Comparison of the Effect Administration Ketamine-Propofol (Ketofol) With Ketamin Single On The Quality Score Of Recovery In Patients Post Intravenous General Anesthesia As Measured By Qor-40 In Patients Undergoing Gastrointestinal Endoscopic Procedure

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Abstract
Introduction: Gastrointestinal endoscopy procedures cause discomfort to patients. Administration of sedation to relieve anxiety and discomfort, improve the results of the examination, and reduce the patient's memory of the event. Effective sedation can be judged by how well the drug achieves rapid onset of sedation, hemodynamic stability and fast recovery time. Ketamine maintains hemodynamic stability and sufficient depth of sedation during EGI procedures. Administering ketamine prevents bradycardia, hypotension and achieves sufficient and prolonged sedation..
Objective: This study aims to compare the effect of giving ketamine-propofol (ketofol) with ketamine alone on the recovery quality score of patients after intravenous general anesthesia as measured by QoR-40 in patients undergoing gastrointestinal endoscopy procedures.
Methods: This study is a randomized blinded clinical trial. This research was conducted fromJuly to September 2022. A total of 30 research subjects who underwent gastrointestinal endoscopy were divided into 2 groups. Group A (n=15) was given intravenous sedation Ketamine 0.5 mg/KgBW + Propofol 0.5 mg/KgBW, group B (n=15) was given Ketamine 1 mg/KgBW. The patient's recovery score was measured using the QoR-40 questionnaire 60 minutes after the endoscopy procedure was completed. Data were analyzed by univariate and bivariate. Bivariate data were analyzed by Chi-Square test, Independent T-Test and Mann- Whitney..
Results: The assessment of the safety score and the total score in this study found significant differences between the two groups with a p value <0.05. No significant difference was foundin the assessment of feelings, support for patients, physical independence and pain scoreswith a p>0.05.
Conclusion: The Ketamine-Propofol group on the comfort score and total score had higher scores than the single ketamine group, whereas on feelings, patient support, physical independence and pain scores there was no difference between the two groups.

***Keyword** : Endoskopi gastrointestinal, Ketamin, Ketamin-Propofol*

Introduction

Gastrointestinal endoscopy (EGI) procedures are growing in diagnostic and therapeutic purposes. Adult endoscopy has quadrupled in the last 15 years and a similar situation exists in the pediatric population. More than 50 million endoscopic procedures are performed in the US (Goudra, 2014). Endoscopy has become a common examination for the evaluation of gastrointestinal disorders. Gastrointestinal endoscopy (EGI) procedures are growing in diagnostic and therapeutic purposes. Adult endoscopy has quadrupled in the last 15 years and a similar situation exists in the pediatric population. More than 50 million endoscopic procedures are performed in the US.[1]
EGI is an uncomfortable and burdensome procedure for the patient. In general, topical anesthetics in the pharynx are safer as premedication for EGI procedures without sedation. However, patients may experience anxiety, discomfort and pain, and are generally unable to tolerate this procedure under topical anesthetic of the pharynx alone. The clinical goals of administering

sedation for EGI are to relieve the patient's anxiety and discomfort, improve the results of the examination, and reduce the patient's memory of the event. Likewise endoscopy in children can be done without sedation, with intravenous sedation, or with general anesthesia.[2]

Ketamine maintains hemodynamic stability and sufficient depth of sedation during EGI procedures. Administering ketamine prevents bradycardia, hypotension and achieves sufficient and prolonged sedation. Cardiac toxicity and episodes of psychosis in induction and prolonged recovery time are drawbacks of ketamine. The combination of ketamine and various other sedative drugs helps reduce side effects.[3]

The effect of propofol on blood pressure as a general anesthetic agent is significant. The study conducted by Hug et al., on the use of propofol for intravenous general anesthesia showed that there was an occurrence of hypotension during the first 10 minutes of induction. This retrospective study noted that approximately 15.7% of patients experienced a drastic reduction in blood pressure to 90 mmHg. Kamakashi et al., also conducted a study of changes in MAP of general anesthesia ketamine and propofol on hemodynamics and found that the combination of these two trans-intravenously would provide better hemodynamic stability compared to other general anesthetics. For ketamine itself, in several studies it was used for prehospital intubation installation, which often causes hypertension during the procedure. Administration of ketamine can increase blood pressure and hemodynamic stability. In many studies, the combination of ketamine and propofol is the best intravenous anesthetic compared to other anesthetics.[4,5,6]

The study conducted by Marko et al., administration of anesthesia in laparotomy showed changes in hemodynamics, both during induction, intubation and after intubation. However, administration of ketofol did not show any significant effect on systolic, diastolic, MAP, and heart rate. This effect provides significant hemodynamic stabilization during the procedure. Bardrinath et al., in their study used propofol-ketamine in monitoring anesthesiain female patients undergoing breast biopsies and it was shown that there was no respiratory depression effect. The hypotensive effect of propofol will be neutralized by administering a combination of ketamine. Studies comparing propofol-fentanyl and propofol ketamine combinations in pediatric patients undergoing gastrointestinal endoscopy showed that propofol-ketamine provides better hemodynamic stability.[7,8]

Recovery after general anesthesia is an important thing to be assessed as the final result of anesthesia services. Recovery after general anesthesia was assessed objectively fromawareness, vital signs, some side effects such as pain, nausea, and readiness to leave the recovery room and treatment room. However, these things are not sufficient to describe recovery after general anesthesia comprehensively. Evaluating patient-reported outcomes (PROs) is a term that is currently being developed in health services. The importance of quality recovery aims to shorten the treatment period, reduce treatment costs, reduce complications, and increase patient satisfaction.[9]

The QoR-40 instrument is a questionnaire developed in 2000 in Australia. QoR-40 specifically assesses the quality of recovery after general anesthesia comprehensively, not only from clinical aspects, but also from aspects that affect patient satisfaction with anesthesia services. The Qor-40 questionnaire questions represent all aspects that are considered as the concept of post-anesthesia recovery quality, namely comfort, feelings, physical independence, support for patients, and pain.[10]

Research conducted by Mulier in 2018 examined the comparison of giving opioids with Opioid-Free Anesthesia (OFA) on the quality of patient recovery as measured by qor-40. The OFA group was given dexmedetomidine, ketamine and lidocaine. The results of this study showed that the hemodynamic stability was the same between the two groups, intra- operatively, opioid-free patients required less analgesics, had an increased quality of recovery after surgery and milder side effects in the PACU. OFA reduces postoperative opioid requirements in the PACU, reduces postoperative hypertension and desaturation and improves the VAS score and quality of recovery as measured by the QoR-40 score.

Subjects and Methods

This study is a randomized blinded clinical trial. This research was conducted from July to September 2022. A total of 30 research subjects who underwent gastrointestinal endoscopy were divided into 2 groups. Group A (n=15) was given intravenous sedation Ketamine 0.5 mg/KgBW + Propofol 0.5 mg/KgBW, group B (n=15) was given Ketamine 1 mg/KgBW. The patient's recovery score was measured using the QoR-40 questionnaire 60 minutes after the endoscopy procedure was completed. Data were analyzed by univariate and bivariate. Bivariate data were analyzed by Chi-Square test, Independent T-Test and Mann-Whitney.

Result

Table 1. Characteristics Sample

Characteristics	Treatment		p-value
	Group A(n=15)	Group B(n=15)	
Age (years), Mean (SD)	5 1,5 (8 , 8)	50.7 (1 3.5)	0.8 49[a]
Type Gender , n (%)			
Man Woman	7 (23.3) 8 (26.7)	8 (26.7) 7 (23,3)	0.715[b]
ASA classification, n (%)			
ASA-I	4 (26.7)	3 (20)	0.666[b]
ASA-II	11 (73.3)	12 (80)	

BMI, Mean (SD)	23.1 (1.4) _	2 1 .9 (2.2)	0, 103[a]
Duration , Median (min-max)	15 (12-40)	15 (14-30)	0.255[c]

a) Independent Samples T-Test , b) *Chi - Square* , c) *Mann -Whitney,*

Table 2. Change hemodynamics before ,during and after treatment

Hemodynamics	Group A (n= 15)		Group B (n= 15)		p-value
	Means / Median	SD /Min-Max	Mean/ Median	SD/ Min-Max	
MAP (T0)	90	8,9	9 0.4	8,2	0.904[a]
MAP (T1)	87.8	6,8	94.9	7,5	0.012*[a]
MAP (T2)	88.4	7,2	9 4,0	7,6	0.045*[a]
Heart Rate (T0)	8 8	68-98	85	6 8-93	0.317[b]
Heart Rate (T1)	77,2	5,9	86, 8	5,5	0. 001*[a]
Heart Rate (T2)	77,4	6,9	8 5,3	5, 2	0.002*[a]
Breathing Frequency (T0)	18	14-22	20	17-22	0 ' 151[b]
Breathing Frequency (T1)	18	16-2 0	19	16-22	0.011*[b]
Breathing Frequency (T2)	18	14-20	20	16-22	0.364[b]
SpO2 (T0)	99	98-99	99	98-99	0.417[b]
SpO2 (T1)	99	97-99	99	98-99	0.095[b]
SpO2 (T2)	99	97-99	99	98-99	0.374[b]

Description : - P-value obtained from test a) *Independent Samples T- Test* , b) *Mann -Whitney*,
- The difference or change stated * means if $p < 0.05$
- T0 = initial value before treatment ; T1 = Value of 5 minutes after action start ;T2 = 10 minutes value after action done .
- Data presented as mean ± SD if the data is normally distributed while data which is not normallydistributed is presented in median value (min/max).

Table 3. Relationship of Ketamine-Propofol (Group A) and Ketamine alone (Group B)against score quality recovery the patient being measured with QoR-40

Questionnaire	Group A (n= 15)		Group B (n= 15)		p-value
	Means / Median	SD /Min-Max	Mean/ Median	SD /Min-Max	
Comfort	51.9	7	44.9	8,1	0.017*[a]
Condition Feeling	37,2	5,4	36,9	8,1	0.896[a]
Support to patient	29.6	3,3	28	25-35	0.400[b]
independence physical	23	20-25	23	20-25	0.863[b]
Painful	31,3	3,4	29	23-35	0.418[b]
Total score	**172.3**	**15,2**	**162.2**	**9,1**	**0.038*[a]**

Description : - P-value obtained from test a) *Independent Samples T- Test* , b) *Mann -Whitney*,
- The difference or change stated * means if $p < 0.05$
- Data presented as mean ±SD if the data is normally distributed while data which is not normally distributed i is presented in median value (min/max).

Table 4. Details of comfort score in QoR- 40

Questionnaire	Group A (n= 15)		Group B (n= 15)		p-value
	Median	Min-Max	Median	Min-Max	
Could breathe with easy	4	3-5	4	2-5	0.482 _
Could sleep rest well	4	3-5	4	2-5	0.606 _
Could eat with enjoyment	5	3-5	4	2-5	0.409 _
Could enough rest _	4	3-5	4	2-5	0.692 _
Feel tired	4	3-5	4	2-5	0.071 _
Nauseous	5	3-5	4	2-5	0.004*
Throw up	5	3-5	4	2-5	0.007*
Throw up dry	5	3-5	4	2-5	0.029*
Shaking and twitching	4	3-5	3	2-5	0.024*
shivers	5	2-5	3	2-5	0.025*
Feel freezing	2	3-5	3	2-5	0.106
Feel dizzy	2	2-5	3	2-5	0.002*

The p-value is obtained from the *Mann -Whitney* test . The difference or change stated * means ifp < 0.05. Data presented with Median (min/ max) .

Discussion

In this study, there were no statistically significant differences between the groups given ketamine-propofol and the single ketamine group, with p>0.05. Ketamine has a side effect called emergence reaction, which is a psychological reaction that occurs when the patient wakes up after administration of ketamine in the form of hallucinations, nightmares, delirium,agitation, and mood changes that affect the assessment of these three aspects. Ketamine has side effects that can reduce the anesthetic recovery score in all three aspects, namely hallucinations, nightmares, delirium, and agitation on the emotional aspect. The side effects of delirium, agitation, and mood swings affect the aspect of patient support, while the side effects of ketamine hallucinations, delirium, and agitation affect the recovery score of anesthesia on the independence aspect. In this study, a subanesthetic dose of ketamine (0.5 mg/kg BW) was used so that the side effects that appeared were reduced or minimal.[11]

There was no statistically significant difference in the pain score in this study betweenthe group given ketamine-propofol and the single ketamine group with p>0.05. Ketamine has an analgesic effect at sub-anaesthetic doses. Ketamine acts on pain modulation and perception pathways by inhibiting the effects of the excitatory membrane neurotransmitter glutamic acid on the NMDA receptor subtype.[12]

The total score in this study found that there was a statistically significant difference between the group given ketamine-propofol and the single ketamine group with p<0.05. This is in accordance with Yalcin's research in 2018, assessing the comparison of single propofol, single ketamine and ketamine-propofol administration on patient parent satisfaction, anesthesiologist satisfaction and operator satisfaction, with the results of the study showing that ketamine-propofol administration had satisfaction rates for patient parents , anesthesiologist and operator satisfaction were higher than the other groups. In this study we reported periods of hypotension and bradycardia that were not significant in the Ketamine- propofol Group and we concluded that reducing the dose of propofol in combination with ketamine as a sympathomimetic agent resulted in a more stable cardiovascular hemodynamics.[13]

Mizrak et al. found lower levels of anxiety with ketamine sedation than with propofol sedation and they discussed that the combination of low-dose fentanyl with ketamine provided their results. In our study, we found a significant reduction in anxiety levels in Group P and Group KP (p = 0.001; p = 0.003 respectively) whereas in Group K we found a numerical decrease in anxiety levels but the level of statistical significance of these findings was deemed insufficient. (p > 0.05). We suggest that the anxiolytic effect of propofol plays an important role in reducing anxiety levels that we found in the ketofol group It can be concluded that several factors, including higher rates of hallucination complications, nausea, vomiting, hemodynamic changes and long recovery periods seen after ketamine sedation, significantly affect the parental satisfaction score. On the other hand, administration of ketamine-propofol makes patients more comfortable which ultimately results in higher levels of dentist and anesthesiologist satisfaction.[13]

Conclusion

Based on this study, it was found that the administration of Ketamine-Propofol had a patient recovery score measured by QoR-40 which was higher in terms of comfort score and total score compared to the single Ketamine group, while the administration of single Ketamine had a patient recovery score measured by QoR-40 lower on the overall score compared to administration of Ketamine-Propofol.

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