EFFECTS OF PROPOFOL FOR REPEATED PROLONGED DEEP SEDATION IN PEDIATRIC PATIENTS UNDERGOING RADIOTHERAPY IN ONCOLOGY CENTRE OF HUE CENTRAL HOSPITAL

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ABSTRACT

Objective: *Immobilization of pediatric patients undergoing radiotherapy (RT) often requires anaesthesia. The aim of this study is to evaluate the safety and sufficiency of a propofol injection for repeated prolonged deep sedation in pediatric patients for RT.*

Patients and methods: *Patients who underwent anesthesia for RT between March 2014 and June 2016 were included in the study. Sedation was introduced with a repeated small boluses of intravenous propofol 0.045 mg.kg^{-1} until unconsciousness and inactivity occurred. When unwanted movement was observed, an additional dose of propofol was administered. We assessed the patient characteristics, oncologic diagnosis, duration of sedation, sedation scores and complications related to sedation.*

Results: *Total 136 sedative anaesthetics performed in 9 consecutive paediatric oncology patients, mean age 38.6 (8.0) months (range 30-54). A loading dose of 3.3 (0,4) mg.kg^{-1} propofol was administered for induction. Patients breathed spontaneously and do not have unwanted movements during the radiation procedure. Mean duration of sedation was 6.9 (0.7) mins. Mean awakening time was 8,1 (2,0) mins and could be discharged about 30 mins later. There was no clinical important complication of involving respiration, circulation or neurology during and after sedation.*

Conclusion: *Deep sedation with propofol seems to be an excellent method to immobilize paediatric patients during RT procedures.*

Keywords: *Sedation, pediatric, radiotherapy, propofol.*

I. INTRODUCTION

Conformal radiation techniques require precise positioning of the patient, and additional positioning check-ups are performed before each radiation procedure [1], [2], [6], [9]. Therefore, RT is a somewhat more time-consuming procedure than another diagnostic or intervention procedures, prolonging the time of sedation required. The safetyof paediatric patients undergoing RT depends on absolute immobilization duringthe procedure. However, timidity and anxietyproduced by strange hospital environment orpersonnel cannot be assuaged by persuasion and despite the presence of their parents, it is mostly impossible to keep pediatric patients quiet

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without any sedative drug.

Unfortunately, none of the sedative regimens usually applied in paediatrics can absolutely prevent children from moving and therefore, a deeper level of sedation is required when younger children require radiation treatment.General anaesthesia, however, combined with tracheal intubation involves risks such as subglottic oedema, and if anaesthesia has to be performed daily over a lengthy period of radiation therapy, it may be difficult to manage out-patients. In addition, the time needed for anaesthetic preparations and posttreatment monitoring usually exceeds by a multiple the duration of the RT procedure. The ideal method should be quick in onset, have few side effects, and promote short awakening time with rapid psycho-motor recovery [6]. Tracheal intubation would be unnecessary if there are a reliable and safe alternatives that does not produce serious respiratory depression.

Propofol is an interesting hypnotic drug to provide sedation for diagnostic procedures in young patients [2], [5]. It is increasingly used for pediatric patients undergoing repeatedradiation procedures, since it provides reliable sedation and short recovery periods. In our opinion an anaesthetic technique based on continuous application of hypnotics is the best way available to achieve the aims desired. Therefore, we prefer total intravenous anaesthesia with propofol and spontaneous breathing in paediatric patients undergoing RT.The aim of this study is to evaluate the safety and sufficiency of a propofol injection for repeated prolonged deep sedation in pediatric patients for RT.

II. PATIENTS AND METHODS

Patients who underwent anesthesia for external beam RTin Oncology Centre of Hue Central Hospital from March 2014 to June 2016 were included in the study. After carefully informing the parents concerning the anaesthesia procedure, written consent was obtained. A peripheral venous catheter via the internal jugular vein was inserted a few days prior to radiation treatment. It was recommended to all patients for preprocedural fasting time 2h for clear fluids, 4h for breast milk and 6h for solids, non human and formula milk. All patients were evaluated by the anesthesiologist of the clinic before undergoing RT, and anesthesia was administered by the anesthesiologist and a technician.

Table 1.Ramsey Sedation Score

1. Nervous, agitated and/or restless
2. Cooperative, orientated, quite patient
3. Only obeying the orders
4. Sleeping, hitting the glabella and responding to high voice suddenly
5. Sleeping, hitting the glabella and responding to high voice slowly
6. No response to any of these stimulations

During induction of sedation and awakening, patients' families were also in the RT room. Sedation was introduced with a repeated small boluses of i.v. propofol 0.045 mg.kg-1 until sufficient depth of sedation was obtained. When unwanted movement was observed in patients, an additional dose of propofol was administered. O_2 was provided from the central medical gas system through the face mask. Patient's blood pressure noninvasively, peripheral oxygen saturation (SpO_2), single lead electrocardiogram and Ramsey sedation score (Table 1) were recorded. All patients were treated in the supine position, immobilized with fixation bandages to prevent falls, and monitored with two cameras, one of which could focus on the patient's monitor, the other being able to adjust to the patient's chest movements and the RT procedure. All equipment necessary for managing emergency situations were readily available throughout the RT procedure.

Table 2. Modified Aldrete Score

Activity	
Voluntary movement of all limbs to command	2
Voluntary movement of two extremities to command	1
Unable to move	0
Respiration	
Breathe deeply and cough	2
Dyspnea, hypoventilation	1
Apneic	0
Circulation	
BP +/– 20 mm Hg of preanesthesia level	2
BP >20-50 mm Hg of preanesthesia level	1
BP >50 mm Hg of preanesthesia level	0
Consciousness	
Fully awake	2
Arousable	1
Unresponsive	0
Color	
Pink	2
Pale, blotches	1
Cyanotic	0

After termination of the RT procedure, the time until spontaneous opening of the eyes (awakening time) was registered.Patients were observed in the recovery room until their modified Aldrete'sscores was greater than nine (Table 2).

III. RESULTS

Retrospectively, we reported upon a total of 136 sedative anaesthetics performed in 9 children who received radiation therapy daily for differing oncological diseases in Oncology Centre of Hue Central Hospital from March 2014 to June 2016. The age, weight, gender, diagnosis and RT procedures for patients are presented in Table 3.

Table 3. Patients' characteristics

Case	*Age (month)*	*Weight (kg)*	*Gender*	*Diagnosis*	*No. of treatment*	*i.v access*	*Position*	*Area treated*
1	45	13	M	Rhabdomyosarcoma	7	Peripheral	Supine	Subframe
2	36	15	F	Nephroblastoma	10	Peripheral	Supine	Kidney
3	35	13	M	Rhabdomyosarcoma	28	Peripheral	Supine	Chest
4	32	12	F	Neuroblastoma	7	Port-a-cath	Supine	Head
5	54	18	M	Neuroblastoma	24	Peripheral	Supine	Head
6	42	13	M	Neuroblastoma	11	Peripheral	Supine	Head
7	30	12	M	Neuroblastoma	13	Peripheral	Supine	Head
8	34	14	M	Nephroblastoma	14	Peripheral	Supine	Kidney
9	30	15	F	Neuroblastoma	22	Peripheral	Supine	Head
Mean (SD)	*38.6 (8.0)*	*13.9 (1.9)*			*15.1 (7.7)*			

The repeated small boluses of i.v. propofol 0.045 $mg.kg^{-1}$ was sufficient in all patients to avoid inadvertent movements and to guarantee safe cardio-respiratory conditions. No additional propofol boluses were needed after final positioning until the end of the RT procedure. The average propofol bolus dose for induction and patient positioning was 3.3 (0.4) $mg.kg^{-1}$. Requirements of propofol induction dose were quite stable over the successive weeks of treatment.Mean duration of sedation was 6.9 (0.7) min and the patients awakened 8.1 (2.0) min after the last bolus of i.v propofol (Table 4). In all cases the patients could be assessed by the attending anaesthesiologist as having completely recovered within 30 min after awakening.

Table 4. Summary of sedation times and doses of propofol

Case	*No. of treatment*	*Weight (kg)*	*Loading dose ($mg.kg^{-1}$) Mean (SD)*	*Sedation time (min) Mean (SD)*	*Ramsey score (after induction 3 min) Median (min-max)*	*Awakening time (min) Mean (SD)*
1	7	13	3.2 (0.9)	6.1 (0.6)	6 (4-6)	9.9 (2.1)
2	10	15	2.8 (0.4)	6.5 (1.0)	6 (5-6)	9.5 (1.2)
3	28	13	3.4 (0.9)	6.2 (0.7)	6 (5-6)	7.9 (1.6)
4	7	12	3.9 (1.0)	5.7 (0.3)	6 (5-6)	6.1 (1.3)
5	24	18	4.1 (0.8)	5.3 (0.5)	6 (4-6)	7.8 (2.4)
6	11	13	3.2 (0.5)	6.0 (0.8)	6 (4-6)	8.2 (1.7)
7	13	12	3.4 (0.5)	6.3 (0.9)	6 (5-6)	9.2 (2.7)
8	14	14	3.2 (0.2)	6.2 (1.1)	6 (5-6)	7.4 (3.6)
9	22	15	2.9 (1.1)	5.5 (0.4)	6 (5-6)	6.8 (1.5)
Mean(SD)	*15.1 (7.7)*	*13.9 (1.9)*	*3.3 (0.4)*	*6.9 (0.7)*		*8.1 (2.0)*

In all cases induction of sedation with propofol was smooth and without respiratory side-effects. Airway maintenance and SpO2 while breathing air were well maintained, although following the occasional bolus, SpO2 fell to about 90%. The anesthetic techniques and the related complications are summarized in Table 5.

Table 5. Complications related to sedation

	No. of Patients n (%)
HR increase >20% compared with baseline	0
HR decrease >20% compared with baseline	2 (22.2)
SpO_2 decrease >5 point compared with baseline	2 (22.2)
Convulsion	0
Laryngospasm	0
Bradycardia	0
Agitation	0
Hiccup	0
Shivering	0
Increased oral secretion	1 (11.1)
Nausea and Vomiting	1 (11.1)

Although respiratory complications were the most common complications, there were no episodes of laryngospasm or bronchospasm and no use of advanced airway interventions, such as endotracheal intubation, laryngeal mask usage, or tracheostomy. No vomiting was observed in any patient.

IV. DISCUSSION

Propofol is an excellent hypnotic drug for repeated radiation procedures in young children. It offers reliable sedation and immobilization, rapid and pleasant awakening as well as short duration of hospital stay [9]. Based on our preliminary experiences in 9 patients undergoing repeated RT procedure, deep sedation using repeated small boluses of i.v. propofol 0.045 $mg.kg^{-1}$in our patients was safe with regard *(1)* to maintaining sufficient spontaneous breathing without the need for an artificial airway, *(2)* to avoiding coughing and bucking, *(3)* obtaining a motionless child and *(4)* maintaining stable cardiovascular conditions.

For rapid and safe induction of anaesthesia with propofol in children usually a loading dose of 2.5$mg.kg^{-1}$ has to be administered intravenously[8]. The dose must be increased in unprernedicated children5 and therefore a mean induction dose of 3.3 mg.kg was necessary for our patients. All children had fallen asleep after administration of the induction dose. Overall, the induction dose in our study population was similar to that reported by Scheiber and colleagues [6]. In contrast to other authors using a fixed dose of propofol for induction, with the presented technique the induction dose was titrated until sufficient depth of sedation was obtained.

Regarding the duration of anesthesia, our results have demonstrated that a briefer anesthetic session carries less risk. Although, a limit to the duration of anesthesia is unlikely to be feasible in this setting, a heightened awareness of the increased risk during longer procedures might be helpful in anticipating possible complications. The mean time until awakening for our patients was 8.1 min and after about 30 min they were completely recovered. This corresponds to the observations of Motsch & Boullaywho reported that following a totally intravenous anaesthetic with propofol, lasting about 45 min, children opened their eyes spontaneously after 12.8 min and were able to answer questions correctly 17.5 min later [4]. Fast awakening after stopping propofol infusion is due to the short elimination half life (t1/2β) and also to the lack of substantial cumulation during administration over a longer period. Elimination half life after a single injection is even shorter with children than with adults [8].

Airway and respiratory complications comprised most of the problems in our research. The chin lift and jaw thrust may need to be stabilized with application of paper tape under the chin and/or a shoulder roll. The airway position can be challenged by positioning the head and neck in an immobilization device or thermoplastic mask (as indicated by the RT regimen). Other factors that can contribute to a low incidence of oxygen desaturation are preoxygenation by face mask before induction and a regimen of successive 1 mg/kg intravenous boluses of propofol until loss of consciousness, followed by continuous infusion. We have found that this standardized method of administering propofol by practitioners who use it frequently is safe and effective. We are unaware of any previous analysis of the factors associated with the risk of anesthesia-related complications in pediatric patients undergoing RT. Both an increased duration of anesthesia and greater total doses of propofol adjusted by weight were associated with a greater risk of complications.

V. CONCLUSION

The results of our experience demonstrate that sedative anaesthesia with propofol is an excellent method for immobilizing children during radiotherapeutic procedures. In our estimation, this anaesthetic technique offers considerable advantages over other methods of sedation and general anaesthesia.

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