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Recurrent anesthesia applications in pediatric radiotherapy: a retrospective observational study

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ABSTRACT

Aims: Pediatric radiotherapy is used for various indications in childhood malignancies. This descriptive study aims to describe the demographic data, anesthesia method and complications of pediatric radiotherapy patients.

Methods: This study was conducted retrospectively and observationally in a tertiary care center. Patients aged 18 years and younger who received anesthesia for radiotherapy were included. Data were obtained from the hospital information system and anesthesia observation forms. Demographic data, radiotherapy indication, fraction number and dose, anesthesia method, anesthetic drug and dose, patient position, complications and recovery time were analyzed.

Results: 485 patients received radiotherapy and anesthesia was administered to 19 of these patients (3.91%). 3 patients were excluded due to missing data, and 16 patients received anesthesia 417 times. Patients were between the ages of 1-17 years, mean age was 4.9 years. Sedation was used in 92.3% of the procedures and general anesthesia in 7.7%. The most common indication for radiotherapy was glial tumor. The number of radiotherapy fractions ranged between 8-33 sessions, the median number of sessions was 30 and the mean number of sessions was 24.8. Treatment doses were 150-200 Gray. Complication rate was 2.87%. A statistically significant difference was found when the doses of propofol, fentanyl, midazolam used in the first and last fractions and recovery times of the patients were compared ($p<0.01$).

Conclusion: Anesthetic management in pediatric radiotherapy requires multidisciplinary treatment due to the unique requirements of the procedure. Patients should be thoroughly re-evaluated at each session and protected from the potential for addiction.

Keywords: Pediatrics, radiotherapy, radiation oncology, anesthesia, pediatric oncology

INTRODUCTION

Malignancies in childhood are not as common as they are in adulthood, accounting for fewer than 1% of all new pediatric cancer cases.[1] The most common childhood malignancies are acute lymphoblastic leukemia (ALL) (26%), central nervous system tumors (21%), and neuroblastoma (7%).[2] Childhood malignancies require multidisciplinary treatment management, whereby treatment success rates increase accordingly.[3] Radiotherapy (RT) was first applied under general anesthesia by Harrison and Bennet in 1963 and continues to be applied for palliative and therapeutic purposes.[4]

The aim of RT treatment is to protect normal tissues and to deliver an appropriate and effective dose to target cancerous tissue. Although RT is a painless procedure, immobilization is required during treatment.[5] Repeated general anesthesia and sedation applications are required for immobilization, particularly in young children who are unable to cooperate and stand still.[5] Anesthesia applications are required in almost all patients aged 0-3 years and the need for anesthesia during RT increases inversely proportional to age.[6]

Although there is no surgical procedure, such as a large incision or blood loss, in RT treatment, it is uncomfortable for most anesthesiologists due to the necessary special physical conditions.[7] These include the physical distance from the patient during RT, lack of access to the patient during treatment, difficulty in airway access due to a thermoplastic mask, lack of support in emergencies, complex patient positions, and the high number of RT fractions.[7]

In this retrospective study, we aimed to present and discuss 417 recurrent anesthesia experiences due to RT of 16 pediatric patients aged 1-17 years. Our primary objective was to describe the demographic characteristics of the patients in our center and the secondary objective was to report anesthesia-related complications and anesthesia techniques.

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METHODS

This study was conducted retrospectively and observationally in a tertiary-level training and research hospital. Our study was approved by the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 10.07.2024, Decision No: AEŞH-BADEK-2024-580). The study was conducted in accordance with the Declaration of Helsinki. Inclusion criteria were patients aged 18 years and younger who had received anesthesia for RT treatment in our center between October 1, 2022 and June 1, 2024. Patients who had not completed RT treatment, turned 19 years of age during treatment, or had missing data were excluded from the study. Data of the patients were obtained from the hospital information system and anesthesia observation forms. Demographic data, RT indication, RT fraction number and dose, anesthesia method used, anesthetic drug and dose, patient position, complications, and recovery time were analyzed.

Medical records are susceptible to bias and human error, including missing or inaccurate data, particularly concerning the perioperative period and patient or parent perceptions of disease severity. In this study, discrepancies in information and interventions may arise due to underreporting by patients or parents during the pre- and post-anesthetic periods for both inpatient and outpatient cases. Additionally, certain subjective and objective complications may have been underreported among outpatient patients.

Statistical Analysis

For statistical analysis of the research data, Statistical Package for Social Sciences (SPSS), version 22.0 for Windows (SPSS Inc. Chicago, USA) computer package program was used. In the descriptive statistics section, categorical variables were presented as numbers and percentages, and continuous variables were presented as mean±standard deviation or median (minimum-maximum value). Compliance with normal distribution of continuous variables was assessed using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). In the study, paired T test was preferred to compare the anesthesia drug doses and recovery time in the first and last cycles for each patient. Due to the small sample size, nonparametric tests (e.g., Wilcoxon signed-rank test) were evaluated as alternatives. However, since normality tests gave appropriate results, paired T test was preferred. It was examined whether the data were affected by extreme values and outliers that should be excluded from the analysis were determined. In this study, the statistical significance level was accepted as $p<0.05$.

RESULTS

Between October 1, 2022 and June 1, 2024, a total of 485 patients aged 18 years and younger received RT treatment, with 3.91% of these patients (19 patients) undergoing anesthesia. Data of 19 patients were analyzed; three patients were excluded due to missing data and the study was conducted on 16 patients (Figure). The patients included in the study were aged between 1-17 years, with a median age of four years and a mean age of 4.9 years. A total of 62.5% of the patients were female and 37.5% were male. There were no patients with American Society of Anesthesia (ASA) physical status scores of 1 and 4. Of the patients, 19% were classified as ASA2 and 81% as ASA3. There was a preoperative fasting period of 4-8 hours (Table 1).

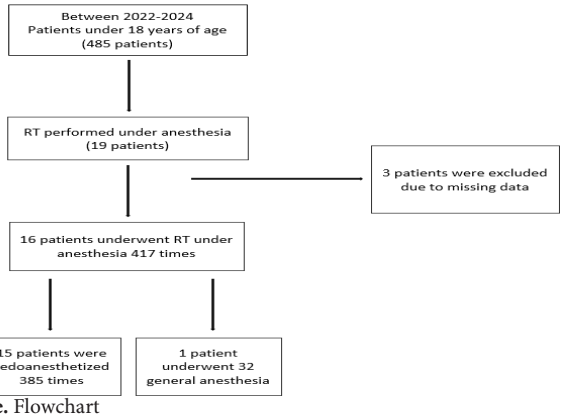

Figure. Flowchart

Table 1. Demographic data of the patients and indications for radiotherapy

	n=16
Age	
Median	4
Mean	4.9
Range	1-17
Gender	
Female	10 (62.5)
Male	6 (37.5)
Weight (kg)	
Median	15.75
Range	10-58
Height (mt)	
Median	0.98
Range	0.71-1.68
ASA score	
1	0
2	3 (19)
3	13 (81)
4	0
Disease	
Brain tumor	8
Chemoterapy	8
VP shunt	1
Nephrectomy	2
Bone marrow transplantation	2
Epilepsy	5
Hypothyroidism	1
Tracheostomy	1
Puberty precocious	1
Fasting period	
4 h	1
6 h	14
8 h	1
RT indication	
Glial tumor	8 (50)
Ependymoma	3 (18 8)
Neuroblastoma	2 (12.5)
Rhabdomyosarcoma	1 (6.3)
Wilms tumor	2 (12.5)

kg: Kilogram, mt: Meter, h: Hours, RT: Radiotherapy

Anesthesia was administered a total of 417 times on 16 patients who needed it during RT. Of the anesthesia applications, 385 (92.3%) were sedation and 32 (7.7%) were general anesthesia. Only one patient-who had a tracheostomy-received general anesthesia. Sevoflurane and midazolam were used for general anesthesia. Propofol, midazolam, ketamine, and fentanyl were the other anesthetic agents used. Ketamine was used in only one patient. Sixteen patients received anesthesia for CT simulation a total of 20 times (Table 2).

Table 2. Anesthesia management and radiotherapy data of the patients

	n=417
Sedation	385 (92.3)
General anesthesia	32 (7.7)
RT fraction time	
Median	30
Range	8-33
RT dose (Gy)	
Median	180
Range	150-200

RT: Radiotherapy

All patients received RT in the supine position and no patients in the prone position. The indications were Glial tumor in 50%, Ependymoma in 18.8%, Neuroblastoma in 12.5%, Wilms tumor in 12.5%, and Rhabdomyosarcoma in 6.3% (Table 1). The most common treatment site was the cranium (69%). The number of RT fractions of the patients ranged between 8-33 sessions; the median number of sessions was 30 and the mean number of sessions was 24.8. Treatment doses were in the range of 150-200 gray (Table 2).

Complications occurred in 12 of the 417 anesthesia procedures with a complication rate of 2.87%. The complications encountered were as follows: mobilization (four times), desaturation (three times), bradycardia (three times), hypo-hypertension (once) and nausea-vomiting (once) (Table 3). Complications were detected with a camera in the RT room. Interventions were made on patients who developed complications and no patient required cardiopulmonary resuscitation. Desaturated patients were treated with mask ventilation and the treatment was completed without any problems. An intervention was made on one patient who became mobile and was about to fall off the treatment table.

Table 3. Complication rates and types of complications encountered in radiotherapy sessions

	First cure	Last cure	p
Propofol (mg/kg)	1.8±0.48	3.2±0.52	<0.001
Fentanyl (mg/kg)	0	0.75±0.62	<0.001
Midozolam (mg/kg)	0.06±0.025	0.09±0.028	<0.001
Recovery time*	19.6±3.68	36.9±7.84	<0.001

*Paired T test, mg: Miligram, kg: Kilogram

Vascular access was provided with port catheters in two patients, central venous catheters in four patients, and peripheral venous cannulas in 10 patients. There were no complications related to central venous access. Peripheral venous cannulas were changed every five days. When the doses of propofol, fentanyl, and midazolam used in the first and last RT fraction anesthesia applications and recovery times of the patients were compared, a statistically significant difference was found (p<0.01) (Table 4).

Table 4. Comparison of the amount of anesthetic drugs used and recovery times in the first and last RT sessions of the patients

	n=417
Number of complications	12 (2.87)
Type of complication	
Mobility	4
Desaturation	3
Bradycardia	3
Hypo/hypertension	1
Nausea-vomiting	1

Recovery time is the time when the modified aldrate score is 9 and above, RT: Radiotherapy

DISCUSSION

The frequency of non-operating room anesthesia (NORA) applications is gradually increasing with the developing technology. One of the NORA applications is RT, which is a multi-purpose treatment method in various malignant diseases. It allows for the treatment of damaged tissues with high and homogeneous doses of ionizing radiation while preserving normal tissues. Immobilization is very important for RT treatment to be effective and successful, and to avoid negative consequences. Anesthesia is used for immobilization in the pediatric population who cannot cooperate, cannot understand the procedure, have bad experiences in their medical history, and feel anxiety and discomfort.[8] In our study, we presented the experience of anesthesia 417 times for RT treatment in 16 pediatric patients who met these criteria.

The need for anesthesia increases inversely proportional to age in RT.[9] In the literature, the incidence of anesthesia for RT in the pediatric population varies and different incidences-such as 11.8%, 12.8%, 25.7% and 45% have been reported.[10-13] We think that this difference in incidences is due to the treatment modalities of the centers, differences in the population, and behavioral modified therapies adopted over the years. In our center, the incidence of anesthesia for pediatric RT is 3.91%. In the literature, the need for anesthesia for RT has been reported in 100% of children younger than three years of age and 10% of children older than 12 years of age.[14] According to the results of our study, 85.5% of the anesthetized children were younger than eight years of age and the mean age was 4.9 years. Only one patient was 17 years old. In a study conducted by Lydia et al.[10] in 2021, no patient aged 16 years or older was reported. Similarly, only one patient in our study was older than 12 years of age. Despite the patient's age, when the need for anesthesia was questioned, it was observed that the patient had undergone poor medical experiences. Studies have also shown that the need for anesthesia decreases with various behavioral modified therapies, especially in children aged 3-12 years and older than 12 years.[15] In line with the literature, there is a playground in the RT unit in our center to reduce the children's anxiety. Parental anxiety should not be neglected, since children may also be affected by their parents' emotions during RT sessions, which is a long and tiring treatment program.[11] Parents and children should participate in modified therapy programs together.[11,16] For this reason, both children and parents are routinely informed

in detail about the process in our clinic. All questions of both children and parents are answered. We think that the lower incidence rate in our center compared to the rates reported in the literature is due to the modified behavioral therapies we apply and the active participation in the therapies of both children and parents.

Anesthetic management is a challenging process due to the anatomical and physiological variations of children, as well as the physical conditions and unique features of RT treatment. The "thermoplastic mask" used particularly in head and neck malignancies limits airway access. In RT, late recognition of potential complications may be caused by the lack of possibility of instant intervention, physical barriers with the patient, complexity of the positions, and the fact that patient follow up can only be performed with a camera.[3] Considering both the difficulty of physical conditions and the effects of RT treatment, patients should be evaluated and followed up in detail at each session to prevent complications.[6] We routinely subject our patients to a complete physical examination and evaluate them in detail in the preoperative period before each anesthesia application. There is a limited number of studies in the literature, most of them retrospective. In the studies, anesthesia-related complication rates differ according to anesthesia management (0.3%-10.57%).[6,10,17,18] While nausea-vomiting and hypotension are common in patients under general anesthesia, respiratory complications are prominent in patients under sedation. According to the results of our study, the anesthesia complication rate in pediatric RT in our clinic is 2.87%. Our complication rates are similar to those in the literature. The complications we encountered are shown in **Table 3**. In addition, none of the patients with complications required cardiopulmonary resuscitation and the procedures were successfully completed. In our clinic, routine Bispectral Index (BIS) monitoring is performed in NORA procedures. We believe that, particularly in patients sedated for RT, it would be beneficial to fix the patient on the RT table with auxiliary equipment and additional monitoring and to monitor the depth of anesthesia with BIS monitoring.

RT can be performed on an outpatient basis in appropriate patients. In long and repetitive anesthesia applications, outpatient treatment increases the tolerability of the process. Therefore, the postoperative period is as important as the intraoperative period. The method of anesthesia (general anesthesia/sedation) and anesthetic drugs used for RT are among the most important parameters affecting the postoperative period.[6] Compared with general anesthesia, sedation is a more feasible method in recurrent daily procedures.[19] Therefore, in our clinic, the sedation rate is 92.3% and the general anesthesia rate is 7.7%. In line with our clinical practice and results, we believe that sedation is more feasible in recurrent anesthesia procedures.

The drugs used, as well as the preferred method of anesthesia, affect the postoperative period.[20] In a study conducted by Sane et al.[18] in 2022, when ketamine and propofol were compared, it was found that ketamine prolonged the return time of cognitive functions and increased secretions. According to the results of our study, ketamine was used in only one patient with tracheostomy, who was followed up on with a mechanical ventilator. The reason for this was that the patient was hypotensive at the beginning of treatment. We preferred ketamine because of its better hemodynamic stabilization in hypotensive patients. In another study, it was emphasized that the use of propofol for RT can be safely used without the need for an airway device, as well as its anti-emetic efficacy and short duration of action.[21] Therefore, we preferred to administer anesthesia with propofol in our routine practice.

In our center, the number of sedation for anesthesia method was higher compared to general anesthesia (92.3%/7.7%). This may be due to the higher number of outpatients in our clinic, and the preference for sedation for rapid postoperative recovery in frequently recurrent anesthesia applications. The combined use of the agents used in the ideal sedation method has gained a place in anesthesia practice as a general opinion. For this reason, no single agent is used alone in our clinic and a balanced anesthetic regimen is applied. In addition, when the anesthetic agents used in the first RT session were examined, a combination of midazolam and propofol was mostly used. In repeated sessions, it was determined that the patients' need for anesthetic increased. In the following sessions, the dose requirement for midazolam and propofol increased and fentanyl was added. When the doses of propofol (1.8±0.48/3.2±0.52), midazolam (0.06±0.025/0.09±0.028), and fentanyl (0/0.75±0.62) used in the first and last fractions of the patients were compared, a statistically significant difference was found between the first and last fraction ($p<0.001$). We surmise that this statistical difference is due to the development of tolerance to anesthetic drugs because of frequent and repeated anesthesia applications.[22] When the recovery times of the patients in the first and last sessions were compared, there was a statistically significant difference, which we surmise that this was due to the increase in the amount of anesthetic drugs used in the increased number of sessions ($p<0.01$) (19.6±3.68/36.9±7.84).

Limitations

The implementation of pediatric RT anesthesia in our center within the protocol and sharing the results of patients treated according to this protocol may be a guide for other centers. Although our study is a single-center study, it may be a guide for future multicenter studies with participation from different regions of the world in terms of long-term anesthesia management and clinical practices. For this purpose, we determined the incidence of anesthesia in pediatric patients who received RT in our hospital for the first time and created a step for future studies. Of course, there were some limitations to our study. These limitations are; the retrospective design of the study, reflecting single-center results, exclusion of 3 patients who received anesthesia due to incomplete data, inability to include patients with incomplete data in the study, and especially the subjective nature of the reports of outpatients.

CONCLUSION

In conclusion, anesthesia management in pediatric RT is a special procedure that requires multidisciplinary management due to its unique requirements. Because of inadequate sedation doses based on anesthesiologists feeling themselves outside the safe zone, mobilization and repetition of the procedure may occur. In order to prevent undesirable results, patients should be re-evaluated in detail at each session of repeated anesthesia applications, all necessary equipment should be prepared in advance, and close monitoring should be conducted on the depth of anesthesia. We recommend the use of behavioral modified therapies in certain age groups to

avoid the potential for addiction due to frequent and repetitive anesthesia. Most studies on this subject are retrospective reviews and we believe that further controlled clinical studies are required.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 10.07.2024, Decision No: AEŞH-BADEK-2024-580).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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