ORIGINAL RESEARCH

A comparative study to assess the efficacy of sedation with dexmedetomedline plus ketamine and propofol plus fentanyl in adult patients undergoing out patients colonoscopy

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ABSTRACT
Aim: For colonoscopy patients, we compared the safety and efficacy of the propofol and fentanyl (PF) and the combination of dexmedetomidine and ketamine (DK) for sedation. **Method:** Sixty patients undergoing colonoscopy were randomized into two groups for the purposes of anesthesia in this study: group A received PF, and group B received DK. 30 patients comprised the PF group, while the remaining thirty patients comprised the DK group. Both groups exhibited comparable demographic characteristics. At 2, 5, 10, and 15 minutes, the sedation score (as determined by the Ramsy scale) and vital signs of the patients were documented. A protocol was utilized to document complications such as apnea, hypotension, hypoxia, nausea, and vomiting, in addition to the satisfaction of the gastroenterologist. The data were analyzed with SPSS V.18 and a significance level of <0.05 using chi-square, independent t-tests, and repeated measure analysis. **Result:** The mean score of sedation was3.78 ± 0.41 in DK group and4.15 ± 0.37 in PF group (p value = 0.002). Serious complications, including hypotension (p value = 0.004) and apnea (p value = 0.20) were significantly higher in PF group. **Conclusion:** Compared to PF, the combination of DK and PF provides adequate sedation with fewer complications in patients undergoing colonoscopy.

INTRODUCTION

By means of colonoscopy, noncancerous lower gastrointestinal diseases can be detected and treated with efficacy, including lesions of the colon.[1] The most efficacious screening procedure for the prevention of colorectal cancer is screening colonoscopy. The effectiveness of colonoscopy is significantly influenced by the overall caliber of its indication, planning, preparation, and execution. In other words, the quality is proportional to the quantity of polyps and adenomas that are detected, or alternatively, to the quantity that are overlooked throughout the procedure. The spectrum over which the incidence and occurrence of colorectal cancer are reduced is directly influenced by the quality. This also applies to the rate of interval carcinoma.[2] While colonoscopy is a readily available and time-efficient outpatient procedure, it frequently induces considerable discomfort and distress among patients. By effectively managing the patient's pain and distress, intravenous sedation enables the physician to utilize this technique to a greater extent. To achieve this, various agents are employed either individually or in combination with one another.[3]Although propofol is commonly prescribed for sedation during colonoscopies, its application is restricted due to complications such as respiratory depression and hypotension.[4,5] In addition to sedation, ketamine is a safe, rapid-acting intravenous anesthetic that has been utilized in a variety of therapeutic and diagnostic procedures.[6] It efficiently traverses the blood-brain barrier and maintains patency of the airway,

ventilation, and cardiovascular stability while providing effective analgesia.[6]Dexmedetomidine, an alpha-2 adrenergic receptor agonist, is administered for sedation during colonoscopy either alone or in combination with other analgesic agents. The extended hospitalization and recovery period are the primary drawbacks associated with this medication, which reduces its popularity as the sole sedative in outpatient settings. When dexmedetomidine is administered concurrently with other drugs, both the dosage needed and the adverse effects can be minimized.[7] It induces a distinct form of sedation known as "arousable sedation," wherein individuals appear to be somnolent but exhibit cooperative and communicative behavior upon stimulation, resembling the state of natural sleep.[8,9] Additionally, within the intensive care unit (ICU), it is correlated with decreased anesthetic needs and maintenance of respiratory function, allowing septic shock patients to maintain hemodynamic stability while utilizing a lower dose of vasopressor.[10]The purpose of the present study was to compare the analgesic and sedative properties of propofol and fentanyl, which are frequently used analgesics, with those of dexmedetomidine and ketamine prior to colonoscopy in patients.

MATERIAL AND METHOD

- The objective of the current randomized, double-blind clinical trial was to compare the analgesic and sedative properties of dexmedetomidine and ketamine (DK) versus propofol and fentanyl (PF) in order to facilitate pain relief during colonoscopy in patients.
- Sixty patients, aged between 18 and 70 years, of either gender, were selected. The utmost number of subjects allowed in each group was thirty, as determined by averaging two population means and taking into account various outcomes such as hypotension, hypoxemia, and apnea.
- Patients were provided with a comprehensive explanation of the study procedure and potential complications. In exchange for their voluntary participation, they were requested to affix their signatures on informed consent forms.

Inclusion criteria

- age above 18 years
- the American Society ofAnesthesiologists physical status (ASA-PS) class 1 and 2
- willingness to participate in the study.

Exclusion criteria

- a history of allergy to the drug.
- drug addictionand use of psychiatric drugs
- ASAclass ≥ 3, known psychological problems
- emergency cases
- unwillingness to participate in the study.

Method

- In order to identify the subjects, consecutive sampling was used. Patients were randomly assigned to two categories, denoted A and B, by means of permuted block randomization. The units had a dimension of four and were determined through the roll of dice. The allocation process for treatment groups A and B involved a straightforward randomization method involving a coin toss. As the research design employed was double-blind, neither the patient nor the physician evaluating the results were informed of the specific treatment modality.
- After assigning patients to treatment groups and obtaining the written informed consent from them, thedemographic information including gender, age, height, and weight as well as primary vital signsincluding systolic blood pressure, mean arterial pressure, blood oxygen saturation (SpO2), and heart ratewere recorded in the checklist of each patient.
- Group A (PF) was sedated with midazolam (0.02 mg/kg), fentanyl (1 µg/kg), and propofol (1 mg/kg); group B (DK) was sedated with dexmedetomidine (0.3 µg/kg), ketamine (0.25 mg/kg), and midazolam (0.02 mg/kg).
- Using the Ramsey sedative scale, the level of sedation was measured at 2, 5, 10, and 15 minutes. The following information was recorded on the checklist of each patient: sedation score and vital signs of each patient at predetermined time points; total dose administered; duration of colonoscopy; intraoperative complications including nausea, vomiting, bradycardia, hypotension, chills, delusions, hallucinations, and apnea; and the gastroenterologist's level of satisfaction with the procedure categorized as totally satisfactory (easy to perform), satisfactory (difficult to perform), or unsatisfactory (impractical).
- Furthermore, the following recovery assessments were documented in each patient's medical record: time of entry into the recovery room, duration of time between completion of the colonoscopy and discharge, pain assessment score using the Wong Baker faces pain assessment scale at discharge, level of patient satisfaction at discharge (categorised as completely satisfactory, satisfactory, or unsatisfactory), and recovery complications including nausea, vomiting, bradycardia, hypotension, shivering, delusions, hallucinations, and apnea.
- Patients were provided with an explanation of the study procedure and potential complications. In exchange for their voluntary participation, they were requested to sign informed consent forms.

RESULTS

Out of the total 60 participants in the present clinical trial, 30 were assigned to the Propofol & Fentanyl (PF) group (10 males and 20 females), while 30 were assigned to the Dexmedetomidine & Ketamine (DK) group (17 males and 13 females). The study involved the random allocation of patients into two treatment groups. Demographic variables, such as gender, age, and weight, were compared between the groups, along with primary vital signs including SpO2, heart rate, systolic blood pressure, and mean arterial pressure.

		Propofol + Fentanyl	Dexmedetomidine + Ketamine	P-value
sex	male	10 (33.3%)	13(43.3%)	0.153
	female	20 (66.6%)	17(56.6%)	
Age		45.34 ± 13.17	37.16 ± 13.11	0.067
Weight		63.06 ± 13.21	65.73 ± 10.34	0.343
Primary O2 Saturation		97.82 ± 1.06	97.90 ± 1.22	0.542
Primary HR		87.32 ± 14.82	85.75 ± 14.43	0.536
Primary MAP		87.74 ± 15.21	89.41 ± 22.01	0.421
Primary SBP		115.13 ± 23.05	121.53 ± 17.21	0.762

Table 1: Patients demographics and baseline parameters in both groups. The mean of the variables as well as the p values for the two groups. No significant difference was observed.

	Colonoscopy		P value	Recovery		Pvalue
	Propofol + Fentanyl	Dexmedetomidine + Ketamine		Propofol + Fentanyl	Dexmedetomidine + Ketamine	
Sedation score	4.15 ± 0.37	3.78 ± 0.41	0.002	-	-	-
Mean SBP	100.42 ± 14.31	107.75 ± 11.54	0.003	112.32 ± 11.40	106.55 ± 10.47	0.200
MAP	67.22 ± 15.32	73.76 ± 14.55	0.002	71.30 ± 7.40	81.32 ± 7.41	0.039
HR	69.61 ± 13.15	68.50 ± 12.41	0.838	67.20 ± 15.96	72.11 ± 11.43	0.567
O2 saturation	92.18 ± 4.33	96.33 ± 1.05	0.000	91.84 ± 1.65	95.41 ± 1.02	0.020
Mean pain score	-	-	-	1.07 ± 0.22	1.26 ± 0.224	0.800

Table 2: Sedation score, pain score and vital signs during colonoscopy and recovery in both groups

The patients who received DK had a mean sedation score of 3.78 ± 0.41 compared to 4.15 ± 0.37 for those who received PF. This difference was statistically significant (p value = 0.002); that is, patients who received PF had a higher mean sedation score.Critical sign evaluations conducted during colonoscopy in two groups revealed that patients undergoing DK had significantly higher SpO2 (p value = 0.000), systolic blood pressure (p value = 0.003), and mean arterial pressure (p value = 0.002) than those undergoing PF; that is, DK group patients experienced lower levels of hypotension and desaturation. Changes in heart rate did not differ significantly between the two groups.

Regarding the recovery of patients' vital signs, systolic blood pressure and heart rate did not differ significantly between the two groups; however, the DK group exhibited higher values of SpO2 (p = 0.020) and mean arterial pressure (p = 0.039). Using a visual analog scale to assess discomfort during recovery, there was no statistically significant difference between the two groups.

Colonoscopy			P-value	Recovery			P-value
Complication	P + F N (%)	D + K N (%)		Complication	P + F N (%)	D + K N (%)	
Bradycardia	3(10)	6 (20)	0.350	Bradycardia	0 (0.0)	1 (3.33)	0.461
Hypotension	14 (46.6)	7 (23.3)	0.004	Hypotension	13 (43.3)	7 (23.3)	0.06
Apnea	5(16.6)	0 (0.0)	0.020	Apnea	2 (6.6)	0 (0.0)	0.321

Agitation	(0.0)	2 (6.66)	0.526	Nausea	0 (0.0)	11 (36.6)	0.000
				Vomiting	0 (0.0)	1 (3.33)	0.616
				Shivering	2 (6.6)	0 (0.0)	0.438
				Dizziness	0 (0.0	8 (26.6)	0.002

Table 3: Complications during colonoscopy and recovery in both groups

Hypotension (p value = 0.004) and apnea (p value = 0.020) emerged as the most significant complications during colonoscopy in the PF group. A lack of substantial distinction was observed between the two cohorts with regard to bradycardia and agitation. An evaluation of recovery complications revealed that the incidence of nausea (p value = 0.000) and disorientation (p value = 0.002) was significantly higher among patients in the DK group. No statistically significant distinctions were observed between the two cohorts with regard to additional complications such as bradycardia, hypotension, apnea, vomiting, or trembling.

DISCUSSION

Under sedation, a colonoscopy is the standard procedure for colorectal cancer screening, diagnosis, and occasionally treatment of colon lesions. The procedure can be completed as an outpatient. Given that the patient does not require hospitalization for the colonoscopy procedure, the optimal sedation should possess the following characteristics: rapid onset and termination of action, minimal side effects, and a seamless recovery process. This is in addition to appropriate analgesics and sedation, with the aim of expediting the patient's readiness for discharge. Presently, numerous protocols for colonoscopy utilize Propofol exclusively, with fentanyl administration not being routinely incorporated. The primary purpose of this measure is to prevent the worsening of respiratory depression induced by the main drug, Propofol, and to accelerate the patient's recovery time. However, such protocols result in severe pain for the patient, which cannot be alleviated with pain medication alone, and since neither midazolam nor Propofol have analgesic properties, removing fentanyl from the protocol is unethical from a patient's perspective, despite the fact that it could be achieved with the assistance of midazolam administered as a substitute. Consequently, Ketamine and Dexmedetomidine were employed in the current investigation to elicit analgesia in the intervention group. Both Ketamine and Dexmedetomidine possess analgesic properties, with Ketamine being particularly noteworthy due to the analgesic effect confirmed at subanesthetic doses and the absence of patient consciousness reduction or respiratory depression independently during the procedure.[11,12]Comparing the outcomes of the PF and DK groups, the present study revealed that patients who received PF experienced substantially greater sedation as measured by the Ramsey score. Comparing the efficacy and adverse effects of Dexmedetomidine and Propofol in sedation of patients undergoing colonoscopy, Karanth et al.[13] found that the analgesic effects of the two agents were not significantly different. This result contradicted the present study's; however, in the present investigation, there was no statistically significant distinction between the two groups with regard to the level of satisfaction expressed by patients during recovery and the satisfaction of both the physician and patient with the procedure, despite the PF group achieving a higher sedation score. This indicates that both medications induced satisfactory sedation and, as such, were not inherently superior. Furthermore, it is worth noting that for numerous outpatient procedures, such as colonoscopy, a moderate level of sedation will suffice, resulting in reduced hemodynamic and respiratory complications.Respiratory complications, such as hypoventilation, apnea, and hypotension, are among the concerns associate with the sedative effect of Propofol.[11,14] In contrast to those receiving DK, patients who received PF exhibited decreased SpO2 and blood pressure, as well as an increased susceptibility to hypotension and apnea, according to the results of the current investigation. A large retrospective study involving 996 patients sedated prior to MRI with Propofol or Dexmedetomidine revealed that Propofol-treated patients had a higher incidence of hemodynamic complications, such as hypotension and bradycardia. Despite the sympatholytic effects of both Propofol and Dexmedetomidine resulting in decreased blood pressure and pulse rate, patients on Propofol exhibited significantly more pronounced alterations in these parameters.[15] Other studies comparing the effects of Propofol and Dexmedetomidine also observed this result; therefore, Dexmedetomidine is a safer agent in terms of hemodynamic stability than Propofol.Typically, the initial dosage of the medication induces sufficient sedation for the duration of the colonoscopy procedure. Lower bolus dosing followed by continuous drug infusion during lengthier procedures was associated with fewer adverse effects than higher doses, according to the findings of studies. [16,17.18]As an agonist of alpha-2-adrenergic receptors, dexmedetomidine acts specifically on the locus coeruleus. In contrast to GABA agonists like Propofol, the distinct chemical characteristics of this medication render it less inhibitive to the respiratory center. As a result, it

offers enhanced sedation gratification during outpatient procedures. Furthermore, due to its limited therapeutic range and potential to induce profound sedation in response to even a marginal alteration in serum concentrations, the administration of Propofol may result in heightened respiratory complications.[8,19,20] Patients assigned to the PF group exhibited a greater incidence of apnea in the current investigation, a finding that is consistent with the research outcomes reported by Wu[17] and Ahmed.[15]A combination of two or more medications decreases the dosage needed and the adverse effects of each individual medication. Patients who were elderly and candidates for upper gastrointestinal endoscopy and were administered Propofol plus Dexmedetomidine had fewer complications and greater satisfaction with the procedure than those who received Propofol alone or in combination with other drugs, such as Ketamine and Sufentanil, according to a study by Yin et al.[21]Patients in the DK group exhibited greater stability and fewer complications in the current investigation than those in the PF group. While the incidence of complications such as vertigo and dizziness during recovery was higher in the DK group of the present study, there was no significant difference in the overall patient satisfaction with sedation between the two groups. The gastroenterologist's level of satisfaction regarding patient sedation was comparable between the two groups. Additional research findings suggest that while patients receiving Dexmedetomidine experienced mild recovery-related side effects, their overall satisfaction with sedation was favorable when this agent was utilized.[22]

CONCLUSIONS

In summary, the results of the current investigation suggest that the inclusion of DK in the administered regiment for patients undergoing colonoscopy, despite its elevated cost, results in a more secure sedation state owing to its hemodynamic and respiratory stability. This is particularly critical during colonoscopies, as patients are frequently positioned laterally and occasionally in a semi-prone position, which hinders airway maintenance and access. However, due to its primary application in colorectal cancer screening among individuals aged 50 and above who are at risk of developing vascular disease, colonoscopy carries a higher propensity for inducing hemodynamic changes. Therefore, the cost-benefit analysis of utilizing DK for colonoscopy appears to be rational.

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