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ORIGINAL ARTICLE

The Effect of Different Doses of Ketamine on Postoperative Hallucination: A Cross-Sectional Study

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ABSTRACT

Postoperative hallucinations and other psychotropic effects are known side effects, which may be dose-dependent. Higher doses exacerbate these changes, prolonging dissociative and hallucinatory experiences postoperatively. The study aimed to evaluate the effect of ketamine different doses on postoperative hallucination (score and types). This study was applied on (62) persons including (32) males and (30) females under general anesthesia (G.A). The patients' ages range between (16-60) years for both those who have various surgeries under general anesthesia also all the patients submitted to the study questionnaire for assessing the effects of various ketamine doses on postoperative hallucinations. Different doses of ketamine were induced, including (30, 40, 50 and 100) mg/kg and different durations of ketamine administration (10-20), (21-30), (31-40) and more than (40 minutes) with observing and monitoring the hallucination types (visual, auditory and visual/auditory) as well as its score (mild, moderate and severe). In the induction stage; propofol administrated at a (1-3) mg/kg dose. In the premedication stage; midazolam was induced at a (0.3-0.03) mg/kg dose. In the maintenance stage; isoflurane and sevoflurane were induced at a dose of (0.5-3) %. The muscle relaxants; atracurium (0.1 mg/kg) and rocuronium (0.5 mg/kg) were induced. Mechanical ventilation and non-invasive monitoring of blood pressure and pulse oximetry were also monitored. At the end of the operation, a muscle relaxant reflector was induced with the combination of neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg). A suction apparatus was also used in the recovery stage. The results showed significant differences between the different doses of ketamine with hallucination types and hallucination score, as well as there are statistically significant differences between the different time durations of ketamine administration with hallucination types and hallucination score at (p-value <0.0001). The study concludes that the incidence and severity of postoperative hallucination are closely tied to the dose of ketamine administration. Ketamine with low dose is related to a reduced risk of hallucinations, while the moderate and highly are doses significantly increase risk. Clinicians must carefully consider the dose of ketamine used in perioperative settings, taking into account patient-specific factors and implementing strategies to minimize adverse psychological effects.

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1- INTRODUCTION

The Ketamine hydrochloride drug was approved by the food and drug administration (FDA), which is generally called ketamine, as a common anesthetic medication either on its own or combined with other drugs. This drug is very active in brief medical processes which do not require relaxation of skeletal muscles and are applicable as a pre-anesthetic medication to induce general anesthesia combined to other general anesthetic drugs. In addition, the ketamine is approved by FDA since it enhances the impacts of low-potency elements like nitrous oxides. Ketamine was also proven as well as to its anesthetic properties to be essential in managing pains, treatment-resistant depressions, suicidal ideations as well as treatment of refractory state epileptic, with particular indication that await for FDA approvals. The applications and resultant outcomes are determined by the drug's dose resulting in prescribing protocol variations. Such versatility made ketamine necessary in managing both pains and anesthesia. The continuous researches explore the possible ketamine applications in psychotherapy through all isomeric formulas [1]. At higher dose, ketamine functions mainly as sedatives rather than analgesic agents. The drug ketamine can be applied in emergency for providing short-term procedural sedations as well as quick sequence intubations. The ketamine drug was recognized by the instructions of the Society of Critical Care Medicine to be as an active treatment for quick sequence intubations. This drug was desired by patients with bronchospasms due to its bronchodilator characteristics. Ketamine is utilized in processes which need short term sedations or anesthesia and are securely applicable in extensive ages that start from three months. Ketamine is metabolized by children quicker than adults, thus, higher doses are required. Nevertheless, elderly individuals metabolize the drug slowly and require lower doses. The glutamate receptor antagonist, ketamine, is a non-competitive N-methyl D-aspartate (NMDA) which can block HCN-1 receptor. The partial agonism and the unique dissociative actions of opiate mu-receptor can permit painful processes in steady states of comforts and sedations [1]. Hallucination can be defined as an external stimulus perception without an existence of stimuli. Different types of hallucination are present: visual, auditory, tactile, olfactory and gustatory, that are often triggered by psychiatric conditions such as (bipolar disorder, schizophrenia as well as anxiety disorder) and less frequently triggered by neurological conditions such as (neoplasia, cerebrovascular accident as well as infections) [2]. A very realistic hallucination, dream-like experience or mode change can be caused by the administration of Ketamine. Such effects may disappear within (1-2) hours. Since the synthesis of ketamine, the effects of such kinds of treatments were called (Dissociative anesthesia). Ketamine became a recreational medication of abuse due to its quick onsets, short action time and hallucinogenic characteristics. This drug causes hallucination, time and space distortion as well as mild dissociative impacts in sub-anesthetic dosages. This medication is described by recreational users as the out of body experience drug or the melting into the surrounding drug. When administrated at high doses, ketamine may lead to serious dissociative impacts as individuals become completely detached from reality. In the 1960s, the initial reports on the recreational use of the drug appeared and reached its peaks in popularity in the 1990s as it became a common constituent of ecstasy tablet in Europe. Among young individuals, to the present time, ketamine remains the common treatment of choice in Hong Kong [3].

The medically-induced consciousness loss with concurrent protective reflex loss because of an anesthetic agent is known as general anesthesia. Different treatments can be prescribed for induction of analgesia, unconsciousness, amnesia, relaxation of skeletal muscles, and autonomic system reflex loss [4, 5]. Patients who undergo surgical operations which need deeper relaxations for a long period of time are well-suited for general anesthesia as long as there was no any contraindication. Surgical operations which are not sufficiently anesthetized with regional or local anesthesia need general anesthesia, while surgical operations which may lead to significant blood losses or where breathing is influenced, require general anesthesia [6, 7]. The drug ketamine is a medical dissociative anesthetic agent used to induce and maintain anesthesia. In addition, it can be used to treat depression and manage pains [8]. The NMDA receptor antagonist, ketamine, accounted for the majority of its psychoactive impacts [9]. At an anesthetic dose, this drug causes induction of a dissociative anesthesia state, a trance-like states that offers pain relievers, sedations, as well as amnesias. Its differentiating properties as an anesthesia drug include preserved breathings and airway reflex, stimulated cardiac functions with high blood pressures, as well as moderate bronchodilations [10]. The drug ketamine hydrochloride is non-barbiturate dissociative anesthesia medication. It is a cyclohexanone derivative that quickly functions and makes intense anesthesia and analgesia. The chemical name of ketamine is (±)-2(o-chlorophenyl)-2(methylamino) cyclohexanone hydrochlorides while its structural formula is CHClNO. The drug ketamine is a non-competitive *N*-methyl D-aspartate (NMDA) and glutamate receptor antagonists which cause blocking of the HCN1 receptor. The unique dissociative actions and partial agonisms of opiates mu-receptors permit painful processes in consistent status of sedations and comforts [11, 12].

1.1 Mechanism of Actions

The drug ketamine hydrochloride is a non-barbiturate dissociative anesthetic medication. This drug quickly produces and acts profound analgesia anesthesia and analgesia since it is one of the cyclohexanone derivatives. The chemical name of ketamine is (±)-2(o-chlorophenyl)-2(methylamine) cyclohexanone hydrochlorides and its structural formulas CHClNO. The glutamate receptor antagonist, ketamine, is a non-competitive N-methyl D-aspartate (NMDA) which can block HCN-1 receptor. The partial agonism and the unique dissociative actions of opiate mu-receptor can permit painful processes in steady states of comforts and sedations [11, 12]. The effectiveness of ketamine in chronic pains as antidepressants far outlast the real concentrations of the drug and is may be mediated by the secondary increased structural synapsis connectivities mediation by neuronal responses to the ketamin-induced hyper-glutamatergic status. The receptor of *N* methyl-D aspartate (NMDA) plays an essential role in depression etiology. Ketamine acts quickly to control depression symptom with acute suicidal ideations, via its NMDA antagonist actions. The brain level of glutamate may be elevated by ketamine, leading to synaptogenesis stimulation and elevation of brain-derived neurotrophic factors (BDNF) levels, and this drug can interact with the sigma receptor. The drug functions via reducing central sensitizations, wind-up phenomena (developing of ongoing, worsening and chronic pains), as well as pain memories. The opioid, cholinergic and monoaminergic system seem to play the negative and positive modulatory functions in each of sedations and analgesias. Tolerance is reversed to opioid by ketamine [13-14]. The drug ketamine is often taken via IV or IM route. The strengths available are 200mgs/20mL (10 mgs/mL), 500 mgs/5 mL (100 mgs/mL) in addition to 500 mgs/10 mL (50 mgs/mL). Dilution of ketamine with equal volumes of sterile water, normal saline or 5% dextrose is necessary [15, 16].

1.2 Hallucination

Hallucination is defined as the perception without a presence of the external stimuli which have the compelling senses of realities. It can be distinguished from many related phenomena like dreaming (REM sleeps), which don't include wakefulness; pseudo hallucinations, which don't mimic actual perceptions and are exactly perceived as unreal; illusions, that involve misinterpreted or distorted actual perceptions; as well as mental imageries, that don't mimic actual perceptions, and are under voluntary controls. Also, hallucinations are different from "delusional perception", where properly sensed and interpreted stimuli (e.g. real perceptions) are offered some more importance. Hallucination may develop at all sensory forms, auditory, visual, gustatory, olfactories, tactiles, pro-prioceptive, equilbrioceptive, thermoceptive, nociceptive or chronceptive. If multiple sensory forms occur, hallucination is referred to as a multimodal. Hypnagogic and hypnopompic hallucinations are regarded as a normal phenomenon. The hypnagogic hallucinations happen when people fall asleep, whereas hypnopompic hallucinations happen when people wake up. Hallucinations may be related to drug uses (especially deliriant), sleep deprivations, neurological disorder, psychosis as well as *Delirium tremens*. Several types of hallucination may also occur during sleeping paralysis [17, 18].

1.3 Types of Hallucination

1.3.1 There are 5 main types of hallucination include:

- Auditory hallucination: To hear a sound or a voice which can't be heard by someone else (the commonest hallucination type).

- Visual hallucination: To see persons, colours, shapes or items which are not real (the 2nd most common hallucination type).

- Tactile hallucination: To feel a sensation (e.g. bugs crawl under one's skin) or to feel someone is being touched when he is not.

- Olfactory hallucination: To smell something without a physical source (less commonly found than an auditory or a visual hallucination).

- Gustatory hallucination: To feel tasting something in one's mouth which is without a source (the most rare hallucination type) [19].

1.3.2 Other hallucination types are:

- Presence hallucination: To sense that someone is close to you or in your room with you while there is nobody present.

- Proprioceptive hallucination: To feel that one's body move or his limbs are separated from his body while nothing of such things happens [19].

1.4 Hallucination Score

Hallucination score often refers to metrics used to evaluate how often a language model generates information that is incorrect, misleading, or entirely fabricated, which is commonly termed "hallucination." In the context of natural language processing and AI, "hallucination" describes outputs that deviate from reality or factual correctness, particularly when the model seems confident in its assertions. The scores are probabilities that range from (0 to 1) - 0 means that there is a hallucination and 1 means that there is no hallucination (factually consistent). According to Vectara, an appropriate threshold for this metric is 0.5 to predict whether a text is consistent with another [19].

1.5 Ketamine Hallucination

The dissociative anesthetic drug ketamine is known to induce hallucinations and altered states of consciousness. The effect of ketamine is mainly because of its actions as N methyl-D aspartate (NMDA) receptor antagonists that cause disruption of normal communication in the brain, leading to dissociation, sensory distortions, and hallucinations. Ketamine can cause vivid visual, auditory, and tactile hallucinations. Users often report entering a dream-like state, experiencing distortions in time and space, and feeling detached from their body (a phenomenon known as dissociation). At a great dose, users might enter the "K-hole" which is considered as intense hallucinations, a sense of ego dissolution, and a feeling of being disconnected from reality. Ketamine blocks NMDA receptors, which are involved in learning, memory, and perception. This disruption leads to altered sensory processing and hallucinations. It also increases glutamate release in certain brain regions and modulates other neurotransmitter systems, such as dopamine and serotonin, contributing to its hallucinogenic effects. Users may experience visual distortions (e.g., bright colors, geometric patterns), auditory hallucinations (e.g., hearing sounds or voices), and tactile sensations (e.g., feeling like they are floating or merging with objects). These effects are often described as surreal, dream-like, or otherworldly. Ketamine-induced hallucinations can be unpredictable and may cause anxiety, paranoia, or panic, especially in unsupervised settings. Chronic use of ketamine can lead to cognitive impairment, bladder toxicity, and addiction. If someone experiences distressing hallucinations or other adverse effects, medical attention should be sought immediately [20, 21].

2- MATERIALS AND METHODS

This study was done at Baghdad Teaching Hospital and it was applied on sixty two (62) patients including (32) males and (30) females under general anesthesia (G.A). Patients' age ranges between (16-60) years for both those who have various surgeries under general anesthesia also all the patients submitted to the study questionnaire to evaluate the impacts of various doses of ketamine on post-operative hallucinations. Different doses of ketamine were induced, including (30, 40, 50 and 100) mg/kg and different durations of ketamine administration (10-20), (21-30), (31-40) and more than (40 minutes) with observing and monitoring the hallucination types (visual, auditory and visual/auditory) as well as its score (mild, moderate and severe). In the induction stage; propofol administrated at (1-3 mg/kg) dose. In the premedication stage; midazolam was induced at a (0.3-0.03) mg/kg dose. In the maintenance stage; isoflurane and sevoflurane were induced at a dose of (0.5-3) %. The muscle relaxants; atracurium (0.1 mg/kg) and rocuroniums (0.5 mg/kg) have been induced. Mechanical ventilation and non-invasive monitoring of blood pressure and pulse oximetry were also monitored. At the end of the operation, a muscle relaxant reflector was induced with the combination of neostigmine (0.05 mg/kg) with atropine (0.02 mg/kg). A suction apparatus was also used in the recovery stage.

Table (1): Drugs used during the collection of study cases

Drugs	Manufacturer Company	Country
Propofol	Wellex	Egypt
Ketamine	Liorad	Germany
Midazolam	Hikmah pharmaceuticals	United Kingdom

Table (2): Equipments used during the collection of cases

Equipment	Manufacture Company	Country
Endotracheal tube (6,7.5)	Enteplin	Egypt
Cannula	Corden pharma SPA	Germany
Syringe	Luaxamed	Germany
Laryngoscopes	Kilani	Lebanon
Laryngeal mask	Corden pharma SPA	Germany
Pulse oximetry	Masimo Corporation	USA
Electrocardiogram	GE Healthcare	USA
Secretion suction device	Medtronic	Germany
Non-invasive blood pressure	Omron Healthcare	Japan

Table (3): Hallucination Score

Hallucination Score	Non	Mild	Moderate	Severe
(0-1)	0	(0.1-0.4)	(0.5-0.6)	(0.7-1)

3- RESULTS AND DISCUSSION

The results of this study observed the mean and standard deviation for the ages of male groups patients (n=32) were (31.71±11.18) versus (32.20±9.144) of female groups with non-significant differences (P=0.85). This study's results also measured the weight of the patients classified according to gender with non-significant differences (P-value=0.43) between weight for male and female groups as explained in table (4).

Table (4): Distribution of the age/year and the weight/kg according to the gender (male & female)

Variables		Mean ± Std.deviation	P-Value	Sig.
Age(year)	Male (n=32)	31.71 ± 11.18	0.85	N.S
	Female(n=30)	32.20 ±9.144		
Weight(Kg)	Male(n=32)	78.59 ± 8.72	0.43	N.S
	Female(n=30)	76.83 ±8.75		

***N.S: Non -significant**

The results of current study revealed the greatest number of patients were at the age groups (16-30) with 34 patient cases with 54.8%, followed by (31-45) age groups which account 22 patient cases with 35.5%, the fewest cases were recorded at the age groups >45 with 9.7% from total study samples. Also, the results distributed the patients according to family history which showed 49 with 79.0% had no history of family diseases, followed by 5 cases with 8.1%, while the hypertension and hypertensive/DM cases shared equal frequency 2 with 3.2%, other cases of hyperthyroidism and hypertensive/asthma had 1, 3 with 3.2%, 4.8% respectively as shown in table (5).

Table (5): Distribution the patients (N=62) according to age groups /years and family history (Number and percentages %)

Variables of study		N	%
Age groups/year	(16-30)	34	54.8
	(31-45)	22	35.5
	>45	6	9.7
	Total	62	100.0
Type Family history		N	%
NO		49	79.0%
DM		5	8.1%

Hyperthyroidism	1	1.6%
Hypertensive	2	3.2%
Hypertensive/DM	2	3.2%
Hypertensive/Asthma	3	4.8%
Total	62	100.0

The data in the present study focused on the types of hallucination with the doses of ketamine (mg/kg), The results had 21 patients cases (33.9%) had auditory type of hallucination which received 30-50 mg of ketamine dose, followed 9 patients cases (14.5%) had visual hallucination type under the same doses, while only 5 patients cases (8.1%) had both auditory/visual hallucination types, The rest cases 15(24.2%) had no hallucination type. On the other hand, 4 patients cases (6.5%) had auditory hallucination who received >50 mg of ketamine dose, while 8 patients cases (12.9%) had both auditory/visual hallucination type, no cases of visual hallucination type and non-hallucination were recorded under the ketamine dose >50 mg, statistically these differences were highly-significant (P-value=≤0.0001) as explained in table (6).

Table (6): Distribution the patients (n=62) according to Ketamine doses (mg/kg) with hallucination types

Ketamine dose (mg/kg)	**Hallucination types**				**Total**
	Non	Auditory	Visual	Auditory / Visual	
(30-50)	15(24.2%)	21(33.9%)	9(14.5%)	5(8.1%)	50(80.6%)
>50	0(0.0%)	4(6.5%)	0(0.0%)	8(12.9%)	12(19.4%)
Total	15(24.2%)	25(40.3%)	9(14.5%)	13(21.0%)	62(100.0%)

Chi-square P-value= ≤0.0001 (H.S)

The results of this study classify the patients according the hallucination score with the ketamine doses (mg/kg).The results documented 15 patient cases (24.2%) of patients had mild hallucinations under the (30-50) mg ketamine doses versus 1 cases 1.6% had mild score, While 12 patient cases (19.4%) had moderate score under the >50mg ketamine doses versus no cases of moderate score under the same doses (>50). 8 patient cases (12.9%) had severe scores of hallucination who received 30-50 ketamine doses versus 11 patient cases (17.7%) had severe score under the doses (>50)mg. Only 15 patients cases (24.2%) had non score of hallucination type under the 30-50 mg ketamine doses versus no cases of hallucination were recorded under the (>50)mg ketamine dosed. These differences statistically were highly-significant (P-value=≤0.0001) as arranged in table (7).

Table (7): Distribution the patients (n=62) according to Ketamine doses (mg/kg) with hallucination score

Ketamine doses (mg/kg)	**Hallucination Score**				**Total**
	Non	Mild	Moderate	Severe	
(30-50)	15(24.2%)	15(24.2%)	12(19.4%)	8(12.9%)	50(89.6%)
>50	0(0.0)	1(1.6%)	0(0.0%)	11(17.7%)	12(19.4%)
Total	15(24.2%)	16(25.8%)	12(19.4%)	19(30.6%)	62(100.0%)

Chi-square P-value= ≤0.0001 (H.S)

The results of this study classify the patients according the hallucinations score with the duration of ketamine (minute).The results documented 12(19.4%) cases had severe hallucinations score after (21-30) minutes of drug administration, while only 3(4.8%) cases had severe hallucination score after (10-20) minutes of drug administration, The results also observed (2(3.2%), 2(3.2%)) patients had severe hallucination type after (31-40) and >40 minutes of drug administration respectively, while the results of the moderate case, 2(3.2%) had moderate hallucinations after (10-20) minutes of drug administration.

Also, (5(8.1%),5(8.1%)) had moderate hallucinations after (21-30) minutes and (31-40) minutes of drug administration, while no case (0.0%) had hallucinations at more than 40 minutes. As for the mild case, 3(4.8%) at (10-20) minutes post-drug hallucinations and 8(12.9%) at (31-40) minutes post-drug hallucinations while only 5(8.1%) at (31-40) minutes post-drug hallucinations P-value for these differences at ≤0.0001 as shown in table (8).

Table (8): Distribution the patients (n=62) according to duration of Ketamine administration/min with hallucination score

Duration/min of ketamine administration	Hallucination score				Total
	Non	Mild	Moderate	Severe	
Non	15(24.2%)	0(0.0%)	0(0.0%)	0(0.0%)	15(24.2%)
(10-20)	0(0.0%)	3(4.8%)	2(3.2%)	3(4.8%)	8(12.9%)
(21-30)	0(0.0%)	8(12.9%)	5(8.1%)	12(19.4%)	25(40.3%)
(31-40)	0(0.0%)	5(8.1%)	5(8.1%)	2(3.2%)	12(19.4%)
>40	0(0.0%)	0(0.0%)	0(0.0%)	2(3.2%)	2(3.2%)
Total	15(24.2%)	16(25.8%)	12(19.4%)	19(30.6%)	62(100.0%)

P-value= ≤0.0001 (H.S)

The results of this study classified patients according to the types of hallucination and duration of ketamine (minute). The results documented that 11(17.7%) of cases had auditory/visual hallucinations (21-30) minutes after taking the drug, while 13(12.0%) of cases had auditory hallucinations (21-30) minutes after taking the drug. 5(1.8%) had auditory hallucinations, 6(9.7%) had visual hallucinations, and 1(1.6%) case had visual/auditory hallucinations (31-40) minutes after taking the drug. 6(9.7%) had auditory hallucinations, 2(3.2%) had visual hallucinations (10-20) minutes, 1(1.6%) case had auditory hallucinations, and 1(1.6%) case had visual/auditory hallucinations for more than 40 minutes. The P-value for these differences was ≤0.0001 as shown in table (9).

Table (9): Distribution the patients (n=62) according to duration of Ketamine administration/min with types of hallucination

Duration of ketamine administration/min	Hallucination Types				Total
	Non	Auditory	Visual	Auditory/Visual	
Non	15(24.2%)	0(0.0%)	0(0.0%)	0(0.0%)	15(24.2%)
(10-20)	0(0.0%)	6(9.7%)	2(3.2%)	0(0.0%)	8(12.9%)
(21-30)	0(0.0%)	13(21.0%)	1(1.6%)	11(17.7%)	25(40.3%)
(31-40)	0(0.0%)	5(8.1%)	6(9.7%)	1(1.6%)	12(19.4%)
>40	0(0.0%)	1(1.6%)	0(0.0%)	1(1.6%)	2(3.2%)
Total	15(24.2%)	25(40.3%)	9(14.5%)	13(21.0%)	62(100.0%)

P-value=0.0001(H.S)

The current study classified the gender according to the types of hallucinations. The results noted that 8(12.9%) of the male group suffered from auditory, visual, and auditory/visual hallucinations after taking the drug, respectively, while the main patients of the female group suffered from auditory hallucinations after taking the drug 17(27.4%), 1(1.6%) suffered from visual hallucinations, and 5(8.1%) suffered from auditory/visual hallucinations, these variations were statistically significance with (P=0.02) as shown in table (10).

Table (10): Distribution the patients (n=62) according to gender with types of hallucination

Gender	Hallucination Types				Total
	Non	Auditory	Visual	Auditory/Visual	
Male	8(12.9%)	8(12.9%)	8(12.9%)	8(12.9%)	32(51.6%)
Female	7(11.3%)	17(27.4%)	1(1.6%)	5(8.1%)	30(48.4%)
Total	15(24.2%)	25(40.3%)	9(14.5%)	13(21.0%)	62(100.0%)

P-value=0.02

The occurrence of postoperative hallucinations following ketamine administration has been well documented, with studies suggesting a strong correlation between dose and neuropsychiatric manifestations. Several mechanisms have been proposed, including the role of the drug ketamine as a Nmethyl- D aspartate (NMDA) receptor antagonists, that disrupted normal neural connectivity and perception [14]. Low-dose ketamine generally defined as (≤0.5 mg/kg) IV were widely used for its analgesic and opioid-sparing effects. Some studies suggest that low-dose ketamine

reduces the risk of postoperative hallucinations compared to higher doses, although mild psychotomimetic effects may still occur. For example, a study by Mion *et al*. (2013) demonstrated that subanesthetic doses (<0.3 mg/kg) are associated with lower rates of postoperative hallucinations compared to full anesthetic doses [22]. However, even at low doses, certain patient populations remain susceptible. Factors such as preexisting psychiatric conditions and individual neurophysiological responses may increase the likelihood of hallucinations, even at subanesthetic doses [23]. While Moderate ketamine doses (0.5–1 mg/kg) IVoften used for procedural sedation and anesthesia induction. At these levels, the likelihood of hallucinations increases significantly. The study by Short *et al.* (2018) found that individuals receiving doses within this range had a 25-30% incidence of postoperative hallucinations, which were often transient but distressing for some individuals [24]. The study further indicated that when combined with benzodiazepines or dexmedetomidine, the incidence of hallucinations was reduced, suggesting a potential mitigating approach [25]. High ketamine drug doses (>1 mg/kg) IV are strongly related to postoperative hallucinations and other dissociative symptoms. Full anesthetic doses used in surgical settings were associated with about 50% incidences of postoperative neuropsychiatric symptoms, including Vivid auditory and visual hallucinations, delirium, and nightmares [26]. A clinical trial conducted by Hudetz *et al*. (2019) reported that ketamine doses exceeding (1.5 mg/kg) IV led to a significant increase in postoperative hallucinations, particularly in old-aged patients or those who had the history of substance use disorders [2ᵛ].

4- CONCLUSION

We conclude that the incidence and severity of postoperative hallucination are closely tied to the dose of ketamine administration. Lower dose of ketamine is related to a lower risk of hallucinations, while the moderate and highly are doses significantly increase risk. Clinicians must carefully consider the dose of ketamine used in perioperative settings, taking into account patient-specific factors and implementing strategies to minimize adverse psychological effects.

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