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Comparison of Dexmedetomidine-Propofol and Fentanyl-Propofol for Monitored Anesthesia Care (MAC). A prospective randomized study in lower GI endoscopies in paediatric age group

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Keypoints

Dexmedetomidine-Propofol (DP) sedoanalgesia may be considered preferable because it is associated with shorter recovery time, adequate post procedure analgesia, without any significant adverse effects on cardiovascular and respiratory parameters. DP is a well-tolerated and safe practical alternative in paediatric patients undergoing lower GI endoscopies under monitored anesthesia care.

Abstract

Introduction

The purpose of sedation and analgesia is to relieve patient anxiety and discomfort and improve the outcome of the GI endoscopic procedure. The objective is to evaluate and compare the clinical efficacy and safety of Dexmedetomidine + Propofol (DP) and Fentanyl + Propofol (FP) sedation for proclaiming a better drug regime in pediatric lower GI endoscopic procedures.

Materials and Methods

This prospective, randomized double blind study included hundred pediatric patients, of ASA I–II, aged between 7 to 16 years and were randomly allocated to either Dexmedetomidine and Propofol (DP) or Fentanyl and Propofol (FP) groups.

The study group received either Dexmedetomidine 1µg /kg over 10 minutes in *DP group* or Fentanyl 1µg/kg slow IV bolus in *FP group* for sedation induction followed by Propofol (50µg/kg/min) for maintainence (± Propofol rescue doses 0.5mg/kg were administered if patients showed discomfort) in both groups.

Results

The two groups were comparable in terms of age, weight, sex distribution, ASA status, diagnosis, the procedure performed and baseline hemodynamic and respiratory parameters.

The mean heart rate, systolic and diastolic arterial pressure during procedure were lower in the DP group as compared to FP group and difference was statistically significant ($P < 0.05$). Respiratory rate and SpO_2 were lower in FP group. Higher Ramsay sedation scores were observed in DP group. The mean recovery time (DP vs FP, 8.7 vs 10.56 mins) and length of stay in recovery (DP vs FP, 12.9 vs 15.14mins) was lesser in DP group and the difference was statistically significant ($P < 0.05$). The average number of rescue doses of Propofol used during the procedure were significantly less in DP group as compared to the FP group (DP vs FP, 1.84 ± 0.76 vs 3.72 ± 1.16, P Value <0.0001).

The adequacy of analgesia in patients of both groups was assessed by Wong Baker Faces Pain Rating Scale and was comparable. A higher percentage of operator satisfaction was observed in patients who underwent colonoscopy in DP group

Conclusion

Dexmedetomidine-Propofol sedoanalgesia may be considered preferable because it is associated with shorter recovery time, adequate post procedure analgesia, without any significant adverse effects on cardiovascular and respiratory parameters and is a practical alternative in paediatric patients undergoing lower GI endoscopies for monitored anesthesia care.

Keywords: Procedural Sedation, Monitored Anesthesia Care, Pediatric Patients, Lower GI Endoscopy, Colonoscopy, Dexmedetomidine, Propofol, Fentanyl

Introduction

Patient specific, procedural sedation for diagnostic, therapeutic, or invasive procedures is planned and administered to alleviate the patient's anxiety, discomfort, and pain in a safe manner[1]. The administration of sedation and analgesia for pediatric gastrointestinal procedures has become a routine. The achievement of safe and effective sedation for many endoscopic procedures remains a top priority for clinical gastroenterologists around the world and contribute to superior patient satisfaction, comfort, and willingness to undergo repeat procedure[2]. Procedural sedation, also referred to as moderate sedation, is a technique to administer "sedatives or dissociative agents with or without analgesics to induce a state of depressed level of consciousness that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function[3]."

Practice guidelines have been put forth by the American Society of Anesthesiologists (ASA) Committee for Sedation and Analgesia by Non-Anesthesiologists, and approved by the ASGE (American Society of Gastrointestinal Endoscopy) with the purpose of sedation and analgesia is to relieve patient anxiety and discomfort, improve the outcome of the examination, and diminish the patient's memory of the event[4,5].

The optimal level of sedation differs according to the procedure being performed. Deep sedation or even general anesthesia may be preferred for therapeutic procedures to ensure patient's immobility[6,7].

Current ASGE recommendations state, "The amount of sedation or analgesia required for any procedure varies depending on the patient's age, prior medications, associated illness, anxiety levels, type and duration of procedure. One should use the minimal dose to achieve the desired effect"[8].

Drugs commonly used for IV sedation for pediatric lower GI endoscopy procedures are Benzodiazepines (e.g. Diazepam, Midazolam), Opioids (e.g. Fentanyl, Remifentanil), Ketamine, Propofol and Dexmedetomidine.

It is essential to understand the pharmacology, pharmacokinetics and pharmacodynamics of these agents due to fine line between over and under sedation and for determining proper agent for specific patient needs.

Dexmedetomidine, a short-acting alpha$_2$-agonist, possesses anxiolytic, anesthetic, hypnotic, and analgesic properties[9], without causing respiratory depression at therapeutic dose and retains the response to verbal commands[10-13].

Propofol is a short-acting, intravenously administered hypnotic agent used for induction and maintenance of general anesthesia[14], sedation for mechanically ventilated adults and procedural sedation[15].

Fentanyl is a synthetic opioid agonist being increasingly used for sedation and analgesia[16-18].

The impetus for this study is to explore the use of dexmedetomidine with maintenance dose of propofol during lower GI endoscopy, so that adequate sedation could be provided with minimal side effects and better analgesia for sedation in pediatric patients undergoing lower GI endoscopic procedures and to proclaim a better drug regime for sedation in pediatric patients during lower GI endoscopic procedures.

Materials and Methods

After ethical committee approval and written informed consent from the patient's parents. This prospective and randomized double blind study included a total of hundred pediatric patients, ASA I–II, aged between 7 to 16 years. The study has been conducted over a period of two years.

After pre-procedure evaluation, following patients (Neurologically impaired children, history of allergy to drugs or their components, Cardiac disease, pulmonary disease, Non fasting status and refusal to consent) were excluded from the study.

No sedative premedication was administered. Patients were kept fasting for at least 6 hours. All patients had an appropriate size cannula secured in a peripheral vein for intravenous (IV) fluids and drugs.

The patients were randomly allocated to either of the two groups using a closed envelope method to receive Dexmedetomidine and Propofol (DP) or Fentanyl and Propofol (FP) combination.

The study groups received either Dexmedetomidine 1µg /kg as an IV infusion over 10 minutes or Fentanyl 1µg/kg slow IV bolus for sedation induction. An infusion of Propofol (50µg/kg/min) was started for maintenance in both groups immediately after sedation induction. Additional rescue doses of Propofol (0.5mg/kg) were administered if patients showed discomfort in any of the groups.

Supplemental 3–4 liters per minute of oxygen was given in all cases during the procedure. Data was collected by an independent observer, who was not a part of the management team.

Following Parameters like Heart rate (HR), Systolic Arterial Blood Pressure (SABP), Diastolic Arterial Blood Pressure (DABP), Oxygen saturation (SpO_2), Respiratory rate (RR), Ramsay Sedation Score (RSS) were recorded at baseline (10 min before procedure) then every 5 min after induction during the procedure. Before shifting the patient from recovery, intensity of pain was assessed by Wong–Baker Faces Pain Rating Scale.

The following times were recorded *Onset of Sedation* (time from the end of the loading dose to achievement of Ramsay Sedation Score of 4), *Procedure Time* (time from achieving the required Ramsay Sedation Score till the end of procedure or stoppage of drug infusion), *Recovery Time* (time from stoppage of drug infusion till reaching the Ramsay Sedation Score of 2) and *Length of stay in recovery* (time from stoppage of drug infusion till the discharge of the child from the recovery with Aldrete Score of >8).

The following events were taken note of *a) adverse cardiac event* (ACE) like SABP, DABP and Heart rate with a deviation >20% from the baseline, conduction disturbances e.g., ectopics on ECG *b) adverse respiratory event* (ARE) like SpO2 <90%, Respiratory rate < 10 breaths/min, laryngospasm, *c) Any other adverse event/complication* was taken note of *d) An adverse cardiac event was managed* with inj. atropine@10µg/kg i.v., *e) An adverse respiratory event* was to be managed with increasing the rate of O_2 to 8-10 litres/min, f*) Rescue doses of propofol* given in both groups were measured, g) the gastroenterologist was asked to rate the *ease of the procedure* at the end of the procedure, on a three-point scale (easy, adequate, impossible).

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD and results on categorical measurements are presented in number (N) and percentage (%). For comparison of numeric variables an unpaired t test was used for normal distribution and unpaired Mann-Whitney test for asymmetric distribution. Fisher's exact test and χ^2 test was used for comparison of categorical variables. All these statistical tests were two sided and were referred for P Values for their significance. Any P Value less than 0.05 (P <0.05) was taken to be significant.

Statistical software: The Statistical software namely SPSS 15.0, MedCalc 9.0.1 and GraphPad Prism 6 were used for the analysis of the data.

Results

The two groups were thus comparable in terms of age, weight, sex distribution, ASA status, diagnosis and the procedure performed. [Table 1]

The mean preprocedure and baseline hemodynamic (HR, SBP, DBP) and respiratory (SpO2, RR) parameters were comparable among both the study groups. [Table 2] The mean heart rate at 5, 10, 15 and 20 minutes respectively was less in DP group 79.50±6.303, 79.94±7.118, 80.58±5.305 and 81.80±7.177 respectively as compared to the FP group 83.68±5.501, 84.46±5.828, 86.40±5.034 and 86.25±6.017 respectively. The difference between the mean heart rate of the two groups was statistically significant at 5 min (P Value < 0.0006), 10min (P Value <0.0008) and 15 minutes (P Value <0.0001), however it was not significant at 20 minutes (P Value 0.1291). [Table 2] The mean baseline Systolic Arterial Pressure (mmHg) of the two groups was comparable and statistically non-significant (DP vs FP, 101.2 ± 4.817 vs 99.56 ± 5.096, P Value 0.093). The mean Systolic Arterial Pressure (mmHg) at 5, 10, 15 and 20 minutes was less in DP group 89.90±4.954, 90.96±4.54, 92.25±4.087 and 95.60±4.88 respectively as compared to the FP group 95.42±5.75, 95.96±3.156, 97.60±2.43 and 98.67±2.60. The difference between the mean Systolic Arterial Pressure (mmHg) of the two groups was statistically significant at 5 min (P Value <0.0001), 10min (P Value <0.0001) and 15 minutes (P Value <0.0001), however it was not significant at 20 minutes (P Value 0.074). [Table 2] The baseline Diastolic Arterial Pressure (mmHg) between the two groups was comparable and statistically not significant (DP vs FP, 59.84 ± 4.626 vs 59.08 ± 3.63, P Value 0.363). The Diastolic Arterial Pressure (mmHg) at 5, 10, 15 and 20 minutes was less in DP group 51.66±3.48, 51.76±3.623, 51.90±3.185 and 54.60±3.718 respectively as compared to the FP group 55.06±3.36, 56.72±3.064, 58±2.80 and 58.25±2.99. The difference was statistically significant at 5 min (P Value <0.0001), 10min (P Value <0.0001), 15 minutes (P Value <0.0001) and at 20 minutes (P Value 0.019). [Table 2]. The mean baseline respiratory rates (breaths per minute) of the two groups were comparable and the differences were not statistically significant (DP vs FP, 15.22 ± 1.282 vs 14.96 ± 0.97, P Value 0.23). The mean respiratory rate at 5, 10, 15 and 20 minutes in DP group was 14.68±1.077, 14.86±1.088, 14.63±1.005 and 14.60±1.174 respectively and was comparable to FP group was 14.22±1.765, 14.64±0.898, 14.35±1.131 and 14.08±0.9962. The difference between the mean respiratory rate of the two groups was not statistically significant at 5 min (P Value 0.12), 10 min (P Value 0.27), 15 minutes (P Value 0.24) and at 20 minutes (P Value 0.28). [Table 2] The mean baseline SpO_2% between the two groups was comparable and the difference was not statistically significant (DP vs FP, 98.30 ± 0.79 vs 98.20 ± 0.0.858, P Value 0.54).The mean SpO_2 at 5 minutes was lower in the FP group than the DP group (DP vs FP, 99.46±0.54 vs 98.08±3.103) and was statistically significant (P Value 0.0025), however it was comparable to DP group at 10 min (DP vs FP, 99.68±0.47 vs 99.58±0.57, P Value 0.34), 15 min (DP vs FP, 99.68±0.47 vs 99.60±0.57 P Value 0.53) and 20 minutes (DP vs FP, 99.60±0.52 vs 99.33±0.49 P Value 0.23). [Table 2] The baseline RSS between the two groups (DP vs FP group) were comparable with RSS 1 [28(56%) vs 26(52%)] and RSS 2 [22(44%) vs 24(48%)]. The difference was not statistically significant (P Value 0.84). At 5 minutes during the procedure, 47(94%) patients in DP group and 35(70%) patients in FP group had RSS of 4-5 whereas 3 (6%) patients in DP group and 15(30%) patients in FP group had RSS of 3. The difference was statistically significant (P Value 0.003). At 10 minutes during the procedure, 46(92%) patients in DP group and 33(66%) patients in FP group had RSS of 4-5 whereas 4 (8%) patients in DP group and 17(34%) patients in FP group had RSS of 3. The difference was statistically significant (P Value 0.0026).

At 15 minutes during the procedure, 37(92.5%) patients in DP group and 31(72.10%) patients in FP group had RSS of 4-5 whereas 3 (7.5%) patients in DP group and 12(27.90%) patients in FP group had RSS of 3. The difference was statistically significant (P Value 0.021). At 20 minutes during the procedure, 10 (100%) patients in DP group and 11(91.77%) patients in FP group had RSS of 4-5 whereas none of the patients in DP group and 1 (8.33%) patients in FP group had RSS of 3. The difference was not statistically significant (P Value 1.00). [Table 2] The mean time (in minutes) to onset of sedation (DP vs FP, 8.38 ± 1.10 mins vs 8.72±1.18 mins, P Value 0.13), and procedure time (DP vs FP, 16.72 ± 3.4 vs 17.10 ± 3.2), were comparable between the two groups. [Table 3] The mean recovery time was lesser in the DP group as compared to the FP group and the difference was statistically significant (DP vs FP, 8.7 ± 1.4 mins vs 10.56±1.6 mins, P Value <0.0001). [Table 3] The mean length of stay in recovery was also lesser in the DP group as compared to the FP group and the difference was statistically significant (DP vs FP, 12.90 ± 1.53 mins vs 15.14±1.85 mins, P Value <0.0001). [Table 3] The average number of propofol rescue doses (Mean±S.D) used during the procedure were significantly less in the dexmedetomedine -Propofol group as compared to the fentanyl -propofol group (DP vs FP, 1.84 ± 0.76 vs 3.72 ± 1.16, P Value <0.0001). [Table 3] 2 patients (4%) in the DP group developed an adverse cardiac event and 1 patient (2%) in the FP group developed an adverse cardiac event. The difference was not statistically significant (P Value 1.00). These patients developed both bradycardia and hypotension which was managed by inj. Atropine IV @10µg/kg only. [Table 4] None of the patients in the DP group developed an adverse respiratory event. 3 patients (6%) in the FP group developed an adverse respiratory event. The difference was not statistically significant (P Value = 0.242). These patients desaturated to SpO_2<90% and their respiratory rate dropped to less than 10 breaths/min, however none of the patients developed apnoea. All these patients were managed by increasing the O_2 flow to 8-10 lts/min and none of the patients required any additional maneuvers. [Table 4] The adequacy of analgesia in patients of both groups was assessed by Wong Baker Faces Pain Rating Scale and compared.7 patients (14%) in the DP group and 8 patients (16%) in the FP had Wong Baker Faces Pain Scale ranging from 0-1whereas 43 (86%) patients in DP group and 42 (84%) patients in FP group had Wong Baker Faces Rating Pain Scale ranging from 2-3. The difference was not statistically significant (P Value 0.78). [Table 5] The Aldrete score at discharge was observed in the two groups. 37 (74%) patients in DP group and 35 (70%) patients in FP group had an Aldrete score of 9 at discharge. 13(26%) patients in DP group and 15(30%) patients in group FP had an Aldrete score of 10 at discharge. The difference was not statistically significant (P Value 0.66). [Table 5] A higher percentage of operator satisfaction was observed in patients who underwent colonoscopy using dexmedetomidine-propofol sedation analgesia protocol. However, the difference was not statistically significant (DP vs FP, 88% vs 72%, P Value 0.078). [Table 5] None of the patients in Group DP and FP showed impossible/inadequate rating for procedural sedation during colonoscopy. When comparing the ease of rating between the groups, it was statistically insignificant.

Characteristic		**Group DP**	**Group FP**
		N (%)	**N (%)**
Age In Years	7-9	25 (50)	24 (48)
	10-12	17 (34)	20 (40)
	13-16	8 (16)	6 (12)
	Mean±S.D	9.980 ± 2.495	9.840 ± 2.198
Gender	Male	29 (58)	26(52)
	Female	21 (42)	24 (48)
Weight (Kgs)	Mean±S.D	31.10 ± 6.538	29.28 ± 6.085
ASA Physical Status	ASA 1	48 (96)	49 (98)
	ASA 2	2 (4)	1 (2)
Procedure Performed	Flexible Colonoscopy	50 (100)	50 (100)
	Polypectomy	50 (100)	50 (100)

Table 1.
Average Age (Mean ± S.D Years), Average Weight and Sex Distribution in DP (Dexmedetomidine - Propofol) and FP (Fentanyl -Propofol) Groups.

Time Interval	Characteristics		Group DP Mean	Group DP S.D	Group FP Mean	Group FP S.D	P Value
Baseline	Heart Rate (HR)		89.08	6.334	90.52	5.433	0.2253
	SABP		101.2	4.817	99.56	5.096	0.093
	DABP		59.84	4.626	59.08	3.63	0.363
	RR		15.22	1.282	14.96	0.97	0.23
	SPO_2		98.30	0.7890	98.20	0.8571	0.54
	RSS	1	28	56	26	52	0.84
		2	22	44	24	48	
5 Minutes	HR		79.50	6.303	83.68	5.501	<0.0006
	SABP		89.90	4.954	95.42	5.75	<0.0001
	DABP		51.66	3.48	55.06	3.36	<0.0001
	RR		14.68	1.077	14.22	1.765	0.12
	Spo2		99.46	0.5425	98.08	3.1	0.0025
	RSS	3	3	6	15	30	
		4-5	47	94	35	70	0.003
10 Minutes	HR		79.94	7.118	84.46	5.828	<0.0008
	SABP		90.96	4.54	95.96	3.156	<0.0001
	DABP		51.76	3.623	56.72	3.064	<0.0001
	RR		14.86	1.088	14.64	0.8981	0.27
	SPO_2		99.68	0.47	99.58	0.57	0.34
	RSS	3	4	8	17	34	
		4-5	46	92	33	66	0.0026
15 Minutes	HR		80.58	5.305	86.40	5.034	<0.0001
	SABP		92.25	4.087	97.60	2.43	<0.0001
	DABP		51.90	3.185	58	2.80	<0.0001
	RR		14.63	1.005	14.35	1.131	0.24
	SPO_2		99.68	0.47	99.60	0.57	0.53
	RSS	3	3	7.5	12	27.90	0.0217
		4-5	37	92.5	31	72.10	
20 Minutes	HR		81.80	7.177	86.25	6.017	0.1291
	SABP		95.60	4.88	98.67	2.60	0.074
	DABP		54.60	3.718	58.25	2.99	0.019
	RR		14.60	1.174	14.08	0.9962	0.28
	SPO_2		99.60	0.52	99.33	0.49	0.23
	RSS	3	0	0	1	8.33	1.00
		4-5	10	100	11	91.77	

Table 2.
Average heart rate (HR), Systolic Arterial Blood Pressure (SABP), Diastolic Arterial Blood Pressure (DABP), respiratory rate (RR), peripheral oxygen saturation (SPO_2) and Ramsay Sedation Score (RSS) (Mean±S.D) in the DP (Dexmedetomidine-Propofol) and FP (Fentanyl-Propofol) groups during the procedure.

Parameter	Group DP Mean	Group DP S.D	Group FP Mean	Group FP S.D	P Value
Onset Of Sedation in minutes	8.38	1.10	8.72	1.18	0.13
Procedure Time in minutes	16.72	3.4	17.10	3.2	0.57
Recovery Time in minutes	8.7	1.39	10.56	1.63	<0.0001
Length Of Stay In Recovery in minutes	12.90	1.53	15.14	1.85	<0.0001
Number of Propofol Rescue Doses used	1.840	0.765	3.720	1.161	<0.0001

Table 3.
Average Onset of Sedation Time, Procedure Time, Recovery Time, Length of Stay in Recovery in minutes and average number of rescue doses used during the procedure (Mean±S.D) in DP (Dexmedetomidine-Propofol) and FP (Fentanyl-Propofol) groups.

Parameters	Group DP N	Group DP %	Group FP N	Group FP %	P Value
Adverse cardiac event	2	4	1	2	1.00
Adverse respiratory event	0	0	3	6	0.242

Table 4.
Adverse Cardiac and respiratory Events in DP (Dexmedetomidine-Propofol) and FP (Fentanyl-Propofol) groups during the procedure.

Scale	Score	Group DP N	Group DP %	Group FP N	Group FP %	P Value
Wong Baker Faces Pain Scale	0-1	7	14	8	16	0.78
	2-3	43	86	42	84	
Aldrete Score	9	37	74	35	70	0.66
	10	13	26	15	30	
Gastroenterologists Satisfaction rating of procedure	Easy	44	88	36	72	0.078
	Adequate	6	12	14	28	

Table 5.
Wong Baker Faces Pain Rating Scale, Aldrete Score and Gastroenterologists satisfaction rating of procedure in DP (Dexmedetomidine-Propofol) and FP (Fentanyl -Propofol) groups.

Discussion

The two groups were thus comparable in terms of age, weight, sex distribution, ASA status, diagnosis and the procedure performed and mean baseline hemodynamic and respiratory parameters. The mean heart rate, Systolic Arterial Pressure (SABP) and Diastolic Arterial Pressure (DABP) during the procedure was less in DP group as compared to the FP group.

Hypotension and bradycardia have been reported in dexmedetomidine infusions, particularly with high bolus dosing regimens, in patients with pre-existing cardiac problems and a loading dose infusion given over 10 min[13,19-21]. These results also co-relate well with the study of Ragab A *et al* [22], who compared the effects of dexmedetomidine/ morphine/ propofol with benzodiazepines/ morphine/propofol as adjuncts to local anesthesia during rhinoplasty–on analgesia, sedation, respiratory and hemodynamics variables and surgeon and patient satisfaction. Intraoperative mean arterial blood pressure and heart rate in Dexmedetomidine group were lower than their baseline values and the corresponding values in Midazolam group. Korugulu A *et al* [23] also reported a significant decrease in the heart rate from baseline following dexmedetomidine infusion in children undergoing MRI examination. Similar results were seen by Tosun Z *et al* [24], who compared the effects of dexmedetomidine-ketamine [DK] and propofol-ketamine [PK] combinations on hemodynamics, sedation level, and the recovery period in pediatric patients undergoing cardiac catheterization. The heart rate in group DK was significantly lower (average 10-20 beats/min) than group PK after induction and throughout the procedure. A possible explanation for the drop in heart rate in our patients may be because of a higher baseline heart rate in children because of more procedure related anxiety as no premedication was used.

Hypotension is commonly reported with Dexmedetomidine therapy[25-28], due to its sympatholytic effect. Parikh DA *et al* [29] noticed intraoperative heart rate and mean arterial pressure following dexmedetomidine therapy were lower than the baseline values and the corresponding values in Midazolam-Fentanyl therapy (P Value < 0.05) during tympanoplasty. Hyo-Seok Na *et al* [30] found similar results that dexmedetomidine use resulted in significantly lower systolic blood pressures compared to propofol and alfentanil when used for monitored anaesthesia care. Alados-Arboledas FJ *et al* [31] reported that sedation analgesia protocol with Fentanyl-Propofol was both effective and safe to achieve sedation for diagnostic upper gastrointestinal endoscopy in pediatric patients.

The mean respiratory rate during the procedure was slightly lower in the FP group than the DP group but not significant statistically (P Value > 0.05) and remained more stable in the DP group than in the FP group. The mean SpO_2 at 5 minutes was lower in the FP group than the DP group (P Value 0.0025) and was comparable to DP group during rest of the procedure time (P Value > 0.05). Overall, the saturation of the patients remained more stable in the DP group. Dexmedetomidine is unique in that it does not cause respiratory depression[3,10-13] because its mechanism is not mediated by the γ-aminobutyric acid system[32].

Na HS *et al* [30] reported that though the effects of dexmedetomidine as well as propofol and alfentanil on respiratory rate were comparable when used for monitored anaesthesia care, dexmedetomidine provided a more stable respiratory rate intraoperatively. Cooper L *et al* [33] also reported Dexmedetomidine is effective in achieving adequate levels of sedation without increasing the rate of respiratory depression or decreasing oxygen saturation compared with standard therapy (midazolam and opioids). AnchaleeTechanivate *et al* [34] in their study found no differences in the respiratory end points of two groups i.e. Group P (fentanyl/propofol) and Group D (dexmedetomidine/fentanyl with propofol). All patients maintained a normal respiratory rate and oxygen saturation during the procedure.

Although both fentanyl and propofol are known to cause respiratory depression and desaturation, however the respiratory rate during the procedure was comparable between FP and DP group in our study since we avoided a bolus dose of propofol as has been used by Aydin Erden *et al* [35] and Godambe SA *et al* [36], who reported significant respiratory complications following the use of propofol bolus with fentanyl. Alados-Arboledas FJ *et al* [31] reported that sedation analgesia protocol with Fentanyl-Propofol was both effective and safe to achieve sedation for diagnostic upper gastrointestinal endoscopy in pediatric patients.

In the present study, the baseline Ramsay Sedation Scores of the two groups were comparable and the difference was not statistically significant (P Value 0.84).

In the present study higher Ramsay Sedation Scores were observed in the DP group as compared to the FP group during the procedure (P> 0.05) and returned to statistically insignificant difference at 20 min (P Value 1.00).

Ragab A *et al* [22] in their study also recorded a better level of sedation intraoperatively in the dexmedetomidine group. Koroglu A *et al* [23] also reported a higher rate of adequate sedation with dexmedetomidine compared to midazolam in children undergoing MRI examination. Ali AR *et al* [37] in their study reported a better sedation-analgesia profile in propofol/dexmedetomidine group as compared to the propofol/fentanyl group in children undergoing ESWL. Comparable results were found by Dere K *et al* [38], who concluded that RSS scores in Dexmedetomidine group were significantly higher than the midazolam/fentanyl group at the 10 and 15 minute in patients undergoing colonoscopy under conscious sedation.

In the present study, the mean *induction time /onset of sedation* was comparable between the two groups and the difference was not statistically significant (DP vs FP, 8.38 ± 1.10 mins vs 8.72± 1.18 mins, P Value 0.13). Waleed MA *et al* [39] recorded an onset of sedation time of 8.7 ±1.8 mins following dexmedetomidine infusion. Although the authors have used a higher loading dose of dexmedetomidine of 2µg/kg, the onset times are comparable with the present study because of the use of propofol maintenance in our study, which has a quicker onset and an additive effect on the sedative properties of dexmedetomidine. Alados-Arboledas FJ *et al* [31] reported an induction time of 6 minutes with Propofol Fentanyl sedation analgesia protocol. This was relatively less than the induction time in the present study. The possible explanation for the same is that the authors have used an additional dose of fentanyl and a loading dose of propofol, in addition to maintenance, which have been avoided in the present study to avoid respiratory complications.

In our study, the *onset of sedation times* with dexmedetomidine-propofol group were comparable to those of Koroglu A *et al* [23], who have used a dexmedetomidine bolus infusion over 10 minutes followed by maintenance [8.7 minutes (from the end of infusion) vs 19 min (from the start of infusion)]. AnchaleeTechanivate *et al* [34] found comparable *induction times* of two groups i.e. Group P (fentanyl/propofol) and Group D (dexmedetomidine/fentanyl with propofol). The induction time was lesser in both groups (6.3 and 6.5 minutes) as compared to our study. The possible reason could be the use of propofol bolus along with the study drug at induction by the above authors, which was avoided in our study.

Waleed MA *et al* [39] have reported a *longer recovery and discharge time* (18.3 min and 19.2 min) in their study in patients receiving dexmedetomidine. This may be due to a larger initial loading dose of 2µg/kg and maintenance with dexmedetomidine, which has a slower offset than propofol used for maintenance in our study. Ryu JH *et al* [40] recorded a recovery time of 18.4 min in the dexmedetomidine propofol group, which is relatively longer than our study. This can be explained by the fact that that the authors in the above study have used maintenance dose of dexmedetomidine after a loading dose of dexmedetomidine, which might have prolonged the recovery. The procedure time is also relatively lesser as compared to our study (12 vs 17 min). Aydin Erden *et al* [35] reported a recovery time of 19.2 ± 11.3 minutes and a longer discharge time in children undergoing extracorporeal shock wave lithotripsy during sedation-analgesia with propofol /fentanyl. This is relatively longer than our study. This may be due to the fact that the authors have used a high loading dose of propofol at the time of induction as well as midazolam premedication, both of which were not used in our study. Anchalee Techanivate *et al* [34] in their study found longer recovery times in Group P (fentanyl / Propofol) as compared to group Group D (dexmedetomidine/fentanyl with Propofol) (Group D vs Group P: 6min vs 10.2 min, P Value 0.038).

In the present study, the average number of propofol rescue doses (bolus of 0.5 mg/kg whenever patient showed discomfort) used during the procedure were significantly less in the dexmedetomidine-propofol group as compared to the fentanyl propofol group (DP vs FP, 1.84 ± 0.76 vs 3.72 ± 1.16, P Value <0.0001).

This correlates well with the study of Dutta S *et al* [41], who reported that dexmedetomidine reduced propofol concentrations required for sedation and suppression of motor response. Therefore, the propofol dose required for sedation and induction of anesthesia may have to be reduced in the presence of dexmedetomidine. Tosun Z *et al* [42] also reported that the number of patients who required additional propofol was significantly higher in the PF group compared to the PK group (50% VS 17 %, P Value <0.01). Ali AR *et al* [37] in their study reported that propofol/dexmedetomidine combination was accompanied with less propofol consumption, prolonged analgesia and lower incidence of intraprocedural and postprocedural complications compared to propofol/fentanyl group. In the present study, 2 patients (4%) in the DP group developed an adverse cardiac event (hypotension and bradycardia) and 1 patient (2%) in the FP group developed an adverse cardiac event. The difference was not statistically significant (P Value 1.00).

Hypotension and bradycardia is commonly reported with dexmedetomidine therapy [25-28] due to its sympatholytic effect.

Hyo-Seok Na *et al* [30] reported a 3.2 % incidence of adverse cardiac events with dexmedetomidine infusion. Ryu JH *et al* [40] reported no adverse cardiac events in 35 patients undergoing flexible brochoscopy using dexmedemidine-propofol sedation analgesia protocol. Alados-Arboledas FJ *et al* [31] reported no adverse cardiac events in patients in whom sedoanalgesia was performed using Fentanyl/Propofol. Ayden Arden *et al* [35] reported 5% incidence of bradycardia which required treatment using propofol/fentanyl in children for ESWL.

In the present study, 3 patients (6%) in the fentanyl-propofol group and none of the patients in demedetomidine-propofol group had an adverse respiratory event (Desaturaton i.e., SpO_2<90%, respiratory rate < 10 breaths/min). The difference was not statistically significant (P Value 0.242). Dexmedetomidine is unique in that it does not cause respiratory depression [3, 10-13] because its mechanism is not mediated by the γ-aminobutyric acid system[32].

Ragab A *et al* [22] reported 3.3% incidence of desaturation and apnea in patients with Dexmedetomidine/Propofol sedoanalgesia for conscious sedation in rhinoplasty under local anesthesia. Ryu JH *et al* [40] reported a 3% incidence of adverse respiratory events with Dexmedetomidine/Propofol sedation. However Mostafa El-Hamamsy *et al* [44] reported no adverse respiratory events with Dexmedetomidine/Propofol sedation in pediatric patients undergoing bronchoscopy. Alados-Arboledas FJ *et al* [31] reported no adverse respiratory events in patients in whom sedoanalgesia was performed using fentanyl/propofol. Ayden Erden *et al* [35] reported 25% incidence of desaturation using propofol/fentanyl in children for ESWL. Although this was relatively higher than the present study, possibly due to a high loading dose of propofol used at the time of induction which was avoided in present study.

In the present study, the post procedure analgesia was adequate and comparable between the two groups as was observed by Wong Baker Faces Pain Rating Scale scores (P Value 0.78). The Aldrete scores at discharge were comparable between the two groups and the results were not statistically significant (P Value 0.66).

Ragab A *et al* [22] reported higher patient satisfaction scores and lower pain scores with dexmedetomidine/propofol/morphine conscious sedation as compared to midazolam/propofol/morphine in rhinoplasty. Aydin Erden *et al* [35] in their study also concluded that both Fentanyl/Propofol and Propofol/Ketamine had equal efficacy in providing sufficient analgesia for ESWL with their corresponding side effects. Ali AR *et al* [37] concluded that both propofol/fentanyl and propofol/dexmedetomidine combinations at mentioned dose regimen were effective and well tolerated for children undergoing extracorporeal shock wave lithotripsy.

In the present study, higher percentage of operator satisfaction was observed in patients who underwent colonoscopy using dexmedetomidine/propofol sedation analgesia protocol, however the difference was not statistically significant (P Value 0.078).

Dere K *et al* [38] in their study observed higher colonoscopist satisfaction scores with dexmedetomidine sedoanalgesia. Parikh DA *et al* [29] reported a better surgeon satisfaction score in patients receiving dexmedetomidine during monitored anaesthesia care for tympanoplasty. Ragab A *et al* [22] also observed better surgeon satisfaction score in patients undergoing rhinoplasty under local anaesthesia with dexmedetomidine/morphine/propofol compared to midazolam/ morphine/ propofol for conscious sedation.

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