ORIGINAL ARTICLE

Open Access

Lidocaine and dexmedetomidine combined infusion as an alternative to propofol for sedation in colonoscopy

Tamer Hamed Ibrahim[1,2]

Abstract

Background: Colonoscopy is one of the commonly performed procedures for the diagnosis of colonic disorders. Several sedation regimens are administered during colonoscopy. To date, the propofol-based sedation regimen is commonly used, although it may have some risks. I studied the efficacy of dexmedetomidine–lidocaine combination as a substitution for propofol for sedation in colonoscopy procedures.

It is a prospective randomized controlled study; 62 patients were recruited and divided into two equal groups: group P is the propofol group which included patients who received sedation with IV propofol using a loading dose of 50–100 mg of propofol and were continued on propofol IV infusion 25–75 μg/kg/min and group D-L is the dexmedetomidine–lidocaine group where patients received a loading dose of dexmedetomidine 1 μg/kg infused over 10 min followed by infusion of dexmedetomidine 0.2–0.7 μg/kg/h and lidocaine 1 mg/kg IV followed by an infusion of 1.5 mg/kg/h. The primary outcome was the median patients' satisfaction scores after recovery assessed by the Likert 5-item scoring system. Other outcomes included postprocedure pain score, mean arterial blood pressure, saturation, heart rate during the procedure, amount of fentanyl and midazolam used during the procedure, and the number of apneic attacks.

Results: Patients in both groups were satisfied by the procedure, and the median and 1st–3rd IQ satisfaction scores were 5 (4.0–5.0) in group P and 4 (4.0–5.0) in group D-L; however, this difference was statistically significant (P value = 0.014), reflecting more satisfaction in patients who received propofol. Patients in group D-L required significantly more doses of midazolam and fentanyl to achieve an adequate sedation score, had a more significant drop in heart rate, and had significantly more postoperative pain scores than those in group P. Patients in group P had significantly more apneic attacks and lower intraprocedural oxygen saturation levels than those in group D-L.

Conclusion: Dexmedetomidine–lidocaine combined IV infusion was found to be effective and safe for sedation in colonoscopy with less side effects in terms of apneic attacks and desaturation, although patient satisfaction was significantly higher in the propofol group, yet as per the sedation scores this was considered to be clinically non-significant.

Trial registration: The study was registered by the Australian New Zealand Clinical Trials Registry (trial ID: 1262 0000249954).

Keywords: Colonoscopy, Dexmedetomidine, Lidocaine, Propofol, Sedation, Patient satisfaction

Correspondence: dr_tamerhamed@yahoo.com
[1]Faculty Of Medicine, Ain Shams University, Cairo, Egypt
[2]NMC Royal Hospital – DIP, P.O. Box 7832, Dubai, United Arab Emirates

Background

Colonoscopy is the standard procedure for diagnosis, screening, treatment, and follow-up of many colorectal diseases. Although some patients can tolerate a colonoscopy procedure without any sedation and analgesia, it is a distressful procedure for most patients. As a result, different techniques have been developed and conscious sedation using propofol is the most widely and frequently used due to its own pharmacokinetic and pharmacodynamics, i.e., fast onset, easy to titrate, and faster recovery (Chelazzi et al. 2009); however, it may cause bradycardia, respiratory depression, and hypotension (Techanivate et al. 2012).

Dexmedetomidine (Dex.) was approved by the Food and Drug Administration at the end of 1999 for use in humans as a short-term medication (< 24 h) for analgesia and sedation in the intensive care unit (ICU). Its unique properties render it suitable for sedation and analgesia during the whole perioperative period. Its applications as a premedication, as an anesthetic adjunct for general and regional anesthesia, and as a postoperative sedative and analgesic are similar to those of the benzodiazepines, but a closer look reveals that the a_2-adrenoceptor agonist has more beneficial side effects (Ralph et al. 2001).

Dex. is a selective α2-adrenergic receptor agonist (Funai et al. 2014) that possesses anxiolytic, anesthetic, hypnotic, and analgesic properties (Young and Prielipp 2002). It acts on the presynaptic receptor and regulates the release of norepinephrine through a negative feedback mechanism (Funai et al. 2014). The analgesic effects are mediated by alpha 2-adrenergic receptors present on the neurons of the superficial dorsal horn in lamina II, by inhibiting the release of nociceptive transmitters, namely substance P and glutamate, and by hyperpolarization of spinal interneurons. Sympatholysis occurs due to the activation of postsynaptic α2-adrenergic receptors that results in hypotension, and bradycardia thus helps in attenuating the stress response (Bloor et al. 1992). It decreases salivation, intraocular pressure, shivering threshold, bowel motility, and insulin secretion and increases glomerular filtration (Bloor et al. 1992). Dex. also reduces the incidence of nausea, vomiting, and agitation (Cheung et al. 2007). In general, presynaptic activation of the α2 adrenoceptor inhibits the release of norepinephrine, terminating the propagation of pain signals. Postsynaptic activation of α2 adrenoceptors in the central nervous system (CNS) inhibits sympathetic activity and thus can decrease blood pressure and heart rate. Dex. combines all these effects producing analgesia, sedation, and anxiolysis and thus avoiding some of the side effects of multiagent therapies (Nakamura and Ferreira 1988).

At the therapeutic doses, the use of Dex. is not associated with respiratory depression (Nelson et al. 2003). It also has minimal adverse effects on respiratory functions even at high plasma dosages (Venn et al. 2000).

The usual dose of Dex. for procedural sedation is 1 mcg/kg, followed by an intravenous (IV) infusion of 0.2–0.7 mcg/kg/h. Its onset of action is less than 5 min and the peak effect occurs within 15 min (Scheinin et al. 1998). Clinically effective sedation has been reported to set in 10–15 min after the start of the loading dose (Nelson et al. 2003).

IV lidocaine is another potentially interesting adjunct to propofol sedation. Lidocaine (lignocaine) is an amide local anesthetic acting primarily via sodium channel blockade in addition to inhibition of G-protein and N-methyl-D-aspartate (NMDA) receptors (McCarthy et al. 2010). When administered intravenously, the concentration of the neurotransmitter acetylcholine increases in the cerebrospinal fluid (CSF), which would exacerbate the inhibitory descending pain pathways resulting in analgesia (Abelson and Hoglund 2003) probably by binding to muscarinic receptors M3 (Hollmann et al. 2001), inhibition of glycine receptors (Biella and Sotgiu 1993), and release of endogenous opioids leading to the final analgesic effect (Cohen and Mao 2003). Besides, when lidocaine reaches the spinal cord, it reduces directly or indirectly the postsynaptic depolarization mediated by NMDA and neurokinin receptors (Nagy and Woolf 1996).

Benefits of IV lidocaine were reported mainly in cases of visceral surgery as it alleviates abdominal pain (Dunn and Durieux 2017). Colonic distension and traction during colonoscopy results in abdominal discomfort and visceral pain potentially amenable to IV lidocaine (Forster et al. 2018).

Some studies observed that IV lidocaine administration during abdominal surgery improved postoperative analgesia, reduced postoperative opioid requirement, accelerated postoperative recovery of the bowel function, and shorted the duration of hospitalization (Tikuišis et al. 2014).

Hence, IV lidocaine combined with dexmedetomidine infusion would be a good alternative to propofol for sedation during colonoscopy.

Methods

A prospective randomized controlled study approved by the hospital Institutional Review Board and written informed consents were obtained from patients who were randomized using block randomization technique and a research randomizer program. Using PASS 11th release, a sample size of thirty patients in each group was calculated to have at least an 80% power to detect the expected differences of at least two out of five in the mean satisfaction scores (40% change) between the two

groups. A P value less than 0.05 was considered statistically significant.

All patients admitted for elective colonoscopy with ASA physical status I, II, or III were included in the study. Patients were excluded if they had bradycardia (defined as a heart rate less than 50/min) and any arrhythmogenic heart disease or if they could not tolerate the planned sedation regimen, a condition which required giving another medication or turning into general anesthesia. Patients with a known history of hypersensitivity to midazolam, propofol, dexmedetomidine, lidocaine, or fentanyl were excluded from the study.

Patients were divided into two groups: group P, the propofol group, included patients who received sedation with IV propofol infusion and group D-L, the dexmedetomidine–lidocaine group, included patients who received a combination of Dex. and lidocaine IV infusion.

All patients were attached to the basic monitors (heart rate, blood pressure, oxygen saturation) and were kept on an oxygen mask 5–6 l/min with continuous end-tidal CO_2 monitoring.

All patients received 0.02 mg/kg of midazolam IV; then, group P patients were sedated using a loading dose of 50–100 mg of propofol and were continued on propofol IV infusion 25–75 µg/kg/min. Group D-L patients received a loading dose of dexmedetomidine 1 µg/kg infused over 10 min followed by infusion of dexmedetomidine 0.2–0.7 µg/kg/h and lidocaine 1 mg/kg IV followed by an infusion of 1.5 mg/kg/h. In both groups, additional doses of IV midazolam were administered if needed to maintain a modified Ramsay sedation score of 3–4 in addition to boluses of 25 µg of fentanyl in case of pain.

Blood pressure, heart rate, saturation, and respiratory rate were continuously monitored and apneic attacks (defined as cessation of airflow for at least 10 s) (American Academy of Sleep Medicine 2005) were recorded.

After the procedure, in the recovery area and when the patients were alert enough to express their experience with the procedure, they were asked to score their level of satisfaction with the sedation during the procedure in terms of recalling any painful or other undesirable intraprocedural events. Patient's satisfaction level was assessed by the Likert 5-item scoring system (1 = not at all satisfied, 2 = slightly satisfied, 3 = somewhat satisfied, 4 = very satisfied, and 5 = extremely satisfied) (Roberts et al. 1999). Sand Likert scores were obtained by one investigator (who was blinded to the drug allocation) to reduce interobserver variability. Patients were discharged from the recovery if they achieved at least 8 points on Aldrete's scoring system.

The primary aim and outcome of this study was to compare the patients' satisfaction with the sedation technique between the two groups. Other outcomes included the *v*isual *a*nalogue *p*ain (VAS) score recorded immediately after patient recovery, mean arterial blood pressure, saturation and heart rate during the procedure, amount of fentanyl and midazolam used during the procedure, and the number of apneic attacks.

Statistical methodology

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013. Quantitative normally distributed data are described as mean ± SD (standard deviation) after testing for normality using Shapiro–Wilk test, then compared using the independent t-test (independent data) and paired t-test (paired-data) if normally distributed and Mann–Whitney test if not normally distributed, while the Pearson test was used for correlations. Qualitative data are described as number and percentage and compared using the chi-square test and Fisher's exact test for variables with small expected numbers. The level of significance taken at P value < 0.050 was significant; otherwise, it was non-significant.
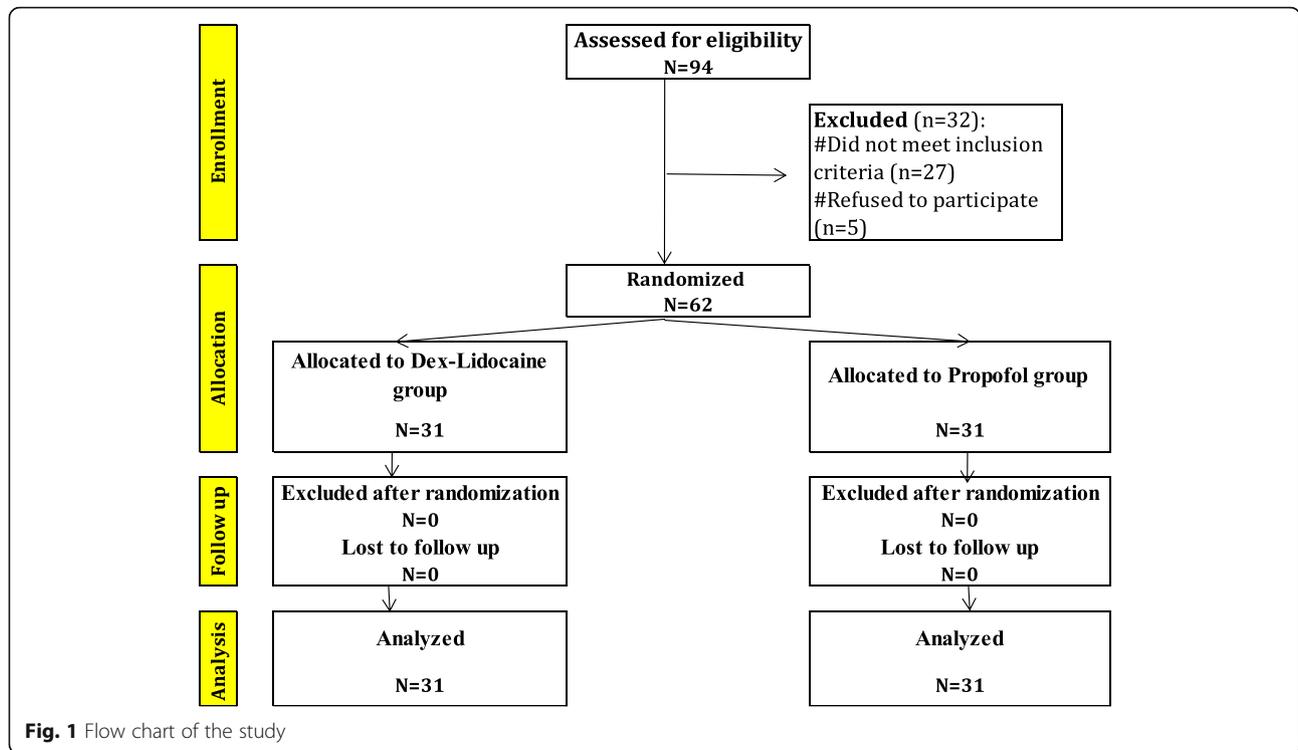
Results

Between March and November 2020, 62 patients were enrolled in the study and were divided into two equal groups: group P and group D-L. The study flow chart is illustrated in Fig. 1.

Patient demographics including age and sex were statistically non-significant between the two groups. There were also non-significant differences regarding the colonoscopy duration, baseline mean arterial blood pressure, and heart rate between the two groups, and the results are illustrated in Table 1.

There were non-significant differences between both groups regarding the intraoperative mean blood pressure and heart rate. The rate of change of blood pressure from the baseline was also non-statistically significant between both groups (decreased by 6.9 ± 9.1 in group P and 4.7 ± 9.2 in group D-L); however, the mean heart rate in group D-L was significantly reduced from the baseline as compared to group P (reduced by 7.4 ± 11 versus 1.4 ± 10.3 respectively, P value 0.03) as illustrated in Table 2.

Patients in group P had significantly more apneic attacks, 11 patients had one attack and 5 patients had two attacks, while none of the patients in group D-L had any apneic attacks (P value < 0.001). The intraoperative mean oxygen saturation was significantly lower in group P (97.8 ± 0.9%) compared to group D-L (98.8 ± 0.9%), P value < 0.001.

Patients in group D-L required significantly more doses of midazolam and fentanyl compared to the propofol group and their first recorded postprocedure pain

Fig. 1 Flow chart of the study

score was also significantly higher; results are illustrated in Table 3.

The median and 1st–3rd interquartile (IQ) patient satisfaction score using the 5-point Likert scaling system was 5 (4.0–5.0) in group P and 4 (4.0–5.0) in group D-L; however, this difference was statistically significant (P value = 0.014), reflecting better patient satisfaction in the propofol group (Fig. 2).

Discussion

Colonoscopy has a major role in the diagnosis of colorectal pathologies, and colonoscopic therapeutic procedures have increased over the recent decades. Although conscious sedation is the ideal method used to reduce anxiety in patients undergoing endoscopy, the choice of agent or combination of agents is still controversial (Ayazoglu et al. 2013). The ideal sedative agent should allow for rapid modification of the sedation level by modifying the dosage, should not have any adverse effects, should be cheap, and

has rapid onset and short duration of action without cumulative effects. The metabolites of the sedative agents should be inactivated at the end of the procedure so that hospitalization is not prolonged (VanNatta and Rex 2006).

In this study, the efficacy of combined Dex.–lidocaine IV infusion compared to propofol in terms of patient satisfaction was examined showing significantly better patient satisfaction scores with propofol sedation compared to sedation using dexmedetomidine–lidocaine. In spite of these results, sedation for colonoscopy using dexmedetomidine–lidocaine was safe and effective as the median satisfaction score in group D-L was 4.0 (4.0–5.0) compared to 5.0 (4.0–5.0) in the propofol group and according to the Sand Likert scoring system we used; a score of 4 means that the patient is very satisfied so the difference between both groups is clinically non-significant. It is clear that this variation in patient satisfaction is related mainly to pain as patients in the dexmedetomidine–lidocaine group had mild median pain

Table 1 Patients' demographics and baseline data

Variables		Group P (N = 31)	Group D-L (N = 31)	P-value
Age (years)		45.6 ± 12.6	46.3 ± 14.3	0.837
Sex (num., %)	Male	22 (71.0%)	20 (64.5%)	0.587
	Female	9 (29.0%)	11 (35.5%)	
Colonoscopy duration (minutes)		29.5 ± 4.2	30.6 ± 4.8	0.355
Baseline mean arterial blood pressure (mmHg)		74.2 ± 10.4	75.6 ± 10.4	0.585
Baseline heart rate (beat/minute)		69.4 ± 10.2	72.9 ± 13.4	0.245

Table 2 Intraoperative blood pressure and heart rate

Variables	Group P (N = 31)	Group D-L (N = 31)	P-value	Effect size Dex.–lidocaine relative to propofol	
				Mean ± SD	95% CI
Intraoperative mean blood pressure (mmHg)	67.2 ± 7.0	70.9 ± 9.9	0.094	3.7 ± 2.2	−0.7–8.1
Change of mean blood pressure from baseline (mmHg)	−6.9 ± 9.1	−4.7 ± 9.2	0.336	2.3 ± 2.3	−2.4–6.9
Intraoperative heart rate (mmHg)	68.0 ± 7.6	65.5 ± 12.8	0.357	−2.5 ± 2.7	−7.8–2.9
Change of heart rate from baseline (mmHg)	−1.4 ± 10.3	−7.4 ± 11.0	**0.030**	−6.0 ± 2.7	−11.5 to −0.6

scores 2.0 (1.0–3.0) but it was significantly higher than the propofol group and I could not find an explanation to the higher pain scores in these patients in spite of receiving lidocaine, dexmedetomidine, and fentanyl while patients in the other group received only propofol and fentanyl boluses.

In order to achieve a suitable sedation situation for colonoscopy, patients who received dexmedetomidine–lidocaine required significantly more midazolam and fentanyl doses as compared to the propofol group; this may be related to the faster onset of action of propofol but this did not affect their hemodynamic stability as there was no significant difference between the mean arterial blood pressure and heart rate during the procedure between both groups. However, the mean heart rate decreased more significantly from the baseline in the dexmedetomidine–lidocaine group and this is explained by the direct negative chronotropic effect of dexmedetomidine.

Patients sedated with propofol had significantly more apneic attacks and thus significantly lower mean intraoperative oxygen saturation values than the other group while patients sedated by dexmedetomidine–lidocaine did not experience any apneic attacks, making this combination safer for high-risk and morbidly obese patients.

Kamer et al. compared the efficacy of dexmedetomidine to midazolam in colonoscopies in terms of perioperative hemodynamics, sedation, pain, satisfaction, and recovery scores where patients in one group

received midazolam and the other group received dexmedetomidine, and fentanyl was given to all patients in their study. They concluded that dexmedetomidine can be used as a sole sedative agent in colonoscopies as in spite that the satisfaction scores were significantly less in patients who received Dex., it showed more efficient hemodynamic stability, higher Ramsay sedation scale scores, and lower numeric rating scale (NRS) scores (Dere et al. 2010). The results are similar to my results in terms of patient satisfaction, yet their patients sedated with dexmedetomidine had lower pain scores and more Ramsay sedation scores which do not explain why they were less satisfied.

Forster et al. studied the efficacy of adding lidocaine infusion to propofol in colonoscopy procedures. Their patients received either IV lidocaine or the same volume of saline. They concluded that intravenous infusion of lidocaine at a rate of 4 mg/kg/h after a loading dose of 1.5 mg/kg resulted in a 50% reduction in propofol dose requirements when added to ketamine during colonoscopy and a significant reduction of post-colonoscopy pain and fatigue (Forster et al. 2018). That was different from my results mostly because they used higher lidocaine loading and infusion doses than what I used; in addition, they used a loading dose of ketamine 0.3 mg/kg.

Using dexmedetomidine as a sole sedative agent was studied by Sula et al. who prospectively studied 231 ASA class I–III patients who underwent colonoscopy. Sedation was accomplished with propofol 1.5 mg/kg and on-

Table 3 Illustration of apnea, oxygen saturation, midazolam, and fentanyl requirements and pain scores

Variables		Group P (N = 31)	Group D-L (N = 31)	P-value	Effect size Dex.-lidocaine relative to propofol	
					Mean ± SD	95% CI
Apnea (number of attacks)	**Zero**	15 (48.4%)	31 (100.0%)	**< 0.001**		
	1	11 (35.5%)	0 (0.0%)			
	2	5 (16.1%)	0 (0.0%)			
Intraoperative mean oxygen saturation (%)		97.8 ± 0.9	98.8 ± 0.9	**< 0.001**	1.0 ± 0.2	0.5–1.5
Midazolam dose (mg)		1.5 ± 0.6	3.3 ± 1.0	**< 0.001**	1.8 ± 0.2	1.4–2.2
Fentanyl dose (μg)		48.4 ± 19.3	64.5 ± 23.5	**0.005**	16.1 ± 5.5	5.2–27.1
Pain score (VAS 0–10) median (1st–3rd) IQ		0.0 (0.0–1.0)	2.0 (1.0–3.0)	**< 0.001**	**Not applicable**	

Fig. 2 Patient satisfaction score
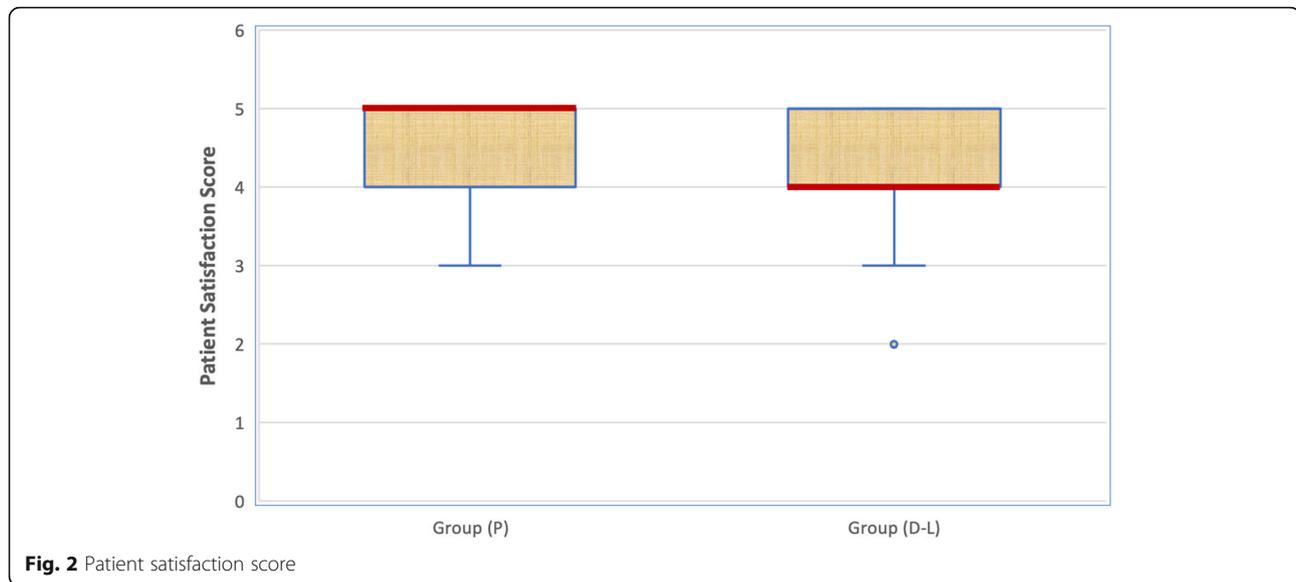
demand bolus dose of 0.4–0.5 mg/kg (group P) and with dexmedetomidine 1 μg/kg (group D). Vital signs as well as patients' satisfaction and the endoscopists' satisfaction were compared. A decline in the systolic blood pressure occurred in 29 patients (12.5%), 17 patients (58.6%) in group D and 12 patients (41.4%) in group P. Eleven patients (4.7%) in group P and one patient in group D had a decline in oxygen saturation and no bradycardia was noted. The satisfaction scores in both groups were comparable. The authors suggested that both regimens were safe and effective for sedation during a colonoscopic procedure (Sula et al. 2012). As noticed in my study, the use of propofol caused more desaturation but that was non-significant in their study, while the use of dexmedetomidine caused more hypotension and this was also non-significant. They used a subjective way to examine the satisfaction which was amnesia for patients and the verbal endoscopist opinion; however, in my study, I used a numerical scale for that which was the reason for the significant difference although clinically I considered that as non-significant.

However, in the study of Jalowiecki et al., the sole use of dexmedetomidine as a sole sedative agent was found inadequate. The study involved 64 patients who underwent outpatient colonoscopic procedures. In group D, patients received 1 mcg/kg of dexmedetomidine over 15 min and maintained by an infusion of 0.2 mcg/kg/h. Group P received 1 mg/kg of meperidine and 0.05 mg/kg of midazolam. Group F patients received 0.1–0.2 mg of fentanyl IV on demand. The study was terminated before recruiting the planned 90 cases because of adverse effects in group D. There was significant bradycardia and hypotension in group D in addition to increased fentanyl usage in 47% of patients compared with 42.8%

and 79.2% of patients in group P and F, respectively. Nausea/vomiting, vertigo, and ventricular arrhythmia were noted only in group D. In addition, group D had the longest time to home discharge (Sula et al. 2012). The increased fentanyl utilization in group D may be related to the fixed low dose of dexmedetomidine they have used while in our study we used 0.2–0.7 μg/kg/h in addition to lidocaine infusion (Jalowiecki et al. 2005).

Conclusion

Combined infusion of dexmedetomidine–lidocaine is an effective and safe alternative to propofol infusion for colonoscopy procedures, even though patients who received propofol were significantly more satisfied, yet the median satisfaction scores of the patients who received dexmedetomidine–lidocaine were 4, indicating clinically good patient satisfaction. Patients who received Dex.–lidocaine did not experience any apneic attacks during the procedures, rendering it more safe than propofol specially in high-risk and morbidly obese patients.

References

Abelson KS, Hoglund AU (2003) Intravenously administered lidocaine in therapeutic doses increases the intraspinal release of acetylcholine in rats. Neurosci Lett 2002(317):93–96

American Academy of Sleep Medicine (2005) International classification of sleep disorders. Diagnostic and coding manual, Second edn. American Academy of Sleep, Westchester, Ill

Ayazoglu TA, Polat E, Polat C, Yasar NF, Duman U, Akbulut S, Yol S (2013) Comparison of propofol-based sedation regimens administered during colonoscopy. Rev Med Chil 141:477–485

Biella G, Sotgiu ML (1993) Central effects of systemic lidocaine mediated by glycine spinal receptors: an iontophoretic study in the rat spinal cord. Brain Res 603:201–206

Bloor BC, Ward DS, Belleville JP, Maze M (1992) Effects of intravenous dexmedetomidine in humans. II. Haemodynamic changes. Anesthesiology 77:1134–1142

Chelazzi C, Consales G, Boninsegni P, Bonanomi GA, Castiglione G et al (2009) Propofol sedation in a colorectal cancer screening outpatient cohort. Minerva Anestesiol 75:677–683

Cheung CW, Ying CL, Chiu WK, Wong GT, Ng KF, Irwin MG (2007) A comparison of dexmedetomidine and midazolam for sedation in third molar surgery. Anesthesia 62:1132–1138

Cohen SP, Mao J (2003) Is the analgesic effect of systemic lidocaine mediated through opioid receptors? Acta Anaesthesiol Scand 47:910–911

Dere K, Sucullu I, Budak ET, Yeyen S, Filiz AI, Ozkan S, Dagl G (2010) A comparison of dexmedetomidine versus midazolam for sedation, pain and hemodynamic control, during colonoscopy under conscious sedation. Eur J Anaesthesiol 27:648–652

Dunn LK, Durieux ME (2017) Perioperative use of intravenous lidocaine. Anesthesiology 126:729–737

Forster C, Vanhaudenhuyse A, Gast P, Louis E, Hick G, Brichant J-F, Joris J (2018) Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: a randomized placebo-controlled study. Br J Anaesth 121(5):1059e1064

Funai Y, Pickering AE, Uta D, Nishikawa K, Mori T, Asada A et al (2014) Systemic dexmedetomidine augments inhibitory synaptic transmission in the superficial dorsal horn through activation of descending noradrenergic control: an in vivo patch-clamp analysis of analgesic mechanisms. Pain 155:617–628

Hollmann MW, Ritter CH, Henle P et al (2001) Inhibition of m3 muscarinic acetylcholine receptors by local anaesthetics. Br J Pharmacol 133:207–216

Jalowiecki P, Rudner R, Gonciarz M, Kawecki P, Petelenz M, Dziurdzik P (2005) Sole use of dexmedetomidine has limited utility for conscious sedation during outpatient colonoscopy. Anesthesiology 103:269–273

McCarthy GC, Megalla SA, Habib AS (2010) Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. Drugs 70:1149–1163

Nagy I, Woolf CJ (1996) Lignocaine selectivity reduces C fibre-evoked neuronal activity in rat spinal cord in vitro by decreasing N-methyl-D-aspartate and neurokinin receptor-mediated postsynaptic depolarizations; implications for the development of novel centrally acting analgesics. Pain 64:59–70

Nakamura M, Ferreira SH (1988) Peripheral analgesic action of clonidine: mediation by release of endogenous enkephalin-like substances. Eur J Pharmacol 146:223–228

Nelson LE, Lu J, Guo T, Saper CB, Franks NP et al (2003) The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 98:428–436

Ralph G, Cleighton Brown H, Mitchell DH, Silvius EN (2001) Dexmedetomidine: a novel sedative-analgesic agent. Bumc Proceed 14:13–21

Roberts JS, Laughlin JE, Wedell DH (1999) Validity issues in the Likert and Thurstone approaches to attitude measurement. Educ Psychol Meas 59(2):211–233

Scheinin H, Aantaa R, Anttila M, Hakola P, Helminen A, Karhuvaara S (1998) Reversal of the sedative and sympatholytic effects of dexmedetomidine with a specific alpha 2-adrenoceptor antagonist atipamizole: a pharmacodynamic and kinetic study in healthy volunteers. Anaesthesiology 89:574

Sula H, Domi R, Ohri I, Broqi I, Beqiri A, Gani H (2012) Propofol versus dexmedetomidine for sedation in colonoscopy: a prospective, randomized study. Eur J Anesthesiol 29:32

Techanivate A, Verawattaganon T, Saiyuenyong C, Areeruk P (2012) A comparison of dexmedetomidine versus propofol on hypotension during colonoscopy under sedation. J Anesth Clin Res 3:11

Tikuišis R, Miliauskas P, Samalavičius NE, Žurauskas A, Samalavičius R, Zabulis V (2014) Intravenous lidocaine for post-operative pain relief after hand-assisted laparoscopic colon surgery: a randomized, placebo-controlled clinical trial. Tech Coloproctol 18:373–380

VanNatta ME, Rex DK (2006) Propofol alone titrated to deep sedation versus propofol in combination with opioids and/or benzodiazepines and titrated to moderate sedation for colonoscopy. Am J Gastroenterol 101:2209–2217

Venn RM, Hell J, Grounds RM (2000) Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 4:302–308

Young CC, Prielipp RC (2002) Sedative analgesic, and neuromuscular blocking drugs. In: Murray MJ, Coursin DB, Pearl RG et al (eds) Critical care medicine: perioperative management, 2nd edn. LippincottWilliams &Wilkins, New York, pp 147–167

Publisher's Note

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