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The effect of dexmedetomidine vs. atracurium on intubation condition in children - a randomized clinical trial

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Abstract

Background Using neuromuscular blocking agents (NMBA) in pediatric induction protocol is a challenging matter. Therefore, in this study, we aimed to find a safer way for anesthesia in children. We compared the effects of dexmedetomidine with atracurium on intubation conditions in children aged 6–12 years under general anesthesia. If dexmedetomidine has the similar effect as atracurium, we can use it for intubation and anesthesia of children in situations where the use of atracurium is challenging for any reason.

Methods This clinical trial was carried out on children between 6 and 12 years in Mashhad University of Medical Sciences, Mashhad, Iran between January 2018 and February 2020. Participants candidates for tracheal intubation and general anesthesia were enrolled. Patients were distributed into two groups: Patients received Dexmedetomidine (Group D) and patients received Atracurium (Group A).

Results We enrolled 25 patients in each group. Most of them were male. The intubation quality score consists of 5 items including laryngoscopy, vocal cord, coughing, jaw relaxation and limb movement was assessed between two groups. This score had no statistically significant difference between study groups. Immediately after induction and one minute after it, heart rate was statistically significant higher in group A than group D ($P<0.001$ & $P=0.04$ respectively). All of the intubations in our study were successful. More coughing was seen in group A compared with group D ($P=0.01$).

Conclusion In children aged 6–12 years, the administration of intravenous dexmedetomidine 1mcg/kg over a period of 10 min before the induction of anesthesia with sufentanil 0.3 µg/kg and propofol 3 mg/kg showed no statistically significant difference in quality of intubation score when compared to the use of 0.5 mg/kg atracurium to facilitate intubation. Decreased heart rate and less coughing were observed when using dexmedetomidine. This trial was registered retrospectively in the Iranian Clinical Trials Registry at 2021-24-05 (https://www.irct.ir/), and its registration number is IRCT20201028049177N1.

Keywords Intubation, Neuromuscular blocking agents (NMBA), Dexmedetomidine, Anesthesiology, Pediatric

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Background

As using neuromuscular blocking agents (NMBA) like atracorium, rocuronium and vecuronium in some situation of pediatric induction protocol is challenging, most anesthesiologists prefer to perform intubation without NMBA or to use non-depolarizing NMBA's [1, 2]. In some condition including allergy to these type of drugs, neuromuscular diseases, minor cranio-maxillo-facial surgery and who are in risk of malignant hyperthermia and also in very small Children, the use of NMBA is more challenging [3, 4]. On the other hand, some anesthesiologists believed that omitting NMBA can lead to adverse events in patients [5]. Evidence revealed that the condition of tracheal intubation is an important factor in the incidence of laryngeal morbidity. In standard intubation conditions, compared to less acceptable conditions, postoperative hoarseness and vocal cord consequence are less observed [6]. In not excellent intubation conditions, children intubation in general anesthesia may cause concern in anesthesiologists [5]. Sugammadex or neostigmine are used to reverse neuromuscular blockage effect of NMBA. Sugammadex can more easily reversed the effect of NMBA compared to neostigmine. Neostigmine needs more time, about 15 to 17 min, to reach its peak effect. But the cost and low availability of sugammadex in Iran is often another reason to avoid NMBA in pediatric anesthesia, especially in short elective surgery.

Intubation condition is an important factor in postoperative laryngeal injury [7]. Although intubation becomes easier by increasing doses of propofol or remifentanil, but complications such as bradycardia and hypotension are also possible [8]. Therefore, an ideal protocol for inducing intravenous anesthesia is one that provides easy intubation conditions with minimal complications. Dexmedetomidine is an anesthetic drug with both analgesic and hypnotic features. The use of this drug reduces the need for volatile anesthetics, although further information is need for humans, especially for children [9, 10]. It has been shown that this agent, significantly reduce the need for analgesics and anesthetics as well as the hemodynamic reaction to pain stimulants [11]. There are growing evidences in using this drug in pediatric population. Also, its safety profile is documented [12, 13].

There is limited data on this issue. Therefore, this study was conducted to compare the effects of dexmedetomidine with atracurium on intubation conditions in children aged 6–12 years under general anesthesia. If dexmedetomidine has the similar effect as atracurium, we can use it for intubation and anesthesia of children in situations where the use of atracurium is challenging for any reason.

Methods

Study participants

This double-blind randomized clinical trial carried out on children in first affiliated hospital (Ghaem hospital) of Mashhad University of Medical Sciences, Mashhad, Iran. It was done between January 2018 and February 2020. children between 6 and 12 years, who were candidate for general anesthesia and tracheal intubation were enrolled. The inclusion criteria *were as follows*: (1) Pediatric patients between 6 and 12-years old candidate for elective surgeries; (2) Under general anesthesia and tracheal intubation; (3) Physical status of ASA 1 or 2; (4) Informed consent of parents or guardians. The exclusion criteria included: (1) Coexistence of upper respiratory infection within past 3 weeks before intubation; (2) Patients with cardiovascular disorders; (3) Children with difficult airway for intubation; (4) Children with morbid obesity (child BMI-sex-age percentile higher than 85th -95th percentile accords with the definition of overweight and obesity in adult).

Study design

All children who were candidate for general anesthesia were randomly assigned into dexmedetomidine or atracorium group in a 1:1 ratio, using computer-generated series. The consecutive numbers from 1 to 50 for subjects were noted on each individual envelope, so 25 sheets of papers marked with #D (dexmedetomidine group) and the other 25 sheets marked with #A (atracorium group). In operating room, a technician of anesthesiology who was not involved in the study open the envelope No: 1 and prepared the medication based on the writing appeared on the sheet, either #A or #D. Atracorium and dexmedetomidine were exactly similar in color, smell and appearance. Patients, anesthesiologist and who analyzed data were blinded to study groups.

After entering the operating room, all patients in both groups monitored with non-invasive blood pressure (NBP), O2 saturation measurements (SpO2) and electrocardiography (ECG). Around 10 min before induction, 1 μg/kg Dexmedetomidine (group D) or 0.5 mg/kg Atracurium (group A) were injected with pump infusion to two study groups. Induction was done with 3 mg/kg propofol and 0.3 μg/kg Sufentanil in both groups. The time of injection of Dexmedetomidine was adjusted to be at its peak effect at the time of induction. Bradycardia and hypotension are two main adverse reactions of dexmedetomidine. We were aware of this complication and to deal with it, Atropine is available at the patient's bedside. All patients were followed up to 24 h after the operation in terms of the probability of similar complications. Figure 1 shows the flowchart of study.

Then all patients were intubated by Macintosh laryngoscope size 2–3 and tracheal tube 4 to 6. General

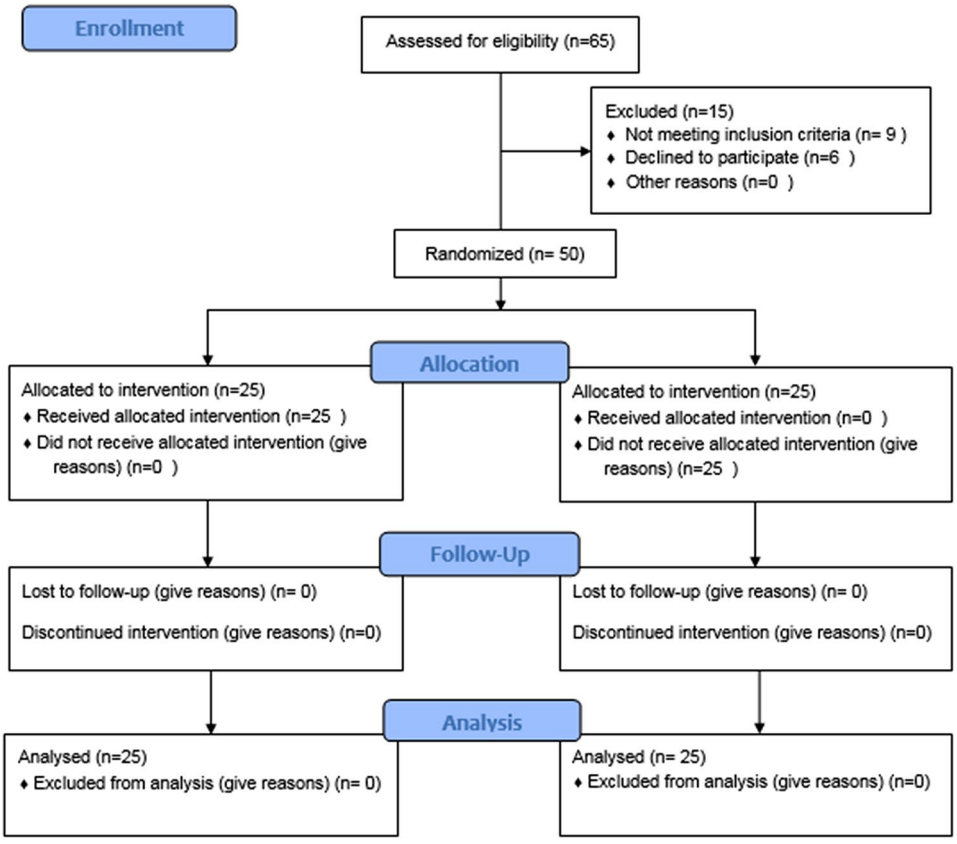

Fig. 1 Consort diagram. Flowchart of the study

Table 1 Scoring of intubation condition

Score	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cord	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Jaw relaxation	Complete	Slight	Stiff	Rigid
Limb movement	None	Slight	Moderate	Severe

anesthesia was maintained with 1–2% Isoflurane and 0.1–2 µg/kg/min remifentanil. Ventilator rate was adjusted in order to maintain PCO2 between 35 and 40 mmHg. Atropine 0.02 mg/kg and neostigmine 0.04 mg/kg were used as neuromuscular blocking revers agent before extubation. Extubation was done with the children resumed consciousness and could breathe spontaneously after surgery.

Primary and secondary outcomes

The primary outcome of this study was the Scoring of intubation in two groups. Intubation scoring was assess according to Table 1 [14, 15]:

The best score is one for all factors (excellent condition). The acceptable status is two for all factors and poor condition was considered when each factor was more than two. We considered excellent and acceptable conditions as successful intubation and poor condition as failed intubation. Secondary outcomes included non-invasive measurements of mean blood pressure and heart rate before and after induction and one minute after intubation were assessed too. Also, complications during anesthesia were also recorded if occurred.

Ethical approval and consent to participate

This study was approved by the ethical committee of Mashhad University of Medical Sciences with reference number IR.MUMS.MEDICAL.REC.1399.381. The study protocol was registered in Iranian Registry of Clinical Trial on 24/05/2021 and its IRCT registration number is IRCT20201028049177N1(https://www.irct.ir/search/result?query=@irct_id:IRCT20201028049177N1). All parents or guardians were informed about the study protocol and signed the written informed consent.

Sample size and statistical analysis

The sample size based on the similar study assumption (the rate of successful intubation in two study group 90% and 53%) [16] and type one error 5%, type two error 20% was calculated 20 patients in each study group and because of probable loss, 25 participants in each group were considered.

Table 2 Demographics of patients in study groups

Variable	Group D ($n=25$)	Group A ($n=25$)	*P* value
Gender n (%)	Male 15 (60) Female 10 (40)	Male 21 (84) Female 4 (16)	0.05*
Age (mean ± S.D) year	7.98 ± 2.06	8.52 ± 2.14	0.55**

** Fisher exact test, ** Mann Whitney; Group D = Dexmedetomidine, Group A = Atracurium*

Table 3 Comparison of heart rate and blood pressure immediately and one minute after induction in study groups

Characsteristics	Group D ($n=25$)	Group A ($n=25$)	*P* value
Before induction			
Heart rate (mean ± S.D) per minute	102.48 ± 13.89	103.96 ± 11.03	0.07
Mean atrial blood pressure (mean ± S.D) mmHg	82.40 ± 11.63	90.28 ± 9.18	0.005
Immediately after induction			
Heart rate (mean ± S.D) per minute	75.08 ± 16.23	95.44 ± 14.03	0.001>
Mean atrial Blood pressure (mean ± S.D) mmHg	81.16 ± 10.75	82.32 ± 8.42	0.77
One minute after intubation			
Heart rate (mean ± S.D) per minute	89.80 ± 13.01	101.56 ± 12.35	0.04
Mean atrial Blood pressure (mean ± S.D) mmHg	88.16 ± 11.47	88.92 ± 10.77	1

Group D = Dexmedetomidine, Group A = Atracurium

All data were entered into SPSS 19. To compare categorical variables between two groups, Chi square test or Fisher's exact test was used. For comparing quantitative variables, Mann Whitney test or Independent T-test was used based on the results of kolmogrov-smirnov test. P value less than 0.05 considered as statistically significant.

Results

We enrolled 25 participants in each group. The mean age of participants in each group and distribution of gender is shown in Table 2.

Table 4 Comparison of cough and limb movement in two groups

Characsteristics	Group D ($n=25$)	Group A ($n=25$)	*P* value
Cough			
None Cough n (%)	13 (52)	21 (84)	0.01
Slight Cough n (%)	12 (48)	3 (12)	
Severe Cough n (%)	0	1 (4)	
Limb Movement			
None n (%)	11 (44)	15 (60)	0.19
Slight n (%)	9 (36)	9 (36)	
Moderate n (%)	5 (20)	1 (4)	

Group D = Dexmedetomidine, Group A = Atracurium

Table 3 shows comparison of blood pressure and heart rate, immediately and one minute after induction in two study groups. The heart rate before induction had no significant difference in two study groups ($P=0.07$). Immediately after induction and one minute after it, heart rate was statistically significant higher in group A than group D ($P<0.001$ & $P=0.04$ respectively). O2 saturation was 100% in three measurements in both groups.

Intubation quality scores are shown in Fig. 2. According to Fig. 2, intubation scores were better in group A than group D, but all patients in both study groups got the intubation scores between 5 and 9, and thus they were in excellent intubation condition category. All the intubations in our study were successful.

Limb movement and cough were assessed after induction. According to Table 4, there was no significant difference between two groups in limb movements ($P=0.19$) but coughing was significantly higher in group A rather than group D ($P=0.01$). We did not detect any complication in both groups.

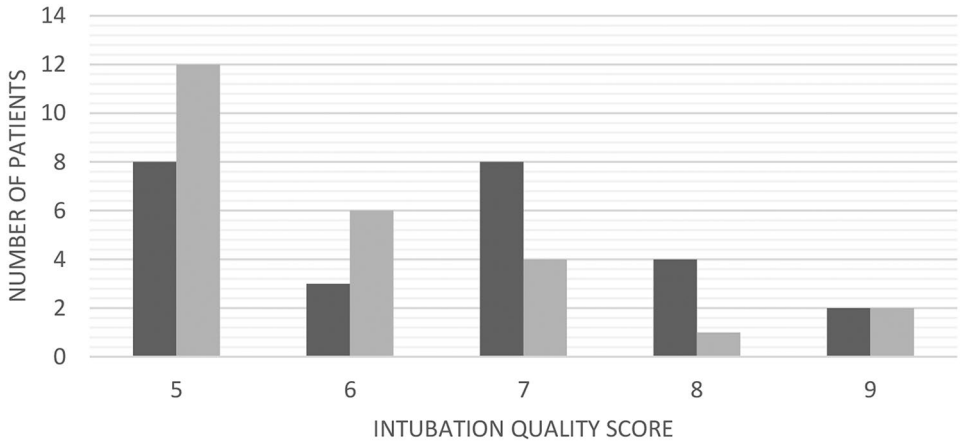

Fig. 2 Histogram of intubation quality score; Black column = Dexmedetomidine, Gray column = Atracurium

Discussion

Our findings showed that dex-sufenta-propofol is a valid alternative to the use of atra-sufenta- propofol to create acceptable intubating conditions in children between 6 and 12 years of age. It should be noted that all of our intubation in both groups were successful and, in this respect, there is no difference between the two groups. Priority of group D rather than Group A was in lesser cough and hemodynamic consistency during and after induction. The same efficacy was observed in both study groups.

Typically, the scoring system of Viby-Mogensen and colleagues, compares intubation conditions with and without the prescription of neuromuscular blocking agent [15]. In this system, both 'excellent' and 'good' categories, specify a successful intubation. But this combination occult the differences between two techniques [6]. Whichever approach is used for scoring, intubation conditions without neuromuscular blocking agents have serious consequences [17]. Complications of intubation without neuromuscular blocking agents are more common than the side effects of neuromuscular blocking agents itself [18]. Generally, the intubation conditions were categorized as excellent, acceptable, and poor based on the easy or hard laryngoscopy, jaw relaxation, vocal cord condition, coughing, and limb movement. It is obvious that postoperative pharyngolaryngeal complications are less common in patients who are classified in "excellent" category. In our study, due to the slow injection of dexmedetomidine and only in one loading dose we did not detect any complications such as bradycardia or hypotension etc. Moreover, the rate of excellent intubation conditions in group D was 32% and in group A was 48% and all intubations were successful. In a previous study, the results showed that induction with 3 mg/kg propofol and 1, 2, and 3 μg/kg remifentanil, lead to 50%, 69%, and 82% successful intubation respectively. Also, this study demonstrated that 29%, 35%, and 48% of cases had excellent intubation conditions respectively. The authors mentioned that the combination of propofol (3 mg/kg), remifentanil (2 μg/kg) and dexmedetomidine (1 μg/kg) improved the intubation condition rather than propofol (3 mg/kg), remifentanil (2 μg/kg) and a higher dose of remifentanil [19].

Dexmedetomidine is a widely used drug in pediatric perioperative management. It is administered orally (2.6 μg/kg) 30 min before surgery and also intra-nasally (3 μg/kg) 60 min pre-induction of anesthetic drugs [20]. In pediatric perioperative management, dexmedetomidine facilitates the separation of the child from their parents due to its sedative and anti-anxiety properties. Intravenous infusion of dexmedetomidine (1 μg/kg) as a general anesthetic drug reduces the concentrations of propofol and remifentanil need for intubation by 1.29 μg/ml and 0.64 ng/ml, respectively [21]. Dexmedetomidine (1 μg/kg) is a cost-effective drug that reduces the need for sedatives and analgesics drug during surgery, also in children who were under sevoflurane anesthesia, decrease the occurrence of postoperative agitation, nausea and vomiting [22].

Dexmedetomidine (1 μg/kg) is usually administered as an IV infusion within 10 min. However, the study showed that in patients without underlying disease, rapid infusion of 0.25, 0.5, 1.0, or 2.0 μg/kg dexmedetomidine in 2 min was tolerated without any consequence and a biphasic hemodynamic effect was observed [23]. Following the administration of dexmedetomidine, initially and temporarily, arterial blood pressure increases, then within 3 min due to stimulation of α2-adrenoceptors in vascular smooth muscle cell, arterial blood pressure reaches its peak and then due to stimulation of α2-adrenoceptors in CNS, a long-term reduction in blood pressure occurs. Another study showed that increasing the concentrations of dexmedetomidine in plasma from 0.5 to 3.2 ng/ml could cause a significant increase in blood pressure [24]. The results of the study showed that, after administration of dexmedetomidine, heart rate was significantly lower in comparison with Atracurium. There was no effect on blood pressure. Wei et al. showed that following administration of dexmedetomidine, systolic and diastolic blood pressures increased and returned to baseline with propofol and remifentanil. In this study, the blood pressure of three patients increased, which returned to normal condition after prescription of propofol and remifentanil [25].

The negative chronotropic effects of dexmedetomidine and sufentanil should be considered.

Bradycardia may be due to stimulation of the central vagus nerve and peripheral μ-opioid receptors by dexmedetomidine and sufentanil, respectively [26]. The results of the study demonstrated that although the time to peak of atracurium was respected in all patients but severe cough was more prevalent in group A compared with group D.

In this study we enrolled children with ASA class I or II and the results of the study cannot be used for critically ill patients. This is a limitation of our study. Also, safety aspects such as delayed awakening, sore throat, hoarseness, evidence of airway trauma, quality of recovery, and etc were not measured, making it hard to make any remarks on safety. Further large-scale and multi-center studies can be helpful and recommended.

Conclusion

In children aged 6–12 years, the administration of intravenous dexmedetomidine 1mcg/kg over a period of 10 min before the induction of anesthesia with sufentanil 0.3 mcg/kg and propofol 3 mg/kg showed no statistically significant difference in quality of intubation score when

compared to the use of 0.5 mg/kg atracurium to facilitate intubation. Decreased heart rate and less coughing were observed when using dexmedetomidine.

Abbreviations

ASA American Society Anesthesiologists
IV Intra Venous
CNS Central Nervous System

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13104-024-07072-4.

Supplementary Material 1

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Author contributions
M.A. designed the study, collected data, and cooperated in drafting the manuscript. S.G. supervised the study protocol implementation, collected data, and cooperated in drafting the manuscript. S.S. supervised the study protocol implementation, collected data, and cooperated in drafting the manuscript. A.N. collaborated in writing manuscript. M.G. Check the accuracy of the data and enter the data into the SPSS file and cooperated in drafting the manuscript. S.N. participated in the design of the study protocol, data analysis, and interpretation of the results, cooperated in drafting the manuscript, and amended the manuscript according to the editor's comments. All authors reviewed the manuscript.

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Data availability
The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Mashhad University of Medical Sciences controlled this randomized clinical trial study from 2018 until 2020, and 50 participants between 6 and 12 years who were candidate for tracheal intubation under general anesthesia were included. All methods were carried out in accordance with Helsinki guidelines. The Ethical Committee of Mashhad University of Medical Sciences approved the study method with approval number IR.MUMS.MEDICAL.REC.1399.381 and written informed consent was obtained from a parent or guardian for participants between 6 and 12 years.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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