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# Effects of Inhalation Anesthetics on Respiratory Mechanics in Children with Reactive Airway Dysfunction Syndrome

İnhalasyon Anesteziklerinin Solunum Mekaniklerine Etkileri

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Abstract: This study aimed to compare the effects of sevoflurane and desflurane on respiratory mechanics during general anesthesia in pediatric patients with respiratory problems. This prospective, randomized study included 40 pediatric patients (6 girls and 34 boys), aged 1-6 years, who underwent elective lower urinary tract surgery (e.g., orchiopexy and hypospadias repair) under general anesthesia at our university hospital between February 1, 2015, and May 1, 2015. Patients were assigned to two groups based on the administered inhalation agent: sevoflurane or desflurane. Airway resistance (RAW), dynamic compliance (Cdyn), peak inspiratory pressure (PIP), and plateau pressure (Pplato) were measured at multiple time points during general anesthesia at 1, 3, 6, 10, 15, 20, 30, 40, 60, 90, 120 min and after intubation. The values were then compared between the groups There were no statistically significant differences between the sevoflurane and desflurane groups regarding RAW, Cdyn, PIP, and Pplato values (p> 0.05). Sevoflurane and desflurane are both viable options for maintaining general anesthesia in children with RADS. However, additional studies are required to identify the safest anesthetic agents, especially in pediatric patients with underlying respiratory issues.

**Keywords:** Reactive Airway Dysfunction Syndrome, Respiratory Mechanics, Inhalation Anesthetetics, Sevoflurane, Desflurane

Özet: Reaktif hava yolu disfonksiyon sendromu gibi solunum problemleri olan pediatrik hastalarda, genel anestezi sırasında kullanılan inhalasyon anesteziklerinin (sevofluran ve desfluran) hastalarda introperatif dönemde solunum mekanikleri üzerindeki etkilerinin karşılaştırılması hedeflenmiştir. Prospektif, randomize olarak dizayn edilen bu çalışmada, elektif alt üriner sistem cerrahisi (örneğin, orşiopeksi ve hipospadias onarımı) nedeniyle genel anestezi verilen, RADS tanılı, 1-6 yaş arası 40 pediatrik hasta (6 kız ve 34 erkek) bulunmaktadır. Hastalar, anestezi idamesi için uygulanan inhalasyon ajanına göre, sevfluran ve desfluran olacak şekilde, iki gruba ayrılmıştır. Hava yolu direnci (RAW), dinamik kompliyans (Cdyn), pik inspiratuar basınç (PIP) ve plato basıncı (Pplato) değerleri, genel anestezi süresince entübasyondan sonra, 1, 3, 6, 10, 15, 20, 30, 40, 60, 90 ve 120. dakikalarda kaydedilmiş ve karşılaştırılmıştır. Gruplar arasında RAW, Cdyn, PIP ve Pplato değerleri açısından istatistiksel olarak anlamlı fark saptanmamıştır. (p > 0,05). RADS'lı çocuklarda genel anestezinin idamesinde sevofluran ve desfluran kullanımı ile hastalarda intraoperatif havayolu basınçları üzerinde gruplar arasında istatistiksel anlamlı fark saptanmamış olup, daha çok hasta sayıları ile yapılacak çalışmalara da ihtiyaç olduğu vurgusu ile, RADS tanılı hastalarda anestezi idamesi için sevofluran ve desfluranın güvenle kullanılabileceğini düsünmekteviz.

**Anahtar Kelimeler:** Reaktif hava yolu disfonksiyon sendromu, solunum mekanikleri, inhalasyon anestezikleri, sevofluran, desfluran

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# 1. Introduction

Reactive Airways Dysfunction Syndrome (RADS) and irritant-induced asthma represent significant respiratory conditions typically arising from acute exposure to high concentrations of irritant substances. Originally described by Brooks et al. in 1985, RADS is characterized by the sudden onset of asthma-like symptoms following a single high-level exposure to irritant agents, in individuals with no previous respiratory complaints (1). This condition persists for at least three months after the initial exposure and is accompanied by airflow obstruction and bronchial hyperreactivity. The global prevalence of irritant-induced asthma is substantial, with reports indicating it constitutes approximately 5-18% of all occupational asthma cases (2).

The pathophysiology of RADS involves direct damage to the bronchial epithelium following exposure to irritant agents. This damage triggers a complex inflammatory cascade involving oxidative stress, neurogenic inflammation, and airway remodeling (2). Chlorine and chlorine-releasing agents remain the most frequently reported causative agents, accounting for approximately 14% of RADS cases(3). Other common triggers include toluene diisocyanate, paint fumes, smoke inhalation, acids, alkalis, and various industrial chemicals.

In the perioperative setting, patients with a history of RADS or irritant-induced asthma present unique challenges. These patients typically demonstrate increased airway reactivity, which significantly elevates their risk of perioperative respiratory including bronchospasm, adverse events laryngospasm, perioperative cough, desaturation, and airway obstruction. Studies have demonstrated that children with increased airway reactivity, including those with RADS, have a higher incidence perioperative bronchospasm (2.2-5.7%)compared to those without such conditions (0.2– 4.1%) (4).

Anesthetic management of patients with RADS requires careful consideration of medication choices and airway management strategies. Both inhalational and intravenous anesthetic agents can affect respiratory mechanics in different ways. For instance, under inhalational anesthesia, closing pressure at the mask is significantly higher in patients with airway reactivity compared to control subjects. Additionally, these patients often demonstrate reduced spontaneous ventilation and elevated PCO2 levels despite adequate airway patency. Furthermore, opioid analgesics may

precipitate respiratory depression and even central apnea in patients with increased airway reactivity(5).

The fact that inhalation anesthetics, which are indispensable in general anesthesia. respiratory physiology in many ways, from various forces controlling ventilation and pulmonary blood flow to surface tension, mucus secretion, and airway smooth muscle tone, highlights the importance of inhalation anesthetic selection in patients with respiratory risks. Sevoflurane and desflurane are the most commonly used inhalational anesthetics for general anesthesia. Sevoflurane is a colorless, nonirritating, nonflammable, and nonexplosive volatile anesthetic agent(6). Desflurane is also a colorless, nonexplosive gas. Owing to its pungent odor, desflurane may cause respiratory symptoms, increased such secretion, cough as laryngospasm, during the induction period of anesthesia and may limit the rate of induction. Its pungent odor does not cause problems in the maintenance of desflurane anesthesia Desflurane can be used for maintenance of anesthesia but is not preferred for induction anesthesia.

Respiratory complications (e.g., bronchospasm and laryngospasm), which are frequently encountered during general anesthesia induction, are especially important in pediatric patients and require rapid diagnosis and treatment. Compared to adults, there are many anatomical differences between the upper and lower airways in children. These differences must be considered before attempting airway manipulation. (8)

We aimed to investigate the effects of sevoflurane and desflurane on the respiratory mechanics in children with reactive airway dysfunction syndrome (RADS) who underwent lower urinary tract surgery under general anesthesia.

# 2. Materials and Method

This prospective randomised study was approved by the Institutional Review Board of Cerrahpaşa Medical Faculty of Medicine (approval no.: 12.01.2015; 83045809/604.01//02-7639). Since the patients included in the study were under 18 years of age, informed consent was obtained from their parents both verbally and in writing. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as revised in 2000 (protocol number E.27336).

A total of 40 patients with RADS, who underwent elective lower urinary tract surgery (e.g., orchiopexy and hypospadias repair.) under general anesthesia at the Cerrahpaşa Medical Faculty Anesthesiology and Reanimation Clinic, between February 1, 2015, and May 1, 2015, were evaluated. The diagnosis of RADS was made according to the American Chest Physicians Criteria (9).

#### 2.1. Inclusion criteria

Patients aged between 1 to 6 years and with American Society of Anesthsiologists Physical Status (ASA) between I to II who were previously diagnosed with RADS (New onset symptoms simulating asthma, symptoms occuring after a single exposure incident, onset of symptoms no longer than 24 hours, symptoms persistent for more than 3 months, airflow obstruction in pulmonary function test, metacholine challenge test positivity, ruling out other types of pulmonary diseases) were included in the study (1).

#### 2.2. Exclusion criteria

The exclusion criteria were as follows: Patients who declined participation in the study, ASA III and higher classification, Age younger than 1 year or older than 6 years, Patients undergoing total intravenous anesthesia, Patients with a surgical duration exceeding 2 hours.

## 2.3. Randomization

Prior to anesthesia, patients were assigned to a group by drawing lots from a bag containing papers labeled with either sevoflurane (Group S) or desflurane (Group D), with the procedure conducted by an individual who was unaware of the study details.

#### 2.4. General Anesthesia

Preoperative sedation was performed midazolam according to the body weight of the patients. Peripheral oxygen saturation (SpO<sub>2</sub>) and heart rate were continuously monitored, systolic diastolic and mean arterial pressures were monitored at 10-minute intervals. Anesthesia induction was performed with 2 µg/kg fentanyl, 2 mg/kg propofol, and 0.6 mg/kg rocuronium IV in all children. Patients were orotracheally intubated appropriate intubation tubes. The appropriate intubation tube size was determined using the following formula: inner diameter of the tube (mm)=age (years)/4+4. A cuffed tube was not

preferred because it may affect the airway pressure by causing edema.

To maintain anesthesia, one MAC of sevoflurane was used in Groups S, and one MAC of desflurane was used in Groups D.

All patients were ventilated intraoperatively using the Datex Ohmeda S/5 Avance anesthesia device in the volume-controlled mode. The respiratory frequency was adjusted to FiO2:40%, I:E 1/1.5, PEEP: 5 cmH2O, tidal volume 6-8 ml/kg, and endtidal carbon dioxide of 35-40 mmHg. Once the surgery was completed, atropine sulfate 20 mcg/kg and neostigmine 60 mcg/kg IV were administered in order to reverse neuromuscular blockade for every patient.

#### 2.5. Outcomes

PIP, Pplato, and Cdyn were recorded using a Datex Ohmeda S/5 Avance anesthesia device. RAW was calculated using the formula: PIP (cmH<sub>2</sub> 0)-Pplato (cmH<sub>2</sub> 0)/flow (lt/min). The airway flow value for each patient was calculated by dividing the tidal volume by the inspiratory time for each measurement. Respiratory mechanics (PIP, Pplato, RAW, and Cdyn) were recorded immediately after intubation and at 1, 3, 6, 10, 15, 20, 30, 40, 60, 90, and 120 minutes. Patients were monitored for respiratory and hemodynamic functions for 2 hours during the early postoperative period.

### 2.6. Statistical methods

Power analysis was performed using G\*Power (v3.1.7) to determine the sample size. The power of the study is expressed as 1- $\beta$  ( $\beta$ =probability of type II error) and in general, studies should have 80% power. According to Cohen's effect size coefficients, according to the calculation made by assuming that the evaluations to be made between two independent groups will have a large effect size (d=0.8), we decided that there should be at least 18 people in each group. Considering that there may be losses during the study process, we decided to include 20 people in each group.

Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 Statistical Software (Utah) were used for statistical analysis.

In addition to descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, and maximum), the Student's t-test was used to evaluate variables with normal distribution, and the Mann–Whitney U test was used to compare

quantitative data. A paired-sample t-test was used for intragroup comparisons of normally distributed parameters and the Wilcoxon signed-rank test was used for intragroup comparisons of non-normally distributed parameters. Yates Continuity Correction, Fisher's exact test, and Fisher-Freeman-Halton test were used to compare the qualitative data. Significance was evaluated at p<0.01 and p<0.05 levels.

#### 3.Results

Our study included 40 (6 girls and 34 boys) The age of the patients who participated in the study ranged between 1 and 6 years with a mean age of  $3.39\pm1.57$  years. There were no statistically significant differences between the groups in terms of sex, age, body weight, or duration of anesthesia (P >0.05). (Table 1)

**Table 1**. Evaluation of descriptive characteristics by groups

		Group S	Group D	P
Sex	Female	1 (5,0)	5 (25,0)	°0,220
Sex	Male	19 (95,0)	15 (75,0)	0,220
	Mean±SD	$3,55\pm1,79$	$3,05\pm1,57$	
Age	Min-Max (Median)	1-6 (3,5)	1-6 (2,5)	<sup>a</sup> 0,176
Body weight (kg)	Mean±SD	$16,85\pm6,08$	13,30±4,03	<sup>b</sup> 0,119
	Min-Max (Median)	6-26 (16,5)	6-22 (13,0)	
Duration of	Mean±SD	$87,00\pm33,10$	$85,00\pm35,76$	
anaesthesia	Min-Max (Median)	30-120 (90)	30-120 (90)	<sup>a</sup> 0,823
		n (%)	n (%)	

(Min: minimum, Max:maximum, SD:standart deviation)

The mean sevoflurane PIP value were found to be  $16.15\pm1.70$ , while the mean desflurane values were found to be  $16.45\pm3.95$ , and no statistically significant difference was found between them (p>0.05) (Table 2)

Table 2. Comparison of PIP values

PIP	Sevoflurane (n=20) GRUP S		Desflurane (n=20) GRUP D		а <b>р</b>
(cmH <sub>2</sub> 0)	Mean±SD	Median	Mean±SD	Median	_
After Intubation	16,15±2,70	16	16,45±3,94	16,5	0,780
1 min	16,35±2,52	16	17,20±3,91	17,5	0,419
3 min	17,05±2,42	17	17,65±3,76	18	0,552
6 min	17,05±2,28	17	18,25±3,48	18,5	0,205
10 min	17,50±2,16	17	18,50±3,61	18,5	0,294
15 min	17,30±2,39	17	18,60±3,60	18	0,187
20 min	18,25±2,55	18	18,68±3,58	18	0,664
30 min	17,95±2,56	18	19,47±3,43	19	0,132

40 min	17,58±2,32	17	19,56±3,14	19	0,039*
60 min	18,06±2,29	18	19,13±2,83	18	0,255
90 min	18,15±2,41	18	19,42±2,87	19	<sup>b</sup> 0,272
120 min	18,88±2,70	18	20,00±4,59	19	<sup>b</sup> 0,529

<sup>a</sup>Student's t test

<sup>b</sup>Mann Whitney U test

\*p<0,05

(PIP:Peak inspratory pressure, Min:minute)

The mean sevoflurane Pplato values were found to be 14.40±2.87, while the mean desflurane values were found to be 14.75±3.55, and no statistically significant difference was found between them (p>0.05) (Table 3).

**Table 3.** Comparison of Pplato values

Pplato (cmH <sub>2</sub> O)	Sevoflurane (n=20) GRUP S		Desflurane (n=20) GRUP D		а <b>р</b>
	Mean±SD	Median	Mean±SD	Median	
After Intubation	14,40±2,87	14	14,75±3,55	15	0,734
1 min	14,65±3,12	14,5	15,65±3,44	15,5	0,341
3 min	15,35±2,32	15	16,00±3,26	16,5	0,472
6 min	15,60±2,26	16	16,50±3,00	17	0,290
10 min	15,65±2,50	15,5	16,60±3,22	16,5	0,304
15 min	15,60±2,28	16	16,95±3,50	16,5	0,157
20 min	16,50±2,65	16	16,79±3,39	16	0,767
30 min	16,35±2,43	16	17,88±3,14	17	0,104
40 min	15,68±2,43	15	17,56±2,85	17	0,043*
60 min	16,56±2,45	16	17,33±2,79	17	0,420
90 min	16,62±2,50	16	17,75±2,60	17	<sup>b</sup> 0,271
120 min	17,38±2,92	16,5	18,3±4,35	17,5	<sup>b</sup> 0,623

<sup>a</sup>Student's t test

<sup>b</sup>Mann Whitney U test

\*p<0,05

(Pplato: Plaeau pressure, Min:minute. SD:standart deviation)

The mean sevoflurane RAW values were found to be  $18.41\pm7.45$ , while the mean desflurane values were found to be  $19.37\pm9.40$ , and no statistically significant difference was found between them (p>0.05) (Table 4).

Table 4. Comparison of RAW values

RAW (cmH <sub>2</sub> O/lt/dk)	Sevoflurane (n=20) GRUP S		Desflurane (n=20) GRUP D		а <b>р</b>
	Mean±SD	Median	Mean±SD	Median	
After Intubation	18,41±7,45	19,8	19,37±9,40	18,3	0,723
1 min	17,55±7,65	16,3	16,90±7,10	17,7	0,782
3 min	17,85±8,58	17,4	18,17±7,34	17,7	0,900
6 min	15,62±8,99	12,5	19,25±7,01	19,1	0,162
10 min	19,91±10,35	19,1	21,27±10,41	19,1	0,681
15 min	18,05±7,26	17,8	18,26±8,10	15,5	0,930
20 min	18,92±5,3	19,1	20,20±8,35	21,4	0,567
30 min	17,99±8,31	16,3	13,96±8,90	12,9	0,147
40 min	20,08±16,91	18,3	16,95±10,33	19,4	0,485
60 min	13,53±10,75	13,2	14,24±9,94	13,8	0,831
90 min	11,23±10,99	12,2	10,62±10,27	11,5	<sup>b</sup> 0,967
120 min	7,14±9,71	0	9,01±10,15	5	<sup>b</sup> 0,543

<sup>a</sup>Student's t test

<sup>b</sup>Mann Whitney U test

(RAW: Airway resistance, Min:minute, SD:standart deviation)

The mean sevoflurane Cdyn values were found to be  $18.20\pm7.44$ , while the mean desflurane values were found to be  $14.15\pm5.19$ , and no statistically significant difference was found between them (p>0.05) (Table5).

Table 5. Comparison of Cdyn values

Cdyn (ml/cmH <sub>2</sub> o)	Sevoflurane (n=20) GRUP S		Desflurane (n=2 GRUP D	Desflurane (n=20) GRUP D	
	Mean±SD	Median	Mean±SD	Median	
After Intubation	18,20±7,44	17,5	14,15±5,19	12	0,053
1 min	16,35±6,66	15	13,05±4,65	11,5	0,077
3 min	15,60±6,88	14,5	12,70±4,62	11	0,126
6 min	15,50±6,73	14,5	12,70±4,53	11	0,131
10 min	14,60±6,36	14	12,60±4,54	11	0,259
15 min	14,85±6,56	13,5	12,35±4,60	11,5	0,171
20 min	14,75±6,87	12,5	12,37±4,63	11	0,215

30 min	14,80±7,23	13	11,82±4,30	11	0,146
40 min	14,00±5,96	14	11,88±4,76	11,5	0,259
60 min	13,25±5,76	13	12,13±5,07	11	0,572
90 min	12,54±5,55	13	11,33±5,00	10,5	<sup>b</sup> 0,548
120 min	12,50±6,74	11,5	11,00±5,01	10	<sup>b</sup> 0,656

<sup>a</sup>Student's t test

<sup>b</sup>Mann Whitney U test

(Cdyn:Dynamic compliance, Min:minute, SD:standart deviation)

There were no statistically significant differences between Group S and Group D in terms of PIP, Pplato, RAW, or Cdyn values (p>0.05). Lastly, 2 patients developed bronchospasm in the postoperative 2-hour follow-up period which was statistically insignificant (p>0.05).

#### 4. Discussion

In this study, we investigated the effects of inhalational anesthetics (sevoflurane and desflurane) on respiratory mechanics in children with Reactive Airways Dysfunction Syndrome (RADS). Our findings show that there were no statistically significant differences between sevoflurane and desflurane groups in terms of airway resistance (RAW), dynamic compliance (Cdyn), peak inspiratory pressure (PIP), and plateau pressure (Pplato) values.

Inhalational anesthetics, as essential components of general anesthesia, are known to affect respiratory physiology in many ways, from various forces controlling ventilation to pulmonary blood flow, surface tension, mucus secretion, and airway smooth muscle tone. This highlights the importance of inhalational anesthetic selection in patients with respiratory risks (6,7).

In a study by Goff et al. (10), in adults, intravenous thiopental (5 mg/kg) was administered for anesthesia induction, orotracheal intubation was performed with a cuffed tube after succinylcholine (1.25 mg/kg) injection, and 1 MAC of sevoflurane or desflurane was used for anesthesia maintenance. Respiratory mechanics values measured using the isovolume technique were recorded at 5 and 10 minutes after the inhalation agent Sevoflurane significantly decreased RAW, whereas desflurane had no significant effect. In our study, no statistically significant differences in RAW were observed between the two agents.

Dikmen et al.(11) investigated the effects of inhalation agents on respiratory mechanics in adult patients and reported that isoflurane, sevoflurane, and desflurane decreased RAW at 1 MAC and caused a statistically significant increase in Cdyn. In the present study, no difference was observed in the effects of sevoflurane and desflurane on RAW and Cdyn.

Britta et al.(12) examined the effects of sevoflurane and desflurane on RAW and lung elastance in children aged 1-6 years with and without airway sensitization using a previously described low-frequency oscillatory technique. Inhalation agents increased RAW and elastance in children with airway sensitivity compared to healthy children. Desflurane caused a greater increase in RAW and elastance than sevoflurane in these children. In our study, which is similar in terms of age groups and included patients, elastance was not evaluated, but compliance was observed to be reduced in patients receiving both sevoflurane and desflurane.

In a double-blind randomized controlled trial of 200 pediatric patients aged 2 to 6 years who underwent general anesthesia for strabismus surgery, Kim et al. (13) compared the use of sevoflurane or desflurane. Maintenance was with sevoflurane or desflurane at a dose of 0.8-1.2 MAC. The results of the study showed that the number of general respiratory adverse events during maintenance anesthesia and on emergence was similar between the groups. Consistent with our study, the incidence of cough, secretions, breath holding, and laryngospasm was similar in both groups.

In a study evaluating the effects of sevoflurane, desflurane, and propofol on respiratory mechanics and integrated pulmonary index (IPI) scores during laparoscopic sleeve gastrectomy, Öztürk et al.(14) found that comparison between groups revealed no significant differences in the values of PIP, Pplateau, Cdyn, Rrs, and IPI. Similarly, in our study, we found

no statistically significant differences in intraoperative PIP, Pplateau, Cdyn, and Raw values between groups using sevoflurane and desflurane in pediatric patients undergoing urinary system surgery.

Ozdogan et al. (15) compared the effects of sevoflurane and desflurane on hemodynamics and respiratory functions in the laparoscopic sleeve gastrectomy procedure and reported that there was no statistically significant difference in the preoperative and postoperative pulmonary function tests between the groups. In our study, we evaluated the effects of sevoflurane and desflurane on respiratory functions in patients undergoing lower urinary tract surgery, and similarly, found no significant difference between the groups.

In another study evaluating the effects of propofol, sevoflurane and desflurane on respiratory functions, Oguz et al.(16) analyzed the forced expiratory volume in 1 second (FEV1) % and forced vital capacity (FVC) % values before and after anesthesia and intraoperative dynamic lung compliance and airway resistance values. The researchers found that FVC, FEV1/FVC, arterial blood gases (ABG) analysis, compliance, and airway resistance values were similar between the groups. Similarly, in our study, no statistically significant difference was

found between sevoflurane and desflurane in terms of intraoperatively recorded airway pressures and airway resistance. However, pediatric population is not well-suited for performing pulmonary function tests which limits our ability to interpret data from this perspective.

Due to the single-center design, the generalizability of our findings is limited, and also several confounding factors are present such as surgery duration and given fluid amount. Moreover, data regarding the number of intubation attempts are missing which would provide more insight regarding nature of airway obstruction. Lastly, ethnic and genetic factors may also influence common physiology and anesthetic response. Our participants consisted Turkish origin which may also limit the findings' generalizability.

In this study, we examined the effects of sevoflurane and desflurane on respiratory mechanics and found no statistically significant differences in terms of RAW, Cdyn, PIP and Pplato values measured in patients using sevoflurane and desflurane. These two anesthetic agents can be safely used as inhalation anesthetics for maintenance of general anesthesia in children with RADS. More studies are needed to select the safest anesthesia method, especially in pediatric patients with respiratory problems.

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