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Comparative evaluation of dexmedetomidine as a premedication given intranasally vs orally in children between 1 to 8 years of age undergoing minor surgical procedures

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Key points

Dexmedetomidine is an attractive alternative, as a pre-medication, to conventional drugs because of its non-interference with respiration. Dexmedetomidine, as a premedication, has been most widely administered via nasal route. Oral dexmedetomidine is as effective as nasal dexmedetomidine as a premedication. Dexmedetomidine given via both routes blunts hemodynamic response at induction equally and effectively.

Abstract

Background

Dexmedetomidine has been used as a premedication in children primarily via nasal route. Concerns regarding bioavailability and onset of action has restricted its use via oral route. However, oral route is natural and more pleasurable compared to nasal. We compared dexemedetomidine given as a premedication via nasal and oral routes in children undergoing minor surgical procedures.

Methods

54 children of ASA PS I grade, aged 1to 8 years, were randomised to one of the two groups. Group I received 1mcg/kg dexmedetomidine intranasally while group II received 3 mcg/kg dexmedetomidine orally, 45 minutes prior to induction of anaesthesia. Depth of sedation was assessed using modified Observer Assessment of Alertness/Sedation Scale just before premedication and every 10 minutes thereafter, till parental separation. Mask acceptance , baseline, minimum and maximum heart rates, at induction were recorded along with post operative complications.

Results

Though initial sedation scores dropped rapidly in group I compared to group II, final sedation scores were similar in both the groups. There were no difference in the two groups in terms of mask acceptance and hemodynamic parameters at induction. Both the groups showed blunting of hemodynamic response (<20% increase in heart rate) at induction.

Conclusion

Oral dexmedetomidine (3 mcg/kg) is as effective a premedication as intranasal dexmedetomidine (1 mcg/kg). Dexmedetomidine premedication, in doses and via routes used in this study, blunts hemodynamic response at induction of anaesthesia.

Keywords: dexmedetomidine, premedication

Introduction

The preoperative period is a stressful event for the majority of individuals undergoing surgery. This is especially true in the pediatric patients. The separation from parents and the alien environment of operating rooms is dreadfull to most children. In order to alleviate physiological and psychological effects of preoperative anxiety in children, most anesthesiologists use either parental presence or sedative premedication.

Concerns regarding parental presence on induction of anesthesia include a negative behavioral response to stress in some children when a parent is present and an upsetting experience to the parents, especially if watching their child going limp or when leaving their child after induction.[1,2] Oral midazolam has been shown to be more effective in reducing a child's anxiety than parental presence and parental presence combined with oral midazolam was not superior in reducing a child's anxiety than sedation alone [3].

However, midazolam premedication can be associated with respiratory depression, excessive sedation and prolonged recovery. Alpha2 agonist, dexmedetomidine, has an advantage of providing analgesia in addition to sedation with no respiratory depression. Intranasal dexmedetomidine, 1 $\mu g \cdot kg^{-1}$, has been found to be effective and safe alternative for premedication in children; providing superior sedation in comparison to 0.2 $mg \cdot kg^{-1}$ intranasal midazolam.[4] Intranasal dexmedetomidine provides satisfactory sedation with no adverse hemodynamic effects[5,6]. Intranasal drug administration, however, may not be accepted by some children. Given by oral route, dexmedetomidine is an effective premedicant prior to anesthesia induction or procedural sedation[7]. Oral dexmedetomidine has been shown to provide dose-dependent effective analgo-sedation, comparable to ketamine, with less adverse effects[8]. The efficacy of dexmedetomidine, as a premedication in children, via oral route with respect to nasal route has not been evaluated before. This study evaluated the efficacy of Dexmedetomidine as a premedication given intranasally vs orally in children between 1 to 8 years of age undergoing minor surgical procedures.

Methods

A study was conducted on 54 children of ASA PS I grade of both sexes undergoing minor surgical procedures at department of anaesthesia, BJ Wadia hospital for children, Mumbai. Careful pre-anaesthetic examination was done. A written informed consent was obtained from the parents of all children. Children with anticipated difficult airway, BMI> 30, liver or renal dysfunction, known allergy to dexmedetomidine, OASS < 5 on day of surgery, were excluded. Standard fasting protocols were followed for all the children. Patients were divided into two groups using table of random numbers. Baseline sedation scores were recorded, using modified OASS, for all patients just before premedication. Patients in two groups were premedicated approximately 45 minutes before induction as follows-

1. GROUP I received Dexmedetomidine 1 mcg/kg in 1ml of 0.9% saline intranasally + 3ml of rose syrup orally .
2. GROUP II received Dexmedetomidine 3 mcg/kg in 3 ml of rose syrup orally + 1 ml of 0.9% saline intranasally .

Subsequent sedation scores were assessed using modified OASS at 10 minutes intervals following premedication, till parental separation (Table 1). Patients were shifted to operation theatre and SpO2 and ECG monitors were attached. Baseline heart rate and saturation were recorded and anaesthesia induced with O_2/Air (50:50%) with high concentration of Sevoflurane (3-4 MAC%) on spontaneous respiration (tidal volume breathing) using Ayre's T-piece circuit via face mask. Mask acceptance score was recorded at this point. Intravenous access made, iv fentanyl, 1mcg/kg, administered and Ringer's lactate 10 ml/kg/hr, started simultaneously. I-gel of appropriate size inserted and secured. Maximum and minimum heart rates at induction were recorded. Induction time was defined as the time from application of mask till securing of I-gel (Table 2). The occurrence

of perioperative adverse events such as hypotension, bradycardia, tachycardia, the occurrence of postoperative shivering, postoperative nausea and vomiting, were noted. Descriptive statistics i.e. mean and standard deviation have been used for continuous variables like age, weight, sedation scores and heart rates. Statistical methods used are independendent student's t-test. Pearson chi-square test was used for categorical data.

5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Response only after name is called loudly and/or repeatedly
2	Response only after mild prodding or shaking
1	Response only after painful trapezius squeeze
0	No response after painful trapezius squeeze

Table 1. Modified Observer Assessment of Alertness/Sedation Scale

Score	Response
1 (good)	Patient allows mask over his face without any resistance
2 (average)	Patient allows mask over his face with some resistance, that can be overcome by the person holding the mask.
3 (poor)	Patient allows mask over his face with significant resistance, that cannot be overcome by the person holding the mask alone and requires additional help

Table 2. Mask acceptance score

Results

Demographic variables were comparable in two groups, including age and weight (Figure 1). Mean sedation scores were comparable in two groups at 10 minutes (4.73 vs 5.00). Mean sedation score at 20 minutes was significantly lower in nasal group compared to oral group (3.50 vs 4.18; p,0.05). However, the mean sedation scores in both the groups at 30 minutes were again comparable (2.64 vs 2.79). The mean sedation scores in both the groups at parental separation were also comparable (2.18 vs 2.04) (Figure 2). The mean mask acceptance scores in the two groups were comparable (2.00 vs 2.14) (Figure 3). The number of patients with mask acceptance score of 1, 2 and 3 were also comparable in two groups (Figure 4). The mean baseline, maximum and minimum heart rates were similar in two groups. The mean maximum heart rate in Group I was 10.39% (<20%) of baseline, while that in Group II was 11.89% (<20%) of baseline (Figure 5)

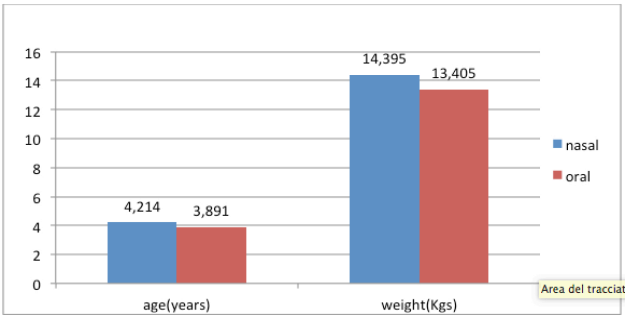

Figure 1. Demographic comparison of two groups

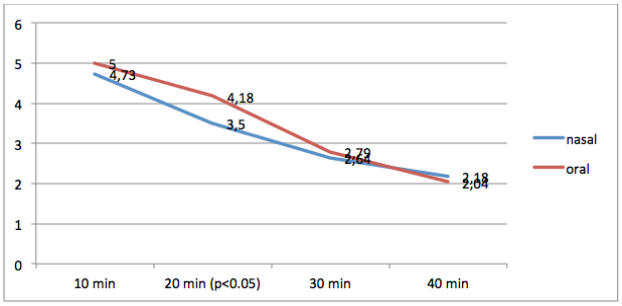

Figure 2. Comparison of sedation scores between the two groups, at 10 minutes intervals, commencing from 10 minutes after premedication upto 40 minutes after premedication. Difference was statistically significant at 20 minutes. However , the final sedation scores at 40 minutes were similar.

Figure 3. Comparison of mask acceptance between the two groups. No statistically significant difference found.

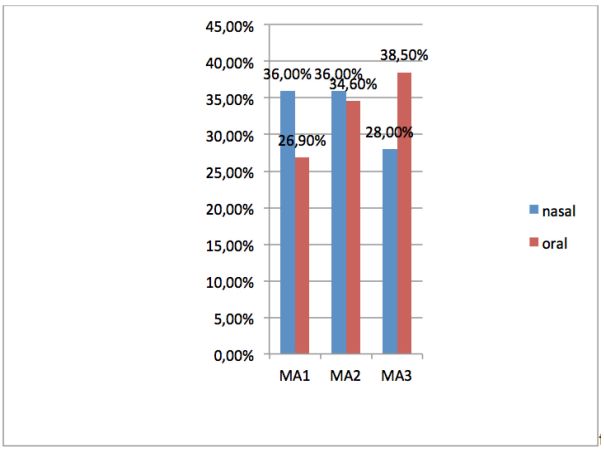

Figure 4. Percentage of children with mask acceptance scores of 1, 2 and 3, in both the groups. No statistically significant difference found.

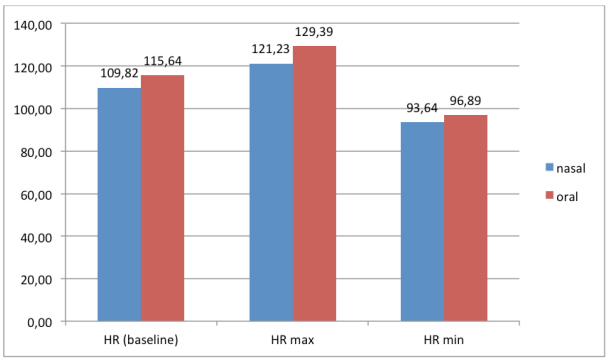

Figure 5. Comparison of heart rates at induction between the two groups. No statistically significant difference found.

Discussion

The present study shows that both intranasal dexmedetomidine (1 mcg/kg) and oral dexmedetomidine (3 mcg/kg) are equally effective as premedications. Also dexmedetomidine, in doses and via routes used in this study, blunts hemodynamic response at induction of anaesthesia. Dexmedetomidine is an alpha-2 agonist and acts at various levels to produce different effects (Figure 6).

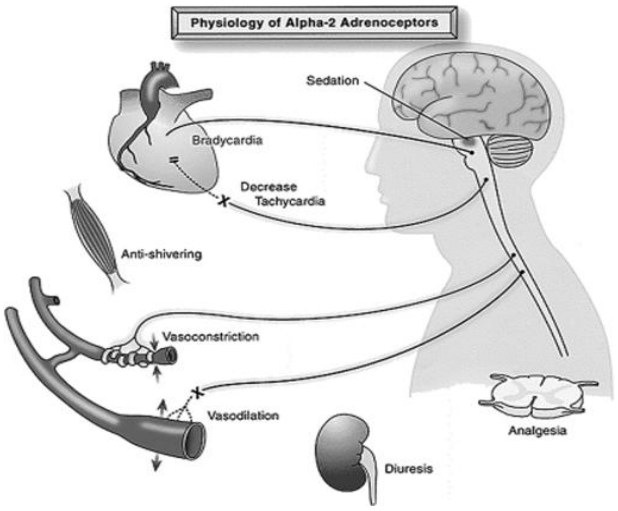

Figure 6. Diagram showing different actions of dexmedetomidine.

When given as a pre-medication, it acts on locus ceruleus to induce sedation. Its action on the same center also modulates nociceptive neurotransmission. Various studies have compared deexmedetomidine premedication with conventional premedications. Sheta SA et al compared intranasal dexmedetomidine with intra nasal midazolam in children aged 3-6 years. They concluded that intranasal dexmedetomidine (1 ug/kg) resulted in superior sedation in comparison to 0.2 mg/kg intranasal midazolam[4]. In a meta-analysis of randomised control trials, Pasin L et al concluded that dexmedetomidine is effective in decreasing anxiety upon separation from parents, decreasing postoperative agitation, and providing more effective postoperative analgesia when compared with midazolam[9].

Ibrahim M showed that intranasal dexmedetomidine (3 mcg/kg) is as effective as intranasal ketamine (7 mcg/kg) to induce a state of moderate conscious sedation and to facilitate parents' separation and IV cannulation in children undergoing MRI[10]. Also dexmedetomi-

dine used as an adjuct to ketamine produces more satisfactory sedation than ketamine alone[11].

Oral dexmedetomidine has not been as extensively studied as nasal dexmedetomidine. A preliminary data published by Zub D et al suggests that oral dexmedetomidine may be an effective premedicant prior to anesthesia induction or procedural sedation[7]. Singh C et al compared oral dexmedetomidine and oral ketamine in children aged 3-10 years, undergoing dental procedures and concluded that oral dexmedetomidine (4 ug, 5 ug) produced sedation comparable to oral ketamine (8 mg/kg)[8]

Questions on bio-availability of dexmedetomidine when given orally has limited its use via this route, making nasal route more popular for premedication[12]. However, nasal premedication is not always accepted by children. Sneezing, coughing, limits the effectiveness of nasal premedication. However, in this study we found that dexmedetomidine given orally (3mcg/kg) produces sedation similar to that produced when given nasally (1 mcg/kg). Also the hemodynamic response at induction was blunted equally in two groups.

Conclusion

Oral route is a good alternative to nasal route using dexmedetomidine as a premedication in children. Though the onset of action of nasal dexmedetomidine is faster, the final sedation scores achieved are similar to those achieved by oral route.

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