Intranasal dexmedetomidine versus intranasal midazolam as pre-anesthetic medication in pediatric age group undergoing adenotonsillectomy

Bassem B. Saad, Ayman I. Tharwat, Haidi N. Ghobrial* and Sanaa M. Elfawal

Abstract

Background: The pre-operative period is a very stressful event for most of the individuals undergoing surgery especially the pediatric patients. So, relieving their pre-operative anxiety becomes an important concern for an anesthesiologist. Many anesthetic pre-medications are used to relieve this stress response. Of these pre-medications, midazolam and dexmedetomidine are effectively used as sedatives. The present study was planned to compare intranasal dexmedetomidine with intranasal midazolam as a pre-anesthetic medication in children. Forty-eight children aged 3–7 years, of either sex, weighing 13–22 kg, with American Society of Anesthesiologists (ASA) physical status 1 and undergoing elective adenotonsillectomy surgery were enrolled in this comparative prospective, double blinded, randomized clinical study. The children were divided into 2 groups: group D and group M, of 24 each. Forty-five minutes before induction of anesthesia, group D (n = 24) received intranasal dexmedetomidine at a dose of 1 μg/kg and group M (n = 24) received intranasal midazolam of 0.2 mg/kg.

Results: Children who were pre-medicated with dexmedetomidine had lower sedation scores, lower anxiety levels, easier child-parent separation, better mask acceptance, and lower pain scores than those who received midazolam. The incidence of emergence agitation was decreased in both groups with no significant difference.

Conclusion: Intranasal dexmedetomidine seems to offer some advantages compared with midazolam. Thus, it can be used effectively and safely as a pre-anesthetic medication in children undergoing any surgical procedures under general anesthesia.

Keywords: Dexmedetomidine, Midazolam, Pediatric, Intranasal, Pre-medication

Background

Pre-operative anxiety leads to hemodynamic instability, metabolic side effects, increased post-operative pain, and emergence agitation (Kumar & Ganguly, 2015). So, pharmacological measures are used to relieve pre-surgical anxiety and facilitate anesthetic induction without prolonging the recovery (Ghali et al., 2011). The pre-medicant used must have a non-traumatic, acceptable route of administration and be devoid of significant side effects. Intranasal administration has been shown to be very effective, easy, non-invasive route with high bio-availability and rapid onset of action due to the high vascularization of the nasal mucosa (Wang & Bu, 2002).

Midazolam, a water-soluble benzodiazepine, is widely used as a pre-anesthetic medication in children because it has a number of beneficial effects: sedation, anxiolysis, anterograde amnesia, fast onset, and short duration of action. Despite the advantages, it is far from being an ideal pre-medicant as it causes some side effects such as restlessness, paradoxical aggressive
reactions, cognitive decline, and respiratory depression (Bergendahl et al., 2006).

Dexmedetomidine, an α2-adrenoceptor agonist, has excellent sedative and analgesic properties with no respiratory depressant effect. Also, it attenuates hemodynamic stress response because of its sympatholytic action. These properties make it potentially useful as an anesthetic pre-medication (Patel et al., 2015).

So, considering all these aspects, the present study was planned to compare sedation level, ease of child parent separation, hemodynamics, post-operative analgesia, and emergence agitation using intranasal dexmedetomidine versus intranasal midazolam as a pre-medication in pediatric patients posted for adenotonsillectomy.

**Methods**

After ethical committee approval and written informed parents’ consent, this randomized comparative prospectively double-blinded clinical study was performed in our university Hospitals, Cairo, Egypt, during the time period from April 2018 to March 2020. Forty-eight children, aged 3–7 years with ASA physical status 1, were scheduled for adenotonsillectomy surgery. Patients with known allergy or hypersensitivity reaction to any of the drugs used in the study, with nasal infection, nasal pathology, or with huge adenoids and patients on any other sedatives were excluded from this study. All patients fasted 6 h for solids but clear fluids were allowed up to 4 h before anesthetic induction. The children were randomly divided into 2 groups of 24 each by using a computer-generated random sequence, Group D (n = 24) received intranasal dexmedetomidine at 1 μg/kg and group M (n = 24) received intranasal midazolam at 0.2 mg/kg. The intranasal dexmedetomidine and midazolam were prepared according to the patient’s body weight so as the calculated dose of the drug diluted to a total volume of 2 ml. Forty-five minutes before induction, in the pre-operative holding area, in the presence of one parent, equal volume of the drug was dripped into both nostrils using a 3-ml syringe with the child in a recumbent position. Drug administration was done by an anesthetic technician who was not blinded to the group arrangement. And in order to create a double-blinded study, neither the anesthesiologist who was responsible for monitoring the patients and recording the data nor the parents were informed which drug was administered.

**Measurements**

In the pre-operative holding area, vital signs (heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO2)) were recorded before administering the intranasal drug and every 10 min for 45 min with continuous monitoring. The degree of sedation was assessed every 10 min for 45 min by using Modified Observers Assessment of Alertness/Sedation Scale (MOAA/S) (Table 1) (Cohen et al., 2007) and Anxiety scale (Table 2) (Akin et al., 2012).

The response to their separation from the parents was assessed at the time of their transferral to the operation theatre (OT) using Child Parent Separation Scale (Table 3) (Patel et al., 2015). Children were transported to the OT where face mask induction was carried out using sevoflurane in oxygen, while another anesthesiologist was securing an

---

**Table 1** Modified Observer’s Assessment of Alertness/Sedation Scale (Cohen et al., 2007)

| Score | Description                                      | Level of sedation |
|-------|--------------------------------------------------|-------------------|
| 1     | Does not respond to mild prodding or shaking.   | Deep              |
| 2     | Responds to mild prodding or shaking.           | Moderate          |
| 3     | Responds only after name is called loudly or repeatedly. | Moderate |
| 4     | Lethargic response to name spoken in normal tone. | Moderate          |
| 5     | Appears asleep but responds readily to name spoken in normal tone. | Minimal           |
| 6     | Appears alert and awake, responds readily to name spoken in normal tone. | Alert             |

**Table 2** Anxiety scale (Akin et al., 2012)

| Score | Description                  | Level of anxiolysis |
|-------|------------------------------|---------------------|
| 1     | Calm and cooperative         | Excellent           |
| 2     | Anxious but could be reassured | Good               |
| 3     | Anxious and could not be reassured | Fair     |
| 4     | Crying or resisting          | Poor                |

**Table 3** Child-Parent Separation Scale (Patel et al., 2015)

| Score | Description                                      | Behavior   |
|-------|--------------------------------------------------|------------|
| 1     | Patient unafraid, cooperative, or asleep         | Excellent  |
| 2     | Patient slightly fearful and/or crying; quieted with reassurance | Good       |
| 3     | Patient fearful and crying; not quieted with reassurance | Poor      |

**Table 4** Mask Acceptance Scale (Mountain et al., 2011)

| Score | Description                  | Mask acceptance |
|-------|------------------------------|-----------------|
| 1     | Calm, cooperative            | Excellent       |
| 2     | Cooperative with reassurance | Good            |
| 3     | Moderate fear of mask, not easily calmed         | Fair            |
| 4     | Combative, crying            | Poor            |
intravenous line. Pulse oximeter, non-invasive blood pressure, and electrocardiogram were attached. Acceptance of a face mask was assessed using the Mask Acceptance Scale (MAS) (Table 4) (Mountain et al., 2011). The dial setting was increased by 1% every 2–3 breaths until loss of eyelash reflex. One microgram per kilogram of fentanyl was injected intravenously. Oral endotracheal tube was inserted. Anesthesia was maintained with 0.8–1 MAC level of isoflurane in oxygen. Spontaneous breathing was maintained and monitored using capnography. All patients received intravenous paracetamol 15 mg/kg. Intraoperative HR, SBP, DBP, and SpO2 were noted every 10 min. After completion of surgery, isoflurane was discontinued and extubation was done in the lateral decubitus position when the patient had reached certain criteria (purposeful movements, eye opening and regular breathing). Then, they were brought to the Post-Anesthetic Care Unit (PACU). Once the modified Aldrete score ≥ 9, the patients were transferred to the Surgical Day Care Unit (SDCU). Every 20 min for 2 h, post-operative HR and SpO2, emergence agitation using a 4-point scale (Table 5) (Sikich & Lerman, 2004) and post-operative pain using Modified Objective Pain Scale (MOPS) (Patel et al., 2015) were assessed. MOPS based on five parameters, i.e., crying, movements, agitation, posture, and verbalization of pain, and each parameter was given a score of 0–2 depending upon severity (Patel et al., 2015). Injection of pethidine 0.5 mg/kg intramuscular was used in children with MOPS ≥ 5 as a rescue drug.

Statistical analysis
Sample size was calculated using PASS 11.0 sample size calculation program and based on a study carried out by Patel et al. (Patel et al., 2015) who mentioned that the sedation score in dexmedetomidine group is 2.53 ± 0.74; while in midazolam group is 3.69 ± 0.87; group sample sizes of 24 and 24 achieve 99% power to detect a difference of −1.2 between the null hypothesis that both groups are 2.5 and the alternative hypothesis that the mean of group M is 3.7 with known group standard deviations of 0.7 and 0.9 and a significance level (alpha) of 0.01000 using a two-sided Mann-Whitney test assuming that the actual distribution is uniform.

Data were collected, revised, coded, and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean and standard deviation (SD) or as median and inter-quartile range (IQR). Comparison of quantitative variables between the two study groups was done by using independent t test when the data were normally distributed and Mann-Whitney test in non-parametric data. Qualitative data were presented as number and percentage and the differences between the two groups were compared using the chi-square (χ²) test and/or Fisher exact test when the expected count in any cell found less than 5. The confidence interval was set to 95% and the margin of error accepted was set to 5%. p < 0.05 was considered statistically significant (S).

Results
There were no significant demographic differences between both groups as regards age, sex, body weight, and duration of surgery (Table 6).

### Table 5 Emergence Agitation Scale (Sikich & Lerman, 2004)

| Score | Description                  |
|-------|-----------------------------|
| 1     | Awake and calm, cooperative |
| 2     | Crying, requires consoling  |
| 3     | Irritable/ restless, screaming, inconsolable |
| 4     | Combative, disoriented, thrashing |

### Table 6 Patients’ demographic data

| Demographic data          | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | t/χ²# | p value |
|---------------------------|--------------------------------|--------------------------|-------|---------|
| Age (years) (mean ± SD)   | 5.04 ± 1.49                    | 5.13 ± 1.54              | −0.191| 0.850   |
| Sex N (%)                 |                                |                          |       |         |
| Female                    | 9 (37.5%)                      | 10 (41.7%)               |       |         |
| Male                      | 15 (62.5%)                     | 14 (58.3%)               | 0.087# | 0.768   |
| Weight (kg) (mean ± SD)   | 17.83 ± 2.78                   | 18.08 ± 3.09             | −0.295| 0.770   |
| Duration of surgery (min) (mean ± SD) | 25.38 ± 3.00                 | 24.79 ± 2.70             | 0.707 | 0.483   |

# Independent t test; χ² chi-square test. p value > 0.05 was considered statistically non-significant.
Baseline pre-operative HR, SBP, DBP, and SpO₂ were statistically comparable in both groups. Similarly, after 10 and 20 min of intranasal drug administration, no statistically significant difference was observed in vital parameters between both groups \((p > 0.05)\). But, after 30 min of pre-medication onwards, the HR and BP were significantly lower in group D than in group M \((p < 0.05)\) (Figs. 1, 2, and 3). There was no significant difference in SpO₂ between both groups \((p > 0.05)\), and no oxygen desaturation was observed with both drugs throughout the whole procedure (Fig. 4).

The sedation scores were assessed in both groups before administration of the intranasal drugs and every 10 min after that for 45 min. The sedation score was significantly lower in the midazolam group at 10 and 20 min after the administration of the drug \((p < 0.001)\). However, at 30 and 45 min, there was a statistically significant decrease in sedation score in group D compared with group M \((p = 0.002\) and \(< 0.001, \text{ respectively})\) (Table 7). Just before anesthesia induction, 58% of children in group D achieved a sedation score of 2 and 42% of them achieved a score of 3 while in M group 87% achieved a sedation score of 3 (Figs. 5 and 6). Regarding the anxiety score at 10 min of drug administration, there was no statistically significant difference between both groups. However, at 20 min, there was a significant decrease in anxiety score in group M compared with group D \((p < 0.001)\). But, at 30 and 45 min, there was a statistically significant decrease in anxiety score in group D compared with group M (Table 8). Just before anesthesia induction, 83% of children in group D achieved anxiolytic score 1 and 75% of children in group M achieved anxiolytic score 2 (Figs. 7 and 8).
A greater number of children in group D achieved easier parental separation when compared with that in group M but this was not statistically significant ($p = 0.801$) (Table 9). There was an excellent mask acceptance in group D compared with group M which was statistically significant ($p = 0.028$). Seventy-one of children in group D showed a mask acceptance score of 1 or 2 in comparison with 54% of that in group M (Table 10).

Post-operatively, children in group D had significantly lower values on MOPS for the first 2 h (Table 11). Post-operative agitation score of 1 and 2 were achieved in both groups with no significant difference ($p > 0.05$) (Table 12).

**Discussion**

The population sample studied was homogenous regarding the pre-anesthetic characteristics (age, gender, weight) of both groups. Our study showed that there was no statistically significant difference between the two groups regarding the HR and the BP at 10 and 20 min after intranasal drug instillation. But, after 30 min of pre-medication onwards, there was a significant decrease in the HR and the BP in the dexmedetomidine group in comparison with midazolam group. But the fall in HR and BP was within the acceptable limits for the age of the child and did not require the use of chronotropic or inotropic agents. The reduction in HR and BP were expected because dexmedetomidine decreases sympathetic outflow and circulating catecholamine levels and increases cardiac vagal activity (Lester et al., 2018). Similarly, Abdelmoneim et al. (Abdelmoneim et al., 2016) had found that mean BP and HR decreased significantly at 30 min after intranasal dexmedetomidine of 1 μg/kg, compared with that in children who received intranasal midazolam of 0.5 mg/kg. Also, a study by Singla et al. (Singla et al., 2015)
has found that dexmedetomidine of 1 μg/kg reduces both HR and BP in pre-operative period significantly. In our study, the SpO₂ was well maintained throughout the perioperative observation period. But it is not a guarantee that midazolam does not cause respiratory depression. So, more studies are needed with larger group sample size than ours.

We found in our patients that MOAA/S was significantly lower in the midazolam group at 10 and 20 min than in dexmedetomidine group. On the contrary, at 30 min, it was significantly lower in the dexmedetomidine group. This shows that intranasal midazolam has a faster onset of sedation than dexmedetomidine. What correlates with the slow onset of sedation in dexmedetomidine group that we found significant decrease in HR and BP at 30 min of the drug administration. As in agreement with our study, Abdelmoneim et al. (Abdelmoneim et al., 2016) stated that intranasal dexmedetomidine was more capable of causing more sedation than midazolam at 30 and 45 min pre-operative. Likewise, Singla et al. (Singla et al., 2015) showed that the MOAA/S was significantly less at 30 min after intranasal dexmedetomidine. Midazolam produces sedation by stimulating GABA receptors in the cerebral cortex that inhibits normal neuronal function (Patel

Figure 5 The Sedation scores at 45 min after dexmedetomidine administration

Table 7 Comparison between group D and group M as regards Modified Observer’s Assessment of Alertness/Sedation Scale (MOAA/S)

| MOAA/S | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | z test | p value |
|--------|-------------------------------|--------------------------|--------|---------|
| At 0 min | 6 (6–6) | 6 (6–6) | 0.000 | 1.000 |
| At 10 min | 6 (5–6) | 4 (4–5) | 7.373 | < 0.001** |
| At 20 min | 5 (4.5–5) | 3 (3–4) | 10.153 | < 0.001** |
| At 30 min | 3 (2–3) | 3 (3–3) | −3.278 | 0.002* |
| At 45 min | 2 (2–3) | 3 (3–3) | −5.038 | < 0.001** |

Data are presented as median (IQR). *p value < 0.05 was considered statistically significant, **p value < 0.001 was considered highly significant.
et al., 2015). On the other hand, dexmedetomidine produces sedation by stimulating alpha2-adrenergic receptors in the locus coeruleus, so reduces central sympathetic output, resulting in increased firing of inhibitory neurons (Buck, 2010). Also, in this study, intranasal dexmedetomidine was superior to midazolam as anxiolytic, with lower anxiety score at 30 and 45 min pre-operative. Singla et al. (Singla et al., 2015) also proved that dexmedetomidine was more anxiolytic than midazolam at 30 min. In disagreement with that, Akin et al. (Akin et al., 2012) found lower anxiety scores in the patients who received intranasal midazolam 0.2 mg/kg than in those who received dexmedetomidine 1 μg/kg in the OT.

Concerning the child parent separation, children in group D were more easily separated from parents than in group M but it was not statistically significant. Our study confirms Singla et al. (Singla et al., 2015) study that found better parental separation with dexmedetomidine. Mostafa and his colleague also stated that the number and percentage of children achieved child–parents separation score grade 1 was significantly higher in D group than M group (Mostafa & Morsy, 2013).

As for the mask acceptance in the present study, there was better mask acceptance in group D compared with group M. In agreement, Sun et al. (Sun et al., 2014) compared midazolam and dexmedetomidine intranasally. They stated that the dexmedetomidine group was associated with more satisfactory sedation upon mask acceptance compared with the midazolam group. But, Akin et al. (Akin et al., 2012)

---

Table 8 Comparison between group D and group M as regards Anxiety scale

| Anxiety scale | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | z test | p value |
|---------------|-------------------------------|-------------------------|--------|---------|
| At 0 min      |                               |                         |        |         |
| Median (IQR)  | 4 (4–4)                       | 4 (4–4)                 | 0.000  | 1.000   |
| At 10 min     |                               |                         |        |         |
| Median (IQR)  | 3 (3–3)                       | 3 (2.5–3)               | 0.700  | 0.488   |
| At 20 min     |                               |                         |        |         |
| Median (IQR)  | 2 (2–2)                       | 1.5 (1–2)               | 4.153  | < 0.001**|
| At 30 min     |                               |                         |        |         |
| Median (IQR)  | 1 (1–1)                       | 2 (1–2)                 | −2.890 | 0.006*  |
| At 45 min     |                               |                         |        |         |
| Median (IQR)  | 1 (1–1)                       | 2 (1.5–2)               | −4.897 | < 0.001**|

Data are presented as median (IQR). *p value > 0.05 was considered statistically non-significant, *p value < 0.05 was considered statistically significant, **p value < 0.001 was considered highly significant.
showed that midazolam was superior in providing satisfactory conditions during mask induction because the authors stated that intranasal dexmedetomidine sedative effect did not reach its peak before mask induction.

With respect to the post-operative effects of anesthetic pre-medication, we found that both drugs decreased post-operative agitation, with no statistically significant differences among both groups. In agreement with our study, Özcengiz D et al. (Özcengiz et al., 2011) who compared oral dexmedetomidine 2.5 μg/kg with oral midazolam 0.5 mg/kg as pre-medication in children who were given sevoflurane. In disagreement with that, Kamal et al. (Kamal et al., 2008) who studied the effect of oral dexmedetomidine 3 μg/kg versus oral midazolam 0.5 mg/kg as pre-medication in 60 pediatric patients prior to a standardized sevoflurane.

Emergence agitation (EA) is related to multiple factors: pre-operative anxiety, pain, certain surgical procedures (ophthalmological and otorhinolaryngology), personality traits, pre-school age, too rapid emergence and type of inhalational anesthetics (high incidence with sevoflurane). Not a sole factor can lead to EA (Silva et al., 2008). In spite of the fact that pain is a major cause of EA, its adequate management may not prevent EA from occurring. So, giving pre-anesthetic medication to ameliorate pre-operative anxiety has been tried, hoping that it might decrease the incidence of EA (Özcengiz et al., 2011).

In our study, the number of children who required rescue analgesia was higher in the group M as
comparing to group D. Forty-two percent of children in group M in comparison to 21% in group D required rescue analgesia. Dexmedetomidine produces profound analgesia by reducing pain transmission through activation of central α2 adrenoceptors, present in the neurons of the dorsal horn of the spinal cord (Afonso & Reis, 2012). Similarly, Akin et al. (Akin et al., 2012) reported the number of children requiring post-operative analgesia was lower in the dexmedetomidine group. Also, Schmidt et al. (Schmidt et al., 2007) found that dexmedetomidine was related to lower levels of post-operative pain.

The major study limitation is the timing of drug administration. Dexmedetomidine reaches its peak sedative effect approximately at 30–45 min of intra-nasal administration while midazolam peak sedative effect at 10–20 min of administration. So, giving midazolam 45 min before anesthesia induction is a long time as its maximum sedative effect will be wearing off. For dexmedetomidine, if intranasal drug administration is given before anesthesia induction by less than 45 min, this length of time may be too short. But, for some children, the drug may have an effect. Greater sedative effects in the dexmedetomidine group could have been noted if we had waited longer, but in this circumstance, the effect of midazolam would have been disappeared. Another study limitation is not using nasal atomizer spray that deposit drug solutions more anteriorly result in slower drug removal and increased absorption as the drug remains within the nasal cavity for longer. To solve this problem in our study, we tried not to exceed absolute maximum volume of pre-medication 1 mL per naris. As larger volume tends to flow into the nasopharynx and is swallowed (Pires et al., 2009).

**Table 9** Comparison between group D and group M as regards child parent separation score

| Child parent separation score | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | z test | p value |
|------------------------------|---------------------------------|--------------------------|--------|--------|
| Median (IQR)                 | 1.5 (1–2)                       | 2 (1–2)                  | 0.253  | 0.801  |

Data are presented as median (IQR). *z* Mann-Whitney test. *p value > 0.05 was considered statistically non-significant

**Table 10** Comparison between group D and group M as regards Mask Acceptance Score

| Mask acceptance score       | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | z test | p value |
|-----------------------------|---------------------------------|--------------------------|--------|--------|
| Median (IQR)                | 2 (1.5–3)                       | 2 (2–3)                  | 2.052  | 0.028  |

Data are presented as median (IQR). *z* Mann-Whitney test. *p value < 0.05 was considered statistically significant

**Table 11** Comparison between group D and group M as regards Modified Objective Pain Scale (MOPS)

| MOPS                    | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | z test | p value |
|-------------------------|---------------------------------|--------------------------|--------|--------|
| At 20 min               | 3.975 0.024*                     | 3 (2–5)                  | 2.975  | 0.024* |
| At 40 min               | 2.5 0.016*                       | 3 (2–4)                  | 2.884  | 0.016* |
| At 60 min               | 1.5 0.025*                       | 3 (2–3)                  | 3.638  | < 0.001** |
| At 80 min               | 1 0.019*                         | 2 (1–3)                  | 2.417  | 0.019* |
| At 120 min              | 1 0.016*                         | 2 (1–2.5)                | 2.511  | 0.016* |

Data are presented as median (IQR). *z* Mann-Whitney test. *p value < 0.05 was considered statistically significant. **p value < 0.001 was considered highly significant

**Table 12** Comparison between group D and group M as regards Emergence Agitation Score

| Emergence Agitation scale | Dexmedetomidine group (n = 24) | Midazolam group (n = 24) | z test | p value |
|--------------------------|---------------------------------|--------------------------|--------|--------|
| At 20 min                | 1 0.000 1.000                   | 1.5 1.000                | 0.245  | 0.808  |
| At 40 min                | 1 0.000 1.000                   | 1.5 1.000                | 0.245  | 0.808  |
| At 60 min                | 1 0.000 1.000                   | 1.5 1.000                | 0.245  | 0.808  |
| At 80 min                | 1 0.000 1.000                   | 1.5 1.000                | 0.245  | 0.808  |
| At 120 min               | 1 0.000 1.000                   | 1.5 1.000                | 0.245  | 0.808  |

Data are presented as median (IQR). *z* Mann-Whitney test. *p value > 0.05 was considered statistically non-significant

**Conclusion**

Pre-medication with intranasal dexmedetomidine 1 μg/kg appeared to be associated with lower sedation score and anxiety score, easier child parent separation, excellent mask acceptance, and better post-
operative analgesia in comparison with intranasal midazolam 0.2 mg/kg. Also, both drugs were similarly effective in preventing emergence agitation in children. Thus, it can be concluded that intranasal dexmedetomidine can be used effectively and safely as a pre-anesthetic medication in children undergoing any surgical procedures under general anesthesia.

Abbreviations
ASA: American Society of Anesthesiologists; DBP: Diastolic blood pressure; EA: Emergence agitation; HR: Heart rate; IQR: Inter-quartile range; MAS: Mask Acceptance Scale; MOAA/S: Modified Observers Assessment of Alertness/Sedation Scale; MOPS: Modified Objective Pain Scale; OT: Operation theatre; PACU: Post-Anesthetic Care Unit; S: Significant; SBP: Systolic blood pressure; SD: Standard deviation; SDCU: Surgical Day Care Unit; SpO2: Oxygen saturation

Acknowledgements
Not applicable.

Authors’ contributions
HN designed the study, revised literature, followed the patients, and critically reviewed the manuscript. BB designed the study, analyze the data, wrote, and critically revised the manuscript. AI and SM revised literature, followed the patients, collected the data, performed the analysis, and wrote the manuscript. All authors read and approved the final version of the manuscript.

Funding
None.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Approval of research ethical committee of Faculty of Medicine, Ain Shams University was obtained (code number:FMASU M D 44/2018) and written approval of research ethical committee of Faculty of Medicine, Ain Shams University was obtained (code number:FMASU M D 44/2018) and written informed consent was obtained from all parents of the patients.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 18 June 2020 Accepted: 26 August 2020
Published online: 15 September 2020

References
Abdelmonim HM, Hamouda SA, Mahfouz GA, Hashem AE (2016) Intranasal dexmedetomidine versus midazolam in preoperative sedation for non-complex pediatric congenital cardiac surgeries. Research and Opinion in Anesthesia & Intensive Care 3:129–137
Afonso J, Reis F (2012) Dexmedetomidine: Current Role in Anesthesia and Intensive Care. Rev Bras Anestesiol 62(1):118–133
Akin A, Bayram A, Esmauglu A et al (2012) Dexmedetomidine vs midazolam for premedication of pediatric patients undergoing anesthesia. Paediatr Anaesth 22:871–876
Bengendahl H, Lönnqvist PA, Eksborg S (2006) Clonidine in paediatric anaesthesia: review of the literature and comparison with benzodiazepines for premedication. Acta Anaesthesiol Scand 50:135–143
Buck ML (2010) Dexmedetomidine use in pediatric intensive care and procedural sedation. J Pediatr Pharmacol Ther 15(1):17–29
Cohen LB, DeLegge MH, Aisenberg J et al (2007) AGA Institute Review of Endoscopic Sedation. Gastroenterology 133(2):675–701
Ghali AM, Mahfouz AK, Al-Bahrani M (2011) Pre anesthetic medication in children: a comparison of intranasal dexmedetomidine versus oral midazolam. Saudi Journal of Anaesthesia 5(4):387–391
Kamal K, Soliman D, Zakaria D (2008) Oral dexmedetomidine versus oral midazolam as premedication in children. Ain Shams J Anesthesiol 1
Kumar KS, Ganguly T. Preoperative anxiety in pediatric population: anesthesiologist’s nightmare. Translational Biomedicine 2015; 6(4).
Lester L, Mitter N, Berkowitz DE, Nyhari D (2018) Pharmacology of anesthetic drugs. In: Kaplan JA (Ed.) Kaplan’s Essentials of Cardiac Anesthesia. 2nd edition. Elsevier, Philadelphia. pp. 112–131.
Mostafa MG, Morsy KM (2013) Premedication with intranasal dexmedetomidine, midazolam and ketamine for children undergoing bone marrow biopsy and aspiration. Egyptian Journal of Anaesthesia 29:131–135
Mountain BW, Smithson L, Cramolini M et al (2011) Dexmedetomidine as a pediatric anesthetic premedication to reduce anxiety and to deter emergence delirium. AANA Journal 79(3):219–224
Özçengiz D, Gunes Y, Ozmete O (2011) Oral melatonin, dexmedetomidine, and midazolam for prevention of postoperative agitation in children. J Anesth 25:184–188
Patel DO, Lisha M, Upadhyay MR (2015) Pre anaesthetic medication in children: a comparison of intranasal dexmedetomidine versus oral midazolam. The Journal of Medical Research 1(2):59–63
Pires A, Fortuna A, Alves G, Falcão A (2009) Intranasal drug delivery: how, why and what for? J Pharmacy Pharmaceutical Sci 12:288–311
Schmidt AP, Valinetti EA, Bandeira D et al (2007) Effects of preanesthetic administration of midazolam, clonidine, or dexmedetomidine on postoperative pain and anxiety in children. Pediatr Anesth 17:667–674
Silich N, Lerman J (2004) Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology 100(5):1138–1145
Silva LM, Braz LG, Mo’dolo NS (2008) Emergence agitation in pediatric anesthesia: current features. J Pediatr 84:107–113
Singla D, Chaudhary G, Dureja J, Mangla M (2015) Comparison of dexmedetomidine versus midazolam for intranasal premedication in children posted for elective surgery: a double-blind, randomised study. Southern African Journal of Anaesthesia and Analgesia 21(6):154–157
Sun Y, Lu Y, Huang Y, Jiang H (2014) Is dexmedetomidine superior to midazolam as a premedication in children? A meta-analysis of randomized controlled trials. Paediatr Anaesth 24:863–874
Wang J, Bu G (2002) Influence of intranasal medication on the structure of the nasal mucosa. Chin Med J 115(4):617–619

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.