Arab American University

Faculty of Graduate Studies

Post-Operative Pain Management of Urgent General Surgeries: A Comparison Between Single Paracetamol &Ketamine plus Paracetamol in Tubas Governmental Hospital.

A Randomized Control Trial Study

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Thesis Approval

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Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student’s name:

Signature:

Date:

Student ID:

Dedicated

To

My Father

A strong and gentle friend….

Who taught me to climb the mountain so I can see the world,

Notso, the world can see me…

My Mother

My beloved, the symbol of patience and continuous giving ….

Who brought me up, always accompanied with long prayers and wishes...

Special thanks to ***Dr. Nour Tqatqa*** *who was the anesthesiologist who made this research possible with his guidance, patience and encouragement.*

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To those who taught me letters of gold, and words of gems, to those who gave me so much, to my ***teachers****.*

To the comrades of the path, to those who always supported me, to the shining candles in my life to my ***friends*** *and my* ***colleagues****.*

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"So many of our dreams at first seem impossible, then they seem improbable, and then, when we summon the will, they soon become inevitable"

Christopher Reeve.

It is not a fair task to acknowledge all the people who made this M.A thesis possible with a few words. However, I will try to do my best to extend my great appreciation to everyone who helped me scientifically, financially and emotionally throughout this study.

I shall begin with God the Almighty: without His will, I would have never found the right path. His mercy was with me throughout my life and ever more in this study. I thank Him for enlightening my soul with the respected love and compassion for the other humans and allowing me to enter a field where I could practice this desire.

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Abstract

Many patients suffer from severe pain after general surgeries like inguinal hernia, where the traditional pain management methods (giving patients 1g of Perflgan (Paracetamol)) are usually insufficient to relieve the pain which increases the need for more doses of analgesia and sometimes the need for a combination of analgesia agents. Moreover, this not only increases the analgesia consumption but also may increase the possibility of post-operative complications. Therefore, we shall be using a combination of Paracetamol and ketamine to achieve full pain relief and patient satisfaction, comparing it to using Paracetamolsingly and thus prove that it is more effective.

The present study aims to compare patients' post-operative pain by using ketamine plus Paracetamol vs Paracetamol singly among urgent general surgery patients.

This study is a true experimental randomized, controlled, prospective study, conducted at Tubas Turkish Government Surgical Hospital in Tubas, Palestine. The study is conducted on 60 male and female patients undergoing urgent general surgeries under the department of general snuggeries. American Society of Anesthesiologists (ASA) physical status I and II patients, Ages ranging from 15 to 60 years.

The sample is divided into two groups (30 patients each): Paracetamol 1g group, Paracetamol 1g plus ketamine group. Ketamine has proven to be an effective analgesic drug, which came with less opioid consumption, prolonged analgesia, and more pain relief satisfaction.

The findings of the study revealed that the K group is established to be more effective than the NK Group in terms of postoperative analgesia with reduced rescue analgesic requirements.

The study recommended using ketamine in post-operative urgent general surgeries either singly or adjunct to opioids such as Pethidine, to apply ketamine in ED to achieve better pain relief for several procedures such as fractures or dislocations.

Keywords: Ketamine Pain management, Pain, general surgeries, knowledge, post-operation, Paracetamol.

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LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologists
IV	Intravenous
GA	General Anesthesia
O2	Oxygen
VAS	Visual Analog Scale
K Group	Ketamine Group – Ketamine plus Paracetamol
SPSS	Statistical Package for Social Science
NK Group	Non-Ketamine group (Paracetamol singly)
ED	Emergency Department
COX-2	cyclooxygenase-2

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Chapter One

Introduction

1.0Background

According to International Association for the Study of Pain, pain is defined as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". [1]

Post-operative pain is caused or defined as a condition of damaged tissues after a surgical procedure that can be combined with a muscle spasm in the side of surgery. Postoperative pain is considered to combine Inflammatory & Neuropathic components of pain. [2]

The trauma caused by the surgical procedure comes with inflammation resulting from the damaged tissue injury or direct nerve injury is backed with systemic changes, and chemical release; such as hypertension, tachycardia, and increase in blood glucose if it is left untreated and was not managed at the right time. The postoperative pain could lead chronic pain, depression, and anxiety, which may end with the beginning of developing psychological morbidities.[3]

In most cases, patients who come out after urgent general surgeries such as hernia, appendectomy, or cholecystectomy are given painkillers such as IV Paracetamol, IV diclofenac, COX 2 inhibitors, and opioids may not be enough to achieve good pain management satisfaction of post-surgical patients, which is insufficient to reduce the pain.[4] Since Paracetamol is insufficient to reduce the pain, physicians often tend to use other analgesic drugs to achieve satisfactory pain relief such as opioids[5,6]. Therefore, Multimodal analgesia approach which means adding an

adjutant drug such as ketamine to the Paracetamol will reduce the pain & minimize the dose of opioids after the general surgeries.[7]

1.0.1 Physiology of Pain

Nociception is a part of the functioning of the normal physiological structure, and involves four main stages which are transduction, transmission, modulation, and perception.[8]

-Transduction

When the Nociceptors are stimulated by painful Stimulus such as chemical or physical stimulation, the ions channels (Calcium, sodium, potassium) on the sensory nerve endings opens, generating electrical signal to pass through axons of two main category of nociceptors that are transmitted to the brainstem, thalamus, cortex and spinal cord.[8]

-Transmission

It refers to transport of the action potential from the peripheral terminal passing through axons reaching the central nervous system, this is the time when pain can be managed or controlled, which takes us to the most fundamental part of this process, the mechanism of pain management that the opioids block the release of neurotransmitters[8].

-Perception:

Perception described the awareness of the pain, recognition of pain can be determined by several factor levels of health, social and cultural status, the pain suffered in the past , gender, psychological structure of person and genetics[8].

-Modulation:

Modulation point out the change (decrease or increase) of sensory input whether it is inhibition or enhancement through Supraspinal stimulation, which rises from the midbrain, pons, and medulla. In order to clarify the modulation, we need to imagine an individual that had a painful experience or painful stimulation but does not feel any pain; the opposite situation is when someone has a superficial cut but feels extreme pain. [8]

1.0.2 Multimodal Analgesia:

Multimodal pain management or balanced therapy came into light for the first time in 1993 as documented article by Kehlet and Dahl. It is a method to manage postoperative pain. The fundamental purpose of it is improve the pain relief , analgesic effectiveness, reduce the amount of opioids used to control and decreasing the side effects of the analgesic medications by involving combination of different categories of analgesics to cover multiple sites of pain receptors in the brain , eventually improving the pain management satisfaction and pain relief. [9,10]

1.1 Paracetamol

Paracetamol is tended to be used widely for its antipyretic and analgesic effect. It can be used in children from an early age, is one of rare medications approved for pregnant or breastfeeding women, its analgesic effects are similar to NSAIDs but weaker than them and their effects NSAIDs covers COX-2 selective inhibitors, even though the Paracetamol mode of action is uncertain it is believed that it covers COX-1 and COX-2 by inhibiting them through metabolism to achieve the expected pain relief. However, its abuse is also the main cause of native liver transplantation[14,15]

Chemistry and Distribution

Rapid spread across all tissues allows rapid action regardless of skin area. Plasma protein binding is low. Metabolism: Primarily hepatic metabolism, mainly through two major pathways and one minor the main pathways with glucuronidation (account for 60% of the metabolism total) and sulfate conjugates (35%) which, by adding the relevant groups Glucuronides and sulfates will convert Paracetamol into inactive, soluble metabolites. These paths are interchangeable to quickly saturate if therapeutic doses are exceeded. a secondary pathway, catalyzed by cytochromeP450 (5%), by the formation of Reactive intermediate: N-acetyl benzoquinone imine (NAPQI) which will be next It detoxifies by reducing glutathione and is finally excreted in the urine after conjugation Cysteine and Mercapturic acid. This metabolite (NAPQI) is responsible for the hepatotoxic effects of overdose. [14,15,16,17]

Pharmacological Activities

Table 1 Summary of pharmacological and clinical activities of paracetamol, selective COX-2 inhibitors and non-selective NSAIDs

Pharmacological activity	Paracetamol	Selective COX-2 inhibitor	Non-selective NSAID
Analgesia	Active	Active	Active
Antipyresis	Active	Active	Active
Anti-inflammatory	Active in mild inflammation	Active	Active
Anti-platelet	Low activity	Inactive	Active
Damage to stomach and small intestine	Low activity	Low activity	Active
Aspirin-induced asthma	Weakly active	Inactive	Active
Blood pressure	Variable data	Increase	Increase
Renal	Lesser effects than both NSAID classes	Impaired function in stressed kidneys	Impaired function in stressed kidneys
Increased risk of thrombosis	Inactive	Active	Active

Table 1: Summary of pharmacological and clinical activities of Paracetamol, selective COX-2 inhibitors and non-selective NSAIDs (1)

Pharmacokinetics:

Paracetamol which gets quickly absorbed through the intestine, affected by the presence of food, reaching its maximum plasma concentration after 10-10 minutes of oral ingestion. Distributed to all, it increases with the concentrations using body tissues, crosses the placenta, and is excreted in breast milk. It binds to proteins weakly processing.

It is mainly metabolized by the liver and forms glucuronide-related compounds, which are excreted through the urine, and 9% of it is excreted unchanged through urine.

In an oxidation reaction by cytochrome oxidase enzymes, it forms an independent active spot A urine. The remaining percentage is also metabolized in the liver a chemically imine-benzoquinone-p-Acetyl-N (NAPQI), this compound has a short half-life because it binds quickly to glutathione. A hepatic and sulfhydryl radicals so that it is inactivated and excreted renal ally.

In the case of excess production of NAPQI, as in cases of poisoning, glutathione stores are depleted by the liver, and NAPQI is bound by covalent bonds.(shared) with cysteine sulfhydryl groups involved in the synthesis of cellular proteins, and gets oxidative damage and initiates an inflammatory response that results in for it: mitochondrial dysfunction, hepatic necrosis, and then death. Similar reactions may occur in other organs such as the kidney. [16,17,18]

Intravenous Route:

Paracetamol exists in ready to use as liquid solution thought intravenous route name as perflgan which contains 1g of Paracetamol, giving Paracetamol through IV make its action rapid twice time than oral intake, in other words it equal to two doses of giving it orally. More over the bioavailability of Paracetamol IV is 100% but via oral route can reach maximum of 79%[19]

Pharmacodynamics

Mostly Paracetamol is used in combination of other medications such as NSAIDs to enhance the analgesic potency and activity mean while it has some Interaction with other medications. It is not forbidden to use Paracetamol with any other drug, but there are precautions for use with:

-Vitamin K (AVK) oral anticoagulants, combination can cause increased mitigating effect when Paracetamol is taken in doses a maximum of 4 grams per day for at least 4 days. In this case, the patient is required to check the INR regularly and AVK dose adjustment is possible.[20]

-Chelated resins such as Questran® (cholestyramine): This type of the resin can reduce the intestinal absorption of Paracetamol and thus reduce the intestinal absorption of Paracetamol Efficacy if taken simultaneously. Therefore, it is recommended to take Paracetamol after at least two hours.[21.22]

- Flucloxacillin, an antibiotic from the penicillin family and some others

Cases of metabolic acidosis have been observed, particularly for affected patients

As a risk factor of glutathione deficiency.[23]

Contraindications

Contraindications to the use of the molecule can be summarized in two points:

- Hypersensitivity to Paracetamol or any of its ingredients (allergic reaction).
- severe hepatic impairment reduces the rate of metabolism of Paracetamol,(e.g., Child-Pugh score is greater than or equal to 10).

There are other contraindications related only to the pharmaceutical form in general, such as using suppositories if you have a history of rectal bleeding or even take the capsule or tablets before the age of 6 years due to the risk of miscarriage.[24]

1.2 Ketamine

Ketamine is a molecule that was synthesized in 1962 and is widely used as a general anesthetic. Today, ketamine is still the reference anesthesia agent in some clinical settings, but it is mostly used as an adjunct to general anesthesia. In fact, ketamine is the only effective injectable N-methyl-D-aspartate (NMDA) receptor antagonist available clinically to date. It is well known that the NMDA receptor plays an important role in the phenomenon of central desensitization. In fact, when used in low doses, ketamine has a powerful anti-hyperalgesia effect. It is used around surgery to reduce postoperative pain, opioid consumption, and to prevent delayed pain 2, 4, 8, 14, 18 hours. Its use is gradually extending to other indications such as pain management in the emergency room, and chronic, intractable neuropathic pain. Treatment-resistant depression [25,26]

Chemistry

Ketamine is initially an anesthetic agent present in the clinic in a racemic form. However, the S-ketamine form has 2 times more efficacy than the elemental form or the R-form (-) and above all it has fewer side effects than the psychoactive type, but it is not marketed in France, unlike Germany (Ketanest®). The ketamine-induced state of anesthesia is characterized by deep and prolonged analgesia, and a loss of consciousness that causes the patient to detach more than from true sleep. The analgesic effectiveness of ketamine is related, among other things, to its N-methyl-D-aspartate (NMDA) receptor blocking properties. [27]

From a pharmacokinetic point of view, its half-life of distribution is about 10 minutes, so its effect is fast but rapidly diminishing. The elimination half-life is approximately 2-4 hours and increases if hepatic metabolism is impaired. This drug may accumulate with repeated injections or continued administration. Metabolism occurs through the cytochrome P450 pathway. By D-demethylation, ketamine is converted to nor ketamine, the potency of which is about 20% of the original molecule.[28,29,30]

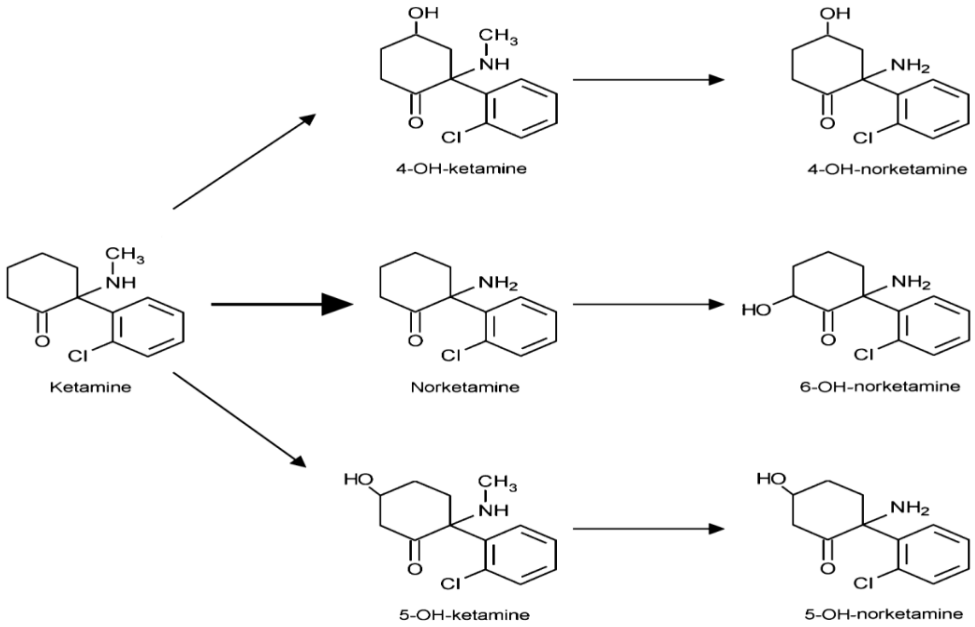


Figure 1: "Metabolism. Ketamine is metabolized mainly to nor ketamine (80%), itself secondarily transformed into hydroxyl-norketamine (15%), mainly 6-hydroxy-norketamine. Accessory pathway passes directly through the transformation of ketamine in hydroxy-ketamine (5%)"

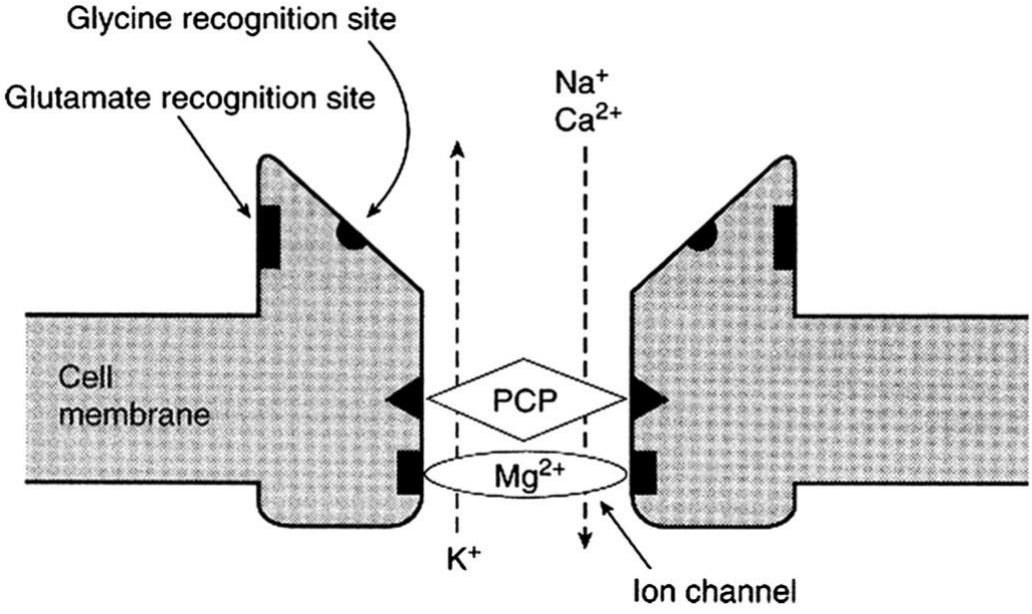


Figure 2: Diagram of NMDA (excitatory) receptor-channel complex. (24)

Side Effects:

Depending on the duration of the surgery, the contraindications are determined alongside with side effects and warnings.

-The drug should not be used in patients with increased intraocular pressure.

-preeclampsia (pre-eclampsia).

-The drug should be used with caution in patients with arterial hypertension or increased intracranial pressure, mitral insufficiency, and mental disorders.

Ketamine may cause high blood pressure, hypersalivation, hallucinations upon awakening (less often in children or with intramuscular injection), and apnea following rapid intravenous injection. Premedication of anesthesia to prevent hypersalivation.[31,32]

1.3 Significance of the Study

Many patients come to the ED department in need of urgent surgery[11,12] ,after they wake up from the surgery they are given the typical Pain killers like Paracetamol, and nonopioid analgesics don't seem to be enough to relieve the pain, and what is worse that some patients are suffering from dependence on opioid of analgesic drugs[5,6,13].Thus, here comes the role of ketamine due to its unique pharmacological structure in a certain dose of 0.3-0.5mg/kg it works as analgesic instead of the hypnotic drug because it works on nonselective NMDA receptors, and it is used for those who Suffers from opioid addiction, and It helps avoid second doses of analgesic drug as clarified approve.[6]

1.4 Study Objectives

1.4.1 Primary Research Objective

To assess the analgesic effect of ketamine &its impact on the postoperative pain reduction & Minimize opioids consumption.

1.4.2 Secondary Research Objectives:

-To assess the effect of ketamine as analgesic agent in reducing post-op pain among urgent general surgeries patients.

-To compare the effect of ketamine in reducing of post-op pain in urgent general surgeries with using Paracetamol versus Paracetamol only.

-To assess the effect of ketamine as pain management drug in reducing other painkillers consumptions in urgent general surgeries

-To assess the effect of ketamine as analgesic agent in reducing hospital length stay among urgent general surgeries patients.

1.5 Research Hypothesis

Administering there is a higher post-operative pain relief among ketamine plus Paracetamol group than the Paracetamol alone group of urgent abdominal surgery patients at the 0.05 significance level.

1.6 Research Questions:

Q1- Does ketamine enhance the effect of Paracetamol in terms of pain management of urgent abdominal surgery?

Q2- How much can the combined drug with Paracetamol provide a better analgesia in comparison of using Paracetamol alone?

Q3- What is the most effective dose of ketamine that can be used in combination to Paracetamol, to provide more pain relief after urgent abdominal surgery?

Chapter Two

Literature Review:

PUPMED, MEDLINE, and Google search engines were utilized for the purpose of this literature review. Key words used for the search were as follows: Ketamine, Paracetamol, analgesia, general surgeries, knowledge, awareness and compliance. Quantitative or qualitative studies, written in English language, that reported the effect of ketamine in reducing pain& achieving more pain relief satisfaction.

2.0 Ketamine Analgesic Effect as Nebulizer after Tonsillectomy:

To start with, a study conducted by **Abdel-Ghaffar, in 2019** at Egypt in cooperation with Assiut University about Preventative nebulized ketamine, for pain control after tonsillectomy in children: randomized controlled trial, a double-blind controlled trial randomized the study design. The study had a main purpose of exploring the analgesic effect of nebulized ketamine as a unique method of pain relief.

The study included 100 children aging between seven and twelve years. The participants were randomly divided in four groups. group 1 had been given Placebo, group 2 had been given Ketamine IV intravenous ketamine, group 3 had ketamine nebulized, group 4 had ketamine nebulized with double dose of group 3 each group 25 patient, data entry and analysis were carried out by SPSS with a confidence interval of 95% the study showed that ketamine reduced the consumption Paracetamol within 24h, significantly reduced the score of visual analogue scale (VAS). Nebulized Ketamine considered as an alternative in case of difficulty of administrating it IV.[33]

2.1 Effects of Adding Ketamine to Bupivacaine in Thoracic Paravertebral Block:

A study conducted by **El Mourad & Amer** in 2018, at Egypt Tanta university hospital. Titled: "Effects of adding dexamethasone or ketamine to bupivacaine for ultrasound-guided thoracic paravertebral, block in patients undergoing modified radical mastectomy: A prospective randomized controlled study." Aimed to assess the effectiveness of adding ketamine or dexamethasone as accompaniment to bupivacaine in thoracic paravertebral block to assist the quality of analgesia postoperatively in patients undergoing modified radical mastectomy.

The study type was a controlled prospective randomized study, conducted on (ninety adult females) programmed for MRM. participants were allocated randomly into three groups (thirty each) to have ultrasound-guided TPVB before induction of general anesthesia, participants were randomized into three groups thirty for each; Group B, Group D, and Group K.B took bupivacaine 0.5% + 1 ml normal saline, D took bupivacaine 0.5% + 1 ml dexamethasone (4 mg) and K took bupivacaine 0.5% + 1 ml ketamine (50 mg).

Participants were observed for 24 hours postoperatively to record the first-time rescue analgesia as a primary outcome, total rescue morphine consumption pain scores, and incidence of complications, SPSS 16 were used for the statistical analysis, the results showed that patients with ketamine group had the lowest VAS score comparing it to the other group.[34]

2.2 A comparison between Paracetamol Singly versus Ketamine and Paracetamol after Pediatric Aden tonsillectomy to Assess Postoperative Pain, Nausea and Vomiting:

This study conducted by **Alsadi**, in 2016 at hospital of eastern Ontario about "The Effect of Administration of Ketamine and Paracetamol Versus Paracetamol Singly on Postoperative Pain, Nausea and Vomiting After Pediatric Adenotonsillectomy" it aimed to compare the efficacy of the combination of ketamine and Paracetamol versus Paracetamol alone in tonsillectomy surgeries, the study was a randomized controlled trial conducted on 98 children (American society of anesthesiologists (ASA)) class I/ children aged between 3 and 12 years candidate for tonsillectomy were randomly assigned into two groups .

Their pain was measured by using CHEOPS pain scale then evacuated the data on SPSS for analysis, the results revealed that there was a significant difference between the group who took the Paracetamol with ketamine and group who took Paracetamol alone, the CHEOPS scale was lower in ketamine group versus the other group in the first 0.5 – 6 hours.[35]

2.3 Ketamine Plus Midazolam with Continuous Local Anesthesia vs Bupivacaine Plus Fentanyl:

A study by **Vincenzi**, In 2020 at Italy in the Italian National Research Center on Aging, about the continuous thoracic spinal anesthesia with local anesthetic plus midazolam and ketamine is superior to local anesthetic plus fentanyl in major abdominal surgery, the study aimed to highlight the analgesic Superiority of ketamine plus bupivacaine over bupivacaine plus fentanyl , the study was designed as retrospective cohort study, the study included 98 patients divided in two groups , 60 patients with fentanyl group and 38 patients with ketamine group, the data was

analyzed with IBM SPSS Statistics version 24 (SPSS Inc, Chicago, IL) was used for statistical analysis, the pain was assessed through VAS (visual analogue scale) , the main results were that ketamine group had the lowest pain score than the fentanyl group and had less respiratory depression complications .[36]

2.4 Postoperative Pain Management Using Ketamine for Idiopathic Scoliosis Surgery:

In his study, **Ricciardelli,** (2020) in USA in corporation with Anesthesiology and orthopedic department, on "The efficacy of ketamine for postoperative pain control in adolescent patients undergoing spinal fusion surgery for idiopathic scoliosis".

This study aimed to highlight the role of ketamine as a key changer in terms of analgesia and to increase the satisfaction of patients. The study adopted double blinded randomized controlled trial which was directed on 50 patients whom their ages were eighteen and under suffering from posterior spinal fusion subjected to ASA score I to III. Half the patients were given placebo, and the other half of the patients were allocated in experimental group.

Data were investigated through GraphPad Software however, the results showed that the combination of ketamine and morphine has achieved a better pain management for the patients and limited the occurrence of nausea and vomiting.[37]

2.5 The Effect of Small Dose of Ketamine on Morphine Requirement after Intestinal Surgery:

A study conducted by **AbdelRady,**(2021) at Egypt in general surgery department. About the "Effect of small dose ketamine on morphine requirement after

intestinal surgery: A randomized controlled trial", the study explored the efficiency of ketamine as pain killer for the skin incision in abdominal surgeries.

The study adopted randomized controlled trial design, applied on sixty patients between 18-60 years old. Subjected to ASA score I and II who were arranged for abdominal surgery which was intestinal surgery. The arranged time for the surgery was between(one – three hours). The patients were allocated in to two groups each one had thirty members. Controlled group were given placebo while ketamine group were given IV ketamine infusion IBM SPSS statistics version 20, analyzed the study collected data.[38]

2.6 The Rolle of Ketamine Subcutaneously Dose on Postoperative Pain Management.

A dose-finding study was conducted by **Jon Tuchsvherer** ET in 2017 in sub-Saharan Rwanda in cooperation "The Canadian Anesthesiologists' Society International Education Foundation and with the Department of Anesthesia at the University of Rwanda". for patient whose undergoing for a major surgery about the effect of applicating low dose of ketaminesubcutaneously a dose finding studyto assist postoperative pain management efficacy of ketamine in Rwanda, in order to make more studies about it in the future.

The study was conducted on 31 patients undergoing major surgeries. Their ages between (18 -65) years old with exclusion criteria for hypertension, allergy to ketamine, increased intracranial pressure, arrhythmias, refusal to participate in the study. The pain measurement was assessed through numerical pain score in which zero means no pain till ten equals' worst pain. ketamine has proven itself in pain reduction and achieving better pain relief without serious side effects.[39]

Chapter Three

Research Methodology

3.0. Study Design:

This is a Controlled, experimental randomized, and prospective study. The study is likely to discover the post-operative pain management of urgent general surgeries: between single Paracetamol& ketamine plus Paracetamol. The study structure is developed to be adjusted a long side with the study objectives and in the same time to fit with the related intervention procedures to assist intervention outcomes. The study was accomplished in operation unit then in the post anesthesia care unit, and final following up the patients in post-surgical wards at Tubas Turkish Governmental Hospital in Tubas, Palestine.

3.1 Study Setting:

The study was conducted in operation unit, post anesthesia care unit, and post-surgical wards at Tubas Turkish Government Hospital in Tubas, Palestine.

3.2 Study Population:

The targeted population is going to be the patients who arrive to ED with severe abdominal pain and needs for urgent surgery, in Tubas Turkish governmental hospital in Tubas. The population is the patients who were admitted to the Ed then directed to the operation room for Urgent abdominal surgery at this hospital.

3.3 Sample Selection:

All patients, whether male or female, underwent urgent general surgery after they were directed from the ED. Those patients must meet the standards of the (American Society of Anesthesiologists (ASA). Agesvary between 15and 65 at Tubas Turkish Governmental Hospital. The predictable sample size was selected from the literature, which is 60 patients separated into two groups K group and the NK group.

Patients were randomly selected due to a lack of cases number, and the researcher was in charged to do the randomization. Review and research were assisted by using first time rescue analgesia requirement as the main variable alongside with pain assessment and other variables.[35,36]

3.4 Inclusion Criteria

- Patient undergoing urgent general surgery under the department of ED or General surgery ward.
- Male and female.
- American Society of anesthesiologist (ASA) score I and II patients.
- Ages between 15 and 65 years old.

3.5 Exclusion Criteria

- Coagulopathy.
- History of Neurological disorders or epilepsy.
- Patients with cardiac disorders or severe respiratory distress.
- History of Allergy to ketamine or Paracetamol.
- Patient refusal.
- History alcohol or drugs abuse.

- History of psychological disorder or Trauma.
- Hepatic or renal insufficiency.

3.6 Subject Recruitment & Sampling:

Coordination was made with the ED, general surgery ward, and general surgeons about the pain management methodologies so we will not lose any participants by wrong interaction. The researcher chosen 60 patients randomly chosen by the dividing them into two groups, the K group will be given ketamine and Paracetamol; P group will be given Paracetamol singly.

The selected participants were aware of the study and they were insured that in case of persistent pain, they will take painkillers and will be taken care of. Those who met the inclusion criteria were contacted face to face and initial verbal consent was obtained to participate in the research.

3.7 Study Variables:

Study variables: The comparison of postoperative pain management effect of ketamine IV vs Controlled group is studied regarding to the variables summarized as following:

Independent Variables:	**Dependent Variables:**
Age (year)	Postoperative pain (Visual analogue scale)
Sex (male/female)	First time of rescue analgesia
Level of Education	Total amount of rescue analgesia in the first 24 hours post surgically
Occupation	Incidence of nausea, vomiting

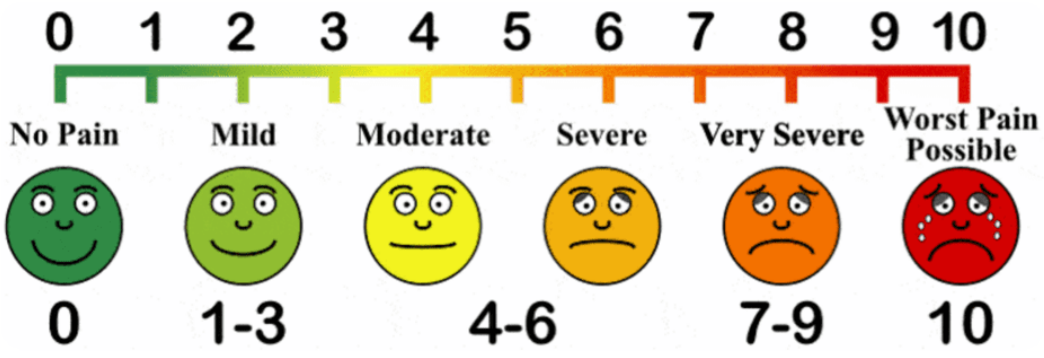
3.8 Data Collection Tools:

3.8.1 Questionnaire Content

A questionnaire was generated based on previously published research articles and studies and it was reformed by the research team to fulfill the objectives of the study. The generated questionnaire included about 10 questions consisting of three sections as follows: Section 1 was designed to assess demographic data including: age, gender, educational level, place of living, work occupation, social status section 2 was made to assess the hemodynamic status, heart rate, blood pressure and oxygen saturation section 3 was dedicated to assess the pain intensity thought Visual analogue Scale (VAS), to assess the amount analgesia consumption postoperative and to assess nausea , Vomiting postoperative.

3.8.2 Postoperative Pain Assessment: one of our most important aims of this research is to measure the pain intensity in the postoperative period. Pain assessment is a vital indicator in postoperative patients and must be looked over periodically. Preoperative patient education of postoperative pain is essential for postoperative pain assessment because it helps to clarify the patent knowledge which leads to decrease any kind of fear and anxiety regarding pain, by achieving this awareness it aids the approach towards better experience and pain relief satisfaction. Postoperative pain management supports the process of quantitating the intensity of pain to generate analgesic regimen, to determine the patient response to the treatment and its efficacy, meanwhile there are several pain assessment tools that must be easy to understand and simple to the patients. One of the most common scales are visual analogue scale, Wong baker faces rating scale, numerical rating scale and verbal rating scale[40,41].

3.8.3 Visual Analogue Scale: Hayes & Pattersonfirst used the VAS in 1921, which was used to measure the pain intensity of patients in clinical and epidemiological researches. It is a 10 cm line anchored by verbal description, most of the time 'no pain' and 'worst pain every imaginable'. The patient is asked to point out thought 100 mm line to indicate the pain severity. The score in measured on the scale from the zero anchor to the patient's mark, 101 levels of pain intensity is assisted through millimeter scale that measures the patient's score of pain. The VAS has limitations for example it must be presented on a paper or electronically[42,43]. Attention is essential when photocopying the measure or scale to avoid significant changes in its length. Even though the VAS proved its validity and reliably, even statistically in comparison with other scales like The Verbal Rating Scale and The Numerical Rating Scale. Postoperatively Visual. Analogue Scale was assisted for all the patients starting from 5 min, 10 min, 15 min, 30 min, 1h, 4h, until 24h by the researcher and a trained health care team member.[42,43]



The Visual Analogue Scale in a simple demonstration thought Picture

3.8.4 Time for the First Rescue Analgesia: patients were all monitored postoperatively to assess the pain score periodically when the pain score exceeds the patient ability of endurance which was between 4 to 6 score they were given analgesia that suites their situation whether it is Paracetamol or Pethidine IV or Diclofenac IM.

3.8.5 Total Amount of Rescue Analgesia Administered in First 24 Hours Postoperatively: In this study we have measured the mean of dosage of rescue analgesic Diclofenac or Pethidine or Paracetamol IV (gm. /24 hours) administered in the first postoperative 24h.

3.8.6 Incidence of Nausea and Vomiting: Postoperatively nausea and vomiting are very common after the surgery and especially after taking pain killers (PONV) are defined as Vomiting or retching, nausea, which occurs during the first 24– 48 hours after surgery. It has been shown that post-operative pain increases the occurrence of emesis. In this study, the patients were asked if nausea or vomiting have occurred during the first 24 hours postoperatively[44,45]

3.9 Study Protocol:

In this study, 60 patients undergoing urgent general surgeries under general anesthesia were enrolled, and randomly allocated in two groups: K group received ketamine 0.5mg\kg alongside with 0.03 midazolam and NK group did not receive ketamine. Both groups received Paracetamol 1g IV, and the surgeries for the two groups had durationof 1h +- 20 min. Paracetamol was administrated before 20+- 10 min in the end of each surgery.Ketamine was administered postoperatively after taking the hemodynamic status of each patient in this group, and after assuring that, the patient is in pain, as patients who did not suffer from moderate to severe pain have not established the necessity to take ketamine beforeadministrating ketamine then

after administrating ketamine. None of the patients suffered from any allergic reaction to any of the administrated drugs.

Blinding: Employees, the persons who are collecting the data and patients who were included in assessing patient pain intensity and care were not aware of the treatment or group's allocation.

Randomization: The patients enrolled in the study were randomly by using lottery method assigned to one of the two previous mentioned groups by simple randomization.

3.10 Anesthesia Protocol:

Preoperatively, all patients were asked to fast for 8 hours at least. as the patient enters the operating room standard hemodynamic monitors were placed (electrocardiogram, heart rate, noninvasive blood pressure, pulse oximeter oxygen saturation, capnography), a urinary catheter was placed to monitor urine output, a suitable gauge intravenous cannula was established, N.S 0.9% and Ringer Lactate were used to for the fluid maintenance according to the surgical ward protocol. Pre-oxygenation was applied using a face mask for 3 minutes minimum at 6 L, followed by the anesthesia induction of 3mcg/kg of fentanyl and 2.5 to 3 mg/kg of Propofol, then 0.5 mg/kg atracurium for smooth tracheal intubation and ventilation, intraoperatively patients were given Dexamethasone 0.1 mg/kg and Paracetamol 1g at the end of the surgery before 20+-10 min.

The mechanical controlled ventilation mode was applied and modified as needed to preserve the Carbon Dioxide end-times between 35 and 43 mmHg and the anesthesia was maintained by sevoflurane to stabilize end tidal concentration 1

minimum alveolar concentration. After anesthesia induction, patients were put in supine position for the entire tine of the surgery. Intraoperative intravenous fluid maintenance was achieved with N.S 0.9% and Ringer Lactate. Fentanyl and Atracurium were administrated according to clinical indications. Neuromuscular block was rescinded to revoke muscle relaxation and the removal of endotracheal tube by using Neostigmine 0.05mg/kg with atropine 0.01mg/kg IV.

When the surgery has ended, patients were ex-tubated after being fully awake and moved to the recovery unit, their pulse, noninvasive blood pressure and oxygen saturation were monitored. Oxygenation was maintained as needed some patients needed 3 or 6 L of oxygen in dependence of their statue after ensuring that patients are fully awake, the control group was transferred to the post-surgical ward and the K group was given ketamine and stayed for 30 minutes under supervision untilthe members of the groupwere ready to be transferred to the post-surgical ward.

In the recovery unit patients were assisted for pain scores by applications VAS score at 5, 10, 15 ,30 min postoperatively by the researcher and the trains medical team then in the 1, 4 ,6 ,12 and 24 hours the patients were followed by the researcher in corporation with post-surgicalward, giving them the full postoperative medications that were given to follow up correctly without interrupting the study.

3.11 Data Analysis:

The data analysis was conducted thought SPSS software statistical package version 20. Percentages, means, standard deviation and frequencies were applied to describe data for each group. Cross tabulation analysis and chi-square teats were used for the examination of the differences in percentages, pairwise differences between means were examined by post-Hoctest, one Way Analysis of Variance (F-Test),

ANCOVA and ANOVA wereused to examine the differences between means. Chi-square and cross tabulation analysis were applied as a univariate analysis.

3.12 Ethical Consideration:

This study was conducted after obtaining the approval of Arab American University Alongside with an approval of the ministry of health to start the data collection and to approve the subject of the study. All the patients were informed about the study aims and purposes, including the drugs that they will be used to relief their pain postoperatively, alongside with their action and potential side effects. Postoperative data collection and pain assessment the whole information collected in relative with the study subjected to confidentiality, anonymity and the patients had the right to withdraw from the research at any time they want. The patients were asked for permission to proceed the study that allowed the researcher and the researcher team to proceed the study according to its protocol.

Chapter Four

Results and Analysis of Data

4.0 Introduction:

Post-operative pain still one of the most important health care concerns, so this thesis was conducted in order to assess the effect of administering ketamine as an adjunct agent to mitigate patients' pain during the post-operative period.

4.1Baseline Comparison between the Participants Characteristics:

By looking at the first table, we find that the majority of the sample was female (93.5%), but this percentage was similar between the two ketamine & Non-ketamine groups (52.6% &47.4% respectively), and there was no statistically significant difference between the two groups due to gender (p=0.285).

While the age group between 25-35 years was the most prevalent (65.5%) among the participants as seen in figure one, the age had no statistical significance between the two groups (p=0.294). As for marital status, most of the participants were married, and there was no statistically significant difference between the two groups due to their marital status (88.5%, p=0.294).

As for profession and educational level, there is a statistically significant difference between the ketamine & Non-ketamine groups due to profession (p<.001) and education level (p<.001), where government work and secondary school level are the most frequent between the ketamine & Non-ketamine groups (54% &37.7% respectively) as presented in figure 2.

Table 1: Baseline Comparison between the Two Groups' Characteristics

		Group		X^2	*P* value
		Ketamine	**Non-ketamine**		
Gender	Male	1 (25.0%)	3(75.0%)	1.142	.285
	Female	30(52.6%)	27(47.4%)		
	Total	31(50.8%)	30(49.2%)		
Age	Less than 20	2(100.0%)	0(0.0%)	3.718	.294
	20- <35	18(45.0%)	22(55.0%)		
	35- <50	10(62.5%)	6(37.5%)		
	≥ 50	1(33.3%)	2(66.7%)		
	Total	30(49.2%)	61(100.0%)		
Occupation	Governmental	29(87.9%)	4(12.1%)	29.961	**<.001**
	Private	2(25.0%)	6(75.0%)		
	Other	0(0.0%)	10(100.0%)		
	Total	20(39.2%)	51(100.0%)		
Education Level	Not Educated	0(0.0%)	1(100.0%)	28.954	**<.001**
	Basic school	3(21.4%)	11(78.6%)		
	High school	10(43.5%)	13(56.5%)		
	Diploma	0(0.0%)	5(100.0%)		
	Bachelor	17(100.0%)	0(0.0%)		
	Post Graduate	1(100.0%)	0(0.0%)		
	Total	30(49.2%)	61(100.0%)		
Social Status	Single	3(75.0%)	1(25.0%)	.802	.370
	Married	28(51.9%)	26(48.1%)		
	Total	27(46.6%)	58(100.0%)		

***X^2*: Chi-Square**

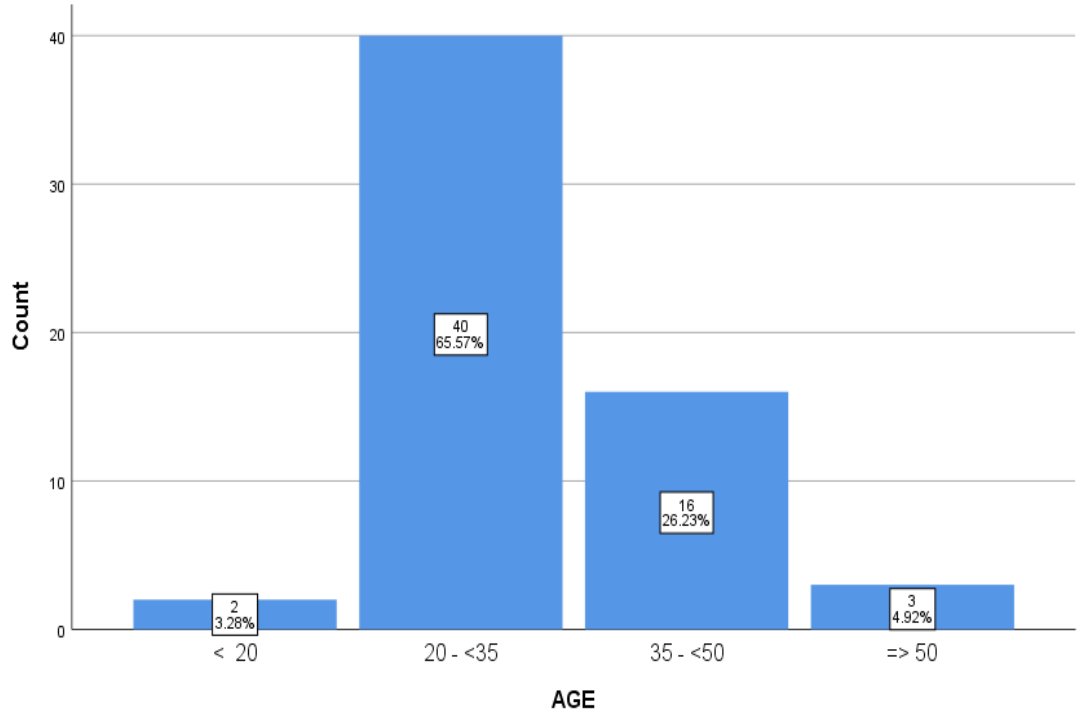


***Figure 1*: frequency distribution of participants' age**

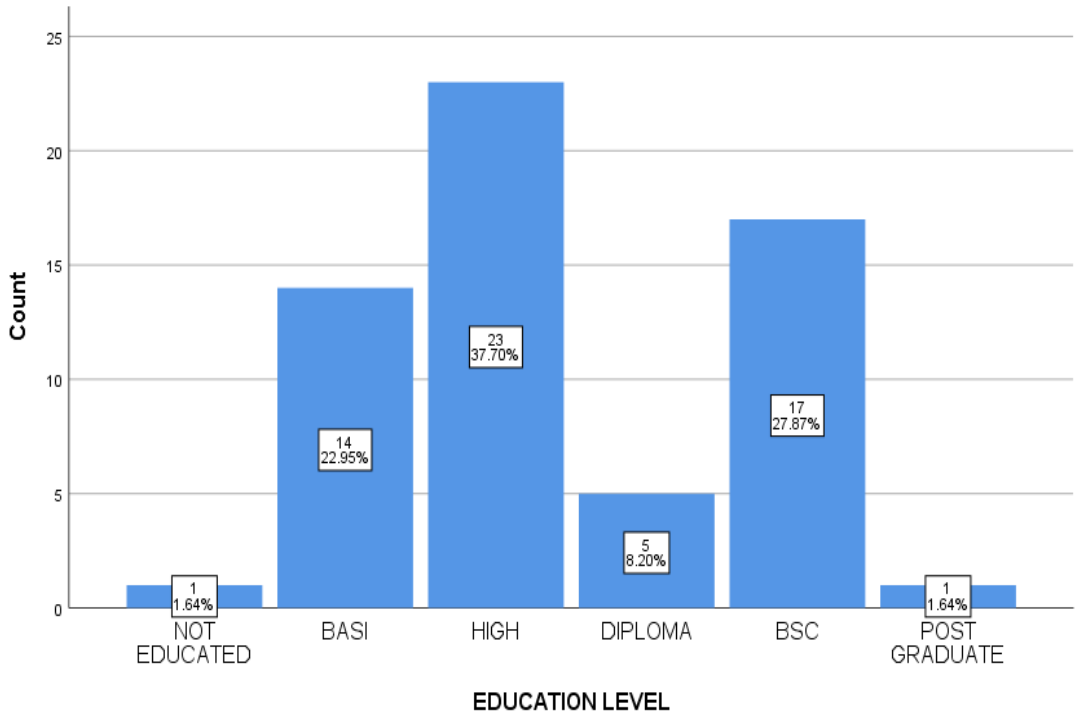


***Figure 2*: frequency distribution of participants' educational level**

4.2Hemodynamic Parameters for Both Groups before Taking Ketamine.

Although there was a statistically significant difference between the two groups (Ketamine & Non-Ketamine) with regard to systolic and diastolic pressure and pulse speed, this difference was not clinically significant, as the values for these readings were within the normal level between the two groups (Ketamine & Non-Ketamine).

Table 2: The Hemodynamics Parameters Before Ketamine between Two Groups (Ketamine & Non-ketamine)

Post-op before ketamine	Group	N	Mean	SD	Mean Rank	MWU	Wilcoxon W	Z	Sig.
SBP	Ketamine	31	125.0	13.5	26.37	321.5	817.5	-2.07	0.038
	Non-ketamine	30	129.8	10.7	35.78				
DBP	Ketamine	31	74.1	8.7	26.56	327.5	823.5	-1.98	0.047
	Non-ketamine	30	79.4	10.8	35.58				
HR	Ketamine	31	81.7	12.6	23.95	246.5	742.5	-3.15	0.002
	Non-ketamine	30	91.7	11.4	38.28				
SPO2	Ketamine	31	96.8	4.5	28.95	401.5	897.5	-0.93	0.351
	Non-ketamine	30	98.0	1.6	33.12				

MWU: Mann-Whitney U

4.3 Pain Score for Both Groups before Taking Ketamine.

Table No. (3) Shows that there is a statistically significant difference (p= 0.017) in the average pain level between the two groups (Ketamine & Non-Ketamine). As the average post-operative pain level among the participants in the Non-Ketamine group was less than the average pain level among the Ketamine group participants (4.25 vs. 6.32 out of 10).

Table 3: The Pain Level before Ketamine between Two Groups (Ketamine & Non-Ketamine)

Post op before ketamine	Group	N	Mean	SD	Mean Rank	MWU	Wilcoxon W	Z	Sig.
VAS	Ketamine	31	6.32	1.40	24.77	100	178	-2.38	0.017
	Non-ketamine	12	4.25	2.76	14.83				

MWU: Mann-Whitney U

4.4 Post-operative Pain Level for Both Groups after Taking Ketamine.

Table No. (4) Shows that there are statistically significant differences (p= 0.017) between the two groups (Ketamine & Non-Ketamine), as the average pain level during the first three readings in the first and fifth minutes, and after fifteen minutes, the average pain level was higher among the participants in the Non-Ketamine control group (3.21, 5.34, & 5.60 vs. 0.26, 0.16 & 0.45 respectively), and this also led to that the Non-Ketamine group needed pain relievers at a higher rate than the Ketamine group, and this difference was statistically significant (p<.001).

Table 4: The Interval Post-operative Pain Level between Ketamine & Non-Ketamine Groups after Ketamine Administration

Post-oppost Ketamine	Group	N	Mean	SD	Mean Rank	MWU	Wilcoxon W	Z	Sig.
VAS at 0	Ketamine	31	.26	.631	19.92	121.5	617.5	-5.27	<.001
	Non-Ketamine	29	3.21	2.33	41.81				
VAS at 5 m	Ketamine	31	.16	.374	16.74	23	519	-6.64	<.001
	Non-Ketamine	29	5.34	2.38	45.21				
VAS at 15 m	Ketamine	31	.45	.723	16.68	21	517	-2.91	0.004
	Non-Ketamine	5	5.60	3.50	29.80				
Analgesia	Ketamine	25	NA	NA	18.00	125	450	-4.21	<.001
	Non-Ketamine	29	NA	NA	35.69				
Analgesia cat.	Ketamine	31	NA	NA	28.60	390.5	886.5	-1.94	0.052
	Non-Ketamine	30	NA	NA	33.48				

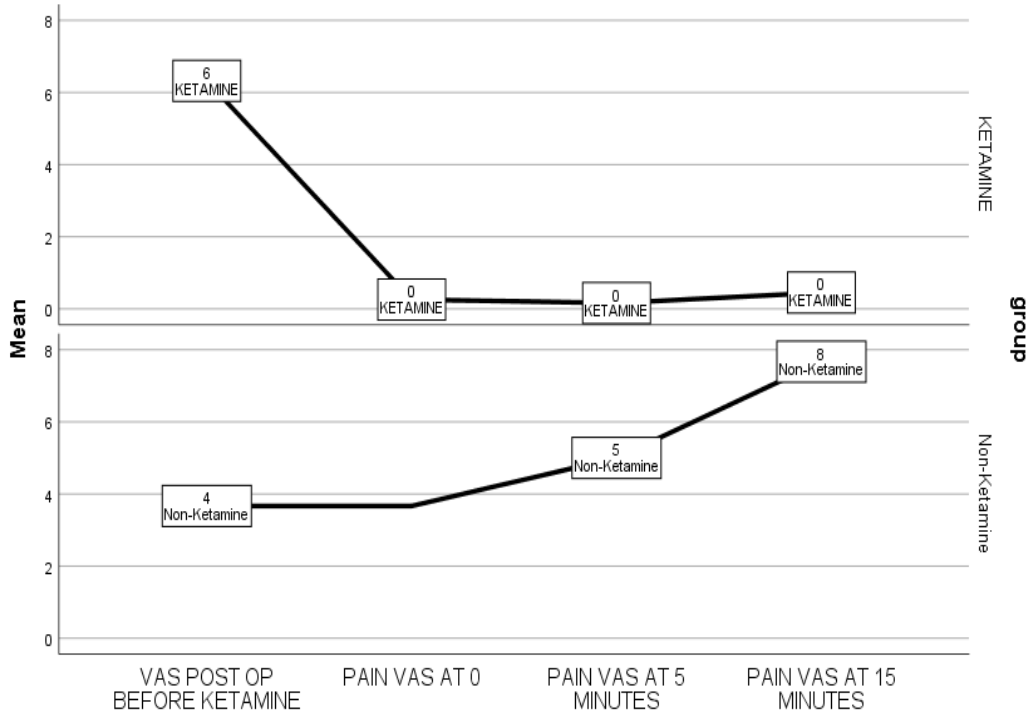


***Figure 3*: VAS means of ketamine and non-ketamine groups participants at baseline, 0, 5, and 15 minutes post-operative**

4.5Hemodynamics' Parameters Comparison of pre and after Ketamine Administration Among Participants of Ketamine Group

Table (5) shows that there is no effect of ketamine on hemodynamics, as there is no statistically significant difference (p>0.05) between diastolicpressure, systolic pressure and heart rate, before and after Ketamine administration, but there is a statistically significant difference between the pre- and post-spo^2 rate (p=0.005). After giving Ketamine, the difference has no clinical significancebecause the results before and after Ketamine were within the normal range.

Table 5: Hemodynamics' Parameters Comparison of pre and after Ketamine Administration Among Participants of Ketamine Group

Post-Operative	Ketamine	Mean	Std. D	Min	Max	Median	Z	Sig.
SBP	**Before**	125.00	13.533	102	159	122.00	-.093	.926
	Post	124.81	15.145	98	155	123.00		
DBP	**Before**	74.16	8.783	58	94	74.00	-1.696	.090
	Post	76.48	7.715	65	90	75.00		
HR	**Before**	81.71	12.663	63	110	80.00	-1.883	.060
	Post	78.32	11.365	60	99	77.00		
SPO_2	**Before**	96.84	4.583	75	100	97.00	-2.802	.005
	Post	95.35	3.852	80	100	96.00		

Wilcoxon Signed Ranks Test

4.6 Comparison Between pre and post Ketamine Administration in Terms of Pain Levels for the Ketamine Group.

Table (6) shows that ketamine has an effect on the average of post-operative pain level, where a statistically significant difference was found between the pain average before administering ketamine and between the pain average after administering ketamine, and this difference was statistically significant (p<.001) as the pain average level among the participants in the Ketamine group decreased dramatically from 6 out of 10 before administering ketamine to less than 1 out of 10after administering ketamine.

Table 6: Comparison of pre and post Ketamine Administration Pain Level (VAS) Among Participants of Ketamine Group

Post-operative	Ketamine	Mean	Std. D	Min	Max	Median	Z	Sig.
VAS	**Before**	6.32	1.400	4	9	7.00	-4.907	<.001
	Post	.23	.617	0	2	.00		

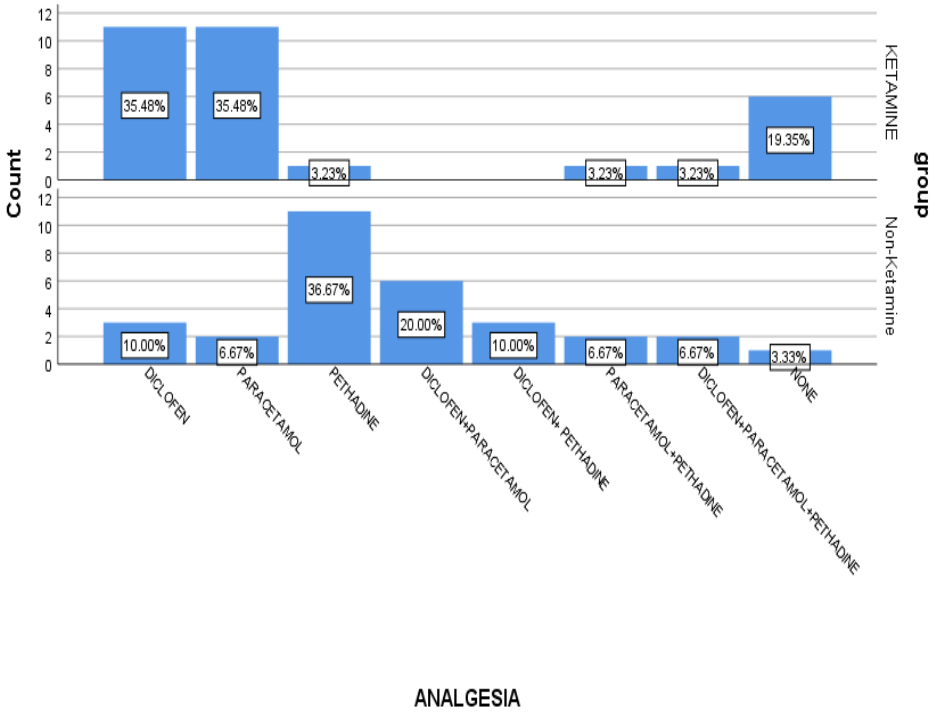


***Figure 4*: analgesia types used by ketamine and non-ketamine groups' participants' post-operative**

4.7 Clarificationof Groups that Needed Analgesia.

Table (7) shows that taking ketamine is a strong predictor of post-operative pain level.Group type showed that it was a significant (p=0.082) predictor of analgesic need in post-operative. Non-ketamine group was 6.96 times more likely to ask forpost-operative analgesia than Ketamine group patients were (OR=6.96, CI=0.784-61.788).

Table 7: Binary Logistic Regression for Groups and the Need for Analgesia

	B	**S.E.**	**Wald**	**df**	**Sig.**	**Exp(B)**	**95% C.I.for EXP(B)**	
							Lower	Upper
Group	1.940	1.114	3.033	1	.082	6.960	.784	61.788
Constant	-.513	1.364	.141	1	.707	.599		

A Variable(s) entered on step 1: group.

4.8 First Rescue Analgesia Time Distribution Among Both Groups.

It is clear by looking at the table 8 that most of the participants in the non-ketamine group requested painkillers during the first five minutes, while the participants of the ketamine group requested painkillers after the 240th minute (80.0% & 35.5% respectively). Likewise, the percentage of participants in the ketamine group who did not request painkillers was much lower than those who did not request painkillers in non-ketamine group (22.6% vs. 3.3% respectively).

Table 8: First Rescue Analgesia Time Distribution Among Both Groups

		Ketamine		**Non-ketamine**	
	Time (Minutes)	**Frequency**	**Percent**	**Frequency**	**Percent**
Rescue Analgesia	5.00	1	3.2	24	80.0
	15.00	0	0	3	10.0
	30.00	1	3.2	1	3.3
	60.00	10	32.3	1	3.3
	120.00	1	3.2	0	0
	240.00	11	35.5	0	0
	None	***7***	***22.6***	***1***	***3.3***

It is clear by looking at table 9 that the average time for rescue analgesia request among the participants in the non-ketamine group was much less than the average time for rescue analgesia request for the ketamine group (5 vs. 240 minutes) and this difference was statistically significant (MWU = 51.0, $p<0.001$).

Table 9: Mann-Whitney U Test to Compare the Rescue Analgesia Time between the Two Groups

	Group	**N**	**Mean**	**Std. D**	**Median**	**MWU**	**Z**	**Sig.**
Rescue Analgesia	Ketamine	31	222.4	173.3	240	51.00	-6.236	< 0.001
	Non-ketamine	30	25.1	90.3	5			

MWU: Mann-Whitney U

Simple linear regression was used to test if ketamine significantly predicted time of first rescue analgesia. The fitted regression model was: [fitted regression equation]. The overall regression was statistically significant (R^2 = [.343], F (1, 59) = [30.75], *p* = [<0.001]). It was found that [group type] significantly predicted [time of first rescue analgesia] (β = [585], *p* = [<0.001]).

Table 10: Simple Linear Regressionfor Groups and the Time for First Rescue Analgesia

			t	**Sig.**	**95.0% CI for B**	
	B	Std. Error			Lower Bound	Upper Bound
(Constant)	419.672	55.965	7.499	.000	307.687	531.657
Group	-197.253	35.571	-5.545	.000	-268.429	-126.076

A Dependent Variable: Rescue Analgesia B: Unstandardized Coefficients

Chapter Five

Discussion, Conclusion, Recommendation, and Limitation

5.0 Discussion

In this chapter, we are going to discuss the results of the previous chapter, which includes the conclusion, limitations and recommendations for the upcoming researches. The interpretation of results is based on the literature review and articles related to the study. Statistical significance interpretation is based on P value < 0.05, which an indicator of the statistical significance. The present study is conducted to assess and identify the ketamine analgesic effect after urgent general surgeries postoperatively. This study was a prospective, randomizeddouble-blinded study conducted by the Department of Anesthesiology, Arab American University-Ramallah Campus in collaboration with general surgery ward and theED at Tubas Turkish Governmental Hospital.

5.0.1 Demographical Characteristics and Hemodynamic Data of Both Groups' Patients:

In this study, there was no privilege for one group over the other group which is proven by the statistical tests as both groups had the similar demographic characteristics in other words there were no statistically significant differences (p value > 0.05) such as (age, gender, work occupation , city, education levels) . In terms of preoperative hemodynamic status, there was a statistically significant between the two groups (0.03 < 0.05) which is not clinically significant.This puts the thesis in balance in terms of comparison between K group NK Group by that we eliminate any impact caused by patients' hemodynamic status or characteristics on the drugs performance.

5.0.2 Dosage and Administration of Ketamine and Paracetamol:

As mentioned before both groups the K group and the NK group had 1g of Paracetamol before the end of the operation which is a protocol after every surgery in Tubas Turkish Governmental hospital, but for the ketamine group according to previous studies in order to activate the NMDA receptors and to achieve the pain relief the dose of ketamine should be between 0.3-0.5 mg/kg IVin this study we applied 0.5 mg/kg , as the ketamine has side effects as explained above, it is favorable and sometimes it necessary to give midazolam 0.03 mg/kg in addition to ketamine to eliminate the side effects of ketamine such as convulsion, hallucination, agitation and any other neurological disorders which is reported by previous studies [31,32,33]

5.0.3 Pain Assessment and Interpretation:

After the patients & research team were well educated about VAS score and the pain management plan after the surgery. The patients' pain assessment started after ensuring that they were fully conscious so that the team does not get false readings for the painby coincidence ,that may interfere the average pain level between the two groups (ketamine & Non-ketamine). As the average post-operative pain level among the participants in the Non-ketamine group was less than the average pain level (p value = 0.017)) among the ketamine group participants (4.25 vs. 6.32 out of 10). Assessment started from 0, 5, 10,15, 30 minutes then 1, 2, 4, 6, 24 hours postoperatively. A study in 2019 by Abdel-Ghaffar et alabout using ketamine not just via IV even nasal or oral by applicate it as nebulizer which resulted in creative method of administrating ketamine as nebulizer for patients who couldn't get ketamine via IVin order to achieve decent pain relief with lower VAS score in comparison with patients who did not get ketamine nor via IV or nasal , in 24h the

patients who has received ketamine experienced less pain which resulted in less VAS score [33],In line with this studywhichrevealed that VAS score for the K group is Less than VAS score for the NK group.

The comparison was limited for the first 15 minutes that is in 0, 5, 10, 15 minutes because the NK group could not last longer because of the pain and they took analgesic drugs after 15 minutes that's why it was not possible to continue the comparison. In this study, the VAS score of K group were significantly lower than the NK group, which is similar to the studies. The K group had lower VAS score than NK group due to the synergistic between ketamine and fentanyl which Paracetamoldoesn't have that's why using ketamine with fentanyl and with opioids in general will be more effective in achieving better pain relief [9,35,36,47,48,49].

5.0.4 Time of the First Rescue Analgesia:

In this study, it was revealed that the time interval for the first dose of rescue analgesic is 240 minutes in the K group where the NK group they couldn't last more than 5 minutes in average to take analgesic drugs (MWU = 51.0, $p<0.001$). Meanwhile, for the patients who didn't request analgesic drugs at all, the K group had 22% of their participants, who didn't take analgesic drugs compared with 3.3% of NK group, who didn't request analgesic drugs after the surgery post-operatively where this is similar to the study made by pain physicians in Egypt in 2016, about using ketamine adjutant to bupivacaine for postoperative pain control in Patients undergoing modified radical mastectomy which increased the time for the first rescue of analgesia and the consumption of opioids such as morphine [52]. Another study found that using ketamine adjunct to opioids such as morphine improved the pain relief and came with less opioids consumption after the cesarean surgeries, which were conducted in Indonesia about using low dose of ketamine in remote areas in

Indonesia for postoperative pain management after cesareans section with limited medical supplies, found that the ketamine prolonged the first time rescue analgesia and reducedopioidsconsumption such as morphine postoperatively [53]

5.0.5 Analgesic Drugs Administrated in the First 24 Hours:

In current study, both groups had the same options in terms of analgesic drugs, which are Pethidine,Diclofenac and Paracetamol. K group had the lower consumption of analgesic medications postoperatively accompanied with lover consumption of Opioids which is Pethidine 3.23% was the consumption of Pethidine postoperatively versus 36.67% in the NK group which is about 10 times less consumption of Pethidine in comparison to NK group, and that confirms the efficacy of ketamine in reducing opioidsconsumption postoperatively such as Pethidine which was used in our study ,Ketamine hasn't just reduced the consumption of opioids it also had less side effects than opioids those results were confirmed by numerous studies[54,55,56,57,58]

5.0.6 Incidence of Nausea and Vomiting:

In this study, there weren't any incidence of nausea or vomiting in both groups as for the K group using low dose or sub-dissociative dose of ketamine comes with less side effects such as nausea and vomiting which is confirmed by systematic review in 2016 about using low dose of ketamine in ED for acute pain emergencies that have filtered more than one thousand studies to confirm that ketamine at low dose comes with side effects, in contrary of high dose of ketamine which may result in several side effects as mentioned such as hallucinations or any alteration on hemodynamic status of the patients and the end nausea and vomiting as most analgesic drugs have the possibility of causing nausea and vomiting [58]. The NK group has notexperienced the incidence of nausea or vomiting that is why there were nocomparison between NK group and K group in terms of PONV[59.]

5.1 Study Limitation:

- The usage of ketamine was not familiar for the anesthesiologist among most of Palestinian hospitals, which made it very difficult to conduct this study.
- Lack of experience of using ketamine as postoperative pain management drug.
- Focusing on the side effects of ketamine and ignoring its efficacy in postoperative pain relief.

5.2 Study Strengths

- The design of the study, which is a true experimental, randomized controlled, prospective Study.
- Postoperative supervision and assessment of the patients for 24 hours, which is enough to cover the analgesia efficacy of ketamine and any incidence of side effects.
- The study sample selection and size, inclusion and exclusion criteria (60 patients) were similar for numerous trustful studies.

5.3 Study Recommendation:

- Using ketamine as adjutant drug postoperatively after urgent general surgeries under general anesthesia on patients under ASA I and ASA II Classifications to achieve better pain relief, less side effects and reduce the consumption of opioids.
- Encouraging physicians (Anesthesiologists) to use ketamine postoperatively and to consume less usage of opioids such as pethidine or morphine.
- Enforcing the hospitals continuing education committee to include sufficient education about multimodal analgesia methodology specially the recovery care unit medical team.
- Enforcing the anesthesiologists to use the ketamine adjutant opioids to reduce their consumption.
- Encouraging Emergency team department to use ketamine in painful procedures such as fractures and dislocations of joints.

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Appendices (1)

RESEARCH CONSENT FORM

Did you use verbal or written consent?

Researcher: Rawad Jehad Fathe Shalbak.

Department of Anesthesiology, College of Graduate Studies, Arab American University**.**

Title of study:

Post-op pain management of urgent general surgeries: a comparison between single Paracetamol& ketamine plus Paracetamol in Tubas Governmental Hospital

A Randomized Control; trial Study

Please read and complete this form carefully. If you are willing to participate in this study, ring the appropriate responses and sign and date the declaration at the end. If you do not understand anything and would like more information, please ask.

Thank you for participating in this study, warm greetings.

Our study aims to identify the efficacy of ketamine as analgesic drug postoperatively.

The data collection will take will take about 10 minutes.

Your participation is voluntary. There are no anticipated risks or benefits to your participation and you can withdraw from the study whenever you want to.. Please sign

---------- This form if you agree to participate ----------, date ------

Thank you for your interest in the study.

Appendices 2: data collection form

الجامعة العربية الأمريكية
Arab American University

Arab American University
Faculty of Health Sciences Department of Nursing
Faculty of Graduate Studies

Assessment sheet to evaluate:

Post-op pain management of urgent general surgeries: a comparison between single Paracetamol& ketamine plus Paracetamol.

Prepared by:
Rawad Jehad Fathe Shalbak

Supervisor: Dr. Jamal Qaddumi

Demographic data

1. Gender: male □ female □

2. Age: less than 20 □ from 20 to less than 35 □

From 35 to less than 50 □ more than 50

3. Occupation: Governmental sector □ private sector □

other □

4. City:…….

5. Educational level: Not educated □ basic level□ high level □

Diploma□Bachelor's degree□ Postgraduate□

6. Social status: single □ married □ widow □ divorced□

Vital signs: post-operation administering Before Ketamine

Bb

HR

SPO2

VAS score

Vital signs: post-operation after administering Ketamine

Bb

HR

SPO2

VAS score

Vomiting episodes during the first 24h post-operative :

.....

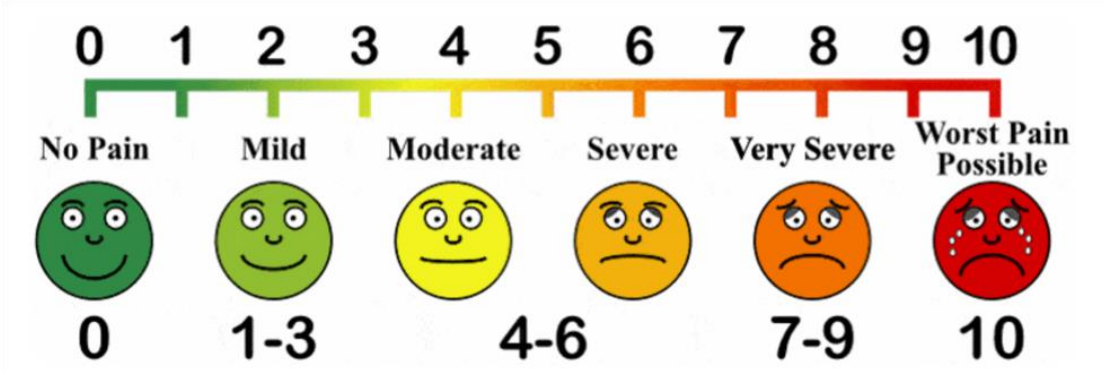
Duration of the operation:

Type of the operation:

Time & Date Post-operation:

Pain measurement via VAS at

0 min:
5 min:
15 min:
30 min:
1 h:
4 h:
24h:



Demographic data

1. Gender: male □ female □

2. Age: less than 20 □ from 20 to less than 35 □

From 35 to less than 50 □ more than 50

3. Occupation: Governmental sector □ private sector □

other □

4. City:…….

5. Educational level: Not educated □ basic level□ high level □

Diploma□Bachelor's degree□ Postgraduate□

6. Social status: single □ married □ widow □ divorced□

Vital signs: post-operation Non-Ketamine Group

Bb

HR

SPO2

VAS score

Vomiting episodes during the first 24h post-operative :

.....

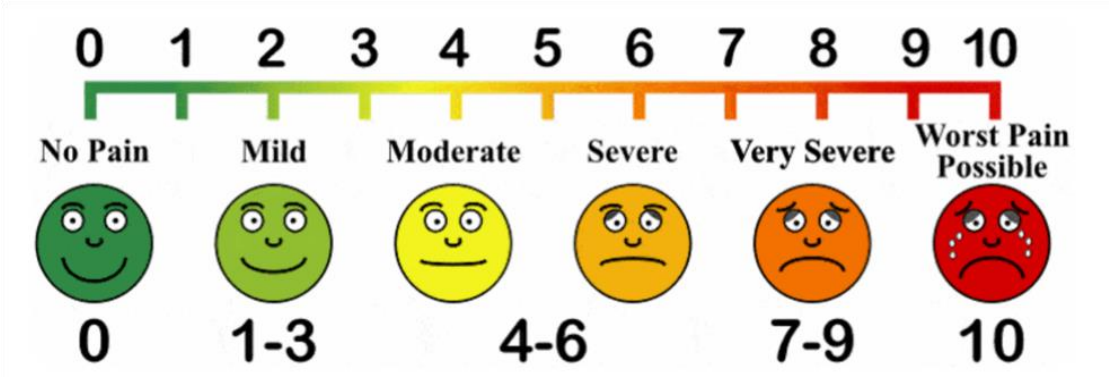
Duration of the operation:

Type of the operation:

Time & Date Post-operation:

Pain measurement via VAS at

0 min:
5 min:
15 min:
30 min:
1 h:
4 h:
24h:



الملخص

يعاني العديد من المرضى من آلام شديدة بعد العمليات الجراحية العامة مثل الفتق الإربي، على سبيل المثال، طرق إدارة الألم التقليدية (إعطاء المريض 1 جم من البيرفلجان (باراسيتامول)) عادة لا تكفي لتخفيف الألم مما سيزيد من الحاجة إلى جرعات أكثر من المسكنات وأحيانًا الحاجة إلى مزيج من عوامل التسكين. علاوة على ذلك، فإن هذا لا يزيد من استهلاك المسكنات فحسب، بل قد يزيد أيضًا من احتمالية حدوث مضاعفات ما بعد الجراحة. لذلك، سنستخدم مزيجًا من الباراسيتامول والكيتامين لتحقيق تسكين كامل للألم وإرضاء المريض، ومقارنته بالباراسيتامول وحده لإثبات أنه أكثر فعالية من استخدام الباراسيتامول بمفرده.

هدفت هذه الأطروحة إلى مقارنة آلام المرضى بعد الجراحة باستخدام الكيتامين بالإضافة إلى الباراسيتامول والباراسيتامول بشكل منفرد بين مرضى الجراحة العامة العاجلة.

المنهجية المتبعة في هذه الدراسة المنهج النوعي التحليلي فهذه الدراسة عبارة عن دراسة تجريبية حقيقية عشوائية، مزدوجة التعمية، خاضعة للرقابة،مستقبلية، أجريت في مستشفى طوباس التركي الجراحي الحكومي في طوباس، فلسطين. أجريت الدراسة على 60 مريضًا من الذكور والإناث يخضعون لعمليات جراحية عامة اختيارية في قسم الجراحة العامة. الجمعية الأمريكية لأطباء التخدير (ASA) الحالة الجسدية للمرضى الأول والثاني، تتراوح أعمارهم من 15 إلى 60 عامًا. تنقسم العينة إلى مجموعتين (30 مريضًا لكل منهما): مجموعة الباراسيتامول 1 جم ومجموعة الباراسيتامول 1 جم بالإضافة إلى مجموعة الكيتامين.لقد أثبت الكيتامين أنه دواء مسكن فعال، والذي يأتي مع استهلاك أقل للمواد الأفيونية، وتسكين طويل الأمد، ومزيد من الرضا عن تخفيف الآلام.كشفت نتائج الدراسة أن مجموعة K تم تأسيسها لتكون أكثر فعالية من مجموعة NK من حيث التسكين بعد العملية الجراحية مع انخفاض متطلبات مسكن الإنقاذ.

أوصت الدراسة بتطوير بروتوكول تسكين الآلام ما بعد عمليات الجراحة العامة الطارئةعن طريق استخدام الكيتامين منفردا او مضافا الى المسكنات الأخرى المستعملة ما بعد العمليات الجراحية العامة الطارئة الذي من شأنه زيادة مفعول و جودة تسكين الألم ما بعد العملية، كما اوصت الدراسة باستعمال الكيتامين و اضافته لقسم الطوارئ و خصوصا خلال عمليات تصحيح الكسور اوخلع بالمفاصل و غيرها من الإجراءات متوسطة الألم او حتى عالية

الألم ، وأخيرًا تدريب الطواقم الطبية على كيف استعمال الكيتامين من اجل ادراجه برتوكولات العلاج بطوارئ و بنفس الوقت ما بعد .

الكلمات المفتاحية: كيتامين إدارة الآلام، الألم، العمليات الجراحية العامة، المعرفة، ما بعد العملية، الباراسيتامول.