



Original Research Article

Comparative Study of Oral Clonidine and Diazepam As Premedicants in Children

Authors

Anoop Prabhakaran¹, Raju Rajan², Geetha N K³

^{1,2}Assistant Professor, Department of Anaesthesia, Govt. Medical College, Thiruvananthapuram

³Professor, Department of Anaesthesia, Govt. Medical College, Thiruvananthapuram

*¹Corresponding Author

Raju Rajan

Assistant Professor, Department of Anaesthesia, Govt. Medical College, Thiruvananthapuram

ABSTRACT

In a prospective observational study, the efficacy of oral Clonidine vis a vis Diazepam as premedicant was assessed in children undergoing elective surgery. Eighty children aged 2-12 years, undergoing general anaesthesia were studied. Forty children received oral diazepam 0.2 mg/kg (group A) and another forty children received oral clonidine 2 µg/kg (group B) 90 minutes before induction of anaesthesia. The level of sedation, parental separation score, quality of mask acceptance and occurrence of complications were noted and compared between the groups. Clonidine 2 µg/kg produced sedation better than diazepam 0.2 mg/kg ($p > 0.001$). Parental separation score and quality of mask acceptance was much better in the clonidine group ($P > 0.001$). Though hypotension and bradycardia were observed in 5% of the clonidine group, it was not clinically significant. Based on composite score, none of the children in diazepam group had an acceptable score as compared to 32.5% children in the clonidine group. 60% of the diazepam group children had an unacceptable score

Keywords: Diazepam, Clonidine, Premedication.

INTRODUCTION

Hospital admission, anaesthesia and surgery are stressful experiences for children, which may lead to psychological trauma and personality changes. Anaesthetic management begins with the pre-operative psychological preparation of patient and administration of a drug or drugs selected to produce specific pharmacological responses prior to induction of anaesthesia. Pre-anaesthetic medication in children is to allay anxiety, to prevent pain and to control the reflex effects of vagal stimulation.

Clonidine, an alpha₂ adrenoceptor agonist, was

introduced into clinical practice as an antihypertensive medication approximately 20 years ago. The alpha₂ adrenoceptor agonist (α_2) clonidine has been shown to exhibit anaesthetic, sedative, sympatholytic and analgesic properties.^{1,2}

It has recently been found to be an effective premedicant in adults, providing preoperative sedation, post-operative analgesia, perioperative hemodynamic stability and reduction in the volatile anaesthetic requirement.

Anxiety and pain are two factors causing considerable emotional stress in children. Recent advances on alpha₂ agonists focus on the possible

use of clonidine as sedative and analgesic. It has excellent bioavailability following oral administration. The prospect of sedation and analgesia provided by one drug in a single oral dose prompted us to study its efficacy as a premedication in paediatric patients.

MATERIALS AND METHODS

The present study was a prospective observational study conducted at the Department of anaesthesia, SAT Hospital Medical College, Trivandrum, after approval of the hospital ethics committee.

Primary objective

To compare the sedative and anxiolytic effects of oral Clonidine and oral Diazepam as premedicant in paediatric patients of 2-12 years during:

1. Separation from parents
2. Level of Sedation on arrival in operation theatre
3. Quality of facemask acceptance

After getting written informed consent from the parents 80 children of age group 2 to 12 years, belonging American Society of Anaesthesiologist (ASA) class 1, they were prospectively divided into two groups of 40, group A and B.

Group A ----oral diazepam was administered to children at a dose of 0.2mg/kg

Group B ---- oral clonidine was administered at 2 µg/kg to children.

Both drugs were diluted in 10ml of 5% dextrose. Children with documented allergy to clonidine, diazepam and systemic disorders were excluded from the group. Children undergoing elective urologic and orthopedic procedures involving minimal blood loss were chosen. All demographic and clinical basal measurements were taken. Clonidine and diazepam premedication were prepared by dissolving crushed tablets of clonidine 100 µg (Arkamine) and diazepam 5mg in 10ml of 5% dextrose. The drug was constituted and given to the child by the nurse in the pre-medication room 90 minutes before the procedure. At 15 minutes interval, we observed the patient's vital parameters- heart rate (HR), systolic BP (SBP), diastolic BP (DBP), and respiratory rate (RR).

Level of sedation was recorded according to three

points scale

1=Tearful/ combative

2 =Alert/ aware

3=Drowsy/sleepy

Parental separation score i.e. behaviour of the child while entering the theatre was assessed using three points scale

1=Poor (anxious and combative)

2=Good (anxious but easily reassured)

3=Excellent(sleepy and calm).

Children were allowed to breathe 50% N₂O and 0.5 to 4% sevoflurane in oxygen through a mask.

Quality of mask acceptance was graded with a four points scale

1=Poor (combative and angry)

2=Fair (fearful and not easily calmed)

3=Good (fearful but easily calmed)

4=Excellent (unafraid and cooperative)

Based on the above three parameters, a composite score is calculated on a scale of 1- 10. Wherein, a composite score of:

1 to 4 - Unsatisfactory

5 to 7 - Satisfactory

8 to 10 - Acceptable

If the child was cooperative, an intravenous access was established. If not, the inhalational induction was continued till the child allowed intravenous access to be secured. Thiopentone followed by vecuronium was administered and trachea was intubated after three minutes. Anaesthesia was maintained with 66% N₂O and 0.5 to 3% sevoflurane in oxygen with controlled ventilation. No other sedative was administered.

Incidence of adverse effects i.e. hypotension (SBP< 70mm of Hg) hypertension(SBP>40 mm of Hg), bradycardia (HR<60/min) Respiratory distress rate < 12 / min, desaturation(SpO₂<90%)for 15 minutes) were noted.

Bradycardia was treated with atropine. Hypotension was corrected using intravenous fluids; Atropine was administered if it was accompanied by bradycardia; if persistent and severe, an infusion of dopamine was planned.

Data analysis

Data was analysed using computer software, Statistical Package for Social Sciences (SPSS)

version 10. Data are expressed in its frequency and percentage as well as mean and standard deviation. To elucidate the associations and comparisons between different parameters, Chi square (χ^2) test was used as nonparametric test. Student's t test was used to compare mean values between two groups. Mann Whitney's U test was employed to compare non-parametric variable between two groups. For all statistical evaluations, a two-tailed probability of value, < 0.05 was considered significant.

RESULTS

The 2 groups were identical with general characteristics like age, weight, sex, ASA score and duration of surgery.

AGE

Table 1. Age distribution in the two groups

Group		Age (in years)
Clonidine	Diazepam	
26 (65.00%)	29 (72.50%)	< 6
14 (35.00%)	11 (27.50%)	>= 6

Chi square = 0.524; $P > 0.05$

It is observed from Table 1, that the mean age was slightly higher in the Diazepam group (72.5%) as compared to clonidine group in the <6 years (65%) category and the mean age was slightly higher in the clonidine group (35%) as compared to diazepam group (27.5%) in the >6 years category. However, statistical test (Chi square = 0.524, $P > 0.05$) revealed that the difference noted was only due to sampling variation. The test happened to be insignificant. Therefore, it is inferred that both the groups were identical with respect to age and hence age will not have any influence over the final outcome measures.

GENDER

Table 2. Gender distribution in two groups

Group		Sex
Clonidine	Diazepam	
22 (55.00%)	21 (52.50%)	Male
18 (45.00%)	19 (47.50%)	Female

Chi square = 0.050; $P > 0.05$

While considering the sex of patients in diazepam group 52.5% were males and 47.5% females and

in the clonidine group, males were 55% and females 45%. There was no difference in final outcome measures due to sex difference. (Chi square-0.05 $P > 0.05$).

WEIGHT

Table 3. Weight distribution in two groups

Group		Weight (Kg)
Clonidine	Diazepam	
17 (42.50%)	22 (55.00%)	< 15 Kg
12 (30.00%)	11 (27.50%)	15 - 19 Kg
11 (27.50%)	7 (17.50%)	>=20 Kg

chi square = 1.573; $P > 0.05$

The two groups were identical with respect to mean weight (Table 3). In diazepam group in the <15 kg category there were 22 (55%) children compared to 17(42.5%) in the clonidine group. In the 15-19 kg category, there were 11(27.5%) children in the diazepam group compared to 12(30%) in the clonidine group. In the >=20kg category there were 7(17.5%) children in the diazepam group compared to 11(27.5%) in the clonidine group. There is only negligible difference between the two groups. Moreover, it is statistically established that both the groups were identical.

DURATION OF SURGERY

Table 4. Comparison of duration of surgery in two groups

Group		Duration of surgery (min)
Clonidine	Diazepam	
31 (77.50%)	30 (75.00%)	60 – 90
9 (22.50%)	10 (25.00%)	90-120

The duration of surgery was not significantly different in the two groups. 75% of the children in the diazepam group had their surgery finished in 60-90 minutes as compared to 77.5% in the clonidine group. Surgery was prolonged to more than 90 minutes in 25% of children in diazepam group and 22.5% children in the clonidine group. All the children belonged to ASA class I and accepted the premedication in the same manner. Despite the bitter taste of both the tablets, which was masked by 5% dextrose, none of the children spit it out. Both the groups accepted premedication well.

PARENTAL SEPARATION SCORE

The clonidine group gave better parental separation scores. None of the diazepam group patients had excellent parental separation scores, whereas only one patient in the clonidine group had a poor parental separation score. The finding is statistically significant. (Chi square =38.839,P<0.001).

Table 5. Comparison of parental separation score in two groups

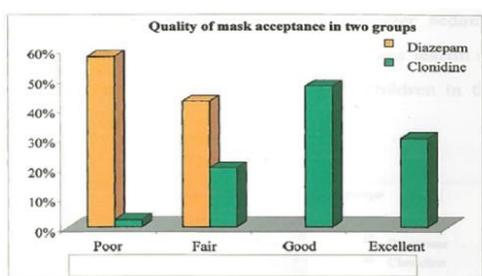
Group		Parental Separation score
Clonidine	Diazepam	
1 (2.50%)	27 (67.50%)	Poor
33 (82.50%)	13 (32.50%)	Good
6 (15.00%)		Excellent

Chi square = 38.839; P < 0.001

QUALITY OF MASK ACCEPTANCE

Mask acceptance scores were also better in the clonidine group as compared to the diazepam group. 77.5% children in the clonidine group had good/excellent quality of mask acceptance. None of the children in the diazepam group had good/excellent mask acceptance scores that was statistically significant. (Chi square = 54.407; P<0.001) (Fig 1)

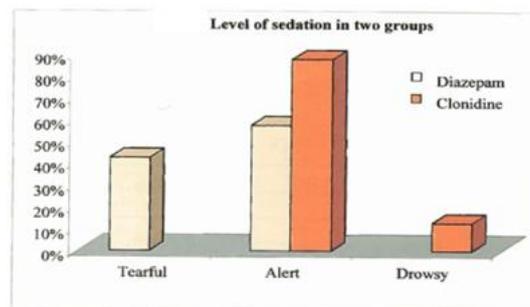
Quality of Mask Acceptance (Fig 1)



LEVEL OF SEDATION

Children of clonidine group had better sedative scores. None of the children in the clonidine group was tearful on arrival to the operation theatre as compared to 42.5% children in the diazepam group. Figure 2 shows, 42.5% children in the diazepam group was tearful on arrival to the operation theatre.

Level of Sedation (fig 2)



COMPOSITE SCORE

- 1 to 4 - Unsatisfactory
- 5 to 7 - Satisfactory
- 8 to 10 - Acceptable

It is observed that the clonidine group shows higher scores on all three (Sedation, Quality of mask acceptance, Parental separation) than the diazepam group. (Chi square = 36.541, P<0.001) (Fig:3)

Comparison of scores in the two groups(Fig:3)

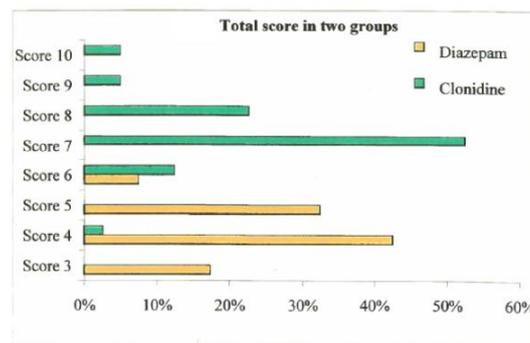


Table 6 shows that although most of the children in both the groups had a satisfactory score, none of the children in diazepam group had an acceptable score as compared to 32.5% children in the clonidine group. Also 60% of the diazepam group children had an unacceptable score <= 4

Table 6. Comparison of total score in two groups

Group		Total Score
Clonidine	Diazepam	
1 (2.50%)	24 (60.00%)	Unsatisfactory (1-4)
26 (65.00%)	16 (40.00%)	Satisfactory (5-7)
13 (32.50%)		Acceptable (8- 10)

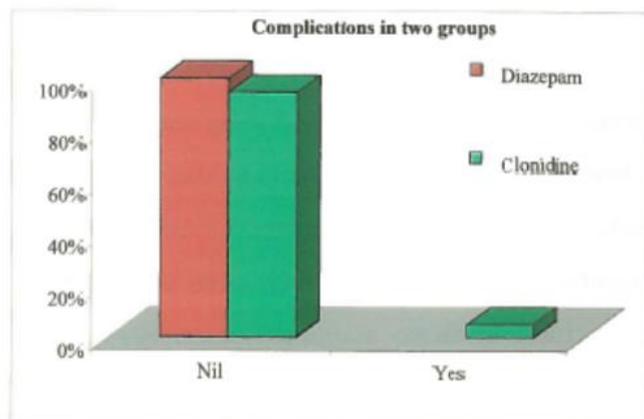
Chi square = 36.541; P < 0.001

COMPLICATIONS

Bar diagram (fig 4) shows a 5% incidence of

complication in the clonidine group which was not statistically significant. ($P>0.05$) 4 children in the clonidine group experienced complications, 2 had bradycardia and 2 suffered from hypotension, which was appropriately managed. None of the children in diazepam group experienced any complications.

Fig: 4 – COMPLICATIONS IN 2 GROUPS



DISCUSSION

So far, we have not yet found the ideal premedicant in children. The search is still on. In the last few years many reports have been published addressing the desirable properties of alpha 2 agonists in the perioperative period. In our study, clonidine has been found to be superior to diazepam as pre-medicant in children. Children premedicated with clonidine had superior level of sedation, parental separation anxiety and face mask acceptance compared to diazepam group. The study was limited to the children older than 2 years as cardiac output in younger ones depend on heart rate and clonidine is known to give rise to bradycardia. Our findings were comparable to the study by Malde et al.³ In their study, they found that, clonidine treated groups had significantly superior sedation compared to diazepam group. A single oral dose of clonidine 2 µg/kg can provide good anxiolysis and postoperative analgesia with minimum side effects. In adults, 0.3mg of oral clonidine produced sedation and anxiolysis.⁴ Carabine et al⁵ noted that higher doses had better sedative effect; 0.2mg is effective for anxiolysis. But some studies concluded that there was no difference between clonidine and diazepam as premedicants.^{6,7,8}

Dhamani et al⁹ in their meta-analysis summarized that premedication with clonidine produces more satisfactory levels of sedation at induction, decreases emergence agitation and produces more effective early post-operative analgesia, when compared with midazolam. Premedication with clonidine is superior to midazolam in terms of producing sedation, decreasing post-operative pain and emergence agitation. Compared with diazepam, clonidine was superior in terms of preventing Post Operative Nausea Vomiting during strabismus surgery without Post Operative Nausea Vomiting prophylaxis.

Mikawa et al¹⁰ found better parental separation and mask acceptance with oral clonidine. In another study by Mikawa et al¹¹, lower pain scores, greater pain free period and less requirement of rescue analgesics in children premedicated with clonidine were demonstrated.

Malde et al³ noted that the incidence of postoperative hypotension was 8% with clonidine 4 µg/kg. In the present study, complications were noted in 5%. Clonidine is suitable as a premedicant in children but the necessity of vigilant post-operative monitoring is very important. There was no incidence of respiratory depression, desaturation, troublesome hypotension or bradycardia. Atropine premedication may be the reason for the same. The 4 children who had complications in the clonidine group were managed appropriately.

In the present study, clonidine premedication resulted in a calm, co-operative child without undue drowsiness, excellent anxiolysis, easy separation from parents, good mask acceptance and no respiratory depression.

Animal experiments and later human studies using neuraxial administration of clonidine have shown significant analgesia.^{12,13,14,15}

Further studies are required to establish clonidine as a safe and effective premedicant in children.

CONCLUSION AND SUMMARY

Level of sedation, parental separation and quality of mask acceptance were the parameters assessed to measure the quality of premedication. Vital

parameters were monitored at regular intervals perioperatively upto 24 hours after surgery. The result of study showed that children who received premedication with oral clonidine had better parental separation, sedation and mask acceptance scores. Based on the present study, oral clonidine is a superior premedicant compared to oral diazepam in producing better parental separation, sedation and quality of mask acceptance without significant side effects.

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