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Research Article

Dexmedetomidine versus propofol for sedation during gastrointestinal endoscopy in pediatric patients

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KEYWORDS

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Abstract *Objective:* To compare the sedative, hemodynamic, respiratory and adverse effects of dexmedetomidine versus propofol during gastrointestinal endoscopy (GIE) in pediatrics.
Methods: After obtaining approval of the research and ethics committee and informed consent of the parents of the patients, eighty pediatric patients ASA I/II aged 1–14 years, scheduled for gastrointestinal endoscopy were randomized into dexmedetomidine group or propofol group. Sedation was achieved with propofol 2 mg/kg bolus then infused at 100 μg/kg/min or dexmedetomidine 2.5 μg/kg over 10 min then infused at 2 μg/kg/h to achieve a Ramsay sedation scale (RSS) $\geqslant 5$. HR, MAP, RR and SPO2 were continuously monitored and analyzed at (T0) baseline, (T1) after induction, (T2) after insertion of endoscope, (T3) during procedure, (T4) recovery period. Times of induction, procedure, and recovery were reported together with any adverse effects.
Results: There were no significant differences in demographic data between the two groups. HR values were significantly lower in dexmedetomidine group at T1, T2 and T3 (83.95 ± 13.79 versus 92.95 ± 12.38, 103.35 ± 15.34 versus 112.75 ± 12.79 and 90.80 ± 13.99 versus 104.05 ± 10.73) beats/min respectively, (p-value < 0.05). No significant differences were found in MAP, RR and SPO2 values between groups at all time points. Induction and recovery times were significantly longer in dexmedetomidine group 10.51 ± 1.75 versus 3.17 ± 0.72 min and 28.55 ± 7.95 versus 13.68 ± 3.35 min (p-value < 0.001). Seven patients in dexmedetomidine group (17.5%) versus

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one patient in propofol group (2.5%) showed unwanted movement (p-value 0.057), and no cases in dexmedetomidine group demonstrated oxygen desaturation versus 6 patients (15%) within propofol group (p-value 0.026).

Conclusion: Dexmedetomidine sedation during GIE provides more respiratory safety and HR stability presenting itself as a suitable alternative agent especially for the relatively longer procedures.

1. Introduction

Gastrointestinal endoscopy (GIE) procedures are performed for diagnosis and management in pediatric gastroenterology [1], and it allows visual examination with the ability to obtain biopsy and culture specimens [2]. Pediatric patients have different physiological effects in response to pain and anxiety [3]. So they need proper analgesia and amnesia to allow optimum procedure circumstances especially for those patients who need repeated procedures [2–4].

Propofol is used commonly in sedation for pediatric GIE procedures as it is a powerful sedative characterized by a rapid onset, short duration of action and rapid recovery [5,6]. Also it causes mild analgesia and minor adverse effects including; transient hypotension, dose dependent respiratory depression and hypoventilation [5].

Dexmedetomidine was approved by the food and drug administration in the United States in 1999 for use in adult sedation. Recently it has been introduced in pediatrics in intensive care units and for procedural sedation outside the operating room. Dexmedetomidine is a highly selective alpha-2 (α2) adrenergic agonist with a relatively high ratio of α2/α1 activity when compared with clonidine [7–10]. It possesses sedative, analgesic, sympatholytic, and hemodynamic stability properties [8,9]. It has the unique feature of lacking respiratory depression even with accidental over dosage giving it the advantage over other sedatives as benzodiazepines, opioids and propofol as all of them cause dose dependent respiratory depression [10].

The use of dexmedetomidine for procedural sedation in pediatric patients was reported in various circumstances [7,10], however to our knowledge no studies have reported its use in pediatric GIE.

So in this study we aimed to compare the sedative, hemodynamic, respiratory, and adverse effects of using dexmedetomidine versus propofol during GIE in pediatric population.

Table 1 Ramsay sedation score (RSS) [11].

Anxious and agitated	1
Cooperative, tranquil, oriented	2
Responds only to verbal commands	3
Asleep with brisk response to light stimulation	4
Asleep without response to light stimulation	5
Non responsive	6

Table 2 Steward recovery score [12].

Consciousness	
Awake	2
Responding to stimuli	1
Not responding	0
Airway	
Coughing on command or crying	2
Maintaining good airway	1
Airway requires maintenance	0
Movement	
Moving limbs purposefully	2
Non purposeful movements	1
Not moving	0

2. Patients and methods

This prospective study was conducted on pediatric patients scheduled for GIE. After obtaining approval of the research and ethics committee and informed consent of the parents of the patients, 80 pediatric patients American society of Anesthesiologists classifications I & II (ASA I/II) aged 1–14 years were included in the study.

Emergency patients and patients with ASA physical status more than II were excluded together with any patient who had bradycardia, or vomiting. Patients on beta blocker management or allergic to any component of the study drugs were also excluded. All GIE procedures were performed with the standard technique while the patients were in the prone position with the head tilted to the right side.

No premedications were given to the patients. Patients were randomized into 2 groups: propofol group (PG) and dexmedetomidine group (DG). In the propofol group sedation was induced with propofol (B. Braun Melsungen AG 34209 Melsungen, Germany) bolus 2 mg/kg to achieve a Ramsay sedation scale (RSS) $\geqslant 5$ then propofol infusion started at 100 μg/kg/min for maintenance of sedation. 0.5 mg/kg of propofol was given as a bolus if there was any sudden movement or agitation during the procedure.

In the dexmedetomidine group, sedation was induced by dexmedetomidine (Percedex; Hospira, Inc., Lake Forest, IL 60045 USA), high dose of 2.5 μg/kg was infused over 10 min to achieve a RSS $\geqslant$ 5, and this was followed with continuous dexmedetomidine infusion at 2 μg/kg/h for maintenance of sedation. 0.4 μg/kg of dexmedetomidine was given as a bolus if there was any sudden movement or agitation during the procedure.

All patients were breathing spontaneously and received 3 L/min oxygen supplementation by nasal catheter during the procedure while monitored with pulse oximetry, and non-invasive blood pressure (NIBP).

The sedation protocol was planned to maintain the Ramsay sedation score equal $\geqslant 5$ in addition to the absence of agitation and signs of insufficient analgesia during introduction of endoscope and during the procedure (see Tables 1 and 2).

We recorded induction time (which was defined as the time from the start of drug intake till achievement of RSS $\geqslant$ 5), procedure time, and recovery time (which was defined as the

time from stoppage of drug intake until achievement of the steward recovery score of 6). Heart rate (HR), mean arterial blood pressure (MAP), respiratory rate (RR), and oxygen saturation (SPO2) were continuously monitored and analyzed in the following five time intervals; before induction of sedation (T0), after induction of sedation and before insertion of endoscope (T1), immediately after insertion of endoscope (T2), throughout endoscopy procedures starting 5 min after insertion of endoscope (T3), and recovery period till the patient achieved 6 points on Steward recovery score (T4). The incidence of any unwanted movement that necessitates an incremental bolus of sedative drugs was reported.

We reported any adverse effects as oxygen desaturation (SPO2 < 90%), need for jaw thrust maneuver or manual ventilation, laryngospasm, any episodes of hypotension (decrease in MAP > 20%), bradycardia (decrease in HR > 20% of initial rate or HR < 55/min), vomiting, or shivering.

2.1. Statistical methods

Continuous variables were presented as mean ± SD, while categorical variables were presented as number and/or percentage of total. Independent samples *t*-test was used to test the differences between the two groups regarding; age, weight, times, HR, MAP, RR, and SPO2. Whereas changes in data within the same group (HR, MAP, RR, & SPO2) were analyzed using repeated measures analysis of variance, data about gender, type of GIE, and incidence of side effects were analyzed with chi-square test or Fisher's exact test as appropriate. A *p*-value <0.05 was considered statistically significant and all analyses were done using SPSS software version 20.

3. Results

No statistically significant differences were found between the two groups regarding age, weight, gender and type of endoscopy (Table 3).

The heart rate values changed significantly over the study period. In the dexmedetomidine group the heart rate decreased after induction of sedation (T1) then increased after insertion of endoscope (T2) when compared with the baseline value (T0) (for all *p*-value <0.001). Also in the propofol group after baseline value (T0) there was initial decrease in HR after induction of sedation (T1) then HR increased after insertion of endoscope (T2) and during recovery (T3) (for all *p*-value <0.001). These changes were less vigorous in the dexmedetomidine group as demonstrated by the fact that the heart rate values in the dexmedetomidine group were maintained significantly lower than in the propofol group at T1, T2 and T3 (83.95 ± 13.79 versus 92.95 ± 12.38, 103.35 ± 15.34 versus 112.75 ± 12.79 and 90.80 ± 13.99 versus 104.05 ± 10.73) beats/min respectively, for all *p*-value was <0.05 (Fig. 1).

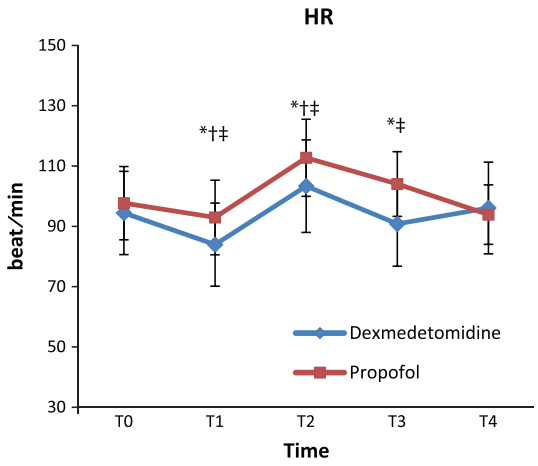

Figure 1 Changes in the heart rate (HR) in the two groups, data are presented as mean ± SD. Dexmedetomidine group ($n = 40$) and propofol group ($n = 40$). T0: before induction of sedation, T1: after induction of sedation and before insertion of endoscope, T2: immediately after insertion of endoscope, T3: during procedure, T4: during recovery till steward recovery score becomes 6. *denotes significance between both groups, *p*-value <0.005, †denotes significance within dexmedetomidine group, *p*-value <0.001, and ‡denotes significance within propofol group *p*-value <0.001.

No statistically significant differences were found in MAP values between the two groups at all time points (Fig. 2). While analysis of MAP within each group showed significant increase at T2 when compared to T0, this occurred in both groups (*p*-value <0.001). The changes in hemodynamics (HR and MAP) were not clinically important (within 20% of baseline values) and no interference needed.

The measurements of RR (Fig. 3) and SPO2 (Fig. 4) were comparable between the two groups all over the study period. No cases in dexmedetomidine group and six cases (15%) within propofol group demonstrated oxygen desaturation SPO2 < 90% (*p*-value = 0.026), which was corrected with chin lift and increasing the oxygen flow to 6 L/min, but no cases needed artificial airway or manual ventilation. Of these six cases five were undergoing upper GIE and one case was undergoing colonoscopy.

The time needed to achieve sedation was significantly longer in dexmedetomidine group than in propofol group (10.51 ± 1.75 versus 3.17 ± 0.72 min) *p*-value <0.001. Also the recovery time was significantly longer in dexmedetomidine group (28.55 ± 7.95 versus 13.68 ± 3.35 min) *p*-value <0.001. The procedure time was comparable in the two groups (Table 4).

Seven patients (17.5%) in dexmedetomidine group showed unwanted movement during the procedure which required

Table 3 Age, weight, gender, and type of endoscopy.

Parameters	Dexmedetomidine ($n = 40$)	Propofol ($n = 40$)	*P*-value
Age (year) mean ± SD	8.35 ± 3.82	9.94 ± 4.82	0.114
Weight (kg) mean ± SD	25.54 ± 9.65	28.11 ± 12.96	0.336
Gender (M/F)	22/18	24/16	0.651
Type of endoscopy (upper/lower)	26/14	25/15	0.816

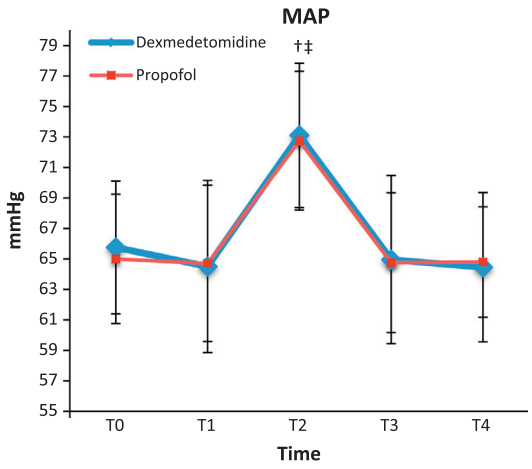

Figure 2 Changes in mean arterial blood pressure (MAP) between the two groups and within each group. Data presented as Mean ± SD. T0: before induction of sedation, T1: after induction of sedation and before insertion of endoscope, T2: immediately after insertion of endoscope, T3: during procedure, T4: during recovery till steward recovery score becomes 6. † denotes significance within dexmedetomidine group, p-value < 0.001 and ‡denotes significance within propofol group, p-value < 0.001.

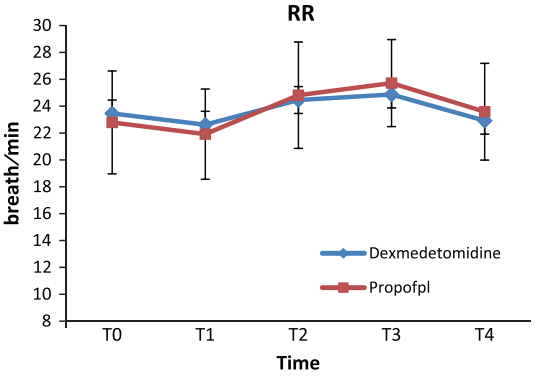

Figure 3 Respiratory rate (RR) changes in the two groups. T0: before induction of sedation, T1: after induction of sedation and before insertion of endoscope, T2: immediately after insertion of endoscope, T3: during procedure, T4: during recovery till steward recovery score becomes 6.

incremental bolus of dexmedetomidine versus only one patient (2.5%) in the propofol group (Table 5).

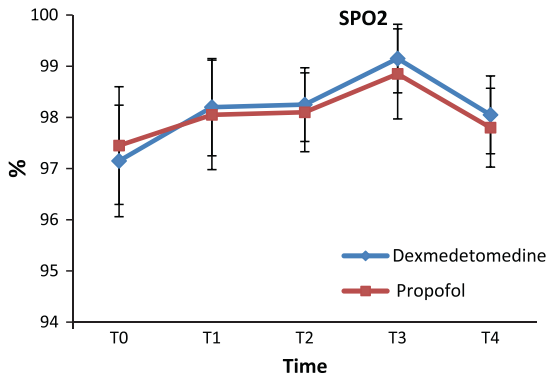

Figure 4 Changes in oxygen saturation (SPO2) in the two groups over the study period. T0: before induction of sedation, T1: after induction of sedation and before insertion of endoscope, T2: immediately after insertion of endoscope, T3: during procedure, T4: during recovery till steward recovery score becomes 6.

Table 4 Times of induction of sedation, procedure and recovery.

Parameters	Dexmedetomidin (n = 40)	Propofol (n = 40)
Induction time (min)	10.52 ± 1.75	3.17 ± 0.72*
Procedure time (min)	20.70 ± 10.71	19.65 ± 7.69
Recovery time (min)	28.55 ± 7.85	13.68 ± 3.35*

* Denotes significant difference between the two groups, p-value < 0.001.

Table 5 Incidence of adverse effects in the two groups.

Parameters	Dexmedetomidine (n = 40)	Propofol (n = 40)
Oxygen desaturation	0	6 (15)*
Unwanted movement	7 (17.5)	1 (2.5)
Vomiting	0	1 (2.5)
Shivering	0	0
Agitation	0	0
Laryngospasm	0	0
Bradycardia	0	0
Hypotension	0	0
Others	0	0

Data are presented as number of patients (%).
* Denotes significant difference between the two groups, p-value 0.026 (by Fishers' exact test).

4. Discussion

In our study, we compared dexmedetomidine versus propofol as a sedative for GIE procedure in pediatric patients.

There were no significant differences between both groups concerning MAP, while HR changes were more limited in dexmedetomidine group and HR values were significantly lower than in the propofol group reflecting more hemodynamic stability.

The incidence of oxygen desaturation was more evident with propofol that gives dexmedetomidine an important advantage regarding the respiratory safety and airway protection.

In pediatrics, there were many doses used in many previous studies ranging from 1 to 3 μg/kg/10 min for induction of sedation and 0.5–2 μg/kg/h for maintenance. In our study we used a high dose of dexmedetomidine 2.5 μg/kg/10 min for induction of sedation and 2 μg/kg/h for maintenance as we used it as a sole agent. The incidence of unwanted movements that needed incremental bolus was more in dexmedetomidine group. Both times of induction and recovery were prolonged with dexmedetomidine than propofol.

All these findings could be explained by the mechanism of action of dexmedetomidine. It acts on the vasomotor center in medulla and on locus ceruleus leading to decreased sympathetic outflow and increased parasympathetic outflow, allows for increased action of inhibitory GABA neurons, this together with triggering neurotransmitters that decrease histamine release leads to analgesia, sedation and natural rapid eye movement (REM) sleep without ventilatory depression [9,10] that explains the low incidence of oxygen desaturation. On the heart sympatholysis decreases tachycardia and produces bradycardia by the vagomimetic action. On the blood vessels central sympatholysis causes vasodilatation that may lead to hypotension, peripheral direct action causes vasoconstriction which may cause initial transient hypertension. Differences in HR and MAP profiles between studies may be rendered to the use of different dose regimens in addition to differences in nature of procedures [10].

The longer induction time with dexmedetomidine was due to the slow initial infusion over 10 min to avoid the undesirable hemodynamic changes that occur with faster infusion. Dexmedetomidine has a short half life (2–3 h) as it is rapidly distributed and extensively metabolized by the liver, still the recovery time was longer than that of propofol as propofol has three times shorter half life (30–60 min) [10].

A previous study [13] compared the effects of dexmedetomidine/ketamine and propofol/ketamine combinations in pediatric patients undergoing cardiac catheterization. It showed similar results as the systolic arterial blood pressure, SPO2, and RR were comparable between the 2 groups while HR was lower at 15, 30, and 45 min in dexmedetomidine group. The sedation scores were comparable between the 2 groups while BIS values and ketamine consumption were more in dexmedetomidine group than propofol group. Also, the recovery time was more prolonged in dexmedetomidine group than propofol group and oxygen desaturation was observed at a higher rate with propofol than dexmedetomidine [13].

Another study [14] evaluated the effects of dexmedetomidine as a sedative in pediatric dental patients versus propofol/midazolam combination. They found that HR, SPO2, & RR were comparable among both groups during all recorded times, while MAP was significantly lower in propofol group than dexmedetomidine group at 5, 10, 15 min. The time of induction of sedation was longer with dexmedetomidine than propofol, but the recovery time was shorter with dexmedetomidine than propofol. They explained that by the addition of midazolam to propofol as previous reports demonstrated that midazolam use in pediatrics resulted in long duration of action [14].

Koroglu et al. [15] compared dexmedetomidine versus propofol in children undergoing MRI examination, they found that dexmedetomidine preserved HR & MAP better than propofol. Also the incidence of oxygen desaturation was more with propofol, but the onset of sedation, recovery and discharge time were significantly shorter with propofol [15].

Another study by the same authors [16] Koroglu et al., compared dexmedetomidine versus midazolam in pediatrics undergoing MRI using a lower dose of dexmedetomidine, they found that the rate of adequate sedation was higher with dexmedetomidine associated with lower requirements of adjunct drugs. HR, MAP and RR were comparable between both groups but the onset of sedation was shorter with midazolam.

Ulgey et al., in their study [17] to test the results of addition of dexmedetomidine to ketamine/propofol combination during pediatric cardiac catheterization found a significant decrease in HR after induction of sedation and throughout the procedure in addition to a decrease in the incidence of oxygen desaturation. Also, addition of dexmedetomidine to ketamine/propofol resulted in shorter recovery time explained by the decreased amount of propofol used [17].

Mason et al., in their study [18] found that IV dexmedetomidine sedation was associated with modest fluctuations in HR and arterial blood pressure independent for age, required no pharmacologic interventions and didn't result in any adverse event and that fall within similar ranges to those published when propofol and inhalational anesthetics are used to achieve anesthesia at a target controlled infusion of propofol of 6 μg/ml or up to 1MAC with sevoflurane.

In summary, dexmedetomidine sedation in pediatric patients undergoing GIE procedures had both favorable and unfavorable aspects as; dexmedetomidine was associated with more HR stability. Also, the respiratory safety of dexmedetomidine as compared to propofol which was associated with higher incidence of oxygen desaturation, this is an important advantage of dexmedetomidine sedation especially in upper GIE procedures which is associated with increased possibilities of oxygen desaturation.

On the other hand, dexmedetomidine was associated with significant increase in the induction time of sedation and the recovery time that could affect the rate of turnover of cases which is an important factor in GIE units. Thus dexmedetomidine may be more suitable for the relatively longer procedures i.e. colonoscopy rather than shorter ones as most of the diagnostic and follow up upper GIE.

Also, in spite of using a higher dexmedetomidine dose than many studies, still some patients needed incremental boluses suggesting that we may need to increase the maintenance dose or add an adjunct drug.

In conclusion, dexmedetomidine sedation during GIE provides more respiratory safety & HR stability presenting itself as a suitable alternative agent especially for the relatively longer procedures.

Conflict of interest

None.

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