surgical treatment and increases the incidence of potentially life-threatening cardiopulmonary events.<sup>8,10</sup>

A variety of anesthesia techniques have been used for infants requiring ROP procedures. Considerable pain during these procedures is related to mydriatic eye drops, forced eyelid opening, insertion of blepharostat, scleral indentation, and intense illumination.<sup>13</sup> Tenon

anesthesia, orbital regional anesthesia such as peribulbar or retrobulbar injections, in combination with sedation has also been used and is associated with excessive head mobility and cardiopulmonary instability.<sup>8,10</sup> The exclusive use of topical anesthesia is associated with severe cardiorespiratory complications during and after ROP surgery. In addition, foveal burns may result since topical anesthesia cannot induce ocular akinesia. More time is needed to complete procedures under topical anesthesia and prolonged treatment is presumed to be more painful.<sup>6</sup>

A lack of evidence exists regarding analgesia protocols for ROP procedures. This is likely due to the limited availability of studies using low-dose opioid therapy in infants receiving laser photocoagulation for ROP. The concern lies with the risks to the infant, especially apnea requiring intubation and mechanical ventilation.<sup>4</sup> Nurse anesthetists are advanced practice registered nurses who may be called to provide anesthesia that is safe and effective. Low dose fentanyl analgesia is a safe and efficacious anesthesia modality in this population. This anesthesia protocol may obviate the need for some hospitals to transfer cases of prematurity with threshold ROP to tertiary hospitals to receive laser treatment and prevent ROP morbidity.<sup>6</sup>

This QI improvement project will help anesthesia providers minimize severe and potentially life-threatening cardiorespiratory complications during and after surgery for ROP. The facilitation of pain management will maintain hemodynamic stability, allow surgery to be successful, and prevent short and long-term consequences associated with prolonged pain.<sup>6</sup> Results of the project will be provided to the NICU leadership team and the anesthesia department. These stakeholders may choose to implement this analgesic protocol identified in the project as a practice change that can subsequently be used to train current and new staff.

## Conclusion

Retinopathy of prematurity remains a frequent comorbidity in preterm infants. Studies have established that infants perceive painful stimuli from ROP screening and therapy.<sup>6</sup> Laser treatment is most commonly used for ROP because it requires less manipulation and causes less trauma than cryotherapy. Premature infants who received topical anesthesia for cryotherapy had protracted and more severe cardiorespiratory complications than with sedation/analgesia or general anesthesia.<sup>10</sup> Complications of tenon anesthesia include rectus muscle damage, scleral perforation, retrobulbar hemorrhage, central retinal artery occlusion, and arrest of the infant.<sup>8</sup> Having an effective analgesic agent such as fentanyl helps to avoid extended procedures, prevents additional pain, and subsequent short and long-term consequences associated with prolonged pain.<sup>6</sup>

There is still no consensus on the best anesthetic approach or standard of care for those at risk for ROP. An anesthesia protocol that provides efficient pain control to vulnerable infants is still needed.<sup>9,10</sup> A good level of analgesia and anesthesia can manage pain in this population while avoiding intubation and mechanical ventilation. Fentanyl and morphine are opioids that have been used for ROP therapy.<sup>10</sup> Less respiratory compromise occurs with fentanyl than morphine.<sup>8</sup> Complication rates suggest that fentanyl is safer when evaluating overall worsening of ventilation status temperature instability.<sup>6</sup> While fentanyl has been used safely, an optimal dose is recommended for future research.<sup>7</sup> The goal remains to confer the best pain control with minimal risk to the infant undergoing laser therapy for ROP.<sup>6</sup> Information gathered from these studies will guide the quality improvement project that educates anesthesia staff on an efficacious analgesic protocol using intravenous fentanyl for ROP procedures. Using these current evidence-based research articles, patient care and outcomes will be improved.

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**APPENDIX A**

Office of Research Integrity  
Research Compliance, MARC 414

Sandy DeJoie

A handwritten signature in black ink, consisting of the letters "EJ" in a stylized, cursive-like font.

March 28, 2022

**"An educational module for improving anesthesia care provider  
knowledge of analgesia in procedures for retinopathy of prematurity: A  
Quality Improvement Project"**

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IRB-22-0115  
111572

03/28/22

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.

or

discontinued.

***Special Conditions:*** N/A

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

EJ



## **APPENDIX B**



### **CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT**

“Improve Knowledge of Analgesia in Procedures for Retinopathy of Prematurity”

#### **SUMMARY INFORMATION**

Things you should know about this study:

- **Purpose:** Educational module to improve knowledge in analgesia modalities in procedures for retinopathy of prematurity.
- **Procedures:** If you choose to participate, you will be asked to complete a pre-test, watch a voice PowerPoint and subsequently a post test
- **Duration:** This will take approximately 20 minutes total.
- **Risks:** The main risk or discomfort from this research is minimal. There will be minimal risks involved with this project, as would be expected in any type of educational intervention, which may have included mild emotional stress or mild physical discomfort from sitting on a chair for an extended period of time, for instance.
- **Benefits:** The main benefit to you from this research is to increase the participant’s knowledge of analgesia for procedural pain in infants undergoing treatment for retinopathy of prematurity.
- **Alternatives:** There are no known alternatives available to you other than not taking part in this study.
- **Participation:** 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. The goal of this project is to improve anesthesia provider knowledge on analgesia in procedures for retinopathy of prematurity.

#### **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:

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 would be expected in any type of educational intervention, which may have included mild emotional stress or mild physical discomfort from sitting on a chair for an extended period of time, for instance.

## **BENEFITS**

The following benefits may be associated with your participation in this project: An increased understanding of analgesia for infants undergoing procedures for retinopathy of prematurity. The overall objective of the program 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 taking part in this project. However, if you would like to receive the educational material given to the participants in this project, it will be provided to you at no cost.

## **CONFIDENTIALITY**

The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, we might publish, 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**

There is no cost or payment to you for receiving the health education and/or for participating 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 at any time 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 at such time that they feel it is in the 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 Sandy DeJoie at 718-781-4687/ [sdejo001@fiu.edu](mailto:sdejo001@fiu.edu) and Dr. Charles Buscemi at 305-348-4870/ [cbuscemi@fiu.edu](mailto:cbuscemi@fiu.edu).

**IRB CONTACT INFORMATION**

If you would like to talk with someone about your rights pertaining to 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](mailto: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 I have about this study, and they have been answered for me. By clicking on the “consent to participate” button below I am providing my informed consent.

**APPENDIX C****Pretest and Posttest Questionnaire:****Analgesia in procedures for retinopathy of prematurity (ROP)****INTRODUCTION**

The primary aim of this QI project is to increase knowledge among anesthesia providers of analgesia in procedures for retinopathy of prematurity in infants to improve patient outcomes in this population.

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 analgesia in procedures for ROP.

**PERSONAL INFORMATION**

1. **Gender:** Male                  Female

2. **Age:** \_\_\_\_\_

3. **Ethnicity:**

Hispanic          Caucasian          African American          Asian

Other \_\_\_\_\_

4. **Position/Title:** \_\_\_\_\_

5. **Level of Education:** Associates                  Bachelors                  Masters

Other \_\_\_\_\_

6. How many years have you been an anesthesia provider?

Over 10          5-10 years          2-5 years          1-2 years

**QUESTIONNAIRE****1. The percentage of premature infants weighing less than 1500g that develop ROP:**

- a. 10%
- b. 20%
- c. 30%
- d. 40%

**2. Irreversible visual impairment due to ROP worldwide may be as high as**

- a. 20,000
- b. 35,000
- c. 45,000
- d. 70,000

**3. Risks of developing ROP is higher in:**

- a. Sicker infants with low birth weights
- b. Infants requiring continuous positive airway pressure (CPAP)
- c. Low apgar scores at five minutes
- d. All of the above

**4. Untreated ROP may lead to:**

- a. Retinal detachment
- b. Development of strabismus
- c. Secondary angle-closure glaucoma
- d. Vitreous hemorrhage
- e. All the above

**5. Consequences of pain in infants include all of the following except:**

- a. Apnea
  - b. Improved visual perceptual ability
  - c. Increased intracranial pressures
  - d. Hemodynamic instability
- 6. Long term consequences of untreated pain in infants include:**
- a. Altered pain processing
  - b. Impaired visual perceptual ability
  - c. Attention deficit disorder
  - d. A and C
  - e. All of the above
- 7. The primary source of procedural pain is related to**
- a. IV insertion
  - b. Eyelid speculum
  - c. Eye drop instillation
  - d. None of the above
- 8. Anesthesia modalities in procedures for retinopathy of prematurity include**
- a. General anesthesia
  - b. Sub-Tenon anesthesia
  - c. Sedation with analgesia
  - d. Topical analgesia
  - e. All of the above
- 9. Sucrose is effective for pain management in procedures for ROP: True or False**

**10. What percentage of infants are intubated to prevent the adverse respiratory effects associated with ROP procedures:**

- a. 50%
- b. 70%
- c. 90%
- d. None of the above

**11. The opioid observed to be a safe analgesic with a rapid onset, penetrates the central nervous system and associated with a decreased pain response is:**

- a. Morphine
- b. Ketamine
- c. Dilaudid
- d. Fentanyl

**12. Which is true regarding a low dose fentanyl infusion for sedation**

- a. Is not well tolerated
- b. Causes frequent life-threatening events
- c. Maintains a stable cardiorespiratory status
- d. Displays unsatisfactory pain scores

**13. What is an effective dose of fentanyl for sedation following a bolus dose?**

- a. 0.5 -1 mcg/kg/hr
- b. 1 -2 mcg/kg/hr
- c. 3-5 mcg/kg/hr
- d. 5-7 mcg/kg/hr

**14. How likely are you to use this analgesic modality to manage pain in infants undergoing procedures for ROP?**

- a. Most likely
- b. Somewhat likely
- c. Somewhat unlikely
- d. Most unlikely

**15. How likely are you to recommend fentanyl sedation as an opioid of choice for ROP treatment?**

- a. Most likely
- b. Somewhat likely
- c. Somewhat unlikely
- d. Most unlikely



## APPENDIX D

**FIU**

### Increasing Knowledge of Analgesia in Procedures for Retinopathy of Prematurity

Sandy DeJoie, MSN, RN

FLORIDA INTERNATIONAL UNIVERSITY

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**FIU**

### Learning Goals

- Describe retinopathy of prematurity (ROP)
- Detail complications of ROP
- Discuss consequences of untreated pain for ROP therapy
- Identify anesthesia modalities
- Explain an effective opioid therapy that maintains hemodynamic stability

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**ROP Background**

- A vasoproliferative disease of developing retinal vessels
- Affects approximately 30% of premature infants weighing less than 1500g
- Risk increases significantly in sicker infants with low birth weights
- May lead to irreversible visual impairment or vision loss in approximately 45,600 infants annually worldwide
- Corrective therapy is painful and requires an effective anesthesia regimen in this vulnerable population

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**Risk factors for ROP**

- Exposure to high oxygen concentrations
- Infants weighing 1250g or less before 31 weeks of gestation at delivery
- Sicker infants with low birth weights
- Infants requiring continuous positive airway pressure (CPAP)
- Low apgar scores at five minutes

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**Scope and consequences of ROP**

- Untreated ROP in premature infants can lead to retinal detachment, development of strabismus, vitreous hemorrhage, myopia, secondary angle-closure glaucoma and vision loss
- Laser treatment is the most effective therapy but is painful with eye speculum use as the primary source of pain
- Pain contributes to instability including increased hemodynamic instability, apnea, increased intracranial pressures, and altered pain processing
- Long term consequences include altered pain processing, impaired visual perceptual ability, and attention deficit disorder

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**Anesthesia modalities for ROP**

- Topical analgesia with tetracaine
- Sub-Tenon anesthesia
- Sedation with analgesia
- General anesthesia

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**Anesthesia management for ROP**

- Opioids used for analgesia
- Maintenance of a stable cardiorespiratory status with fentanyl
- Fentanyl is a safe analgesic with rapid onset and central nervous system that decreases pain
- Fentanyl bolus may precede infusion
- Low dose fentanyl infusion of 1-2mcg/kg/hr is efficacious for pain management

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**Summary**

- Procedures for ROP are painful and cause hemodynamic instability in infants
- Various anesthetic support exist for ROP procedures
- Anesthetic management with the lowest risk of perioperative adverse events should be used
- Low dose fentanyl is efficacious for analgesia in infants undergoing procedures for ROP
- Ideal dosing for fentanyl according to evidence-based research

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