Perioperative Care of Children Undergoing Intra-arterial Chemotherapy for Retinoblastoma

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Retinoblastoma (RB) is a rare cancer of the eye, most commonly seen in children. Intra-arterial chemotherapy for RB is a relatively new treatment modality that has gained increasing popularity worldwide. The principal underlying the intra-arterial approach is delivery of chemotherapeutic agents directly to the site of the tumor. This avoids systemic toxicities normally associated with higher dose of these drugs. The purpose of this continuing education article was to review the features of RB and its treatment, with a focus on the perioperative management of children undergoing intra-arterial chemotherapy at our institution. Intra-arterial chemotherapy for RB is an outpatient procedure and is well tolerated. Adverse events, most often bronchospasm, occur most often during the procedure itself and tend to be easily managed. We focus on the role of peri-anesthesia nursing in the care of the pediatric RB patient, before, during, and after intra-arterial chemotherapy.

Keywords: retinoblastoma, intra-arterial chemotherapy, postanesthesia, PACU.

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OBJECTIVES—1. Discuss the signs and symptoms of retinoblastoma. 2. Describe how a tertiary care institution manages the perioperative care of a patient undergoing intra-arterial chemotherapy.
appearing in the pupil on direct illumination, such as when pictures are taken with a flash. Other signs and symptoms include eyes appearing misaligned (exotropia or esotropia), poor vision, discoloration of iris, and the presence of swelling and redness.

In other locations in the body, cancer is often diagnosed with a biopsy. However, in the case of suspected RB, the biopsy is risky because taking a specimen from the eye can potentially spread the cancer cells to outer parts of the eye and distant sites as well. Therefore, RB is diagnosed by an experienced ophthalmologist who conducts an eye examination under anesthesia using specialized lights and tools. If the examination raises suspicion for cancer cells, the patient undergoes imaging, including x-rays, ultrasound, magnetic resonance imaging, or radioactive tracer imaging.

The location and size of the tumor will impact the plan of care and outcome. If the initial examination suggests that the patient has RB, the physician will then explore the extent of the disease and grade it, and will plan treatment accordingly. Treatment selection is based on stage, location, and size. RB stage is determined according to the International Retinoblastoma Classification. Treatment for RB may involve laser therapy, cryotherapy, intravenous (IV) chemotherapy, and plaque radiation. For larger tumors, surgical removal of the eye or enucleation may be required.

Intra-arterial chemotherapy has gained traction in the recent years as an option, particularly for advanced stage RB (International Retinoblastoma Classification stages D and E) and recurrent RB after IV chemotherapy. Recently, it was suggested that chemotherapy could be used as primary treatment in grades B and C as well. The use of intra-arterial chemotherapy for RB initially began in the 1950s but has now gained rapid widespread recognition in the treatment of RB. Its success is based on the ability for the chemotherapy to reach the retina. During the procedure, an arterial sheath catheter is placed in the femoral artery and is guided to the ipsilateral internal carotid artery under fluoroscopic guidance. Recently the technique was changed by eliminating the guide catheter and using only a microcatheter going from the femoral artery all the way to the ostium of the ophthalmic artery.

Chemotherapy is then introduced directly into the ophthalmic artery to reduce tumor size while minimizing systemic toxicity. Intra-arterial administration of melphalan, a cytotoxic nitrogen mustard derivative alkylating agent that inhibits both DNA and RNA synthesis, and topotecan, a topoisomerase inhibitor that prevents rapidly dividing cells from repairing DNA damage, improves salvage of eyes in advanced stages of the disease.

Literature is limited regarding the nursing care of pediatric patients undergoing intra-arterial chemotherapy for the treatment of RB. The purpose of this article is to highlight the preoperative assessment, intraoperative management procedures, postoperative care, and education of patients and caregivers undergoing intra-arterial chemotherapy. The discussion subsequently will entail protocols that are specific to our institution, but likely generalizable to other facilities interested in performing this procedure. To our knowledge, this is the first article in the nursing literature to describe the perioperative care of pediatric patients receiving intra-arterial chemotherapy.

**Challenges of a Pediatric Patient**

There are several challenges in the care of the pediatric patients. Perhaps the most important and most difficult challenge is the assessment of pain. Very young children do not know how to express themselves verbally or may struggle to express themselves well verbally. Instead, they may cry, become frustrated, or otherwise be unable to express how they are feeling. At our institution we use the Wong-Baker Faces Pain Rating Scale or the Face, Legs, Activity, Cry, Consolability Scale depending on the patient's age and developmental stage. To address child anxiety and discern when interventions should occur, a tailored approach that involves both the child and the parents is needed. Communication and education should vary depending on a patient's knowledge base and developmental stage. Because the hospital encounter may be frightening to the child and parent, it is recommended that staff prepare patients and parents for the entire surgical process. This may include age-appropriate therapeutic games and toys related to the perioperative experience.
Preoperative Preparations

Intra-arterial chemotherapy is an outpatient procedure, performed in an interventional neuroradiology (INR) suite. Therefore, standard guidelines for outpatient surgery in children are applicable. According to the American Society of Anesthesiologists, formula and solids must be avoided 6 hours or more before undergoing anesthesia to prevent aspiration. Infants or neonates may ingest breast milk up to 4 hours before receiving anesthesia. Ingestion of clear liquids, such as water, Pedialyte, clear apple juice, and clear white grape juice, is permitted, but should be avoided at least 2 hours before arrival for surgery.

If the patient is suffering from any symptoms of illness (fever, cough, runny nose, vomiting, or diarrhea) in the days leading up to the procedure, the anesthesia team must address these symptoms because they may increase the risk of respiratory complications postoperatively, such as laryngospasm. Nonsteroidal anti-inflammatory agents, such as ibuprofen and naproxen, should not be given for at least 3 days before surgery. In our institution, acetaminophen is allowed until the day before surgery.

The preoperative nurse should take a detailed health history on the day of surgery. This includes medications, allergies, nothing by mouth status, and whether the child is breast-fed or bottle-fed, if applicable. Initial vital signs are taken. Chemotherapy drugs are ordered at this time, typically melphalan and topotecan. Any medical problems identified at this time are brought to the attention of the attending physician. Because of the young developmental age of the patients, they are given priority on the operating room schedule.

Intraoperative Management

Patients are commonly premedicated with 0.5 mg/kg of oral midazolam in the preprocedure area to provide for amnesia, calmer separation from their parents, and transition to the interventional suite. For those who refuse premedication when indicated, or are contraindicated, parents are offered the opportunity to be present for the induction of general anesthesia. The child is then removed from parents and taken to the INR suite. IV lines are placed while the child is asleep. At our institution, children admitted for intra-arterial chemotherapy for RB are administered general anesthesia throughout the procedure, and sedation for the postoperative period. General anesthesia is required because any movement by the patient could compromise the success of the procedure. Paralysis is especially important during the catheterization of the ophthalmic artery and during the injection of chemotherapeutic agents.

Once arriving to the interventional suite, general anesthesia is induced via mask-inhalation with oxygen and 6% sevoflurane. After the patient is asleep, a peripheral IV is placed and the patient is administered 1 to 3 mg/kg of propofol, 0.1 mg/kg of rocuronium, and 0.5 mg/kg of dexamethasone. The patient is then intubated with a cuffed endotracheal tube. An additional IV is established after intubation. General anesthesia is maintained for the procedure with 1 to 1.3 minimum alveolar concentration of sevoflurane (1.8% to 2.4% Et). Fentanyl 1 to 2 mcg/kg is administered as needed during the procedure, and heparin 60 U/kg and protamine as indicated by the activated clotting times at the conclusion of the procedure.

An arterial sheath catheter is placed in the femoral artery, and then a microcatheter is introduced in the sheath, all the way up to the internal carotid artery and then the ostium of the ophthalmic artery. Chemotherapy is then introduced directly into the ophthalmic artery.

After the injection is complete and during the period of manual groin pressure after the sheath is removed, a dexmedetomidine bolus and subsequent infusion is started. The 2 mcg/kg bolus of dexmedetomidine is administered over 20 minutes, followed by infusion at 1 to 2 mcg/kg/h. This continues until postanesthesia care unit (PACU) admission, approximately 6 hours, while the patient is on flat bed rest. During this time, the reversal agent neostigmine 0.05 mg/kg is administered to the patient, as well as glycopyrrolate 0.01 mg/kg to dry secretions, and ondansetron 0.1 to 0.15 mg/kg as an antiemetic. After spontaneous breathing is verified, the patient is extubated while deeply sedated to minimize moving or coughing. The purpose of this is to avoid any complications at the groin site. The patient is then transferred to the PACU.
Among the most important anesthetic considerations during the procedure are cardiopulmonary events. These typically occur soon after the ophthalmic artery is catheterized. One study reported all adverse events occurring within 2 minutes of catheterization. Kato et al reported that a severe event occurred in 29% of their cases. The most common manifestation was a decrease in lung compliance, which can lead to decreased tidal volumes and increased inspiratory pressures, and if left untreated, to hypoxia. Commonly referred to as bronchospasm, this is typically treated with 2 to 4 mcg of epinephrine. It typically resolves with one dose of epinephrine; however, additional doses may be administered as needed. Hypotension and bradycardia have also been reported.

Postoperative Care

After the procedure, the intra-arterial catheter and sheath are removed and manual site compression is maintained. The INR suite notifies the PACU charge nurse that pressure is being held on the groin insertion site. This typically requires 20 to 30 minutes. The PACU nurse verifies that there is a Broselow cart (a cart with color coded drawers) or similar pediatric resuscitation cart near the bedside, with appropriately sized blood pressure cuffs and bag-mask valves. The patient is escorted out of the INR suite with the anesthesia provider and INR nurse on a portable monitor and oxygen mask. The patient is connected to a monitor, pulse oximeter at the big toe on the ipsilateral side of the sheath, cardiac monitor, and blood pressure cuff, as per hospital policy. Physiological monitoring is continuous and documented every 15 minutes.

Dexmedetomidine is infused for sedation at 1 to 2 mcg/kg/h. The postoperative patient is required to lie with the head of the bed flat for 6 hours during monitoring. The nurses have standing orders to titrate 0.2 mcg/kg/h fentanyl if child awakens. Traditionally a temporary immobilization board such as a papoose board was also used but because of recent changes to interarterial chemotherapy technique and the use of a smaller caliber sheath, these have fallen out of favor. Patient assessment includes the assessing inguinal dressing, observing and reporting hematoma, and checking bilateral pulses. Patients typically stay for 7 to 8 hours before they are discharged, as they must remain in flat bed rest for complete 6 hours.

Standard discharge instructions are provided. Beyond the basic instructions, such as nausea, pain relief, fevers, and activity orders, specific instructions regarding the inguinal dressing must be reinforced before discharge. This includes keeping the groin site clean and dry, thus no swimming or bathing is allowed for 3 days postoperatively. Sudden bleeding or swelling should prompt an immediate emergency room visit. Given that the leg may be relatively immobilized from pain, families are also instructed to give the child a half tablet of 81 mg aspirin tablet. We do not routinely use eye patches as the eyesight itself is unaffected. Finally, because chemotherapy rarely can be absorbed systemically, follow-up laboratory results are crucial to postoperative care.

Discussion

RB can be a devastating life-threatening disease. Overall, this malignancy carries a high fatality rate, with projected patient death in approximately 42% of cases worldwide. Mortality varies by region. In North America, Europe, and other developed nations, the outcomes with RB are more promising, with only 3% to 5% mortality. In less-developed parts of Africa, mortality can reach up to 70% or greater. The main focus of RB management in developed nations remains protection of life, but additional goals of globe salvage and protection of vision are considered. Current therapy involves chemotherapy, radiotherapy, cryotherapy, and laser photocoagulation. To avoid system side effects, localized intraarterial chemotherapy has shown significant benefit.

Intra-arterial chemotherapy for the treatment of RB is typically a quick procedure (less than 3 hours) and relatively low-risk with effective results. In a recent study published at our institution with a mean follow-up of 19 months, globe salvage was achieved in 72% of cases. Moreover, complete regression was achieved for solid tumor in 48 of 51 eyes (94%). The procedure is generally well tolerated, with most adverse events occurring during intra-arterial infusion of chemotherapeutic drugs.

Treatment complications can manifest as a mechanical effect, such as periocular edema and erythema. Edema is seen in 40% of patients and
this may indirectly affect the child’s vision, typically for no more than 3 days. Likewise, chemotherapy infusion can lead to toxic effects on the vascular endothelium. These complications are generally successfully managed in the operating room.

Patients typically require repeat treatments. If the patient has both eyes affected with RB, each eye is treated separately. The procedure for bilateral disease would alternate monthly for each eye. Performing the procedure simultaneously can be risky as if there are thromboembolic events, this may cause bilateral brain injury leading to devastating results. The time period between treatments for the same eye is 3 to 4 weeks.

Conclusions

The treatment of RB has significantly advanced. Specifically, intra-arterial chemotherapy to localized tumor has provided significant benefits to patients. This review of the current perioperative care in the pediatric population was designed to provide insight into the practice at our institution and to encourage dialogue and future research.

References

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1.25 Contact Hours

Purpose of the Journal of PeriAnesthesia Nursing: To facilitate communication about and deliver education specific to the body of knowledge unique to the practice of perianesthesia nursing.

Outcome of this CNE Activity: To enable the nurse to increase knowledge on care of the patient with intra-arterial chemotherapy for retinoblastoma.

Target Audience: All perianesthesia nurses.

Article Objectives

1. Discuss the signs and symptoms of retinoblastoma.
2. Describe how a tertiary care institution manages the perioperative care of a patient undergoing intra-arterial chemotherapy.

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