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Assessment of Analgesic Effect of Ketamine Vs Ketamine Magnesium Infusion and Their Effect on Postoperative Morphine Consumption after Surgical Nephrectomy

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ABSTRACT

Two non-opioid analgesics such as ketamine and magnesium have been investigated for their potential use as adjuvants for opioid analgesics. They were shown to have anaesthetic and analgesic qualities, and it has been proposed that they may have a role in reducing the need for analgesic medication through the post-operative time.

Aim and Objectives: Primarily, we compare intra and postoperative analgesic effect of ketamine versus ketamine magnesium infusion and their influence on postoperative morphine consumption after nephrectomy and secondarily to assess hemodynamic changes and intensity of pain

Methods: This study was conducted in Six October University Hospital, 100 patients presented for elective nephrectomy under general anesthesia in the Department of Anesthesiology were randomly assigned in this prospective double blinded study into one of the two groups using computer generated table. All participants got oral midazolam 0.1 mg/kg in the evening before surgery, ketamine participants (Group I): intravenously injected by ketamine bolus dose (0.3 mg/kg), followed by continued ketamine infusion (0.15 mg/kg/h), Ketamine Magnesium participants (Group II): injected by a bolus dose of magnesium (50 mg/kg) + ketamine (0.3 mg/kg) intravenously, then by continuous infusion of (0.15 mg/kg/h) of ketamine + (10 mg/kg/h) of magnesium sulphate. Following the procedure, VAS score, Ramsay sedation scale, total rescue analgesic doses of morphine taken postoperatively, and unfavorable complications like nausea and vomiting were all documented.

Results: There were statistically significant differences between the two groups in postoperative VAS score, Ramsay Sedation Scale, and hemodynamic changes it was better in group II. Postoperative morphine consumption was remarkably decreased in collection II, with fewer side-effects.

Conclusion: Magnesium sulphate and ketamine together are more effective in curing the postoperative pain and maintaining patient hemodynamics while reducing narcotic side effects.

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1. Introduction

In 1969, renal necrosis factor (RN) therapy, which included ipsilateral adrenalectomy, was used to treat renal cortical tumors. In the surgical procedure known as a radical nephrectomy, the whole kidney is removed, along with the surrounding fat and, in some instances, the adrenal gland and lymph nodes as well. This procedure is performed on an inpatient basis [1].

Opioid use, however, can result in substantial adverse events (like respiratory depression) and side effects (like nausea and vomiting), which may lead to long-term hospital admissions and elevated expensive medical care in the postsurgical environment. The management of postoperative pain with opioids is essential, and however, using opioids has serious unfavorable complications (such as nausea and vomiting) [2].

In light of the fact that patients receiving higher opioid doses are more likely to have the aforementioned negative consequences, it is of the utmost importance to find methods that may minimize the opioids use in the postoperative time. It has been suggested that multimodal analgesia, which entails application of non-opioid analgesic in addition to an opioid analgesic, might be used as a technique of enhancing post-operative pain management while simultaneously lowering the amount of opioids that are consumed [3].

Ketamine and magnesium-ketamine are two non-opioid analgesics that are being studied for uses such as opioid analgesic adjuvants. They were found to have anesthetic and analgesic actions, and it has been proposed that as a result of this discovery, they may have a great contribution in reducing the need for postoperative analgesic medications [4].

This recent study aimed to compare intra and postoperative analgesic effects of ketamine versus ketamine magnesium infusion and their influence on postoperative morphine consumption after nephrectomy and to assess

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hemodynamic changes and the pain intensity as primary and secondary outcomes, respectively.

2. Material and method

The participants for this double-blind randomized clinical trial were recruited from Six October University Hospital from December 2021 to August 2022. Following approval of the study protocol by the medical ethics committee, 100 diseased persons of either sex, aged 35 years older were enrolled and referred to the Department of Anesthesia and Intensive Care for elective nephrectomy.

2.1. Exclusion criteria

Pregnant women, cases with severe chronic disease, cases with allergies to ketamine and magnesium sulphate, cases with a history of current regular use of (analgesic, anticonvulsant, antidepressant), and cases with any postoperative complications (ASA III or higher physical status) are not eligible for participation in this study.

The day before surgery, the diseased persons were given guidelines on how to assess their degree of discomfort using the visual analogue scale [5] (VAS; range from 0 cm = no pain to 10 cm = severe degree of pain).

The diseased persons received 0.1 mg/kg of midazolam orally in the evening before the procedure. The diseased persons were established into one of the two collections to receive the medications using a computer-generated random number database the cases were randomly allocated to one group (50 cases each): As a rescue analgesic, patients received 2–5 mg morphine IV on demand, and the drugs examined in the two groups were diluted in a 50-cc syringe involving 0.9% normal saline with an infusion rate of 1 ml/hr.

A "blinded" anesthesiologist devised the study data and neither the participants nor the anesthesiologist know who is receiving a particular treatment.

Ketamine group (Group I): a 0.3 mg/kg parenteral bolus dose was given, then by a 0.15 mg/kg/h of continued ketamine infusion.

A parenteral bolus of magnesium (50 mg/kg) mixed with ketamine (0.3 mg/kg) was given to Group II, then by continued ketamine infusion at a rate of 0.15 mg/kg/h + magnesium sulphate at rate 10 mg/kg/h.

All cases were given a history and a physical examination of the heart and chest to establish their suitability. Complete blood count (CBC), coagulation profile, liver and kidney functions, and ECG, as well as any additional tests that the patient may need.

Propofol 2–3 mg/kg, fentanyl 3ug/kg, atracurium (0.5 mg/kg), and fentanyl 1 ug/kg every 30 minutes were utilized to establish general anesthesia, which was then maintained by inhaling isoflurane 1 minimum alveolar concentration in 50% oxygen/air, and a forced airway. Ventilation was adjusted to keep CO2 levels between 35 and 40 mmHg at the completion of the tidal cycle, neostigmine (0.08 mg/kg) and atropine (0.02 mg/kg) were administered to treat any remaining neuromuscular blockage by assessing train of four (TOF) using peripheral nerve stimulator after the surgery, and then the patient was extubated.

Cases were moved to the post-anaesthetic care unit after they were fully awake (PACU). The study medications were given in bolus doses, and their infusions began simultaneously with the administration of morphine, according to patient needs. Until 48 hours following surgery, all of the studied solutions were administered by an anesthesiologist blinded to our study.

Vital signs and pain severity (as measured by VAS) were all measured at 30 minutes, 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, and 48 hr before the study ended.

To treat hypotension and bradycardia, ephedrine (0.2 mg/kg) and bolus of crystalloid (10 ml/kg) were administered. Atropine (0.01 mg/kg) was also administered for bradycardia, and desaturation with atropine 0.01 mg/kg (decrease in oxygen saturation more than 5% from the basal value) Vomiting was treated with parenteral granisetron 40 ug/kg, and postoperative discomfort was relieved with morphine 2–5 mg.

To assess postoperative sedation, the Ramsay sedation scale [6] was utilized: 1 = totally awake, 2 = awake but drowsy, 3 = sleeping but responsive to verbal directions, 4 = asleep but sensitive to tactile stimuli, and 5 = asleep and not reacting to any input.

Following the procedure, VAS score, Ramsay sedation scale, total rescue analgesic doses of morphine taken postoperatively, and unfavorable complications like nausea and vomiting were all documented by an anesthesiologist blindly to our study

3. Ethical approval

The research was accepted by the Ethical Committee of October 6 University, and the approval number is PRC-Me-2,112,023. Each study participant provided their signed consent after receiving full information. The Declaration of Helsinki was followed when conducting this research on humans.

Approval on Clinical Trials Registration: RCT approval numbers: NCT05596669.

4. Statistical analysis

IBM-SPSS version 24 was used for data analysis (May 2016). Kruskal-Wallis and Wilcoxon tests, as well as Spearman's correlation and logistic regression analysis, were used to determine statistical significance. Based on the type of data it contained, each variable

was analyzed (parametric or not). We considered that the results were statistically significant if the P-values were less than 0.05%.

5. Sample size calculation

Epi Info STAT-CALC was used to calculate the sample size depending on postoperative total morphine consumption reported in the paper of groups of interest. A sample of 100 Patients undergoing Nephrectomy (50 in each group) was calculated to detect no reduction with power of 90% (power of test) with type I error 0.05 (Alfa). The final minimum sample size taken from the Epi-Info output was 100 diseased persons. We enrolled 100 cases and randomized population by 1:1 ratio into two groups (50 cases in each group).

6. Results

One hundred diseased patients with ASA I and II who had nephrectomy at Six October university hospitals were split into two equal groups. The trial was completed by all 100 participants who were recruited.

As regards age, BMI, sex, surgery time per minutes, kind of surgery, ASA I&II, and gender, no statistically considerable variation among the groups were found ($P > 0.05$) (Table 1).

No remarkable variation was found between the two groups regarding basal characteristics.

Consider heart rate, blood pressure, oxygen saturation, and respiratory rate. The intensity of pain (as defined by a VAS score) was recorded every 30 min, 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, and every 12 hr until the study ended.

There was statistically significant variation among the two group in post-operative mean arterial blood pressure, which was lower in group II at 2 hr, 4 hr, 6 hr, 10 hr, 12 hr, 16 hr, 18 hr, 24 hr, 36 hr, and 48 hr, and no significant variation was found among the two collections at 30 min, 1 hr and 8 hr from postoperative care unit (PACU) until the completion of the first 48 hours following the procedure (Table 2).

The post-operative heart rate shows statically significance differences among the two groups at 1 hr, 2 hrs, 4 hrs, 6 hrs, 8 hrs, 10 hrs, 12 hrs, 18 hrs, 16 hrs, and 24 hrs; it was lower in group II; and there was no statistical significance difference among the collections at 30 min, 36 hrs, and 48 hrs from the start of the first 48 hrs following the surgery (Table 3).

There was statistical significance variation between the two group in post-operative O2 saturation, which was higher in group II at 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, and 18 hr, and of no significant variation among the collections at 30 min, 1 hr, 24 hr, 36 hr, and 48 from postoperative care unit (PACU) until the completion of the first 48 hours following surgery (Table 4).

The post-operative respiratory rate differed significantly between the two groups at 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, and 24 hr from the time the

Table 1. Basal Features of included participants.

	Group I (N = 50)	Group II (N = 50)	P. Value
Age (Years)	52.32 ± 9.86	53.62 ± 8.72	0.49
Sex			
Male	35 (70%)	31 (62%)	0.398
Female	15 (30%)	19 (38%)	
BMI (Kg/m^2)	25.6 ± 2.3	24.9 ± 3.1	0.2
Operation type			
Partial nephrectomy	28 (56%)	26 (52%)	0.69
Radical nephrectomy	22 (44%)	24 (48%)	
ASA physical Status			
I	37 (74%)	35 (70%)	0.66
II	13 (26%)	15 (30%)	
Duration of surgery (Min)	89.56 ± 12.6	92.26 ± 8.89	0.21

Table 2. Mean Arterial blood Pressure (MAP) variations among the two studied collections postoperatively.

	Group I (N = 50)	Group II (N = 50)	P. Value
30 min.	86.02 ± 2.62	85.6 ± 2.34	0.4001
1 hr	83.8 ± 2.47	83.28 ± 2.59	0.3069
2 hr	80.8 ± 2.05	72.8 ± 2.05	< 0.001
4 hr	84.68 ± 2.23	76.28 ± 1.82	< 0.001
6 hr	85.52 ± 2.33	77.04 ± 1.94	< 0.001
8 hr	87.58 ± 3.55	86.66 ± 1.56	0.0963
10 hr	87.6 ± 1.03	78.6 ± 1.03	< 0.001
12 hr	89.12 ± 2.36	80.14 ± 2.33	< 0.001
16 hr	88.3 ± 1.57	79.32 ± 1.53	< 0.001
18 hr	86.88 ± 1.83	78.16 ± 1.52	< 0.001
24 hr	86.02 ± 1.82	77.46 ± 1.43	< 0.001
36 hr	84.06 ± 1.6	75.86 ± 1.32	< 0.001
48 hr	83.58 ± 1.79	75.36 ± 1.47	< 0.001

Table 3. Heart rate changes postoperatively between the two studied groups.

	Group I (N = 50)	Group II (N = 50)	P. Value
30 min.	116.1 ± 10.36	115.78 ± 9.66	0.8734
1 hr	104.06 ± 9.72	95.8 ± 8.86	< 0.001
2 hr	90.7 ± 7.76	83.48 ± 7.14	< 0.001
4 hr	86.36 ± 7.7	79.48 ± 7.03	< 0.001
6 hr	99.64 ± 9.02	91.74 ± 8.35	< 0.001
8 hr	103.62 ± 6.99	95.38 ± 6.48	< 0.001
10 hr	92.86 ± 6.55	85.44 ± 6.01	< 0.001
12 hr	85.26 ± 6.75	78.46 ± 6.18	< 0.001
16 hr	88.58 ± 6.66	81.5 ± 6.03	< 0.001
18 hr	89.34 ± 6.86	82.26 ± 6.27	< 0.001
24 hr	80.82 ± 5.65	74.38 ± 5.19	< 0.001
36 hr	76.8 ± 7.24	74.24 ± 8.67	0.1121
48 hr	75.4 ± 8.02	74.64 ± 7.34	0.6222

Table 4. O2 saturation. Changes postoperatively between the two studied groups.

	Group I (N = 50)	Group II (N = 50)	P. Value
30 min.	95.18 ± 1.91	95.76 ± 4.13	0.3696
1 hr	96.82 ± 1.93	97.08 ± 4.65	0.7159
2 hr	94.28 ± 2.41	96.28 ± 2.41	0.0001
4 hr	95.3 ± 2.94	97.3 ± 2.94	0.001
6 hr	93.1 ± 0.93	95.1 ± 0.93	< 0.001
8 hr	93.4 ± 2.25	95.4 ± 2.25	< 0.001
10 hr	91 ± 0.99	93 ± 0.99	< 0.001
12 hr	96.28 ± 1.11	98.28 ± 1.11	< 0.001
16 hr	95.52 ± 1.76	97.52 ± 1.76	< 0.001
18 hr	94.46 ± 2.11	96.46 ± 2.11	< 0.001
24 hr	96.62 ± 4.8	97.08 ± 2.64	0.5539
36 hr	96.98 ± 5.05	97.6 ± 2.55	0.4403
48 hr	99.02 ± 3.58	99.16 ± 1.56	0.8

patients left the post-operative care unit (PACU) to the completion of the first 48 hr following surgery (Table 5)

In terms of post-operative VAS, there was a statistically significant difference between the two groups at 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, and 36 hr; group II had a lower value. However, there were no statistical significance variations among the collections at 30 min and 48 hr from the beginning of the first 48 hours following the operation (Table 6).

There were statistical significance variation among the two collections in the post-operative Ramsay sedation score at 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 hr, 24 hr, 36 hr, and 48 hr, and there was no statistical significance variation among the collections at 30 minutes, 1 hr, and 2 hr from the postoperative care unit (PACU) until the end of the first 48 hours following the surgery (Table 7).

There were statistical elevated significance variation among the two groups regarding postoperative morphine consumption (mg) as rescue analgesic dose at 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr, 18 h, 24 hr, 36 hr, and 48 hr. It was lower in group II and of no significant variation among the collections at 30 min and 1 hr from the postoperative care unit (PACU) until the completion of the first 48 hours after the procedure. The first requested analgesic dose was taken 30 min postoperatively (Table 8).

Statistical significance variance happened among the two groups in postoperative nausea and vomiting, with lower number of patients suffering in group II at

Table 5. Respiratory rate. Changes postoperatively between the two studied groups.

	Group I (N = 50)	Group II (N = 50)	P. Value
30 min.	24.22 ± 2.53	23.78 ± 4.79	0.5675
1 hr	20.24 ± 2.02	19.24 ± 2.02	0.0148
2 hr	17.42 ± 1.68	16.42 ± 1.68	0.0037
4 hr	16.14 ± 1.5	15.14 ± 1.5	0.0012
6 hr	17.36 ± 1.38	16.36 ± 1.38	0.0005
8 hr	18.28 ± 1.71	17.28 ± 1.71	0.0044
10 hr	16.88 ± 1.91	15.88 ± 1.91	0.0104
12 hr	15.44 ± 1.36	14.44 ± 1.36	0.0004
16 hr	14.24 ± 1.33	13.24 ± 1.33	0.0003
18 hr	14.48 ± 1.33	13.48 ± 1.33	0.0003
24 hr	15.36 ± 1.48	14.36 ± 1.48	0.0011
36 hr	14.94 ± 4.75	14.18 ± 1.35	0.279
48 hr	14.54 ± 4.97	13.92 ± 1.26	0.3942

Table 6. Postoperative VAS Score in the two studied groups.

	Group I (N = 50)	Group II (N = 50)	P. Value
30 min.	2.4 ± 0.49	2.24 ± 0.43	0.088
1 hr	2.92 ± 0.57	2.02 ± 0.55	< 0.001
2 hr	3.54 ± 0.5	1.5 ± 0.51	< 0.001
4 hr	3.06 ± 0.65	1.94 ± 0.59	< 0.001
6 hr	3.02 ± 0.65	1.98 ± 0.51	< 0.001
8 hr	3.92 ± 0.67	1.88 ± 0.59	< 0.001
10 hr	4 ± 0.57	2.12 ± 0.66	< 0.001
12 hr	5.86 ± 0.7	2.68 ± 0.65	< 0.001
16 hr	5 ± 0.53	2.04 ± 0.53	< 0.001
18 hr	2.88 ± 0.56	1.72 ± 0.61	< 0.001
24 hr	2.7 ± 0.46	1.58 ± 0.5	< 0.001
36 hr	2.34 ± 0.48	1.44 ± 0.5	< 0.001
48 hr	1.56 ± 0.5	1.4 ± 0.49	0.1115

Table 7. Ramsay Sedation Scale in the two studied groups.

	Group I(N = 50)	Group II(N = 50)	P. Value
30 min.	1.5 ± 0.52	1.38 ± 0.5	0.492
1 hr	1.44 ± 0.51	1.56 ± 0.51	0.4955
2 hr	2.56 ± 0.51	2.44 ± 0.51	0.4955
4 hr	2.25 ± 0.45	3 ± 0.82	0.0031
6 hr	2.5 ± 0.52	3.13 ± 0.72	0.0083
8 hr	2.81 ± 0.83	4 ± 0.82	0.0003
10 hr	3.06 ± 0.77	4.38 ± 0.72	< 0.001
12 hr	3.81 ± 0.75	5.19 ± 0.83	< 0.001
16 hr	4.19 ± 0.91	5.63 ± 0.5	< 0.001
18 hr	2.88 ± 0.89	5 ± 0.73	< 0.001
24 hr	3 ± 0.82	3.94 ± 0.85	0.0035
36 hr	3.06 ± 0.93	4.56 ± 0.51	< 0.001
48 hr	1.63 ± 0.72	3.13 ± 0.81	< 0.001

Table 8. Postoperative Morphine consumption among the studied groups.

	Group I (N = 50)	Group II (N = 50)	P. Value
30 min.	3.57 ± 0.61	3.58 ± 0.33	0.9347
1 hr	4.71 ± 0.56	4.81 ± 0.45	0.58
2 hr	6.61 ± 0.4	5.26 ± 0.49	< 0.001
4 hr	6.89 ± 0.42	5.48 ± 0.51	< 0.001
6 hr	7.45 ± 0.45	5.93 ± 0.55	< 0.001
8 hr	8.44 ± 0.51	6.71 ± 0.63	< 0.001
10 hr	8.86 ± 0.54	7.05 ± 0.66	< 0.001
12 hr	9 ± 0.55	7.16 ± 0.67	< 0.001
16 hr	9.7 ± 0.59	7.72 ± 0.72	< 0.001
18 hr	10.83 ± 0.66	8.61 ± 0.81	< 0.001
24 hr	10.97 ± 0.67	8.73 ± 0.82	< 0.001
36 hr	13.08 ± 0.79	10.4 ± 0.97	< 0.001
48 hr	14.06 ± 0.85	11.19 ± 1.05	< 0.001

8 hr, 10 hr, 12 hr, and 24 hr but no significant variance among the collections at 36 hr and 48 hr. Until the conclusion of the first 48 hours following the procedure, in the postoperative care unit (PACU) (Table 9)

Statistically remarkable variation in pruritus post-operatively among the two collections, less diseased persons in category II developed post-operative pruritus at 8 hr, 10 hr, and 12 hr, and there were no statistical significance variance among the collections from post-operative care unit (PACU) at 30 minutes or at 48 hours from the end of the first 48 hours following the procedure (Table 10).

7. Discussion

Improved postoperative pain treatment is strongly associated with rapid recovery from surgery, shorter hospital stays, lower morbidity, and lower expenses. Preventing pain systematically before the patient recovers from anaesthesia is necessary since post-operative pain is unexpected [7].

It is a common practice to administer opioid-based patient control analgesia (PCIA) for pain control post-operatively. Numerous adjuvant medications enhance analgesic efficacy and/or spare opioids. At lower dosages, ketamine provides analgesic effects and had shown a rise in popularity [8].

Several medications, including ketamine and magnesium sulphate, may inhibit N-methyl-D-aspartate (NMDA) receptors found in the dorsal horn of the spinal cord, and these drugs have been previously discovered as potential adjuvants for post-operative analgesia [9].

The main finding of the current study is the interaction synergism among the NMDA antagonists such as magnesium sulphate and ketamine. It is known that magnesium blocks calcium influx and inhibits the

Table 9. Postoperative nausea and vomiting among the studied groups.

	Group I (N = 50)		Group II (N = 50)		
	N	%	N	%	P. Value
30 min.	0	0%	0	0%	-
1 hr	0	0%	0	0%	-
2 hr	0	0%	0	0%	-
4 hr	0	0%	0	0%	-
6 hr	0	0%	0	0%	-
8 hr	12	24%	4	8%	0.029
10 hr	10	20%	3	6%	0.037
12 hr	7	14%	1	2%	0.027
16 hr	0	0%	0	0%	-
18 hr	0	0%	0	0%	-
24 hr	8	16%	2	4%	0.046
36 hr	5	10%	3	6%	0.46
48 hr	3	6%	1	2%	0.31

Table 10. Post-operative pruritus among the studied groups.

	Group I (N = 50)		Group II (N = 50)		
	N	%	N	%	P. Value
30 min.	4	8%	2	4%	0.3997
1 hr	0	0%	0	0%	-
2 hr	0	0%	0	0%	-
4 hr	0	0%	0	0%	-
6 hr	0	0%	0	0%	
8 hr	15	23%	5	8%	0.012
10 hr	13	26%	4	8%	0.017
12 hr	9	14%	1	2%	0.008
16 hr	0	0%	0	0%	-
18 hr	0	0%	0	0%	-
24 hr	0	0%	0	0%	-
36 hr	0	0%	0	0%	-
48 hr	4	8%	1	2%	0.169

NMDA receptor channels [10]. Meanwhile, NMDA receptors are modified by allosteric processes when ketamine attaches to the phencyclidine binding site of those receptors [11].

It is not surprising that there is a synergistic pharmacodynamic interaction between the two drugs such as ketamine and magnesium sulphate, which both inhibit NMDA receptor activation through different mechanisms. Both magnesium sulphate and ketamine have a number of other modes of action in addition to NMDA inhibiting activities that may also be accountable for such interaction [12],

In addition to Ketamine opioids – related and anti-inflammatory effects. It also affects calcium and sodium channels, dopamine receptors, cholinergic transmission, noradrenergic, and serotonergic re-uptake [13].

Other presynaptic and postsynaptic calcium channels' activity has been found to be reduced by magnesium sulphate, and the release of neurotransmitters has also been modulated. Additionally, sodium and potassium currents are modulated by magnesium, which has an impact on membrane potentials [14]. Numerous investigations have shown that preoperatively administered ketamine works as an analgesic in the immediate post-operative time [15].

Ketamine's analgesic benefits have been demonstrated by a systematic study, particularly in cases of surgery with severe pain postoperatively, and then paired with morphine to reduce morphine intake [9].

Additionally, Jouguelet-Lacoste et al. [16] said the decreased ketamine dose enhanced post-operative anesthesia, decreased the need for morphine, and decreased the incidence of nausea; these findings are consistent with the findings of our study.

Very high doses of intravenous magnesium sulphate given during surgery have been shown to minimize morphine demand, but not pain levels postoperatively [17].

In the study of **Murphy et al**. [18] they revealed that the reduction in postoperative opioid consumption was connected to the perioperative infusion of magnesium sulphate. However, there was no correlation between the decline in opioid use and the occurrence of opioid-regarding complications (nausea and vomiting postoperatively). Additionally, they clarified that intraoperative magnesium sulphate infusion was connected to a reduction in VAS pain levels for up to 4–6 hours following the procedure.

This study demonstrated that using ketamine with magnesium sulphate was preferable to using ketamine alone since it was associated with improved patient satisfaction, decreased morphine use, and more effective pain management. In the ketamine group, pruritus and nausea occurred more frequently.

The current results were supported by study of **(Bell & Kalso)** [19] as they reported that NMDA receptor antagonists, like ketamine and magnesium sulphate have been used effectively in reducing pain postoperatively and analgesic demands in elder diseased persons facing multiple surgeries. Therefore, it is determined that ketamine with magnesium sulphate is a more potent analgesic than ketamine alone

A recent research by **Jendoubi et al**. [20], they said Ketamine with Magnesium sulphate is a safe and effective adjuvant to reduce opiate intake and regulate early pain. This study focused on acute and chronic pain following an open nephrectomy.

In the study of **Unlugenc et al**. [21], whereas they compared the effect of Magnesium sulphate and ketamine on postoperative analgesia and morphine consumption. It also revealed that the two medications were remarkably decreased morphine intake through the initial 24 hours, both studies agree with ours.

According to **Jabbour et al**. [22], ketamine with magnesium sulphate also lowers pain levels at rest, during movements, and while coughing before patients are discharged from the PACU in fatty participants facing open bariatric procedure during the first 24 hours following surgery. The average VAS in the two collections was consistently less than 4/10, indicating good pain control.

Additionally, **Liu et al.** [23] hypothesized that the "super-additive impact" of these two antagonists could account for the more protracted morphine-sparing effect seen in our study. Each of them supports the findings of our study.

In accordance with the findings of our investigation, **Mohamed and Essam** [24] discovered that boosting ketamine infusion with magnesium sulphate can safely enhance intraoperative and postoperative analgesia while reducing adverse effects in cancer breast surgery.

In the study by **Arkan et al**. [25] they revealed that the overall amount of morphine consumed was remarkably reduced in the ketamine collection, then they did not discover any beneficial benefits of magnesium sulphate on morphine consumption. Postoperative pain scores were similar across all groups. This study disagrees with ours because they employed ketamine and magnesium sulphate independently, and because the types of operations and drug doses were varied.

Patrice F. and Juan C. [26] came to the following conclusion in a systematic review study and meta-analysis of nine researches about ketamine and magnesium sulphate: both differently but constantly decrease hemodynamic variations through surgical procedures and may be realized as complementary not only for pain regulation but also for delivering established anesthesia. This study supports the results of our findings.

8. Conclusion

While ketamine alone is less effective, magnesium sulphate is a useful adjuvant medication for postoperative pain control. Ketamine and magnesium sulphate work better together to relieve surgical pain and maintain patient hemodynamics while minimizing narcotic adverse effects.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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