Ketamine -Propofol For Sedation Of Obese Patients Undergoing Upper Gastrointestinal Endoscopy

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Abstract:

Introduction: Gastrointestinal endoscopy is a prevalent method for diagnosis as well as therapy for several problems. Propofol is frequently used for sedation; however, its negative effects are reduced by the addition of ketamine. Ketamine an NMDA receptor antagonist and it prevents undesirable effects of using propofol especially in obese patients

Aim: This investigation was performed to compare and assess the efficiency of the combination of ketamine and propofol (ketofol) vs propofol alone as sedative medications for obese cases having upper gastrointestinal endoscopy.

Patients and methods: 80 cases aged between twenty-one and fifty years, with American Society of Anesthesiologists status II Obese with BMI > 30 planed for elective upper gastrointestinal endoscopy under sedation in the department of internal medicine at Al Zahra University hospital. Medical Ethical Committee was done and following case written consents, patients randomly assigned by computer generated random number into 2 groups (40 in each group).

Group (P): patient will receive 50 µg fentanyl followed by propofol 2 milligrams per kilogram in boluses manner

Group (KF): patient will receive intravenous propofol–ketamine 3:1 mixture

Results: The total propofol consumption was significantly more in group P than in group KF (258.75 ± 9.041 milligrams and 177.63 ± 63.43 mg, respectively). The recovery duration has been extended in group KF than group P, with times of 6.63 ± 0.628 minutes and 4.85 ± 1.309 minutes, correspondingly. Vomiting attacks were less frequent in group

P than group KF; nevertheless, an insignificant distinction has been observed in case and doctor satisfaction scores among both groups (P=0.122). Furthermore, an insignificant distinction among both groups concerning sex, age, heart rate, BMI, and complications such as bradycardia and nausea **Conclusion:** ketofol (Propofol ketamine combination) is associated with higher safety and cardiovascular stability than propofol group without significant adverse effects in obese patients undergoing upper gastrointestinal endoscopy.

Key words: Ketamine -Propofol - Sedation - obese upper GI Endoscopy.

Introduction

Upper gastrointestinal endoscopy is a prevalent procedure for the diagnosis as well as therapy of many GIT problems, making procedural sedation essential. It pertains to the use of dissociative or sedatives agents, with or without analgesics, to create a state of unconsciousness that enables cases to endure painful and unpleasant sensations related to procedures while preserving cardiac and respiratory function**(1)**

Propofol is a phenolic derivative that is given intravenously and exhibits short-acting sedative as well as hypnotic effects mediated by the GABA receptor, nevertheless it lacks analgesic properties. It became known as the preferred sedative due to its advantages over benzodiazepines, including minimal accumulation, rapid onset, ease of dosage adjustment, and quick recovery following cessation of action. It has served as a sedative drug for endoscopic procedures throughout the past two decades. Nonetheless, propofol may induce deep sedation or potentially hazardous side effects that might require cardiopulmonary assistance **(2)**

Ketamine is an N-methyl D-aspartate receptor antagonist that also binds to opioid and sigma receptors, resulting in a condition known as "dissociative anesthesia." It induces analgesia, amnesia, and preserves normal spontaneous respiration. However, its application as a sole sedative drug isn't recommended due to its tendency to induce alarming sudden responses and vomiting when administered in sedative doses **(3)**

The combination of ketamine and propofol in a single syringe (ketofol) has been demonstrated to be safe, maintaining sedative efficacy while minimizing the various side effects. Combination of ketamine and propofol (ketofol) stabilizes the hemodynamic response analgesia, faster recovery and decrease the incidence of respiratory depression **(4)**

Patients and methods:

This prospective double-blinded randomized research has been undertaken in the Department of Internal Medicine at Al Zhraa University Hospital. In eighty cases, undergoing elective upper gastrointestinal endoscopy with anesthesia. The investigation commenced in June 2019 and ended in March 2020, following permission from the local ethical committee of Al-Zahraa University Hospital, Al-Azhar University, and the acquisition of written informed consent. Cases aged twenty-one to fifty years, of both genders, with American Society of Anesthesiologists class II status and obesity defined by a body mass index exceeding thirty, have been included in this research. Exclusion criteria included cases who had severe bradycardia or any form of atrioventricular block, heart failure, History of Glaucoma, Craniofacial Abnormalities, Epilepsy, Allergy to drugs used, Pregnancy, Current known intracranial mass/lesion, and Patients refuse to participate in the research. Cases were randomly assigned into 2 groups of forty each using computer-generated random numbers.

Group (P): Control group: patient will receive 50 µg fentanyl followed by propofol **2** mg/kg

Group (KF): The case will receive a 3:1 intravenous mixture of ketamine and propofol, consisting of fifteen milliliters of two percent propofol, one milliliter of fifty milligrams per milliliter ketamine, and four milliliters of saline in a twenty milliliters syringe. resulting in concentrations of 2.5 milligrams per milliliter ketamine and 7.5 milligrams per milliliter propofol. Until the Ramsay Sedation Scale reaches three to four (Cases is sleeping, exhibiting a quick response to glabellar tap or loud auditory stimuli). After 8 hrs. When patients completed fasting period before performing the procedure, a peripheral intravenous line was established on the right side with a 20 G cannula, and 8-10 ml/kg/h of crystalloid has been given. No type of sedation was used before the procedure. A nasal cannula with a volume of 3-4 l/min O2 has been administered to all cases from starting the procedure until the patients became fully awake. All cases have been monitored with electrocardiogram, noninvasive arterial blood pressure (ABP), and peripheral oxygen saturation .The hemodynamic parameters were measured form starting (basal level) and every 5 min until the ending of the procedure.

Primary outcome: patient and doctor satisfaction

Secondary outcome: recovery time

Measurements:

- Demographic data (Age, Sex, BMI, ASA status)
- The hemodynamic parameters: peripheral oxygen saturation (SpO2), blood pressure (BP), and Heart rate

(HR), the hemodynamic parameters have been measured from starting (basal level) and every 5 min until the ending of the procedure.

- Recovery time which is the time from the end of procedure until the case became fully awake measured /min
- Cases' and the doctor's satisfaction scores have been done which in general score out of 4 [1 = excellent, 2 = good, 3 = moderate, and 4 = bad]
- Ramsay Sedation Score: The Ramsay Sedation Scale was frequently utilized to evaluate the degree of sedation. The sedative depth has been sustained at levels four to five on the sedation scale throughout the surgery.

Table (1); Ramsay Sedation Score

Score	Level of Sedation
1	Patient is anxious and agitated or restless, or both
2	Patient is co-operative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light tactile stimuli or loud auditory stimulus
5	Patient exhibits sluggish response to light tactile stimuli or loud auditory stimulus
6	Patient exhibits no response

- procedure duration,
- Complications: vomiting, hypotension, and bradycardia were recorded

  Management t of complications:

  - The **management** for bradycardia if occurred by atropine 0.01 milligrams per kilogram

  -The **management** for hypotension if occurred by ephedrine 6 mg/dose

  - The **management** for vomiting if occurred by ondansetron 0.1 mg/kg,
- The total amount of propofol in both groups has been recorded after the procedure was ended

Statistical analysis

The statistical presentation and analysis of this investigation will be undertaken utilizing the standard error, mean, as well as Chi- square. Variance analysis utilizing **Mann-Whitney** tests and T- independent conducted via SPSS V21. Analysis of variation, T-independent tests, and **Mann-Whitney** tests. As for the computer, utilize SPSS software for Windows. T-tests

and **Mann-Whitney** tests have been utilized to compare quantitative data across various times within the same group.

Results:

This prospective double-blind randomized trial had eighty cases undergoing elective upper gastrointestinal endoscopy with sedation. there exists statistically insignificant distinction has been seen among both groups concerning the cases' demographic data (sex, age, BMI). A statistically insignificant distinction has been observed among both groups concerning procedure length and the American Society of Anesthesiologists classification. **(Table 2)**.

Table (2); Baseline characteristics.

Baseline characteristics		Group(P) (number=40)	Group(GKF) (number =40)	p-value
Age		40.08±9.499	38.90±6.44	0.94
Sex	male	60%(24)	70%(28)	0.66
	female	40%(16)	30%(12)	
BMI		32.13±1.96	35.10±3.47	0.81
Procedure duration		14.90±1.499	14.38±1.192	0.12
ASA		2	2	

ASA, American Society of Anesthesiologists. BMI, Body Mass Index

The Hemodynamic parameters:

Concerning systolic blood pressure (SBP), a statistically significant variance has been observed among both groups at five, ten, and fifteen minutes throughout the procedure. Additionally, a statistically significant variance has been noted among both groups at five and ten minutes concerning diastolic blood pressure. Thus, our results indicate that the ketamine-propofol group exhibits greater cardiovascular stability compared to the propofol group.

Table (3); Comparative analysis among both groups as according to SBP

Systolic blood pressure	GroupP (number =40)	Group(GKF) (number =40)	p-value
At baseline	119 ±8.149	120.13±8.281	0.989
After 5min	99.0±9.072	110.0±5.008	<0.001*
After 10min	99±.9.191	112.4±7.677	0.034*
After 15min.	98.9±9.072	112.2±6.483	0.002*
after recovery	117.7±9.191	117.8±9.326	0.093

Table (4); Comparative analysis among both groups as regards DBP.

Diastolic blood pressure	GroupP (number =40)	Group(GKF) (number =40)	p-value
At baseline	70.8 ± 8	68±7	0.307
After 5min	59.88±5	58.88±11	<0.001*
After 10min	57.35±4	57.35±5	0.04*
After 15min.	62.75±4.5	63.75±6	0.120
after recovery	67.3±3.5	67.25±5.8	0.088

As regards the heart rate, A statistically insignificant distinction among the two groups

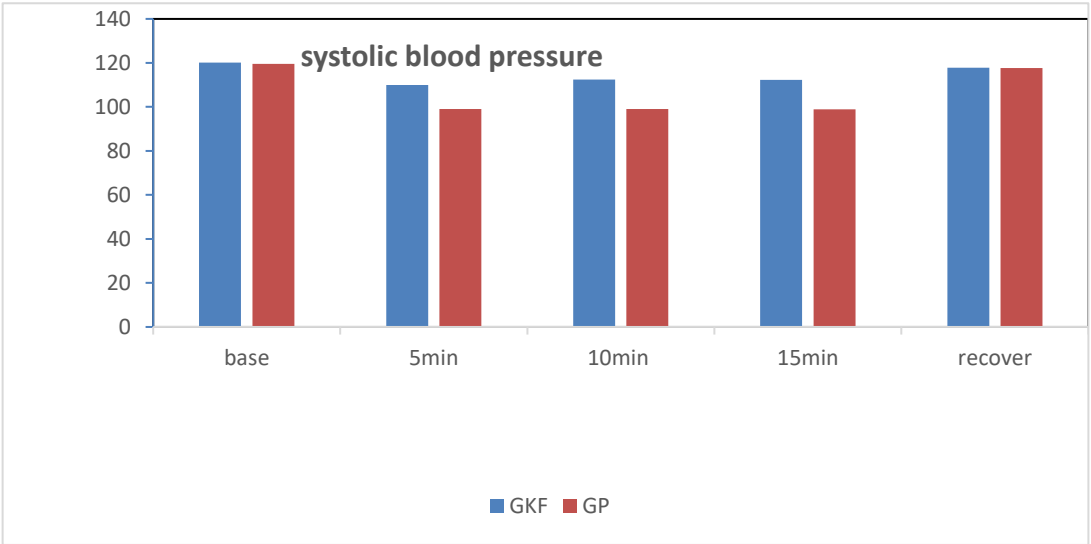

Figure (1); Comparative analysis among both groups as according to SBP.

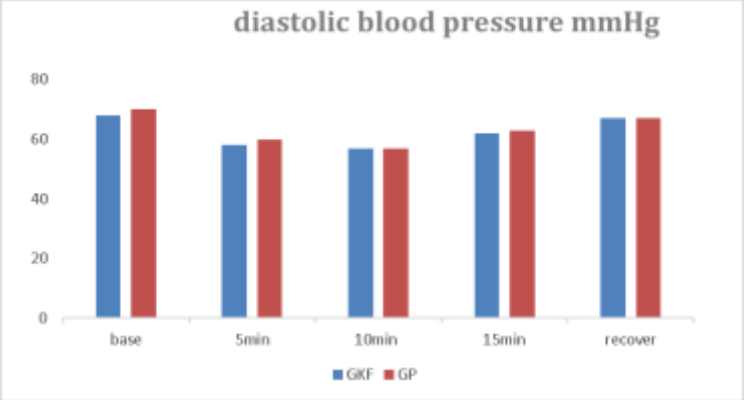

Figure (2); Comparative analysis among both groups according to DBP.

Table (5); Comparative analysis among both groups according to the Heart rate.

Heart rate	**Group(P)** (number =40)	**Group(KF)** (number =40)	p-value
Heart rate At baseline	73.80 ±4.410	78.40±4.539	0.331
After 5min	72.00±2.582	72.10±3.440	0.088
After 10min	72.48±3.658	73.30±4.020	0.469
After 15min.	72.05±2.943	72.33±3.033	0.505
after recovery	72.95±4.032	75.28±5.038	0.093

Figure (3); Comparative analysis among both groups according to the Heart rate.

Table (6); Comparative analysis among both groups according to SPO2.

saturation	Group (P) (number =40)	Group(KF) (number =40)	p-value
SPO2 At baseline	98.25±0.8	97.93±0.764	0.111
After 5min	92.50±1.132	95.48±1.853	0.002*
After 10min	93.75±0.439	95.30±1.067	<0.001*
After 15min.	96.75±0.439	97.10±0.672	0.132
after recovery	98.00±0.716	98.00±0.816	0.179

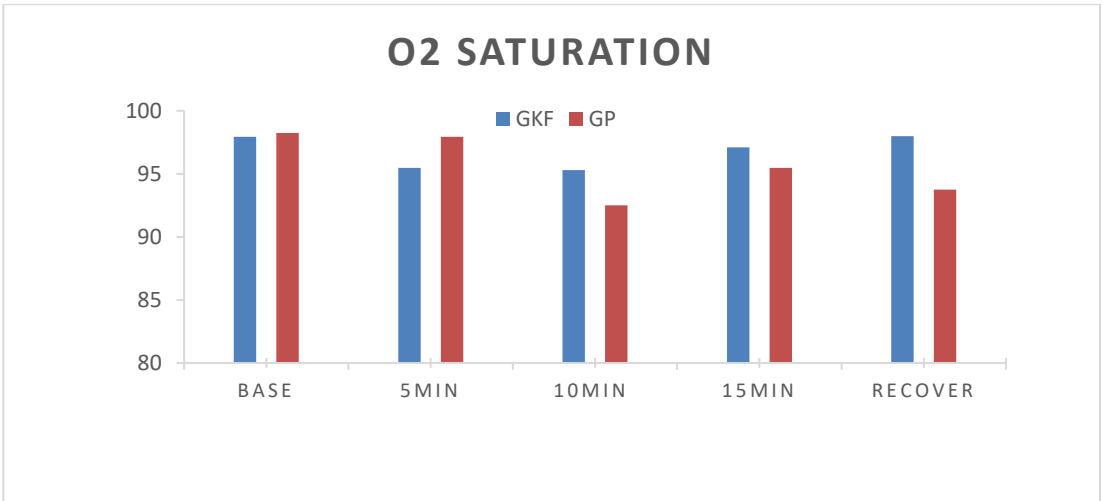

Figure (4); Comparative analysis among both groups according to SPO2.

The results indicate a statistically significant variance in oxygen saturation among both groups at five- and ten-minute post-induction. No significant distinction was observed among group one and group two **(Table 3).**

Our research indicates that the recovery time associated with ketofol is longer than that of propofol alone, demonstrating a statistically significant distinction among both groups .

Concerning case and physician satisfaction, there is insignificant variance among both groups in terms of satisfaction levels for both cases and surgeons.

Table(7); Comparative analysis among both groups according to recovery time, patients' and the doctor's satisfaction score, and the total amount propofol.

Parameters	Group(P) (number =40)	Group(KF) (number =40)	p-value
Recovery Time(minute)	4.85±1.309	6.63±0.628	<0.001*
patients' and the doctor's satisfaction score	2.(1-2)	2.(1-2)	0.122
the total amount propofol	258.75±9.041	177.63±63.438	<0.001*

Concerning the overall quantity of propofol between both groups The total dosage of propofol administered was significantly more in group P than in group KF, as indicated in table (7).

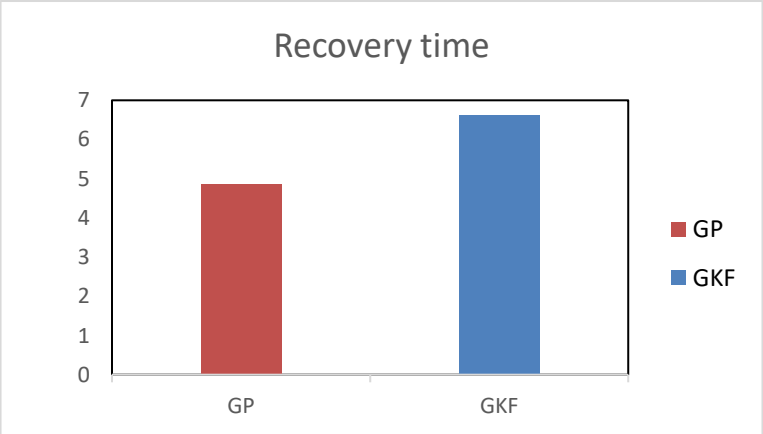

Figure (5); Comparative analysis among both groups according to recovery time.

The Ramsay Sedation Scale indicated that the degree of sedation was consistently maintained at levels four to five throughout the surgery, with results demonstrating a statistically significant distinction among the two groups, as illustrated in Figure 6.

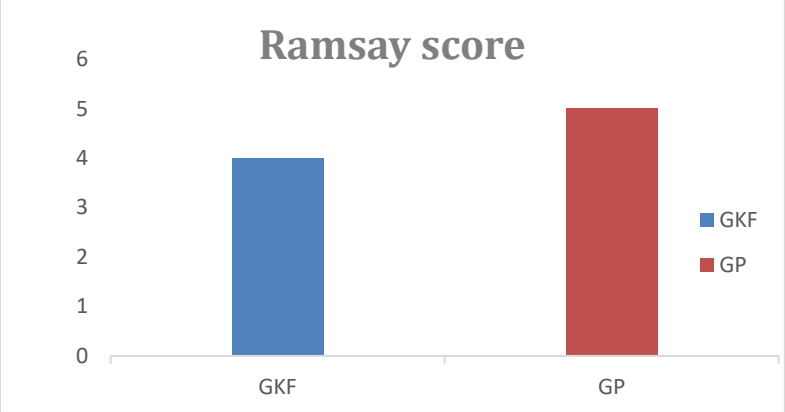

Figure (6); Comparative analysis among both groups according to Ramsay sedation scale

Concerning the complications, the ketofol group exhibited statistically insignificant distinction compared to the propofol group in terms of vomiting and bradycardia; however, there was a statistically significant distinction among the two groups concerning hypotension, as illustrated in Table 1.

Table(8); Comparative analysis among both groups according to complication.

Complication	Group (P) (number =40)	Group(GKF) (number =40)	p-value
VOMITING	10%(4)	20%(8)	0.002*
HYPOTENSION	25%	10%	0.022*
BRADYCARDIA	0%	0%	

Discussion:

While propofol is proposed as a sedative for the upper gastrointestinal endoscopy, its application is constrained, particularly in high-risk cases such as those with obesity, due to difficulties with accurately determining the optimal dosage and the lack of a direct antagonis[5].

Combining propofol with an additional sedative or analgesic may yield certain advantages, although potentially increasing

risks. Adjuvants may enhance the experiences of cases throughout surgical procedures; nevertheless, they also pose a danger of prolonging cases' recovery to normal awareness [6].

The combination of propofol and ketamine decreases the adverse effects of ketamine, including heightened hallucinations, secretion, and vomiting. Simultaneously, the analgesic properties of ketamine augment propofol [7].

The present investigation indicates that systolic blood pressure rose significantly in the KF group relative to the P group, accompanied by a significant fall in diastolic blood pressure at 5 and 10 minutes, but insignificant variance in heart rate has been seen among the groups. Furthermore, oxygen saturation was significantly greater in the KF group in comparison to the P group following five and ten minutes.

The overall dosage of propofol administered was significantly greater in group P than in group KF. The recovery duration has been extended in group KF relative to group P .

Zhang et al. [8] corroborated our findings, indicating insignificant difference in time of recovery; nevertheless, the score of recovery at thirty minutes following operation in the ketofol group was significantly lower than that in the propofol-only group.

Additionally, Yin et al. [9] observed similar results, noting that hemodynamics during sedation remained stable in the propofol-ketamine group relative to the propofol-dexmedetomidine group. Conversely, Tekeli et al. [7] demonstrated that the ketamine-propofol group exhibited lower hemodynamic stability relative to the dexmedetomidine group. The varied outcomes may be attributed to the varying dosages of propofol and ketamine.

El Mourad and his colleagues [10] demonstrated identical findings; they stated a swift onset of sedation and minimal supplementary propofol in the ketamine-propofol group, accompanied by stable hemodynamics.

Consistent with our findings, Abbas et al. [11] demonstrated a significant elevation in MAP within the ketamine-propofol group of cases having Upper Gastrointestinal Endoscopy .

Furthermore, Bachula et al. [12] determined that throughout gastrointestinal endoscopy, the early recovery ratings and during and following-operative hemodynamic parameters remained steady in the ketamine-propofol group.

The specific action mechanism of ketamine is currently unidentified. Nonetheless, the most likely etiology of general anesthesia is the disruption of corticocortical information transmission in a frontal-to-parietal ("top down") manner [13]. Ketamine stimulates medullary cardiovascular centers directly and induces indirect sympathomimetic reactions by inhibiting catecholamine reuptake through multiple mechanisms. The combination of ketamine and propofol for induction reduces

the hemodynamic and cardiac suppression commonly associated with propofol alone [14].

Our findings indicated insignificant variation in consequences, including bradycardia and nausea , among the examined groups. Nevertheless, the incidence of vomiting attacks has been reduced in group P compared to group KF, which exhibited more hypotension .

Likewise, Amornyotin [15] indicated that there were insignificant adverse effects in colonoscopic patients sedated with ketofol.

The current research demonstrated insignificant variations in case and doctor satisfaction scores among both groups.

Zhang et al.[8] demonstrated contrasting findings, indicating that patient satisfaction in the ketofol group was much higher than in the propofol-only group. Moreover, Khajavi et al. [16] established that the combination of ketamine and propofol yields greater satisfaction among cases compared to alternative regimens during colonoscopy. Various patient features may explain the varying results.

The ketamine and propofol combination has been related to hemodynamic stability and an elevated satisfaction score [17].

The research has some limitations. The research was single-centered; hence, the findings lack generalizability. Additionally, the dependence on oxygen saturation instead of capnography might have resulted in an underreporting of respiratory depression. Furthermore, although the investigation didn't explicitly compare the investigational medicines with other recognized procedural sedation and analgesia (PSA) protocols, we believe that the ketamine/propofol combination may surpass benzodiazepines and opioids for procedural sedation and analgesia in morbidly obese cases. A greater sample size may have affected the results that failed to achieve statistical significance. It is advisable to conduct additional research utilizing various additions, types, and concentrations of sedative drugs.

Conclusion: ketofol (Propofol ketamine combination) is associated with higher safety and cardiovascular stability than propofol group without significant adverse effects in obese cases that had upper gastrointestinal endoscopy.

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