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Radiation therapy for children: periprocedural anaesthetic concerns

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Introduction

Radiation therapy has proved to be an important armamentarium for cancer management in children. It remains a multimodal cancer therapy along with surgery and chemotherapy. Radiation therapy is used not only for curative intent but also for palliative management for symptom control. This procedure although painless and of short duration, they pose a considerable challenge for an anesthesiologist. They should work outside their comfort zone of "operating room" with limited means and supply of equipments and drugs. The procedure also requires a motionless child for the delivery of the radiation at the exact site intended and thus to avoid unnecessary radiation exposure. Radiotherapy is used to treat several pediatric malignancies like primary central nervous system (CNS) tumors (28%), retinoblastoma (26%), neuroblastoma (18%), acute leukemia (9%), wilm's tumor (5%), rhabdomyosarcoma (7%); Langerhans cell histiocytosis (4%) and others (3%).[1] In adults, administration of radiotherapy is comparatively easier as they can cooperate well and generally do not require anesthesia unless the patient is mentally unstable, has movement disorders or claustrophobic. The radiation therapy in children have peculiar concerns and is being discussed in this narrative review.

Procedure of external beam radiotherapy

Concerns during Simulation: When the radiation treatment is being planned, the child undergoes a treatment planning session know as simulation. Simulation allows the radiation oncologist to decide the plan of treatment by identification and marking the location of anatomical sites which will be included in the radiation field.[2] The patient's expected position during the actual procedure is determined during simulation which remains major anaesthetic concern in view of anaesthetic management. It becomes more of concern in child with tumors of cranio-spinal axis like medulloblastoma.[2] The plaster immobilization casts for the head and body are made during simulation session and they should be of appropriate size for the delivery of radiation to exact body part and prevent the normal surrounding tissues from radiations.[2] The formation of cast is essential as ill-fitting or tight cast may lead to airway compromise. The child should be motionless for the simulation process. The radiation oncologist will also determine if the patient needs blocks which are radio opaque shields that protect the radiosensitive organs from the ionizing radiations.[2] The simulation phase allows the anaesthesiologists to stay with the patient since the therapeutic dose of radiation is not administered. However, still protective devices are suggested. It can be conducted under general anaesthesia/monitored anaesthesia care (GA/MAC) depending upon the underlying disease site and extent of the tumor. If the patient has any risk of airway compromise, then it would be safe to safe to get the session done with a secured airway. There is radiation therapy planning procedure, which usually precedes the planned treatment. This simulation process is usually of longer duration than the proposed radiation therapy treatment so at times GA may be preferable to sedation. Radiation therapy for tumors like retinoblastoma usually requires a quite eye with muscle relaxation and for posterior fossa tumors prone positioning is preferable for the development of immobilization casts, so GA is suitable.

Concerns during external beam radiation therapy: During the pre-anaesthetic checkup, the child should be thoroughly assessed; age and birth history of the child should be documented. The patient should be evaluated for any associated congenital disorders, effect of the tumor or due to the treatment modalities like surgery or chemotherapy. There are reports of Wilm's tumor with tetralogy of fallot with patent foramen ovale, aortic stenosis and patent ductus arteriosus.[3] Any recent history of upper respiratory, lower respiratory tract, bronchial asthma, seizures, previous episodes of any allergies to medicine, snoring/upper airway obstruction and feeding difficulties should be ruled out.[2] Tumor involving the brainstem or prior craniotomies can affect the lower cranial nerves and swallowing reflex putting the child at considerable risk for regurgitation and aspiration. Review of any previous procedures or surgeries and anaesthesia with complications should be noted. Since these patients undergo continuous repeated treatment, any history of airway compromise during previous procedure should be documented. Physical examination should focus on general examination – weight and airway examination for any tonsillar hypertrophy, mandibular hypoplasia or craniofacial abnormality. Children with supratentorial tumors may have features of increased intracranial pressure like feeding difficulties, irritability, sunset sign and bulging fontanelle; ketamine should be avoided in such patients. Patients with wilm's tumor may present with a large abdominal mass that may impair respiration. Children with hodgkin's and non-hodgkin's lymphoma may have large anterior mediastinal masses, which can compromise the respiration and might cause superior vene cava compression, decreasing the venous return. Any breathing difficulty in supine position should be elicited. Preoperative investigations include chest X-ray, computed tomographic scan and flow volume loops in sitting and supine position. These child may have airway collapse and hypotension with cardiorespiratory arrest on sedation. They should be preferably counseled for monitored anesthesia care if feasible. Cardiovascular system should be examined thoroughly as the patients receiving anthracyclines (used to treat hematological malignancies) may present with acute/chronic toxicity. The acute toxicity may present as rhythm and conduction disturbances. Bleomycin therapy for testicular tumors and lymphomas can cause pulmonary toxicity in the form of new onset cough, respiratory difficulty, and respiratory failure. The radiation suite, bulky equipment and the procedure may incite considerable anxiety in the pediatric patient. The older children may be cooperative and allow the procedure by counselling and under monitored anaesthesia care. The younger age group (2-5 years) may not readily accept the strange surroundings and separation from the caregivers. Fasting should be as per standard American Society of Anaesthesiologists (ASA) guidelines, 2 hours for clear liquids, 4 hours breast milk and 6 hours for formula feed and light meal.[4] Written informed consent should be taken explaining about the procedure, anaesthesia/deep sedation and need for placement of advanced airway if needed.4 The use of supraglottic airways devices is increasing as we can avoid the complications related to endotracheal intubation.

Sedation and anaesthesia for the paediatric patients for simulation process and radiation therapy

Sedation in child is to control the behavior for the completion of the procedure which depends on child's chronological age. There should be supply of all necessary equipment and lifesaving drugs as needed. This can be remembered by the pneumonic "SOAPME": **S**uction (yankauer), **o**xygen, **a**irway (nasopharyngeal and orophyrangeal), laryngoscopes (checked and functional), endotracheal tubes, supraglottic airway devices, face mask and resuscitation bag. **P**harmacy – life saving drugs and antagonists of all sedative medication being used. M- monitors and special equipment (defibrillators).4 Monitoring always remains an issue as the anesthesiologist is away from the patient during the procedure, has to rely on slave monitors placed in the radiation suite. Though, there are no defined guidelines for monitoring during radiation therapy. The American Academy of Pediatrics and American Academy of Pediatric Dentistry in collaboration have set up guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. These guidelines can be extrapolated for monitoring and management of patients in the radiotherapy suite. The monitors include electrocardiogram (ECG), pulse oximeter (SpO_2), non-invasive blood pressure (NIBP), and capnography (end tidal carbon dioxide, $EtCO_2$).[4] Capnography is especially recommended for procedures carried out in dim light.[4] There are usually two monitors in the radiology suite.[5] One is focused on the patient while the other one is focused on the monitor connected to the anesthesia machine. A slave monitor is also attached to monitor vitals outside the radiology suite.[5] A microphone is connected to the loudspeaker of the monitor, so that the pulse oximetry and ECG sounds are heard distinctly.[5] Vitals signs should be recoded after every 5 mins in a time-based record. The process can be interrupted if the anesthesiologist is required to go inside the suite in case need arises. The circuit and the monitoring equipment's should have extension lines so that they can have a desired length and not get entangled during the movement of the operating table. They should be well protected from getting twisted when the operating table's motion occurs.

Since this procedure is painless, only sedation is needed. Various anaesthetic agents are available nowadays for paediatric sedation. The greatest difficulty encountered while starting an intravenous line. Children usually cooperate well in parent's presence. EMLA cream is a good option if time permits and can be applied one hour prior to the expected time for start. There are studies stating the use of intranasal dexmedetomidine, midazolam, and ketamine for preprocedural sedation, before intravenous cannulation is attempted.[6–9] Usually an intravenous line is started on the first day and maintained till the next five days since radiations is delivered in 30 fractions for the subsequent six weeks. Patients who are on ongoing chemotherapy might be having a central venous catheter in situ. Aseptic precautions should be taken during any invasive procedure, as they can be immunocompromised.

Anesthesia for simulation process

The simulation process is of usually longer duration than the radiotherapy treatment. General anesthesia with inhalational anesthetic agents or total intravenous anesthesia and supraglottic airway device is a reasonable option. Endotracheal intubation should be considered if the child is positioned prone or have risk of aspiration.

Sedation - anesthesia for the radiation therapy procedure

The radiation therapy procedure takes place between 5-10 minutes depending upon the number of sites to be irradiated, so sedation is preferred. Indications for general anesthesia stand as discussed for the simulation process. The various drugs are used doe sedation during the radiation therapy (Table 1). Benzodiazepines are hypnotic/sedative, which act via stimulation of gamma-aminobutyric acid (*GABA) (*A) receptor. They have dose dependent cardiorespiratory depression. Midazolam is the most commonly used drug for pediatric sedation. It is used intranasally, oral formulation and intravenously. After an intravenous bolus dose of 0.05-0.1mg/kg, onset of action is 30- 60 sec and peaks around 3-5 mins lasting 20-80 mins and infusion dose of 0.5- 1 mcg/kg/min. It is highly albumin protein so doses have to be reduced accordingly if needed and is metabolized to inactive metabolites.[10]

Propofol is a short acting agent used for induction and maintenance of anaesthesia. Because of it's favorable pharmacokinetic profile, it is suitable for these short procedures.[11] It acts by stimulation of GABA(A) receptors activating chloride channels inhibiting synaptic transmission. It's onset of action is 30-60 sec and duration of action is 5-10 mins due to redistribution.[12] Propofol decreases cardiac output and blunts the compensatory response by causing bradycardia. It is given in a bolus dose of 1.5-2mg/kg after which it can causes apnea in 20-30% cases. Ketamine is a phenycyclidine derivative, which acts on N-methyl-D-aspartate receptor (NMDA) receptors producing dissociative anaesthesia. The i.v dose is 0.5-1.5mg/kg with onset of action 30- 60 seconds and duration of action as 10-20 minutes. However, it can cause increase secretions, agitation and avoided in patients with seizure disorder and increased intracranial pressure. However, it is advantageous in some patients as it causes bronchodilatation and preserves the pharyngeal and laryngeal reflexes.10 Alpha – 2 agonists like dexmedetomidine is being increasingly used for pediatric sedation. This drug acts via alpha – 2 receptors located in periphery, brain (locus coeruleus) and spinal cord. This action on alpha – 2 receptors produces sedation and antinociception. The drug is administered as a loading dose of 1µg/kg over ten mins followed by infusion dose of 0.2-0.7µg/kg/hour titrated to effect.[12,13] Opioids can be used but they are best kept for painful procedures and seldom used because of their respiratory depressant effect.

Post procedure

The vitals of the patient, drug dosages, any complication and measures taken must be documented. The patients should be shifted

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to recovery area post procedure and monitored in propped up position with ECG and pulse oximetry. Supplemental oxygen should be provided as needed. All emergency drugs, airway equipment's, ambu with rebreathing bag with appropriate mask size and suction should be available in recovery room as well. Vital signs should be recorded at specific intervals (10-15 mins). The patients can be discharged once they are conscious and maintain patent airway and fulfils the discharge criteria. They should be able to sit up without support (if age appropriate) and maintain protective reflexes.

Table 1 Dosages of different drugs used for sedation during radiotherapy

Drug	Bolus dose	Infusion dose
Midazolam	0.05 - 0.1 mg/kg	0.025 - 0.5 mg/kg
Propofol	1.5 -2 mg/kg	100 - 200 mcg/kg/min
Ketamine	0 .5 - 1 mg/kg	-
Dexmedetomidine	1 mcg/kg over 10 mins	0.2 - 0.7 mcg/kg/hour

Conclusion

Radiation therapy though a short procedure, takes a toll on the paediatric anaesthesiologists because of entirely unfamiliar environment. The biggest concern is the distance maintained from the patient during the most crucial periods. Therefore, proper vigilance and communication is required among anesthesiologist, radiation oncologists and the technical personnel to prevent any avoidable errors and provide safe procedure sedation.

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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