



## A Comparison of Oral Clonidine and Oral Diazepam as A Preanaesthetic Medication in the Paediatric Patients Undergoing Adenotonsillectomy

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### ABSTRACT

Premedication drugs are used to provide sedation and anxiolysis prior to surgery and achieve optimal intraoperative haemodynamic stability and depth of anaesthesia.

**AIM:** To evaluate the efficacy of oral clonidine and oral diazepam in preoperative sedation, anxiolysis, intraoperative haemodynamics, postoperative analgesia.

**TYPE OF STUDY:** Prospective, double blinded, randomized, comparative parallel group study.

**METHOD:** 40 Patients were given 4 micrograms/kg of clonidine and other 40 patients were given 0.15mg/kg of diazepam. Each patient was assessed as per sedation scores, anxiety scale and postoperative pain scale.

**RESULTS:** Higher degree of sedation (70%) and anxiolysis(67.5%) were observed in clonidine group. Heart rate and blood pressure were significantly lower during surgery in clonidine group. 95% of patients in clonidine group had adequate postoperative analgesia even two hours after surgery.

**CONCLUSION:** Clonidine was proved to be superior to diazepam in children undergoing adenotonsillectomy with regard to preoperative sedation, anxiolysis, Intraoperative haemodynamic stability, and postoperative analgesia.

### KEYWORDS

SEDATION, HAEMODYNAMICS, ANALGESIA

### INTRODUCTION:

In children, premedications are used to provide sedation and anxiolysis before surgery, easy separation from parents, acceptance of face mask, or intravenous cannulation and to provide optimal intubating conditions, cardiovascular stability, and an adequate depth of anaesthesia.

An ideal premedicant should be effective orally, a potent analgesic and a non emetic. It should have the ability to minimize the dose of induction agents, and to not impair cardiovascular stability or quality of respiration.

Many oral premedication drugs have been found to be safe and as effective as intramuscular premedications and do not delay discharge after outpatient surgery.

Recently rapidly acting drugs have been administered via innovative routes just before anaesthetic induction. Intranasal and oral narcotics used for this purpose have associated complication of chest rigidity.

Clonidine by its action on central alpha 2 receptors, controls the outflow of catecholamine and thus maintains preoperative haemodynamic stability and also act as a potent analgesic.

Thus in our study we have assessed the efficiency of clonidine in causing preoperative sedation, Intraoperative haemodynamic stability and postoperative analgesia in children aged 7-12 years undergoing adenotonsillectomy. Thereby clonidine as a premedicant for children, and also its complications have been evaluated.

### AIM:

To evaluate the efficacy of oral clonidine, as premedicant, assessing preoperative sedation and anxiolysis, Intraoperative haemodynamic stability and postoperative analgesia in children undergoing adenotonsillectomy in comparison to the efficacy of oral diazepam.

To evaluate the side effects and complications if any, that may

arise with use of oral clonidine for premedication.

### MATERIALS AND METHODS:

This prospective clinical study was conducted at government hospital, villupuram from june 2015 to june2016 in patients aged 7-12 years undergoing adenotonsillectomy.

### STUDY DESIGN:

Double blinded, randomized, comparative parallel group design was employed.

### SAMPLE SIZE:

80 patients belonging to ASA I of both sexes aged 7-12 years undergoing adenotonsillectomy were randomly divided into two groups of forty each. Group C patients were tablet clonidine 4 microgram/kg per oral and group D patients were given tablet diazepam 0.15mg/kg per oral 90 minutes before surgery. Sedation and anxiety scores were recorded preoperatively. Haemodynamic changes during laryngoscopy and intubation were recorded. Intraoperative haemodynamic changes were also assessed. Post operative pain scores were recorded every half an hour for the first four hours after extubation.

### PROCEDURE:

Preoperative assessment: Patients admitted to surgical units were assessed preoperatively for anaesthetic fitness. Anthropometry, biochemical parameters, ECG, chest roentgenogram and vitals were monitored prior to premedication.

Patients in group C were given tablet clonidine 4 microgram/kg orally 90 minutes before induction and patients in group D were given tablet diazepam 0.15mg/kg as premedication 90 minutes before induction of anesthesia.

Heart rate, blood pressure and O<sub>2</sub> saturation were monitored every 60 to 90 minutes after premedication and just prior to induction of anesthesia. The patients were assessed for sedation and anxiety score prior to induction.

Conduct of anesthesia: Intravenous glycopyrrolate 0.1mg was

given. Fluids were started with dextrose half normal saline and maintained with ringer lactate. Anesthesia was induced with 2.5% thiopentone sodium in a dose of 5mg/kg. Patients in both groups received intravenous fentanyl 2 micro gram/kg. Following this atracurium 0.5mg/kg was administered to produce adequate neuromuscular block. Once the respiration stopped, the patient was ventilated with 100% oxygen. 2 minutes after atracurium, laryngoscopy was performed.

After intubation of trachea mechanical ventilation was started and anesthesia was maintained with 66% N<sub>2</sub>O and O<sub>2</sub>. Heart rate and blood pressure were recorded at 1,2,4,6,8 and 10 minutes after intubation and then monitored constantly throughout surgery and recorded as per the protocol. Intra operatively, additional drugs were administered according to the predetermined criteria. Incremental top up doses of atracurium were given according to surgical relaxation requirements. Anesthetic management was designed to maintain heart rates within 25% and arterial pressures within 20% limits of baseline values and also within clinically acceptable limits.

**CRITERIA FOR INTERVENTION:**

Hypotension was treated by, fluid challenge with 50ml of balanced salt solution and 3mg bolus of intravenous ephedrine if there was no response to the fluid challenge.

Bradycardia was treated by giving atropine 20 microgram/kg increments intravenously.

Hypertension and tachycardia sustaining more than 5 minutes was treated by, halothane inhalation in 0.5% increments to deepen anaesthesia and to maintain baseline HR and BP. Supplemental fentanyl 0.5 microgram/kg i.v if necessary.

Halothane, if administered was terminated about 10-15 minutes before reversing the patient. N<sub>2</sub>O was terminated when the neuromuscular block was being antagonized with atropine 25microgram/kg and neostigmine 50 microgram/kg.

Patients were then extubated and observed for 10-15 minutes by monitoring the vitals including the respiration. They were then shifted to the recovery room and closely observed for any signs of adverse effects. On awakening, assessment of pain was made and it was continued into the postoperative period for four hours. Maintenance intravenous fluids were continued into the postoperative period.

**CLINICAL ASSESSMENT:**

On arrival in the operation theatre each patient was assessed and scored for the effects of premedication on sedation and anxiety.

**SEDATION SCORES**

- GRADE 1: awake and alert
- GRADE 2: awake, calm, lying down quietly
- GRADE 3: drowsy, arousable on oral command
- GRADE 4: drowsy, arousable on mild physical stimulus
- GRADE 5: asleep, sedated, arousable on vigorous physical stimulus

**ANXIETY SCORES**

- GRADE 1: combative
- GRADE 2: tearful
- GRADE 3: apprehensive
- GRADE 4: calm

**POSTOPERATIVE PAIN SCALE**

- GRADE 1: patient restless, screaming with pain
- GRADE 2: patient complaining of severe pain and demands relief
- GRADE 3: patient comfortable, complains of pain on questioning
- GRADE 4: no complaint of pain

**STATISTICAL ANALYSIS**

Z test was applied for studying statistical significance. Epi info

software package was used. P value <0.05 was considered statistically significant.

**OBSERVATION AND RESULTS:**

Patients in group C and D were comparable in distribution of age, sex, ASA status, and baseline values of heart rate and arterial pressures. Clonidine was well tolerated by all patients and no serious drug related side effects were recorded.

**TABLE 1: DEMOGRAPHIC CHARACTERISTICS**

Parameters	Group C n=40	Group D n=40
Age (in years)	10.25 (7-12)	10.375 (7-12)
Sex		
Male	21(52.5%)	17(42.5%)
Female	19(47.5%)	23(57.5%)
ASA status	I (100%)	I (100%)
Baseline values		
Heart rate (beats/min)	99.5 (80-100)	101.88 (85-124)
Blood pressure (mm/hg)		
Systolic	108 (90-120)	107.5 (100-130)
Diastolic	71 (60-80)	69.75 (60-80)

p>0.05

The patients were aged 7-12 years in both the groups. The mean age was 10.25 in group C and 10.375 in group D. All the patients belonged to ASA I medical status. The baseline heart rate was on an average 99.5 in group C and 101.88 in group D. The baseline systolic blood pressure was on an average 108 in group C and 107.5 in group D while the diastolic pressures were 71 and 69.75 in both the groups respectively.

**TABLE 2: SEDATION SCORES**

Degree of sedation	1	2	3	4	5
Group C n=40	0	10	28	2	0
Group D n=40	35	4	1	0	0

P<0.05

There was significantly higher degree of sedation in the clonidine group of patients. Majority (70%) of them were under grade 3 sedation score. Majority of the patients (87.5%) in group D were under grade 1. 10 patients (25%) who received clonidine were under grade 2 and 4 patients (10%) in the diazepam group were under grade 2. 2 patients in group C were under grade 4 sedation score, while none of the patients in group D were under grade 4. None of the patients in both the groups were under grade 5 sedation score. None of the patients had a fall in saturation requiring oxygen by mask. There was statistically significant degree of sedation in group C when compared to group D.

**TABLE 3: ANXIETY SCORES**

Anxiety score	1	2	3	4
Group C n=40	0	0	13	27
Group D n=40	4	24	13	0

P<0.05

Majority of patients(67.5%) in group C were under grade 4 anxiety while in group D majority (60%) were under grade 3 anxiety. Statistical significance was seen between the groups considering grade 3 and 4 anxiety score. 32.5% of patients in both the groups were under grade 3 anxiety.

None of the patients in group C were under grade 1 and 2 while 10% of the group D were under grade 1.

**TABLE 4: INTRAOPERATIVE HAEMODYNAMICS**

At 90 minutes after premedication and also after shifting the patient to the operating table there was a significant difference in heart rate and blood pressure between group C and group D.

	Group C	Group D	
Baseline Heart rate	99.5	101.87	
Systolic pressure	108	107.5	p>0.05
Diastolic pressure	71	69.75	
Intraoperative Heart rate	104.15	119.52	
Systolic pressure	99	120.75	P<0.05
Diastolic pressure	70.65	74.25	

The increase in heart rate associated with laryngoscopy and tracheal intubation was attenuated significantly in group C as compared with group D. The maximum heart rate after intubation was less in group C than in group D. The systolic and diastolic blood pressure changes within 10 minutes after intubation were also similar in group C as in group D. Patients in group C had a statistically significant lower heart rate and blood pressure during the surgery as compared to patients in group D.

Intraoperatively, the incidence of hypertension and tachycardia was significantly greater in group D as compared to group C. But none required intervention for tachycardia or hypertension since they did not exceed the higher limits. Intraoperatively patients in group C had a mean heart rate of 104.15 beats per minute, a mean systolic pressure of 99 mm of Hg and a mean diastolic blood pressure of 70.65 mm of Hg as compared to the values of 119.52 beats per minute, 120.75 mm of Hg and 74.25 mm of Hg respectively in group D.

**TABLE 5: POST OPERATIVE ANALGESIA SCALE**

	Group C				Group D			
	1 <sup>st</sup> hr	2 <sup>nd</sup> hr	3 <sup>rd</sup> hr	4 <sup>th</sup> hr	1 <sup>st</sup> hr	2 <sup>nd</sup> hr	3 <sup>rd</sup> hr	4 <sup>th</sup> hr
Grade 1	0	0	0	0	0	0	16	25
Grade 2	0	0	2	4	20	22	20	15
Grade 3	30	32	34	36	25	18	4	0
Grade 4	10	8	4	0	5	0	0	0

P<0.05

Post operative analgesia was assessed in all patients every half an hour for a period of four hours after extubation. 95% of patients in group C remained in grade 3 and 4 even after two hours after surgery while only 10% of patients in group D were in grade 3 after two hours requiring analgesic supplementation. This was statistically significant.

The analgesia noted in first two hours after surgery might be attributed to the Intraoperative fentanyl. Children in group C remained in grade 3 and 4 even after two hours postoperatively while children in group D sought relief for pain.

None of the patients in both the groups required intervention intraoperatively with fentanyl, ephedrine, atropine, or halothane. None of the patients in both the groups had postoperative problems like vomiting, airway obstruction. None required intravenous volume replacement or blood transfusion for blood loss

**DISCUSSION:**

Published paediatric experience with oral clonidine is limited. Oral administration of clonidine, as premedication to provide sedation for children undergoing ophthalmological surgery

has been studied by Mikawa et al. a preoperative dose of 4 microgram/kg provided good to excellent sedation, superior to diazepam, allowing separation from parents in their study. This was comparable to the present study where appreciable sedation was noted with clonidine when compared to diazepam (p<0.05).

In a study by Mikawa et al 90 children between 5 and 12 years of age undergoing minor surgery were studied. Patients were randomly assigned into three groups receiving a placebo, clonidine 2 microgram/kg or 4 microgram/kg as premedication 105 minutes before induction for comparison. All children received atropine 0.03 mg/kg 60 minutes before induction. They found that clonidine 4 microgram/kg provided better preoperative sedation than placebo or clonidine 2 microgram/kg.

Hence clonidine 4 microgram/kg was used in this study. Clonidine premedication produced significant sedation in 75% of patients in this study. This was comparable to the study by Mikawa et al. significant anxiolysis was seen in group C while 60% of patients were tearful and anxious in group D. This may be attributed to the central sedative and anxiolytic properties of clonidine combined with its action on nucleus tractus solitarius.

In this study, none of the patients in both the groups required intervention for heart rate or blood pressure. But the heart rate and blood pressure were on higher limits in group D patients while patients in group C were haemodynamically stable and maintained their heart rate and blood pressure to the baseline values. But none required treatment for hypertension, hypotension, tachycardia, or bradycardia. This correlates well with the study by Eleanor et al where 36 children aged 7-12 years undergoing adenotonsillectomy were studied. No incidence of hypotension or bradycardia were reported in their study also.

Eleanor et al 's study demonstrated the effectiveness of clonidine as an analgesic in paediatric adenotonsillectomy. They compared with Intraoperative fentanyl as analgesic. In their study bupivacaine 0.25% with 1:200000 epinephrine to a maximum of 2.5 ml per side was infiltrated into the tonsillar fossa prior to incision by the surgeon. In our study local infiltration was not done, still significant postoperative analgesia is noted (97.5%) as compared to 10% in control group even after 4 hours (p<0.05). 98% of children in control group were in grade 1 and 2 requiring analgesic supplementation within the first 2 hours.

Adenotonsillectomy requires preoperative haemodynamic stability with less postoperative agitation due to moderate to severe postoperative pain. A prolonged analgesic effect of clonidine may be advantageous compared to shorter acting analgesic effects of intravenous opioids. In this study significant postoperative analgesia was seen in the clonidine group during the observation period comparing well with the study by Mikawa et al.

In study by Eleanor et al no adverse effect were noted by sending three children home after six hours observation. Clonidine has haemodynamic side effects. Although no children in this study required treatment for bradycardia or hypotension, younger children may require anticholinergic premedication to prevent important bradycardia and decreased cardiac output. Clonidine also reduced the need for postoperative analgesia more than diazepam (p<0.05).

In this study oral clonidine was comparably superior to oral diazepam as a premedicant in terms of postoperative sedation, anxiolysis, Intraoperative haemodynamic stability and the need for postoperative analgesics.

**CONCLUSION:**

Clonidine in the dose of 4 microgram/kg per oral has proved to be superior to diazepam in the dose of 0.15mg/kg per oral in children in the age group of 7-12 years undergoing aden-

otonsillectomy with regard to postoperative sedation, anxiolysis, Intraoperative haemodynamic stability, and postoperative analgesia.

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