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ORIGINAL ARTICLE

Comparison of propofol versus propofol/fentanyl anesthesia for upper gastrointestinal endoscopy

Medhat Hannallah, MD, FFARCS[1], John Carroll, MD[2], Aline Charabaty, MD[3], Caren Palese, MD[2], Franca Barton, MS[4], Nadim Haddad, MD[3]

[1]Professor, Department of Anesthesia, Medstar Georgetown University hospital, Washington, DC (USA)

[2]Assistant Professor; [3]Associate Professor,

Department of Medicine, Division of Gastroenterology, Medstar Georgetown University Hospital, Washington, DC (USA)

[4] Department of Biostatistics, the EMMES Corporation, Rockville, Maryland, USA.

Correspondence: Medhat Hannallah, MD, FFARCS, Department of Anesthesia, Georgetown University Hospital, 3800 Reservoir Road, NW, Washington DC, 20007, USA; Phone: 202-444-6680; E-mail: hannallm@georgetown.edu.

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ABSTRACT

Background: The rapid onset and short duration of propofol makes it an ideal anesthetic during esophagogastroduodenoscopy (EGD). Fentanyl is frequently used in combination with propofol during EGD to provide an analgesic component. The synergy that results from combining the two drugs may be beneficial but may also increase the potential for apnea, hypotension, nausea, and prolonged recovery. This pilot study was designed to test the hypothesis that propofol/fentanyl anesthesia provides better conditions than propofol alone during EGD and to compare the incidence of side effects between the two techniques.

Methodology: This was an IRB approved, double blinded, prospective, placebo controlled study. One hundred consented patients undergoing EGD were randomly assigned into two Groups. Patients in the first (propofol/fentanyl) Group received fentanyl 1 µg/kg followed by propofol 0.75 mg/kg bolus, while patients in the second (propofol) Group received propofol 1.5 mg/kg bolus. Patients in the Group that received fentanyl received half the initial induction dose of propofol in order to minimize the potential for apnea and hypoventilation due to the synergy between the two drugs. In both Groups, additional 20 mg propofol boluses were given at 1min intervals until adequate depth of anesthesia was reached. Propofol infusion was then started and adjusted to maintain adequate depth of anesthesia during the procedure. The primary end point was the quality of anesthesia as rated by the blinded endoscopist. The secondary end points were the incidence of hypotension, hypoxia, nausea, vomiting, and delayed recovery. Data from the two Groups were compared by the Wilcoxon rank test for the primary endpoint, by t-test for continuous measures, and by chi square for proportions including hypoxia and hypotension.

Results: The endoscopists' evaluation scores were statistically significantly higher in the propofol/fentanyl Group. Fentanyl had a statistically significant sparing effect on propofol induction dose. No statistically significant difference between the two Groups was found in the other study parameters.

Conclusion: The combination of propofol and fentanyl provides better quality of anesthesia than propofol alone during EGD with no apparent additional side effects.

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INTRODUCTION

Propofol is widely used for anesthesia during esophagogastroduodenoscopy (EGD).[1] Its rapid onset and short therapeutic effect provides optimal conditions for the endoscopist, comfort to the patient, and rapid recovery. Because it has no analgesic properties, large doses of propofol are often required to reach the adequate anesthesia depth needed for the initiation of EGD and the attenuation of the gag reflex.[2] This can result in the undesirable side effects of airway obstruction and hypotension. Opiates have anti-gag and anti-cough properties.[3] Fentanyl is therefore frequently used in combination with propofol to provide an analgesic component during EGD. The synergy that results from combining the propofol and fentanyl, however, can increase the potential for apnea, hypotension, and delayed recovery. The use of opiates may also increase the incidence of nausea and vomiting. This pilot study was designed to test the hypothesis that propofol/ fentanyl combination provides better anesthesia conditions than propofol alone during EGD and to compare the incidence of side effects between the two groups.

METHODOLOGY

The study was approved by Georgetown University Institutional Review Board (IRB), and written informed consent was obtained from all subjects. One hundred consenting ASA 1 or 2 adult patients age 18 to 65, undergoing EGD were enrolled in this double blinded, prospective, placebo controlled study. Exclusion criteria included chronic opioid use, substance abuse history, weight more than 100 kg, obstructive sleep apnea diagnosis or characteristics, known or anticipated airway difficulty, obstructive sleep apnea, pregnancy, and allergy to propofol, fentanyl, eggs, or soybean. Patients were randomly assigned into one of two groups using an online randomization program. For the first group the research pharmacy prepared a syringe containing 10 mL fentanyl diluted to a concentration of 10 μg/ mL and a syringe containing 20 mL propofol diluted with normal saline to a propofol concentration of 5 mg/mL. For the second group the pharmacy prepared a syringe containing 10 mL normal saline and a syringe containing 20 mL regular strength (10 mg/ mL) propofol. The anesthesiologist administering the medications and the endoscopist performing the procedure were blinded to the contents of the syringes. Patients in the first (propofol/fentanyl) group received fentanyl 1 μg/kg (1 mL/10 kg of the clear "diluted" fentanyl syringe) followed by IV bolus of propofol 0.75 mg/kg (1.5 mL/10 kg of the "diluted" propofol syringe). Patients in the second (propofol) group received 1 mL/10 kg from the clear normal saline syringe followed by IV bolus of propofol 1.5 mg/kg (1.5 mL/10 kg of the regular strength propofol syringe). In both groups, additional 20 mg propofol boluses were given at 1-2 min intervals until adequate depth of anesthesia was reached which was confirmed by eliciting no response from the patient when a soft rubber nasal airway was inserted deep into the oro-pharynx. Propofol 150 μg/kg/min infusion was then started. The propofol infusion rate was adjusted and additional propofol boluses were administered at the anesthesiologist's judgment to maintain adequate depth of anesthesia during the procedure. The primary end point was the quality of anesthesia as rated by the blinded endoscopist using a 10-point scale (10 = perfect, where there was no patient reaction to the endoscope or any breathing difficulty throughout the procedure, 1 = unacceptable, where the endoscopist was unable to start or complete the examination because of vigorous patient reaction to the endoscope or the patient developing airway or oxygenation difficulty necessitating immediate removal of the endoscope). Cardiovascular and respiratory variables were monitored non-invasively throughout the case and in the Post-Anesthesia Care Unit (PACU). The secondary end points were the incidence of hypotension, defined as systolic blood pressure $<$90 mmHg, and hypoxia, defined as arterial O_2 saturation $<$85%. The time patients spent in PACU was recorded. The patients were contacted the following day to inquire about nausea, vomiting or drowsiness. They were asked to rate their overall anesthesia experience on a 10-point scale (10 = perfect). Data from the two groups were compared by the Wilcoxon rank test for the primary endpoint, by t-test for continuous measures, and by chi square for proportions including hypoxia and hypotension.

RESULTS

There was no difference between the 2 groups in patient demographics or the duration of the procedures (Table 1).

Table 1: Patient demographics and procedure times

Variable	Fentanyl/Propofol (N=49)	Propofol (N=49
Age (years)	44.114.7	46.912.1
Gender (M/F)	27/22(55.1%/ 44.9%	22/27 (44. 0%/55.1%)
Height (cm)	170.211.4	172.211.2
Weight (kg)	75.9 (12.7)	74.711.2
BMI (Kg/m^2)	26.34.5	25.24.3
Procedure time (min)	96	85

Table 2: Endoscopist's Evaluation Score

Sedation Condition Score (1-10, 10 = perfect)	Fentanyl-Propofol Group (n)	Propofol Group (n)
9-10	44	31
7-8	2	9
5-6	3	7
3-4	0	2
1-2	0	1

Table 2 summarizes the endoscopists' evaluation scores. The endoscopists evaluation scores were statistically significantly higher in the propofol/ fentanyl group (Table 3).

Table 3: Study outcomes

Outcome	Fentanyl/ Propofol	Propofol	P-value
Endoscogist's Evaluation Score (1-10,10=perfect)	9.6 ± 0.1	8.3 ± 0.3	<0.001
Fentanyl Dose (mcg)	75.7 ± 1.8	0	
Propofol Induction dose (mg/ kg)	1.6 ± 0.1	2.5 ± 0.1	<0.001
Hypoxia (N)	2(4.1%)	7(14.3%)	0.08
Hypotension (N)	7(14.3%)	2(4.1%)	0.08
PACU time (min)	37.5 ± 1.8	3.6 ± 1.7	
Postop Drowsiness(N)	27(55.1%)	29(59.2%)	
Postop Nausea (N)	5(10.2%)	3(6.1%)	
Patient's Evaluation Score (1-10,10=perfect)	9.3 ± 0.2	9.5 ± 0.1	

Data presented as scpre. n(%), or meanstandard deviation

Fentanyl had a statistically significant sparing effect on propofol induction dose. There was a trend for higher incidence of hypoxemia in the propofol group and higher incidence of hypotension in the propofol/fentanyl group. The difference, however, did not reach statistical significance. No statistically significant difference between the two groups was found in the other study parameters.

DISCUSSION

Propofol is a potent intravenous anesthetic with rapid onset and rapid recovery.[2] These characteristics makes it an ideal agent for anesthetizing patients for short, intensely stimulating procedures such as EGD. Because propofol is devoid of analgesic properties fentanyl is frequently used with propofol when anesthetizing patients for these procedures to provide an analgesic component. Fentanyl is a potent short acting opioid with centrally acting antitussive properties, which makes it a suitable agent to use for that purpose.[3] Many reports demonstrate that the anti-cough and anti-gag properties of opioids enhance the anesthetic action of propofol.[4-6]

Tagaito et al. studied laryngeal reflexes in propofol-anesthetized patients by using a fiberoptic endoscope inserted through a laryngeal mask airway to directly visualize the larynx and then stimulating the vocal cords by spraying them with water.[7-8] The authors described a variety of laryngeal responses to this stimulation, including expiration, panting, coughing, and apnea with laryngospasm. Fentanyl attenuated these reflexes in a dose-dependent fashion.

The incidence of hypoxemic episode was low in both groups but was relatively lower in the fentanyl/ propofol group. The causes of the hypoxemic episodes were not documented during the study. It would have been informative if apnea, airway obstruction, or increased airway reactivity associated with coughing, breath holding, and laryngospasm were identified as the cause of the hypoxemic episodes. A possible question for a future study is whether the use of fentanyl specifically decreases the incidence of hypoxemic episodes resulting from airway hyper-reactivity during EGD.

This study demonstrated that the propofol/fentanyl combination did produce better quality of anesthesia for the procedure than with propofol alone as judged by the blinded endoscopists. The blinded endoscopists' numerical scoring of the quality of anesthesia was subjective, still, it did provide a consistent means of comparison between the two groups.

While the synergy between propofol and fentanyl potentiates propofol anesthesia, there is concern that the addition of fentanyl may prolong recovery, delay patients' discharge, and increase the incidence of nausea and vomiting. Although the study was not

powered to compare the incidence of nausea and vomiting and the discharge time between the two groups, these side effects appeared not to increase by the addition of fentanyl to propofol.

In this study most patients required large doses of propofol. In a prospective study involving patients undergoing colonoscopy during propofol anesthesia, it was demonstrated that the majority of patients were experiencing either general anesthesia or deep general anesthesia.[9] As measured using the SedLine brain function monitor (Masimo Corporation, Irvine, CA) the depth of anesthesia was often found to be deeper than that provided during major surgery. This is an important fact to consider when using propofol based anesthesia at the propofol doses used in this study.

It is also important to emphasize the fact that in this study propofol and fentanyl were administered according to a specific protocol in which the dose of fentanyl was limited to 1 μg/kg and propofol was administered slowly and in a lower induction dose when fentanyl was used. Had different doses or rates of administration of the 2 drugs been used the findings might have been different.

Additionally, this study excluded obese patients and those with obstructive sleep apnea (OSA) diagnosis or characteristics. These patients, who develop airway obstruction during natural sleep, are likely to provide more airway challenges during deep propofol anesthesia than patients with normal airway.[10]

CONCLUSIONS

The combination of propofol and fentanyl provides better quality of anesthesia than propofol alone during EGD with seemingly no additional side effects. More studies are needed to objectively characterize PACU time and post-procedure recovery time as well as the safety of the two regiments when anesthetizing patients with obstructive sleep apnea for such procedures.

Conflict of interest: None declared by the authors

Authors' contribution:

MH: Study design, conducted the study, and wrote the manuscript

JC, AC, CP, NH: Helped conduct the study

FB: Helped design the study, analyze the data, and write the manuscript

REFERENCES

1. Lubarsky D, Candiotti K, Harris E. Understanding modes of moderate sedation during gastrointestinal procedures: a current review of the literature. J ClinAnesth. 2007;19:397-404.doi:10.1016/j.jclinane.2006.11.006. [PubMed]
2. Vuyk J, Sitsen E, Reekers M. Intravenous Anesthestics, Anesthesia, 8th edition. Edited by RD Miller. Chapter 30. New York, Churchill Livingstone. 2015;821-63.
3. Fukuda K. Opioid Analgesics. Anesthesia, 8th edition. Edited by RD Miller. Chapter 31. New York, Churchill Livingstone, 2015;864-914.
4. Moffat AC, Murray AW, Fitch W. Opioid supplementation during propofolanaesthesia. The effects of fentanyl or alfentanil on propofolanaesthesia in daycase surgery. Anaesthesia. 1989;44:644-7. [PubMed]
5. Short TG, Plummer JL, Chui PT. Hypnotic and anaesthetic interactions between midazolam, propofol and alfentanil. Br J Anaesth. 1992;69:162-7.[PubMed]
6. Smith C, McEwan AI, Jhaveri R, Wilkinson M, Goodman D, Smith LR, Canada AT, Glass PS. The interaction of fentanyl on the Cp50 of propofol for loss of consciousness and skin incision. Anesthesiology. 1994;81:820-8.[PubMed]
7. Tagaito K, Isono S, Nishimo T. Upper airway reflexes during a combination of propofol and fentanyl anesthesia. Anesthesiology. 1998;88:1459-66. [PubMed]
8. Warner DO. Laryngeal reflexes: exploring terra incognita. Anesthesiology. 1998;88:1433-4. [Free full text]
9. Goudra B, Mohinder Singh P, Gouda G, Borle A, Carlin A, Yadwad A. Propofol and non-propofol based sedation for outpatient colonoscopy-prospective comparison of depth of sedation using an EEG based SEDLine monitor. J ClinMonitComput. 2016;30:551-7. doi: 10.1007/s10877-015-9769-5. [PubMed]
10. ASA Task Force on Perioperative Management. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology. 2014;120(2):268-286.doi: 10.1097/ALN.0000000000000053. [Free full text]