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Comparison of different therapeutic regimens in pain management during dressing among burn patients

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الإهداء

إلى ينبوع الصبر والتفاؤل والأمل

إلى كل من في الوجود بعد الله ورسوله

أمي الغالية

إلى من أحمل اسمك بكل فخر

إلى من أفتقدك منذ الصغر

إلى من يرتعش قلبي لذكرك

أبي الغالي

أهديكم هذا البحث

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الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Comparison of different therapeutic regimens in pain management during dressing among burn patients

أقر بأن ما اشتملت عليه هذه الرسالة إنما هي نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وأن هذه الرسالة ككل، أو أي جزء منها لم يقدم لنيل أية درجة أو لقب علمي أو بحثي لدى أية مؤسسة تعليمية أو بحثية أخرى .

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: **اسم الطالب :**

Signature: **التوقيع:**

Date: **التاريخ:**

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List of Abbreviations

Abbreviation	Full Name
1st	First
2ed	Second
Ca	Calcium
CHEOPS	Children's Hospital of Eastern Ontario Pain Scale
CHF	Congestive heart failure
COPD	Chronic obstructive pulmonary disease
Cox	Cyclooxygenase
G	Gram
H0	Null hypothesis
H1	Alternative hypothesis
HTN	Hypertension
HVAS	Horizontal Visual analog scale
IM	Intramuscular
IQ	Interquartile
IRB	institutional review board
IV	Intravenous
Kg	Kilogram
Mg	Milligram
Mint	Minute
Na	Sodium
NE	Norepinephrine
NMDA	*N*-methyl-d-aspartate
NSAIDs	Nonsteroidal anti-inflammatory drugs
PCA	Patient controlled analgesia
PGE2	Prostaglandin E2
PO	Per oral
PR	Per rectum
R	Receptor
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
TBSA	Total body surface area
TD	Transdermal
THR	Total hip replacement

USD	United States dollar
VAS	Visual analog scale
VAS	Visual analog scale
VVAS	Vertical Visual analog scale
α2	Alpha 2 adrenergic receptors
α2δ-1	The Gabapentin Receptor
BSPAS	Burn Specific Pain Anxiety Scale

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Abstract

Background: Pain is a major problem after burns even when high doses of opioids are administered. The study focused on the effect of using twodifferent therapeutic regimens of analgesia (Morphine with oral Celecoxib, Morphine with Intravenous Paracetamol) to relive procedural pain for burns patient compared with control group (full dose of Morphine).

Methods: A randomizedcontrol study at burn unit in Rafedia governmental hospital Northern West-Bank, Palestine was carried out. Patients' medical files were used to obtain demographic, medication and clinical information. VAS (Visual analogue scale) used to assess pain post dressing. Descriptive and statisticsanalysis was conducted using Statistical Package for Social Sciences SPSS 19.

Results: Ninety patients hospitalized for burn were recruited for the study from Rafedia hospital. The mean ± SD of the patient's age was 29.69 ± 14.96 years. More than half of the studied patients were males (53/90; 58.8%). The mean total body surface area of the burn in the studied patients

was (19.54% ± 10.85%). The most common burn site among the studied patients was lower limb followed by upper limb (21/90; 23.3%) and (18/90; 20 %) respectively. The majority of the studied patients had second degree burn (55/90; 61.1%). The majority of studied patients were having either a scaled burn (44/90; 48.8%) or a flamed burn (37/90; 41.1%). Finally the majority of studied patients were not having any chronic diseases while (22/90;24.4%) were having chronic diseases.

Each patient was evaluated for three consecutive daily dressings using three different treatment regimens as analgesics for the dressing; the regimen number one was (0.1) mg/kg IV Morphine, regimen number two was (0.025) mg/kg IV Morphine with (200) mg orally Celecoxib and regimen number three was (0.025) mg/kg IV Morphine with (1) g IV Paracetamol.Every treatment regimen was followed by pain assessment using VAS. One Way ANOVA analysis indicated that there is a significant difference among the three treatment regimens in VAS score ($F=22.36$, $p<0.001$, $df=2$). Post-hoc analysis using Tukey test indicated that both treatment regimens number one and two were not significantly different from each other. However, both treatment regimens one and two were significantly lower than treatment regimen number three suggesting that treatment regimen number 3 is the least effective in reducing pain during dressing in burn patients.

Finally, analysis of VAS score of the three treatment regimens among either gender, or among either degree of burn, or type of burn or presence of chronic disease yielded similar significant results.

Conclusion: This is a randomize control study indicates thatMorphine alone or Morphine with Celecoxib demonstrates that using Celecoxib in a multimodal analgesic strategy for procedural pain can achieve favorable efficacy in the management of pain. IV Acetaminophen is ineffective in reducing opioids consumption in procedural burn pain. In fact, the VAS was significantly higher in IV Acetaminophen with Morphine-treated patients than in treated patients by Morphine or Morphine with Celecoxib.

Key words: Burn, Procedural pain, Visual analogue scale.

Chapter 1
Introduction

1.1Background

Anesthesia and intensive care for burns, when required, are important aspect of the anesthetic workload in the hospital with a burn word. An estimation of pain management according to the pathophysiology of the burn is also significant, and the crucial part of the anesthetist role is supporting analgesia for burn patients. The generalist anesthetist cannot totally get away from patients with burns especially because they present initially at local hospitals; the quick control of pain can have a respectable effect on the pain experience thereafter.

Pain resulting from burn is considered severe. An adequate management of pain is substantial for more than one reason and the pain control negative consequences are widespread and shows as reduced quality of life, Impaired sleep, impaired physical function, high economic costs of unrelieved pain and potential physiological problems(Richardson and Mustard 2009).

Management of pain raises a challenge from the initial admission in emergency room through the rehabilitation phase of treatment. It is possible that this pain is a type of severe pains that are more difficult to relive from any type of etiology. The type of the damaged tissues from a burn injury is not the only thing that can induce uncommon high scale of pain, the quality

of standard burn care can also worsen any present pain(!!! INVALID CITATION !!!).Consequently, the pain associated to the burn itself and to other procedures used on patient (diagnostic tests, surgical operations, treatments,etc) is usually a moderate or a severe pain. The management of this pain is important from the point of view of both a humanitarian and a therapeutic (Hedderich and Ness 1999).

Managing of pain that is resulted from burns is considerably challenged for the health team worker partially because of the potential burn pain chronic nature and the complicated physiology(Zor, Ozturk et al. 2010). Even though there may be variability in the burn pain range and etiology, there are a similarity between options of treatment of pain management (Pedersen and Kehlet 1998). In addition to theusual analgesic agents like opioids which are a mainstay for treating various sorts of burn pains, non-pharmacologic technique and adjuvant agents also play a serious role in handling burn pain (Leal Pda, Clivatti et al. , Gregoretti, Decaroli et al. 2008). Multidisciplinary tacticsare not the only ones thathavea role in managing pain,thephysical rehabilitation and psychological support canbe the perfect manner for treating patients who suffer from burns(Honorio Benzon 2014).

An effective treatment needs to assess its nature accurately, recognizing the form and type of pain and to be aware of the preferable treatment. Adequate primary assessment play a role of a baseline in estimating the outcome of the following interventions (Sousa 2002).

Pain management guidelines and protocols have been developed and implemented, unrelieved moderate-to severe pain continues to be reported after burn injury, the improper management of pain is still noticed despite the meaningful modern advances concerning burn patients treatment(McCaffrey M 1999). This is related to the lack of professional team's training and the pain's complicated nature shown by those clients (Twycross 2002, Sen, Martin et al. 2007). In addition, the inappropriate pain management may minimize trust between the medical team members, and this would affect the treatment result in a negative way(Weissman and Haddox 1989). Moreover, it might cause a progression of chronic pains, dysesthesia as well as paresthesia (Olgart 1998, Dworkin 2002, Brenner, Ji et al. 2004, Ikeda, Stark et al. 2006). A relationship is existed between insufficient pain relief and the occurrence of psychiatric disturbances like the posttraumatic stress disorder and depression (Courtemanche and Robinow 1989).

Fright and nervousness are stimulated by losing faith in the health team worker, increasing in pain perception, risk of poor compliance with rehabilitation therapies and an awful severe pain suffering (Loncar, Bras et al. 2006). Risk of chronic pain and associated depression can increases by uncontrolled severe burn pain (Edwards, Smith et al. 2007) which can also cause suicidal conception when discharging from hospital (Edwards, Magyar-Russell et al. 2007).

One of the distinguished complications of major burns is post-traumatic stress disorder which can be an effect for poorly managed burn pain (Taal and Faber 1997, Summer, Puntillo et al. 2007). Stress response can be increased by the inability of achieving a real severe pain control (Kehlet 1989).

Table (1.1): Sedation and Analgesia Guidelines for Acute Burns(Bittner, Shank et al. 2015)

Stage of injury	Background anxiety	Background pain	Procedural anxiety	Procedural pain
Acute burn ventilated	1. Midazolam 2. Dexmedetomidine fusion 3. Antipsychotic 4. Propofol infusion (<48h)	Morphine infusion Morphine infusion Morphine infusion Morphine infusion	Midazolam boluses Dexmedetomidine higher infusion rate Haloperidol (very slow boluses) Propofol boluses	Morphine boluses Morphine boluses Morphine boluses Morphine boluses
Acute burn not ventilated	Dexmedetomie IV or scheduled Lorazepam IV or PO	Morphine IV or PO	Lorazepam IV/PO	Morphine IV/PO or Ketamine IV
Chronic acute burn	Scheduled Lorazepam or antipsychotics (PO)	Scheduled Morphine or Methadone	Lorazepam or antipsychotic (PO)	Morphine PO or Oxycodone
Fentanyl infusion could be substituted for Morphine infusion. In view of the increased incidence of delirium with benzodiazepines , minimal use of them is advocated IV = intravenous ; PO = per oral (by mouth)				

1.2 Definition of the Burn

Burn is a damage that happen to the body due to contact with certain chemicals, flames, electricity, hot substances or radiation (X rays, ionizing radiation from radioactive materials or sunlight,). The major effects of contact with electricity, caustic chemicals, steam, hot water or flame are quickly apparent (Online 2016). A model for understanding the pathophysiology of a burn wound is provided in Jackson's Burn Wound Model. The primary injury is the coagulation area near to the source of heat. This area has non-renewable tissues necrosis at the burn center resulted from exposing to electricity, chemicals or heat. The extent of this injury depends on the duration/ concentration of the exposure and on the temperature ((Ed) 2007).

Although necessary treatments like wound debridement, physiotherapy, multiple dressing and skin grafting may cause more pain initially, theycan minimize the pain experience in general(Richardson and Mustard 2009). However, if direct pain was not managed properly, the patient will suffer immediately and he or she may take a longer time to get better and chronic pain may be extended (Patterson, Hofland et al. 2004). The worrying thing is that studies display the repeatedunder-treatment and under-estimation of pain even in centers that are specialized in burns(Patterson, Hofland et al. 2004).

Burn injuries whether intentional or unintentional vary among genders, income, age groups and global region. In most cases, the majority of burn injuries happen at home as a result of the cooking activity (Attia 1997). Children's burns usually happen in the home (84 percent) due to the lack of supervision (80 percent) (Rossi, Braga et al. 1998, Forjuoh 2006). Likewise, adults are liable to get a burn injury at work, outdoors or at home. Usually, burns happen to adult males at work or outdoor, while it happens to adult females at home (Davies 1990, Hemeda, Maher et al. 2003). The most common place that can cause a burn to older adults is the bathroom; the kitchen comes in the second place. (Mabrouk, Maher et al. 2003).

1.3 Epidemiology of the burn

Death rates resulted from burn injuries differfrom oneregionto another in the world. This is not surprising; the lowest rate exists in the developed countries. This result is inevitable due to the interventions like evolution of using smoke detectors, loweringthe hot water heaters temperatures by using sensors, the designation of sprinkler systems, the advancement of children’s flame-retardant sleepwear and expandingthe safepremises and domestic appliances. Thedeaths number resulted from burns, burns that are related to fire as well as other types of burn injury, was decreased recently in a significant way. The advancement in this way was assisted by the updating of stringent legislation, developing of data collection systems, advocacy and social marketing (WHO 2008). Progress

in treating and caring of burn victims has contributed in reducing death rates due to burn in various developed countries. Moreover, the clinical outcomes were improved for a huge number of burn victims by upgrading the care of burn victims. This synchronized with the increasingof practical and emotional support from burn survivor groupswho managed to lead full, significant lives regardless of their injuries (WHO 2008).

On one hand, there are more than 300, 000 deathsresulted from flamed burn injuries. On the other hand, the deaths resultedfrom scalds, chemical andelectricity burns are greater. Millions more experience from disabilities that are related to burn and deformation. Most of them are permanent, but all of them have a number of economical and secondary personal effects on both the victims and on their families (WHO 2008).

Burn injuries happento almost 1.25 million people in Americaevery year. Almost 71,000 person from themneed hospital treatment(Summer, Puntillo et al. 2007).Most of burns are due toscald burns with a percentage of 40% or burns that are related to flame with a percentage of 55%.(Evers, Bhavsar et al. 2010). In developing countries, people are affected by burns excessively with about 90% of the international burns that occur in countries with a low and middle income (Dissanaike and Rahimi 2009).In addition,burn injuries varies from one gender to the other worldwide. Forexample, there is a high proportion of female injuries due to fires from heating and cooking fuels in the developing countries and a large number of male injuries due to fires resulted from work accidents (Dissanaike and

Rahimi 2009).Palestine is considered a developing country that lives under occupation and depends only in one burn unit in both governmental and privet sector (burn unit in Rafedia governmental hospital) that serves all population in the west bank (about: 2.7 million). Therefore, more research must be recruited to improve the quality of serves in this unit.

Every year in Palestine (West Bank), about 7600 people are being treated from burns. Among those patients, 570 are treated in hospital with a mortality rate of 0.67% (health 2013) and at Least 65% of them are children(health 2013). Most of patients are a result of scald burns (72%) and flame-related (21%)(health 2013).The person's age is connected with the type of injury. For example, scald burns usually occur in children while burns that are related to flame occur more frequently in adults (Evers, Bhavsar et al. 2010, health 2013).The only burn unit in West Bank is in the North (Rafedia hospital) and all burn cases that need to hospitalization will admit to this unit.

1.4 Procedural Pain in Burn Patients

Patients can feel the procedural during medical plan (e.g. debridement, changing dressing, cleaning wound or physiotherapy). Wounds re-dressing, cleaning and debridement can stimulate the nerve endings that are already hyperalgesic regenerated and may resulted in stimulate pain. Moreover, there may be a necessity to repeat these procedures many times per day for weeks or even for months.

The inappropriate management of pain before changing the wound dressing can cause pain anticipation and rises patient suffering and anxiety as a result (Byers, Bridges et al. 2001). Naturally, patients' concerns about pain are connected to the wounded area. Using anxiolytics and opiates throughout special procedure is connected strongly with the prior experience of the patient — if the pain was great last time, the demand for pharmaceuticals would be more this time (Byers, Bridges et al. 2001).

1.5 Pain Mechanisms after Burn

All burn injuries are painful and even 1st-degree burns can lead to moderate pain and disturbance, particularly if something like clothesrubagainst the burned skin. Variable severity of pain can be caused by second-degree moderate to deep partial-thickness burns which depends on the destructive area of the dermis. The most painful burns initially are the superficial dermal burns (Campbell JN 1984).

After burn, patient feels pain because of direct stimulation and injury of the nociceptors that exist in the dermis and epidermis that cause a transmission of nerve impulses by C fibers and A-delta to the dorsal horn of the spinal cord. Descending influences from the brain and the peripheral stimuli modulate the impulse magnitude (Richardson and Mustard 2009).

After injury, the inflammatory process starts immediately and causesthe releasing of many chemical agents that stimulate and sensitize the nociceptors at the burn area for some days. The burn wounds area stays

painful and sensitive to thermal and mechanical stimuli with primary hyperalgesia. Secondary hyperalgesia is referred to the change in sensitivity to mechanical stimuli that can be noticed in injury adjacent tissues. The inflammatory response subsides define the pains quality. Although intensity of pain varies, it reaches its maximum in skin donor areas and places of skin loss. The initial nerve endings destruction causes local insensitivity to pain in case of deep burns. A disorderly regeneration of nerve tissue may be in those places, which will expose to neuropathic pain. It is estimated that chronic pain happens to up to 52% of burn patients (Dauber, Osgood et al. 2002).

1.6 Time-course of pain

An important thing to be noted is that the pain intensity of the post-dressing background is more than the pain which the patient feel before changing the dressing at all times. Moreover, it was suggested that the relationship between pain and the burn size is a direct relation (i.e, the larger the wound, the greater the pain) (Atchison, Osgood et al. 1991). Usually, the time needed for changing the dressing depend on the degree of the damaged tissue. In addition, dressings those are applied on the hands as well as on the face will take a longer time than the ones applied on other parts of the body. In an unpublished study for the French national insurance system, burn specialists evaluated that the number of persons needed to dress a 10-30% burn in a total of 138 minutes (46 minutes for one person) is three persons (excluding the hands or face); three persons to dress a

facial burn in 105 minutes (35 minutes per one person); and three persons to change a hand dressing in 66 minutes (22 minutes per person). (This evaluation did not include the one who is responsible for analgesia).

1.7 Types of Pain in Burn Patients

The pain complexity and severity can be changed due to differences in the burn injury mechanism. A partial-thickness burn (2ed degree) causes pain as a result of losing dermis and epidermis exposing raw nerve fibers. In third-degree burns (full-thickness burn) lower levels of severe pain can be caused by burned nerves and upper skin layers (Pal, Cortiella et al. 1997). The origin of burn pain can be neuropathic as well as nociceptive (Schneider, Harris et al. 2006).In burn patients, pain is divided into four different categories, which can be increased by the healing of tissues:

1. Breakthrough pain that lasts for a short period, intermittent, rapid onset/offset and sometimes can be sever.

2. Rest pain which can be described as continuous and dull background pain.

3. Psychogenic pain. This pain is anticipated if the mechanical stimulation does not exist.

4. Procedural pain that remains for a short period of time and has a great intensity. This type of pain occurs due to certain activities such

as debridement, cleaning wounds, joint range of motion exercises and changing dressing.

1.8 Assessment of pain intensity

In order to establish the analgesia effectiveness and the pain severity, it is necessary to assess pain intensity by clinicians. The burn patients' feeling of pain differs from one patient to another in a significant way(Choiniere, Melzack et al. 1989) . Due to this, treatment protocol stipulates that the initial analgesia doses shall be low. In addition, it allows the adjustments of doses in accordance with the assessment of the individual pain. In order to assess pain for children over seven years old and adults, a verbal numeric scale or a visual analogue scale are being used because they are considered as excellent tools for this purpose (Choiniere, Auger et al. 1994) . The picture-based Children Hospital of Eastern Ontario Pain Scale (CHEOPS) (Eland, 1990) is suitable for burn procedural pain assessment in young children.

1.9 Medications

1.9.1 Opioids for Procedural Pain Management

The basic analgesics for victims who suffer from severe burn are opioids. However, Opioids terrible adverse effects decline their permissiveness in dose for severe procedural pain (Patterson 1992, Patterson 1995, Malchow and Black 2008) . Negative effects of opioid

include vomiting, constipation, respiratory depression, sedation, nausea, immunosuppression, urinary retention, hyperirritability, itching and cognitive impairment (Cherny, Ripamonti et al. 2001, Vallejo, de Leon-Casasola et al. 2004) . Increasing opioid dose can cause both analgesia effects and adverse effects to become more visible. What makes effective pharmacologic treatment of pain for burn patient challenging is that burn patients routinely suffer from one or more painful procedures daily for weeks or even for months. The majority of burn victims suffer from acute to intensive pain throughout procedures of wound care (Choiniere, Melzack et al. 1989, Carrougher, Ptacek et al. 2003). Moreover, expectation of pain in the next procedure may be raised by exaggerated pain on the first one (Colloca and Benedetti 2007).

Despite the fact that opioids should not be prevented for patients who suffer from burn-related pain, opioids immunosuppressant effects could theoretically increase risk of infectious complications for burn victims. (Schwacha, McGwin et al. 2006).

1.9.2 Ketamine effectiveness for Procedural Burn

Ketamine is a strong analgesic. Thus, it is still used to achieve sedation and analgesia during dressing changes. Moreover, it can decrease opioids dose in case if the long use is connected to tachyphylaxis in sedated patients in critical care (Patterson, Hofland et al. 2004, Krauss and Green 2006). The induction of central sensitization can be prevented by using

Ketamine as an antiallodynic and antihyperalgesic agent that can decrease maintenance and progress of opioid tolerance (Haley, Sullivan et al. 1990). Nevertheless, it is connected to 5–30% incidence of emergence delirium reactions, mainly in the elderly (Patterson, Hofland et al. 2004, Krauss and Green 2006).

The effects of ketamine are considered dose dependent. That is, lower doses of the drug produce varying results when compared to higher doses. A dose of 1.0 to 2.0 mg per kilogram of body weight produces an intense experience lasting about one hour. The effects include a sense of floating and dissociation, stimulation, and hallucinations. Larger doses of ketamine may produce what users refer to as a “K-hole.” A K-hole is generally reached when the user is on the brink of being fully sedated and is likened to an out-of-body or near-death experience. High doses of ketamine may result in severe respiratory depression, muscle twitches, dizziness, slurred speech, nausea, and vomiting.16 One of the most dangerous effects of Ketamine is the helpless and/or confused state the user may be put into after use of the drug. This causes the user to have difficulty with balance, combined with numbness, muscle weakness, and impaired vision. The combined effects can leave the user vulnerable to particular forms of crime(Jansen 2000),especially "date rape". Other physical side effects for all users can include:

- Flashbacks
- Amnesia
- Impaired motor functioning
- Delirium (hallucinations or disorientation)
- Dramatic increase in heart rate (tachycardia)
- Loss of touch with reality (derealization)
- Loss of coordination
- Sense of invulnerability
- Muscle rigidity
- Aggressive/Violent behavior
- Death from overdose - in severe instances

1.9.3 Benzodiazepines

Benzodiazepines are usually reliable in burns words (Ashburn 1995). It is exceedingly known that pain is aggravated by anxiety and in burns; Midazolam is the commonly used drugs (Cederholm, Bengtsson et al. 1990, Heinrich, Wetzstein et al. 2004). Burns Patient may administer midazolam by intravenous, intranasal, rectal or oral route. Midazolam help

to decrease discomfort arising from these psychological distress (Doenicke, Kugler et al. 1992).

Benzodiazepines affect a key neurotransmitter in the brain called gamma-amino butyric acid (GABA). This neurotransmitter has an inhibitory effect on motor neurons, thus the presence of GABA slows or stops neuronal activity. Benzodiazepines enhance the activity of GABA, effectively slowing nerve impulses throughout the body. The human nervous system has two different types of benzodiazepine receptors: one that causes the anti-anxiety effect, and one that elicits the sedative effect(Baldwin, Aitchison et al. 2013)

1.9.4 COX-2–Specific Inhibitors

The anti-inflammatory effects of non-steroidal anti-inflammatory drugs depend on their efficacy to prevent cyclooxygenase (COX), reducing prostaglandins production that considered vital mediators for pain and inflammatory response. Cyclooxygenase enzymes metabolize arachidonic acid and form prostaglandin H2, which is consequently metabolized by prostaglandin E synthase into prostaglandin E2 (PGE2) (Vane 1971, Crofford, Lipsky et al. 2000, White 2005). Cyclooxygenase -2 inhibition mediates advantageous actions of non-steroidal anti-inflammatory drugs on inflammation, while primarily Cyclooxygenase-1 inhibition causes undesirable gastrointestinal effects (Sakamoto, Kawai et al. , Hawkey 1999, Chan, Hung et al. 2004, Singh, Fort et al. 2006). Moreover, there are no

side effects for Celecoxib on serum thromboxane and platelet functions. This makes it an effective postoperative analgesic (Leese, Hubbard et al. 2000).

COX-2 enzyme is located specifically in areas of the body that commonly are involved in inflammation but not in the stomach. When the COX-2 enzyme is blocked, inflammation is reduced; however, since the COX-2 enzyme does not play a role in protecting the stomach or intestine, COX-2 specific NSAIDs do not have the same risk of injuring the stomach or intestines.

1.9.5 Morphine

Morphine is the most widely used compound among narcotic analgesics and remains the gold standard when the effects of other analgetic drugs are compared. The most characteristic effect of morphine is the modulation of pain perception resulting in an increase in the threshold of noxious stimuli. Antinociception induced by morphine is mediated via opioid receptors, namely the μ-type opioid receptor. Apart from the μ-opioid receptor, two other classical opioid receptors κ- and δ- and one non-classical opioid receptor, the nociceptin receptor was discovered and cloned so far. At the same time endogenous opioids were also discovered, such as enkephalins, endorphins, and dynorphins. The opioid receptors together with the endogenous opioids form the so called endogenous opioid system, which is highly distributed throughout the body and apart from

analgesia it has several other important physiological functions(Anand, Purington et al. 2012).

1.9.6 Paracetamol

Paracetamol, often known in the US and Asia as acetaminophen, is a widely-used analgesic (painkiller) and the main ingredient in everyday medications such as cold and flu remedies. Although discovered in the 1890s and marketed as a painkiller since the 1950s, exactly how it relieves pain was unknown. Intravenous acetaminophen differs in many ways from the available IV opioids and NSAIDs. It is the only approved IV nonopioid analgesic that does not include a boxed warning on the label and that is indicated for use in pediatric patients. The drug is not associated with the increased incidence of nausea, vomiting, and respiratory depression that can occur with opioids, or the platelet dysfunction, gastritis, and renal toxicity that are sometimes associated with NSAIDs (Pasero and Stannard 2012).

1.10 Pain Management Options

Modern day clinical burn injury care requires a multifaceted process to effective the pain management of the post burn by using the non-pharmacologic as well as the pharmacologic methods.

1.10.1 Pharmacologic agents

A lot of pharmacologic agents (Table 1.1) are available for managing different types of pain resulting from burn injuries. This is explained in more details hereinafter in this text.

Therefore, only a cursory review of the different agents in context that are suitable for burn pain management will be provide

Table (1.2): Pharmacologic Management of Burn Pain

Agents	Examples	Mechanism of Action	Administration
Opioids	Fentanyl, morphine, Hydromorphone	*mu*-R agonism	TD, IM, PO, IV
Methadone		*mu*-R agonism, NMDA-R antagonism, serotonin- and NE-reuptake inhibition	PO, I V
NMDA antagonists	Ketamine Dextromethorphan	Noncompetitive NMDA-R antagonism	IV, PO (dextromethorphan)
NSAIDs	Ketorolac Ibuprofen APAP	Cyclooxygenase (COX-1 and -2) inhibition	PO, IV, PR; intrathecal/local (experimental)
Gabapentinoids	Gabapentin Pregabalin	Ca2+ channel blockade (α2δ-1 subunit-containing channels)	PO
Local anesthetics	LidocaineBupivacaine Ropivacaine	Na+ channel blockade	IV (lidocaine), epidural/intrathecal, perineural, TD
α2 adrenergic agonists	Clonidine Dexmedetomidine	Central and peripheral α2-adrenergic blockade/sympatholysis	IV(dexmedetomidine), PO
R, receptor; NMDA, *N*-methyl-d-aspartate; NE, norepinephrine; APAP, *N*-acetyl-p-aminophenol/acetaminophen; NSAIDs, nonsteroidal anti-inflammatory drugs; IV, intravenous; PO, per os; IM, intramuscular; TD, transdermal; PR, per rectum.			

1.10.2 Non-pharmacologic Analgesia

Even thoughpharmacologic agents can primarily manage burn pain, treatment of burn pain may be achieved mostly by non-pharmacologic techniques (Table 1.2), bearing in mind the long-term nature of rehabilitation and the possibility of developing stress related disorders and chronic pain. (Hoffman, Chambers et al.). A study was conducted on a setof non-pharmacologic modalities such asrelaxation techniques and cognitive therapies, despite the fact that there are significant methodological limitations in many available studies(Haythronthwaite, Lawrence et al. 2001).

Table (1.3): Non-pharmacologic Analgesia

Method	Purported Mechanism of Action
Virtual reality	Mostly visual distraction/decrease in processing of incoming nociceptive signals
Music therapy	Auditory distraction/attenuation of stress response to pain
Relaxation techniques	Behavioral management of anxiety, especially immediately pre-procedure/dressing changes

1.11 Problem statement

Burns pain is an increasingly knownproblem of public health. It affectsalmost every community and every geographical region worldwide. Moreover, burns are considered as one of the most devastating injuries at all times. They cause death, morbidness, long-term somatic sequel, huge psychological and economical effects (LOW 2007).

Usually the pain after burn injury is severe and very difficult to be treated and needs strong opioids doses for analgesia. Severe burn pain depends on mechanism of injury, total body surface of the affected area, burn depth and different patient factors and due to complexity of thesefactor, a multidisciplinary approach is essential to those patients. During hospitalization, doses of analgesia differ due to different procedures experienced by patients and their developing status. This causes a difficulty in calculating the analgesic amount to be administered at a certain time.

1.12 Objectives of the Study

1.12.1 General Objective

To study three treatment regimens of procedural pain management in burn patients at Rafedia governmental hospital.

1.12.2 Specific Objective

To determine the efficacy in using one therapy regimen of Paracetamol with Morphine, Celecoxib with Morphine and Morphine alone for anesthetize patient by (Ketamine and Midazolam) in relieving pain during and post dressing for burn patient.

1.13 Significance of the study

Background pain differs from time to time. Its intensity ranges from mild to severe and can may continue for more than one week without any lowering during this time. Background pain treating can be complicated

without causing annoying side effects (e.g. itching and nausea). The risk of opioids dependency in addition to these factors can cause deficient analgesia (Patterson, Hofland et al. 2004). If various analgesics and different rout of administration were compound, multimodal analgesia would be obtained to relief pain synergistically more than traditional analgesia . Furthermore, enhancing patient safety and multimodal analgesia can decrease analgesics complications as well as incidence of adverse effects.

In some burn injuries, Paracetamol (Acetaminophen) and non-steroidal anti-inflammatory drugs (NSAIDs) can have side effects if taken frequently due to their anti-prostaglandin and anti-inflammatory actions (Pal, Cortiella et al. 1997). Intravenous Acetaminophen is a modern and safe substitution for opioids and non-steroidal anti-inflammatory drugs. There is confirmation that pain postoperative can be relieved by intravenous Acetaminophen (Sinatra, Jahr et al. 2005, Cattabriga, Pacini et al. 2007).Moreover, intravenous Acetaminophen is found to be as useful as opioids in several researches related to postoperative pain; (Sinatra, Jahr et al. 2005, Cattabriga, Pacini et al. 2007). Guidelines for pharmacological wound pain management that are based on the World Health Organization recommendations recommend the use of Acetaminophen or NSAIDs for patients who suffer from mild to moderate pain (Woo, Sibbald et al. 2008). Although synthetic opioids agents like Tramadol can have disappointing effects, they may be helpful in managing burns pain especially when non-

steroidal anti-inflammatory drugs are contraindicated (Ronald Melzack OC FRSC PhD 2003).On the other hand, the influence of intravenous Acetaminophen, and if it is a suitable alternative to NSAIDs and opioids, remains a question of research (Grissa, Claessens et al.).

Nonspecific cyclooxygenase inhibitors such as Ketorolac and Ibuprofen may provide less extensive safety profile if compared to specific inhibitors of cyclooxygenase -2– (i.e.Celecoxib). However, there is a lack in data related to the burn patient population. This subject need more studying and non-steroidal anti-inflammatory drugs may be particularly beneficial for burn pain control. Experimental studies suggest that post burn hyperalgesia and decrease hypersensitivity in skin sensitized may be decreased by local administration or intrathecal of non-steroidal anti-inflammatory drugs through ultraviolet burn (Lundell, Silverman et al. 1996, Eisenach, Curry et al. 2010)

1. A study of the alternative analgesia regimen will serve as a baseline data to help policy makers to implement safe and long term cost effective treatment regarding to complication and side effect protocols in state of Palestine.

2. A review of the literature failed to show studies carried out in Palestine or even in the Arab world regarding procedural pain management for burned patientsin hospitals. Actually studies and published research in

the field of procedural pain relive are few in the Arab world. Therefore, a study on this field will be one of the few in the Arab world.

Chapter 2

Literature Review

Table (2.1): Literature Review

Reference	Description of Study	Conclusions/Comments
(Mammoto, Fujie et al. 2016)	A randomized, prospective, open-label controlled study is to evaluate the effects of celecoxib administration immediately after surgeryon pain after TKA surgery	The administration of oral celecoxib immediately after surgery, along with multimodal analgesia that includes peripheral nerve block and PCA,could reduce VAS pain score after TKA surgery.
(Chen, Zhu et al. 2015)	A prospective randomized study of 62 patients todetermine whether celecoxib is able to ameliorate pain intensity, provide a narcotic-sparing effect, achieve early ambulation and improve rehabilitation following total hip arthroplasty (THA) in elderly patients.	The use of a treatment regimen comprising oral treatment with celecoxib at a dose of 400 mg pre-emptively and 200 mg per 12 h post-operatively in combination with PCA morphine pump should improve pain intensity, reduce opioids consumption, and achieve early ambulation and improved rehabilitation after THA in elderly patients.
(Mahar, Wasiak et al. 2012)	A systematic review study for frequency and use of pain assessment tools implemented inrandomized controlled trials in the adult burns population	25 randomized clinical trials utilizing pain assessment tools. Unidimensional pain assessment tools were most frequently usedpain assessment tools, with multidimensional tools used less often, despite the multifacetedand complex nature of burn pain.

(McGuinness, Wasiak et al. 2011)	Four experimental trials involving 67patients were identified to assess the current literature regardingthe effectiveness and side-effect profile ofintravenous ketamine as a means of pain relief when compared with placebo or as an adjunct toopioid analgesia in patients exposed to burn injury.	Intravenous ketamine showedsome efficacy as an analgesic for burn injuries, witha reduction in secondary hyperalgesia when comparedwith opioid analgesia alone. Combination therapy of ketamine and morphine resulted in theabolishment of windup pain phenomena. The sideeffectprofile did not result in the withdrawal of anyparticipants included in the studies' results.
(Berger, Davadant et al. 2010)	The impact of a pain protocol using hypnosis on pain intensity, anxiety, clinical course, and costs.	study shows that a protocol in pain management including hypnosis reduced patient anxiety and exposure to pain, increased early opioids delivery, and decreased general anaesthesia requirements, hospital length of stay and costs.
(Bektas, Eken et al. 2009)	randomised double-blind study compared the efficacy of intravenous 1 gmparacetamol, 50 mg dexketoprofen and 0.1 mg/kg morphine in patients with acute mechanical LBP. Visual analogue scale (VAS) was used for pain measurement at baseline, after 15 and after 30 min.	Intravenous paracetamol, dexketoprofenand morphine are not superior to each other for thetreatment of mechanical LBP in ED.
(Hoffman, Richards et al. 2007)	Prospective randomized study of 12 patients analyzing virtual reality as an adjunct in the treatment of procedural pain during therapy	Virtual reality may be beneficial as an adjunct in the treatment of procedural related pain

(Ostadalipour A 2007)	Evaluate the analgesic and antisympathetic effect of clonidine, an α2 adrenoceptor agonist in burn patients	Clonidine can produce good analgesia and decrease in sympathetic over activity in burn patients, and also reduce opioids dose requirements
(Echevarria-Guanilo, Rossi et al. 2006)	Translating and adapting the Burns Specific Pain Anxiety Scale - BSPAS and the Impact of Event Scale - IES into Portuguese	The VAS was applied at four different times during the day and, by means of this evaluation, 530 pain records were obtained. These data showed that the highest pain scores were concentrated after bathing and wound dressing (score 82.36), called "painful procedure" in this study.
(Cuignet, Mbuyamba et al. 2005)	Randomized, double-blind study of 81 patients comparing the analgesic efficacy of single-shot versus 72-hour infusion of ropivacaine for donor site pain	There was no benefit with 72-hour infusion. The single-shot group had less paresia and were more satisfied with their pain relief
(Cuignet, Pirson et al. 2004)	Randomized, double-blind study of 20 patients comparing the efficacy of continuous fascia iliaca compartment block for 72 hours with ropivacainevs saline to control donor site pain	The treatment group had significantly reduced postoperative morphine consumption and significantly reduced pain scores during the first dressing change
(Prakash, Fatima et al. 2004)	Prospective randomized double-blinded study of 60 patients using patient controlled analgesia to control pain during burn dressing changes	Loading dose of 1 !g/kg Fentanyl followed by 30-!g demand dose with 5-minute lockout provided the best pain control
(Schulte, Sollevi et al. 2004)	Randomized, double-blind, crossover study of 11 volunteers to evaluate the synergistic effect of a NMDA-receptor antagonist and an opioid	First study in humans to show a synergistic analgesic effect with coadministration of a NMDA-receptor antagonist and an opioid

(Raymond, Nielsen et al. 2001)	Prospective analysis of 28 patients to analyze the relationship between pain intensity and sleep quality	Poor sleep will lead to a more painful procedures the following day
(Bijur, Silver et al. 2001)	An observational prospective cohort design to assess the reliability of VAS pain measurements	VAS is a highly reliable instrument for measurement of acute pain
(Bullus, Gordon et al. 1998)	Prospective study of 40 patients to evaluate the appropriate pain assessment tool	Patients prefer the Faces pain rating scale as a objective measurement tool
(Patterson, Ptacek et al. 1997)	Randomized prospective trial of 79 patients studying the benefit of adding Lorazepam to opioids for the treatment of procedural burn pain	The addition of lorazepam reduces pain ratings for procedural burn pain
(Patterson, Everett et al. 1992)	Prospective randomized study of 30 patients analyzing hypnosis as an adjunct in the treatment of procedural pain during wound care	Hypnosis is a viable adjunct for the treatment of procedural burn pain

2.1 Research Questions and Hypotheses

This exploratory study in the inpatient sector was designed to examine three research questions as detailed below:

1. Is the current regimen of opioids for procedural pain management in burn unit effective to relive the pain during different type of intervention for burned patients?

2. Is the current regimen of opioids for procedural pain management in burn unit able to decreasing dose of opioids?

3. What are the best combinations of analgesia regimen that reliving the pain for patients under different type of care?

2.2 The Hypotheses for the research questions

- The null hypothesis (H0): the non-opioids analgesia is ineffective in reliving procedural burn pain.
- The alternative hypothesis (H1): the non-opioids analgesia may decrease dose of opioids analgesia and may managing severity of the procedural burn pain

Chapter 3

Methodology

3.1 Study Design and Site of the Study

A randomize control study was conducted between November 2014 and February 2016 at Rafedia governmental hospital (Burn Unit) in Northern West-Bank, Palestine.

3.2 Sampling Method and Sample Size

All cases of adult major burn admitted the burn unit at Rafedia hospital during the study period included in the study until the predetermined sample is achieved. Based on the literature, a convenient sample of 90 patients will be included in the study; 30 patients in each group(Wang, Saha et al. 2015).Randomization done by the researcher himself, the first patient will rest randomly in one of the three groups, one, two, or three then the subsequent patients will rested alternately in each group.

3.3 Inclusion Criteria

Every patient was included hade classified by physical assessment, medical history and rule of nines to exclude any case was conflict with the characteristics of major burn or the time of onset, and referred to Medical dictionary, major burn is a

severeburn requiring transfer to a specialized burn center;major burns invol

ve > 20% of the total body surface area or >10% in the elderly or very youn g; > 5% is full thickness

1. Patients presented with major burn which will be defined by non-significantmedical and surgical history, physical examination and rule of nine to determine the total body surface area.

2. Age above 12 years

3. Patients in healing phase; which is determined as following characteristics in table:

Table (3.1): characteristics of healing phases (Rowan, Cancio et al. 2015)

Phase	Characteristics	Key players
Inflammatory	Vasodilation Fluid extravasation Edema	Neutrophils Monocytes Macrophages
Proliferative	Wound closure Revascularization	Keratinocytes Fibroblasts
Remodeling	Wound maturation Scarring	Collagen Edema Fibroblasts/myofibroblasts

3.4 Exclusion Criteria

The following patients will be excluded from the study:

1. Pregnant women, lactating mothers.

2. Past history of (Ketamine, Midazolam, Morphine, Paracetamol and Celecoxib drugs hypersensitivity.

3. Past medical history of seizers, glaucoma, prostatic hyperplasia, Stroke, hepatic impairment, renal impairment and CHF.

4. Respiratory disease (Asthma ,COPD, Respiratory depression) ,liver disease, renal failure circulatory shock and HTN

5. Celecoxib with serious interaction drugs (apixaban, ketorolac, intranasal, methotrexate, pemetrexed, thioridazine)

3.5 Data Collection

A data collection form was developed to cover all data items needed, andit was presented to a group of specialists in anesthesia and pain management and amended based on the recommended notes. The form covered the following areas: demographic details, physical measurements, characteristics of burn, medical and surgical history, date and number of dressing.

3.6 Therapeutic regimens

1. All patients in three groups received Ketamine (1.5) mg/kg IV slowly and Midazolam (2) mg IV slowly as procedural anesthesia.

2. The first group (group 1) received analgesic therapy: Morphine sulfate 0.1 mg/kg (8 mg maximum) I.V slowly 10 mint before dressing.

3. The second group (group 2) received analgesic therapy: Paracetamol intravenous 12mg/kg and total dose not more than 1g slowly (over 15 mint) and started infusion 15 mint before dressing with 0.025 mg/kg morphine I.V slowly 10 mint before dressing.

4. The third group (group 3) received analgesic therapy: Celecoxib tablet 200 mg orally 2 hours before dressing with 0.025 mg/kg morphine I.V slowly 10 mint before dressing.

3.7 Follow up of the patient

It was very important to continuously assess the burn patient for pain in order to guide the management of analgesic and response to drug (Dworkin 2002). Characteristics like pain worsening or improvement, pain location, intensity and type of pain were essential for management.

Each patient in the three groups who treated with any of the three regimens will be followed up after 30 mints from the end of the dressing and each patient will be re examined again after 60 mints and 90 mints. All patients will be evaluated for the severity of pain, type of pain, site of pain and duration. For three groups, evaluation will be made for each patient by the same investigator.

3.8 Measures (variables)

Table (3.1): variables of the study

Dependent variable	**Total body surface area**	**Numerical**
	Degree of burn	Categorical
	Type of dressing	Categorical
	Number of dressing	Numerical
Independent variable	Treatment regimen	Categorical
Background variables	Age	continuous
	Sex	categorical
Confounding variable	Other cause of pain	Categorical

3.9 Safety measures

Tolerability and Safety will be assessed by comparing post-drug symptoms with the baseline symptoms or based on the reported adverse events.

3.10 Side effect of the drugs

Patients assessed about respiratory arrest, hypotension, respiratory depression, bradycardia, apnea, dizziness, circulatory depression, nausea, constipation, headache, vomiting, and seizures by:

1. Oral questionnaires of age, sex, history of the disease was taken by interviewing the patients.

2. Physical examination at the same session which done by using burn chart to evaluate the total body surface area and the degree of burn which was dressed.

3. Visual analog scale: The pain visual analog scale (VAS) is a continuous scale that consist of a vertical visual analog scale (VVAS) or a horizontal visual analog scale (HVAS) line with a length of 10 centimeters (100 mm), anchored by 2 verbal descriptors, one for each symptom extreme(Huskisson 1974, Singer and Clark 1999).

4. The same tools(VAS) were used to evaluate the pain scale for the three groups, consecutively (30,60,90) minutes after the patient became fully conscious and oriented, the same practitioner was assessing each patient and the same questionnaires with same burn chart for each patient. The investigators were trained by plastic surgeon to assess the patients about the TBSA and the degree.

3.11 Ethical consideration

1. IRB consent.

2. The patient was given a consent form prior to participation.

3. Participants were assured that all data collected will be confidential.

4. Patients had the freedom of leaving the study at any time.

Chapter 4

Results

4.1 General demographic characteristics of the study sample

Ninety patients hospitalized for burn were recruited for the study from Rafedia hospital. The mean ± SD of the patient'sagewas 29.69 ± 14.96 years. More than half of the studied patients were males (53/90; 55.8%). The mean total body surface area of the burn in the studied patients was 19.54 ± 10.85. The most common burn site among the studied patients was lower limb followed by upper limb (21/90; 21.1%) and (18/90; 18.9%) respectively. The majority of the studied patients had second degree burn (55/90; 57.9%). The majority of studied patients were having either a scaled burn (44/90; 46.3%) or a flamed burn (37/90; 38.9%). Finally the majority of studied patients were not having any chronic diseases while 22 patients (22.1%) were having chronic diseases. The clinical and demographic characteristics of the studied patients are shown in Table (4.1).

4.2 Regimens used by the study sample

Each patient was evaluated for three consecutive dressings using three different treatment regimens as analgesics for the dressing. Treatment regimen was followed by pain assessment using VAS scale. The mean (95% CI) of the VAS score for each treatment regimen is shown in (table

4.2) and Figure 1. ANOVA analysis indicated that there is a significant difference among the three treatment regimens in VAS score ($F=22.36$, $p<0.001$, $df=2$). Post-hoc analysis using Tukey test indicated that both treatment regimens number one and two were not very different from each other. However, both treatment regimens one and two were significantly lower than treatment regimen number three suggesting that treatment regimen number 3 is the least effective in reducing pain during dressing in burn patients. Figure (2) shows the box-plot presentation of the vas score versus the three treatment regimens. The median (IQ range) of treatment regimen 3 was significantly higher than the median (IQ range) of both regimen1 and 2 (Kruskal Wallis test: Chi-sq=35.06; $p<0.001$; $df=2$).There are no significant differences between three types of regimen for heart rate as shown in table (4.5) a figure 3.

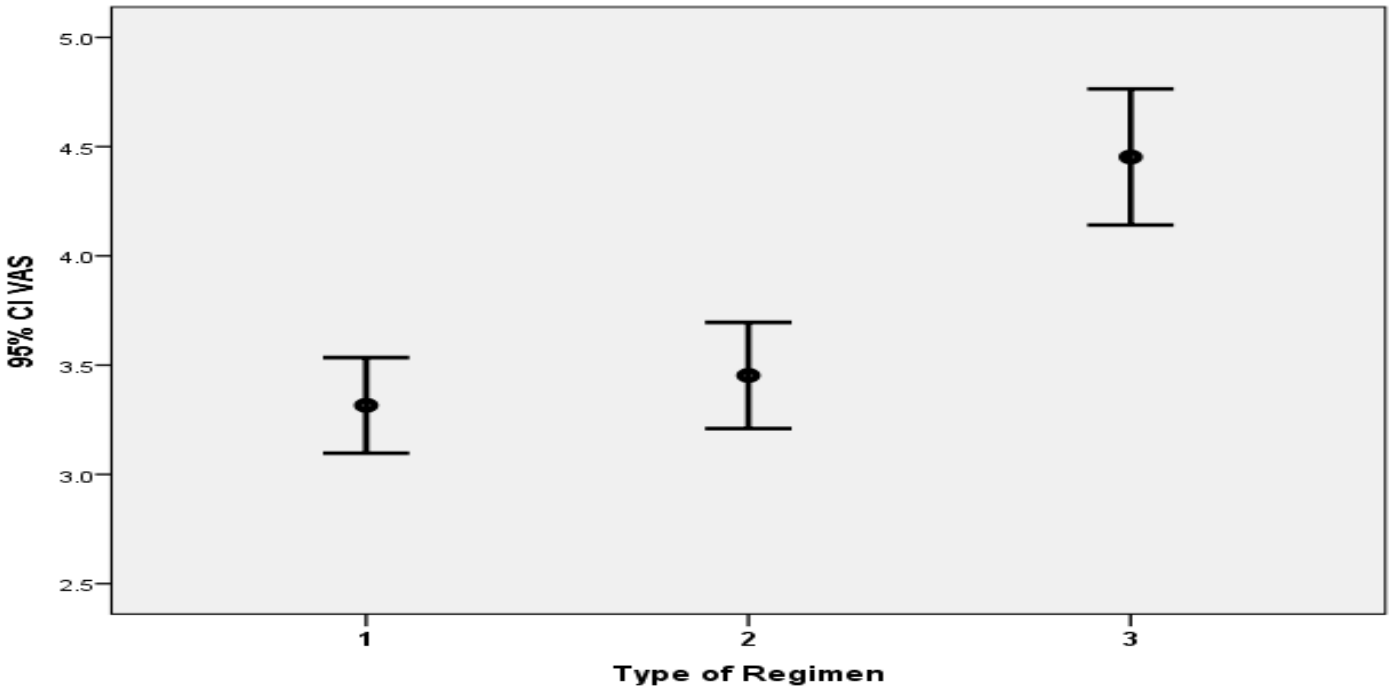
Finally, analysis of VAS score of the three treatment regimens among either gender, or among either degree of burn, or type of burn or presence of chronic disease yielded similar significant results as shown in table (4.3).

Table (4.1): Clinical and demographic characteristics of the studied patients

Variables	Statistics
Age (mean ± SD)	29.69 ± 14.96
Gender:	
Male (n; %)	53 (55.8 %)
Female (n; %)	42 (44.2%)
Total body surface area (mean ± SD)	19.54 ± 10.85
Most common burn site:	
Lower limb (n; %)	21 (21.1 %)
Upper limb (n; %)	18 (18.9 %)
Lower & upper limb (n; %)	14 (14.7 %)
Others (n; %)	45 (45.3 %)
Degree of burn:	
Second degree (n; %)	55 (57.9 %)
Third degree (n; %)	40 (42.1 %)
Type of burn:	
Scaled (n; %)	44 (46.3 %)
Flamed (n; %)	37 (38.9 %)
Others (n; %)	14 (14.8 %)
History of chronic disease:	
Free (n; %)	77 (77.9 %)
With chronic disease (n; %)	22 (22.1 %)
Symptoms post dressing:	
Free (n; %)	21 (21.8 %)
With symptoms (n; %)	78 (78.2 %)

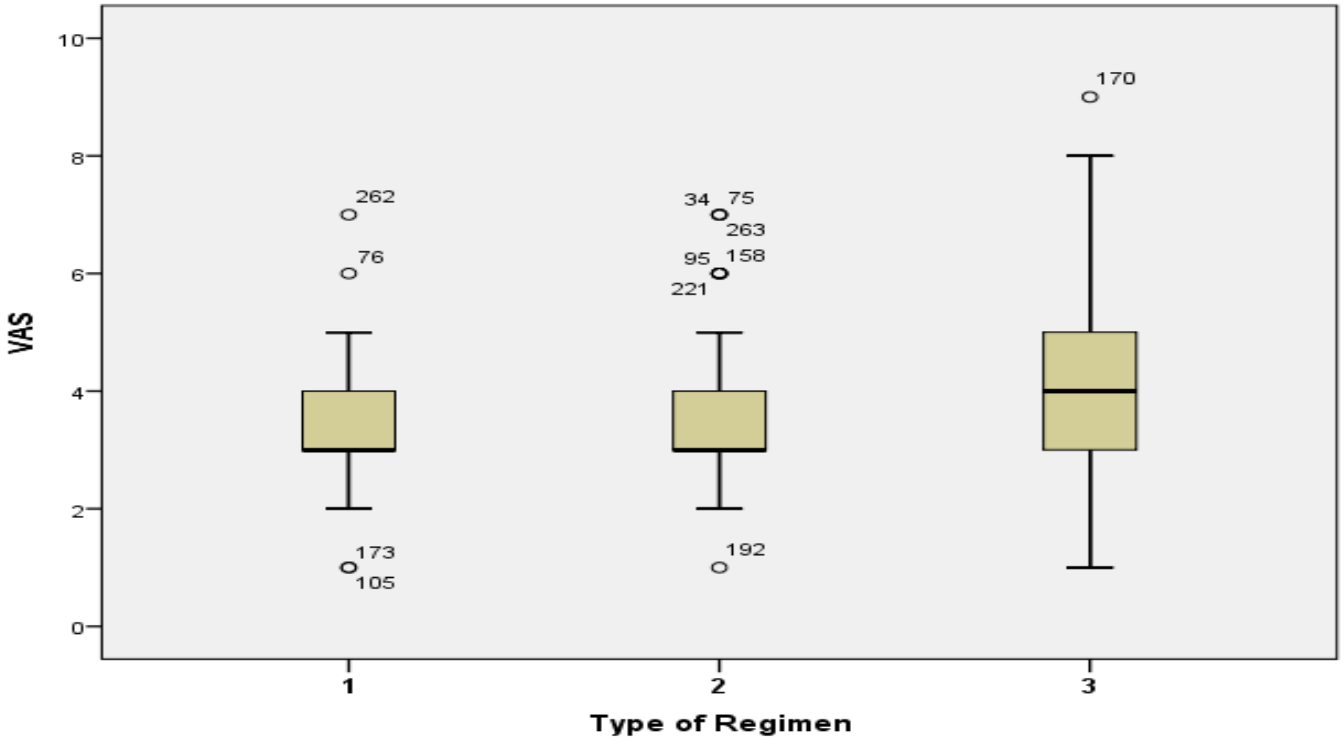
Table (4.2): The mean (95% CI) of the VAS score for each treatment regimen

Statistic	Regimen 1 Morphine	Regimen 2 Morphine + Celecoxib	Regimen 3 Morphine+ Paracetamol	P	Statistical Test
	VAS score				
Mean (95% CI)	3.32 (3.10- 3.53)	3.45 (3.21-3.70)	4.45(4.14-4.76)	F=22.36 <0.001 df =2	Mann-Whitney
Post hoc analysis of the mean	Regimen 1 vs Regimen 2 Regimen 1 vs Regimen 3 Regimen 2 vs Regimen 3			0.74 <0.001 <0.001	Post hoc Tukey test
Median (IQ)	3 (3-4)	3 (3-4)	4 (3-5)	Chi-sq=35.06 <0.001 df = 2	Kruskal-Wallis
Post hoc analysis of the median	Regimen 1 vs Regimen 2 Regimen 1 vs Regimen 3 Regimen 2 vs Regimen 3			0.57 <0.001 <0.001	Mann-Whitney



1= Morphine
2= Morphine + Celecoxib
3= Morphine + Paracetamol

Figure (1): The mean (95% CI) of the VAS score for each treatment regimen



- Regimen 1: Morphine
- Regimen 2: Morphine &Celecoxib
- Regimen 3: Morphine &Paracetamol

Figure (2): The box-plot presentation of the vas score versus the three treatment regimens

Table (4.3): VAS score of the three treatment regimens among different variables

Variable	VAS	P	Test
Gender Male (Mean ± SD) years Female (Mean ± SD) years	 3.75± 1.18 3.73 ± 1.59	0.911	Independent T- test
Degree of burn Second degree (Mean ± SD) % Third degree (Mean ± SD) %	 3.68 ± 1.47 3.79 ± 1.30	0.494	Independent T- test
History of chronic disease Yes (Mean ± SD) No (Mean ± SD)	 3.35 ± 1.36 3.85 ± 1.37	0.012	Independent T- test
Symptoms post dressing Free (Mean ± SD) Others (Mean ± SD)	 3.37 ± 1.02 3.84 ± 1.43	0.04	Independent T- test
Type of burn: Scaled (Mean ± SD) Flamed (Mean ± SD) Others (Mean ± SD)	 3.58± 1.30 4.05± 1.46 3.45± 1.17	0.03 Scaled vs flamed: 0.02 Scaled vs others: 0.76 Flamed vs others: 0.63	ANOVA Post hoc

Table (4.4): VAS score for different regimen based on clinical and demographic data

Variable	Regimen 1	Regimen2	Regimen3	P
Gender:				
Male(mean ± SD)	3.36 ± 0.78	3.42 ± 0.99	4.47 ± 1.35	<0.001
Female (mean ± SD)	3.26 ± 1.36	3.50 ± 1.42	4.43 ± 1.74	0.003
Degree of burn:				
Second degree burn (mean ± SD)	3.29 ± 0.99	3.51 ± 1.03	4.56 ± 1.46	.000
Third degree burn (mean ± SD)	3.35 ± 1.90	3.38 ± 1.39	4.30 ± 1.62	.004
Type of burn:				
Scaled burn (mean ± SD)	3.20 ± 1.09	3.41 ± 1.08	4.11 ± 1.54	.002
Flamed burn (mean ± SD)	3.51 ± 1.09	3.76 ± 1.34	4.86 ± 1.62	.000
Others (mean ± SD)	3.14 ± 1.10	2.79 ± 0.80	4.43 ± 0.94	.000
History of Chronic disease:				
No (mean ± SD)	3.42 ± 1.06	3.55 ± 1.14	4.58 ± 1.53	.000
Yes (mean ± SD)	2.95 ± 1.07	3.10 ± 1.40	4.00 ± 1.50	.023

Table (4.5):Anova test to different effect of treatment regimens on heart rate

	Sum of squares	df	Mean square	F	Sig
Between groups	53.986	2	26.993	0.153	0.859
Within groups	49887.958	282	176.908		
Total	49941.944	284			

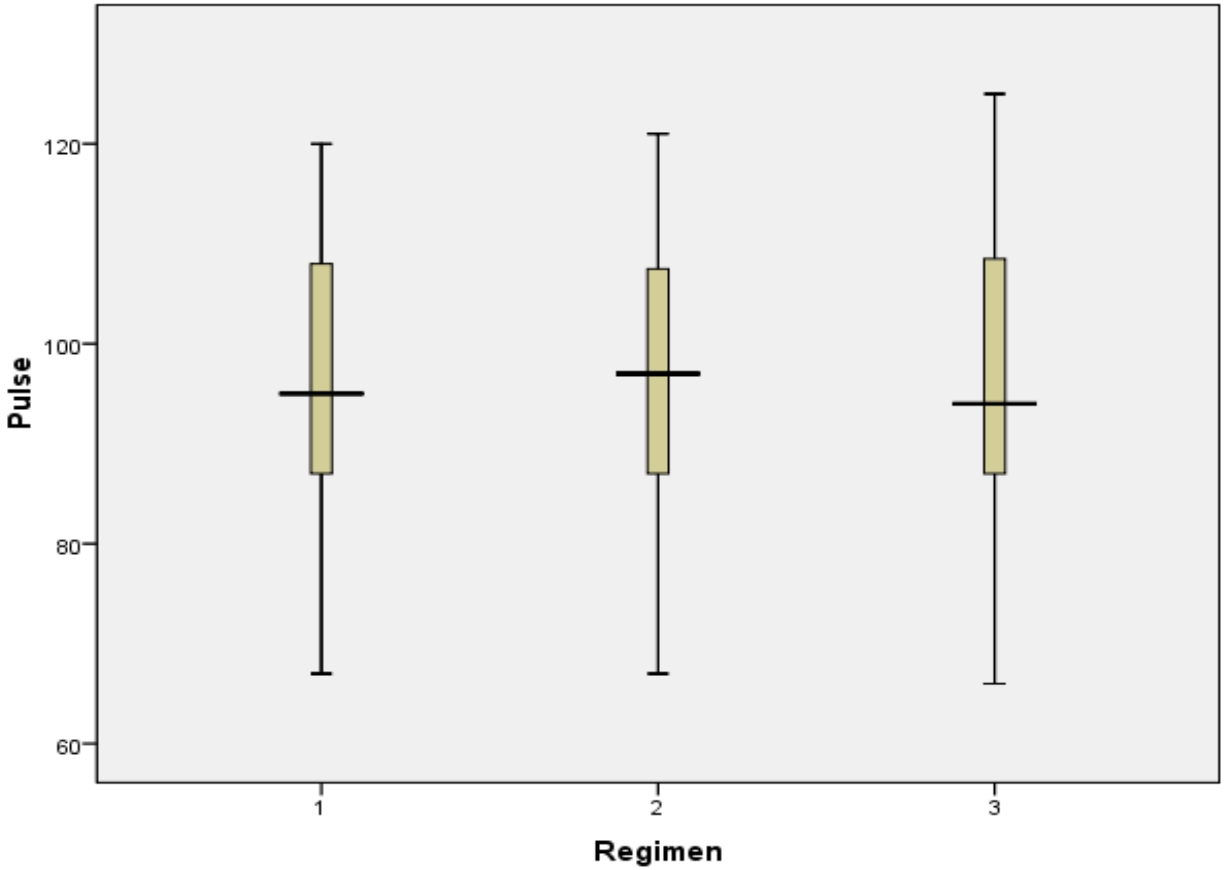


Figure (3): Different effect of treatment regimens on heart rate

Chapter 5

Discussion

This study aimed at investigating the different therapeutic regimens in pain management during dressing among burn patients in burn unit at Rafidia governmental hospital in northern West-Bank of Palestine. The results of the study showed that analgesia combination of NSAIDs (Celecoxib) with Opioids (Morphine) is effective for pain management during dressing for burn patients according to pain score (VAS) and use of this combination decreased the doseof Morphine if used alone.

Many studies conducted to evaluate the effect of different regimen in improving the outcome of procedural pain in burn patients were the maximum sample 92 patients (Birrer 2013). The sample in this study was 90 patients with 270 trials.

Burns mostly cause minor injuries, and scalds are one of the most frequent mechanisms. Although flame injury is the predominant type of bum for which patients are admitted to bum centers, approximately 30% of all bums necessitating admission of a patient to the hospital are caused by scald from hot liquids (Stylianou, Buchan et al. , WHO). In this study, we have (46.3 %) from sample were admitted due to scald burn.

Females accounted for 37% of the total workload in specialized burn injury services, and males for 63% (Stylianou, Buchan et al.). Females

were burned less frequently than males (1:1.27) (Aghakhani, Sharif Nia et al.). Male patients in this study were (55.8%) from sample study.

The most common burned site in children's were in the upper part of the body (51.5 %), while about (26 %) of these patients were burned in lower part of the body (Alsalman, Algadiem et al. , Balseven-Odabasi, Tumer et al. 2009). However, the percentage of the lower part burned of the body was (21.1 %) and the upper part was (18.9 %).

The doses of opioids analgesics that administered for pain management may be very large, and increase the risk of adverse effects (Berger, Davadant et al. , Everett, Patterson et al. 1993).The different side effects post dressing in this study were (78.2 %) from all trials.

Post dressing pain can be classified as mild tosevere forpatients who suffer from burns. Themanagement of such pain needsa combination of high-dose analgesics (opioids) with others having various action mechanisms based on the multimodal concept of analgesia (Garcia Barreiro, Rodriguez et al. 2005). The range of the guidelines used in different burn worddiffer from orally route analgesics for low to moderate pain levels (Methymazol, Paracetamol), to intravenous analgesia using opioids (Morphine, Tramadol, Phentanyl) in continuous intravenous infusion or controlled by the patient (PCA), which is connected in some patients with behavioral procedures, protocols of conscious sedation (Ketamine), hypnotics and benzodiazepines, NSAIDs and other

psychological therapies(Pal, Cortiella et al. 1997, Gallagher, Rae et al. 2000). In this randomized control study, each patient was recruiting and evaluated for three consecutive dressings using three different treatment regimens as analgesics for the dressing and post dressing, andall of these regimens have been carefully selected to suit the purpose for which was chosen for it to provide a lower level of pain and avoid many complications and side effects that may arise in the short or long term.

In the developing world, Ketamine has an important role for being a cheap and flexible mediation (Craven 2007). The addition of Ketamine to a regimen of opioids and benzodiazepines for burn dressing may not only decrease the opioid and benzodiazepine dose but also enhance compliance with physical and occupational therapy(Birrer 2013).Ketamine isa bronchodilator likely by two different mechanisms – the first one isthrough a central effect that encourages the releasing of catecholamine, that waystimulating b2 adrenergic receptors and causes bronchodilation.The second one is through vagal pathways inhibition in order toget the effect of anticholinergic that acts on bronchial smooth muscle in a direct way (Lau and Zed 2001). An increasing in blood pressure, heart rate and stroke volume can be caused by Ketamine causes at the same time as maintaining systemic vascular resistance (Craven 2007). In this study, no respiratory depression or instability of cardiovascular that needsoxygen supplement or urgent intervention was observed. In group,no emergency reaction, laryngospasmor vomitingwas noticed during or after the procedure. In the

current study, Analgesics was combined with Ketamine in order to enhance the analgesia. For the purpose of providing comfort to the patient and to reduce the sense of pain, a sedative (Midazolam) has been added.The effect of Ketamine clearly in pain relief as well as its key role in anesthesia, and did not experience any of the patients for any complications may be related to side effects, and all of the vital signs were within the normal values.

Morphine or other Opioid analgesics are considered cornerstone of pain management for burned patients, but many reviewers report less than adequate pain relief for burned patients with the use of such agents (Krauss and Green 2000).In procedural pain, benzodiazepines are being used as adjuncts to opiates for reducing anxiety (Ang, Lee et al. 2003). Medical teams at the burns word are often amazed at the doses of morphine required to manage pain of differing total burn sizes (Weddell 2004).It was reported in two current studies by Serinken et al and Bektas et al that morphine is not preferable to Paracetamol in patients who have presented with renal colic to the emergency room (Serinken, Eken et al. , Bektas, Eken et al. 2009).In this study, full dose of intravenous Morphine (0.1mg/kg I.V slowly 10 mint before dressing) for anesthetized patients with Ketamine and Midazolam were administered for control group, Mean (95% CI) VAS for this group was acceptable 3.32 (3.10- 3.53), VAS is a scale that is known for pain assessment. In different studies, it was reported that Vas is easy to use, repeatable and sensitive to change (Downie, Leatham et al. 1978, Jensen, Karoly et al. 1986).

Non-steroidalanti-inflammatory drugs are being used as an assistant approach formanaging severe pain worldwide(Chen, Zhu et al. 2015)Analgesia from NSAIDshappens by reducing inflammatory mediators and inflammation through cyclooxygenase-specific inhibition (COX-1 and COX-2). Non-steroidal anti-inflammatory drugs can be used as a useful adjuncts in burn injury victims in order to help the reducing of the burns associated fever as well as the neurogenic inflammatory pain (Promes, Safcsak et al. 2011). Opioids side effects can be decreased by NSAIDs in a significant way. (Malenfant, Forget et al. 1996). Despite the fact that these drugs act synergistically with opioids, they still considered weak when used alone(Marret, Kurdi et al. 2005). In this study, both of variable groups (Celecoxib and Paracetamol) were belong to NSAIDs.

Non- aggregation steroidal anti-inflammatory drugs side effects can be avoided by cyclooxygenase-2 inhibitors that actualized by the cyclooxygenase-1 inhibition which causes impairment of renal function, platelet inhibition and gastrointestinal adverse reactions (Ekman, Wahba et al. 2006). Pre-and post-operative oral Celecoxib in a multimodal analgesic strategy can reduce opioid consumption, achieve favorable pain relief in addition to providingimproved rehabilitation and earlier ambulation if compared with PCA Morphine alone following THA in elderly patients(Chen, Zhu et al. , Kang, Ha et al. , Zhang, Zhu et al. , Reuben and Ekman 2005). In this study, (0.025mg/kg I.V slowly 10 mint before dressing) of intravenous Morphine with (200mg Celecoxib orally two hours

before dressing) for anesthetized patients with Ketamine and Midazolam were administered for variable group, Mean (95% CI) VAS for this group was 3.45 (3.21-3.70).

The American Society of Anesthesiologists has published guidelines for managing severe pain thatrecommend the use of multimodal pain management. This includes around-the-clock NSAIDs and acetaminophen with opioids . The administration of intravenous (IV) Paracetamol to reduce postoperative pain has been effective in diminishing opioid consumption in many surgical populations (Wang, Saha et al.).The safety and efficacy of IV acetaminophen in managing mild-to-moderate pain as monotherapy and in controlling of moderate-to-severe pain in conjugation with opioids were assured by various clinical studies. Due to their anti-prostaglandin and anti-inflammatory actions, NSAIDs like Paracetamol can be noticeably effective in simple burn if taken regularly, (Pal, Cortiella et al. 1997).Some studies have specifically examined Paracetamol alone in burn pain controlling as the most of these agents have been administered as part of a multimodal approach to managing pain in burn patients (Promes, Safcsak et al.). However, Paracetamol exhibits a ceiling effect in their dose response relationship, rendering them inappropriate for the treatment of severe burn pain(Richardson and Mustard 2009). IV Paracetamol is ineffective in decreasing opioid dosing in bariatric surgery patients(Wang, Saha et al.).In this study, the ability of Paracetamol when combined with morphine to control procedural and post dressing pain for burned patients

were less effective, where the Mean (95% CI) VAS for this group was 4.45(4.14-4.76).

In this study, the mean heart rates were acceptable with the baseline, and there was no significant difference between three groups as showed in table (4.5) and figure (3), and this result is correspond with the study that conducted by(Berger, Davadant et al. , Herndon, Hart et al. 2001), There was no significant change in pulse during thepainful procedures between groups of burn patients.

5.1 Strength and limitations of the study

There are certain limitations to the present study. First, due to the rigid inclusion and exclusion criteria, there were limited numbers of patients who were eligible for this study anda larger sample size would be needed to test the hypothesis that intravenous morphine, Celecoxib and morphine are equally effective in ceasing procedural burn pain. Therefore, we believe that this study will provide some insight into procedural multimodal analgesia, which helps to improve pain management in clinical practice.

5.2 Conclusion and recommendation

My randomize control study indicates thatMorphine alone or Morphine with Celecoxib and demonstrates that using Celecoxib in a multimodal analgesic strategy for procedural pain can achieve favorable

efficacy in the management of pain. IV Acetaminophen is ineffective in reducing opioids consumption in procedural burn pain. In fact, the VAS was significantly higher in IV Acetaminophen with Morphine-treated patients than in treated patients by Morphine or Morphine with Celecoxib. I recommend the development of a prospective, randomized, controlled multicenter trial with a high number of patients to further elucidate the potentially beneficial effects of Celecoxib for the management of burn patients.I confirmed that our new pain managementsystem was significantly more effective than the previous system that depends on Opioids alone.

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Appendices

An-Najah
National University
Faculty of Graduate Studies
Dean's Office

جامعة
النجـــاح الوطنية
كلية الدراسات العليا
مكتب العميد

التاريخ : 2015/10/7

حضرة الدكتورة عائدة القيسي المحترمة
منسقة برنامج ماجستير تمريض التخدير

تحية طيبة وبعد،

الموضوع : الموافقة على عنوان الاطروحة وتحديد المشرف

قرر مجلس كلية الدراسات العليا في جلسته رقم (ملحق 296)، المنعقدة بتاريخ 2015/10/1، الموافقة على مشروع الأطروحة المقدم من الطالب/ محمد عطا حسين ابو رجب، رقم التسجيل 11356727، تخصص تمريض التخدير، عنوان الأطروحة:

(المقارنة بين نظم علاجية مختلفة في إدارة الألم أثناء اجراء الغيار لمرضى الحروق : دراسة في مستشفى رفيديا)
(Comparison of Different Therapeutic Regimens in Pain Management During Dressing Among Burn Patients: A Study at Rafidia Hospital)

بإشراف: 1- أ.د. وليد صويلح 2- د. نور الدين المصري

تمت الموافقة على ان يقوم الطالب باجراء التعديلات المبينة على العنوان.

يرجى اعلام المشرف والطالب بضرورة تسجيل الاطروحة خلال اسبوعين من تاريخ اصدار الكتاب. وفي حال عدم تسجيل الطالب/ة للاطروحة في الفترة المحددة له/ا ستقوم كلية الدراسات العليا بإلغاء اعتماد العنوان والمشرف.

وتفضلوا بقبول وافر الاحترام ،،،

عميد كلية الدراسات العليا
د. احمد الرمحي

صادر
جامعة النجاح الوطنية
كلية الدراسات العليا
08. 10. 2015
الرقم المتسلسل :

نسخة : د. رئيس قسم الدراسات العليا للعلوم الطبية والصحية المحترم
: ق.أ.ع. القبول والتسجيل المحترم
: مشرف الطالب

فلسطين، نابلس، ص.ب 707، 7 هاتف:/2345115، 2345114، 2345113 (09)(972)* فاكسميل:2342907(09)(972)
Nablus, P. O. Box (7) *Tel. 972 9 2345113, 2345114, 2345115 هاتف داخلي (5) 3200
* Facsimile 972 92342907 *www.najah.edu - email fgs@najah.edu

بسم الله الرحمن الرحيم

An - Najah
National University
Faculty of Medicine & Health Sciences
Department of Graduate Studies

جامعة النجاح
الوطنية
كليـة الطب وعلـوم الصـحة
دائرة الدراسات العليا

IRB Approval letter

Study title:
Comparison of different therapeutic regimens in pain management during dressing among burn patients.

Submitted by:
Muhammad Ata Abu Rajab
Dr. Nouraldin Almasri

Date Reviewed:
Oct 14, 2014

Date approved:
Nov 5, 2014

Your study titled: " Comparison of different therapeutic regimens in pain management during dressing among burn patients " with archived number 224/Oct/2014 , Was reviewed by An-Najah National University IRB committee & approved on Nov 5, 2014 .

Samar Musmar,MD, FAAFP

IRB Committee Chairman,
An-Najah National University

IRB

نابلس – ص.ب 7 أو 707 هاتف 14/8/7/4/2342902(09)(970) ، فاكسميل 2342910 (09) (970)
Nablus – P.O.Box: 7 or 707 – Tel (970) (09) 2342902/4/7/8/14 – Faximile (970)(09)2342910
Email: hgs@najah.edu Web Site: www.najah.edu

Certificate of Completion

The National Institutes of Health (NIH) Office of Extramural Research certifies that **Muhammad Abu Rajab** successfully completed the NIH Web-based training course "Protecting Human Research Participants".

Date of completion: 10/13/2014

Certification Number: 1555928

نموذج موافقة طوعية للمشاركة في بحث علمي

بعنوان

مقارنة أفضلية الأدوية المسكنة للألم لمرضى الحروق لفترة ما بعد عملية الغيار

الباحث: محمد أبو رجب ,طالب في كلية الدراسات العليا - تخصص تمريض تخدير - كلية الطب وعلوم الصحة - جامعة النجاح الوطنية الفلسطينية

الباحث المشارك: د.نور الدين المصري-أخصائي تخدير وإنعاش- مستشفى رفيديا

مشرف البحث : البروفيسور وليد صويلح – قسم الأدوية والسموم - كلية الطب وعلوم الصحة –جامعة النجاح الوطنية الفلسطينية

دعوة للمشاركة في البحث

الباحث المذكور أعلاه يدعوك للمشاركة في دراسة علمية تهدف للمقارنة بين مجموعة من الأدوية المسكنة للألم في الفترة ما بعد عملية الغيار الجراحي للمنطقة المصابة بالحروق.

أولاً: نود أعلامك أن مشاركتك في هذا البحث هو أمر تطوعي ولك حق الرفض أو الانسحاب بالوقت الذي تريد وفي كلتا الحالتين لن تفقد المزايا التي كنت سوف تحصل عليها وأيضا قد لا يكون هناك أي مزايا سوف تحصل عليه من خلال مشاركتك, وهذا البحث قد يؤدي إلى اكتشاف نتائج جديدة سيكون لها أثار ايجابية على الأفراد مستقبلاً.

ثانياً: بعض الأفراد قد يكون لديها أفكار ومعتقدات دينية وأخلاقية خاصة قد تحد من استعمال بعض الأدوية التي من الممكن أن تستعمل خلال البحث ,إذا كان لديك بعض من هذه الأفكار يرجى منك مناقشتها مع الباحث المسؤول أو الطبيب المشرف على علاجك قبل الموافقة على المشاركة.

الآن سيتم توضيح هذه الدراسة, قبل أن تقرر المشاركة, يرجى منك اخذ الوقت الكافي للاستفسار عن أي تساؤلات مع طاقم قسم الحروق أو أفراد العائلة أو صديق أو طبيبك الخاص.

وصف الدراسة

يحتاج الباحث في قسم الحروق (مستشفى رفيديا) إلى عدد من مرضى الحروق للمشاركة بالبحث المتعلق بصحة المرضى,فهذا البحث يقوم على إعطاء المريض واحدة من مجموعات الأدوية التي سوف تدخل في نطاق البحث قبل وأثناء عملية الغيار اليومي وتحت إشراف أخصائي التخدير والعمل على تقييم درجة الألم بعد الغيار,إن موافقتك على أخذ واحدة من هذه المجموعات الدوائية يعتبر جزءاً من المشاركة في هذا البحث الذي سوف يمكننا من معرفة أكثر هذه الأدوية فاعلية.

المخاطر

قد يكون هناك بعض المخاطر المرتبطة بهذا البحث وهي التي لها علاقة بالآثار الجانبية للدواء المعطى وكحال العديد من الأدوية الأخرى(دواء الكيتامين الذي سوف يستعمل قد يؤدي في بعض الأحيان إلى حدوث بعض الهلوسة لفترة محدودة بعد الغيار) هذا وسوف تعطى بعض الأدوية التي تحد من هذه الظاهرة.

الفوائد المرجوة من هذا البحث

قد لا يكون هناك فوائد ملموسة من مشاركتك في هذا البحث ولكن عملية الغيار اليومي الخاصة بك ستكون أكثر سهولة وأقل الم وستكون نتائج الغيار أكثر ايجابيةً من الناحية الطبية,هذا وقد تساعدنا نتائج هذه الدارسة في تحديد أي من هذه المجموعات الدوائية أكثر فاعلية.

ضمان السرية

إن إجراء هذا الاختبار سوف يكون خلال وجودك في سريرك الخاص في قسم الحروق وسوف يتم إغلاق الستائر المحيطة بك وإخراج جميع المرافقين من الغرفة الخاصة بك وسوف لن يبقى معك سوى الباحث نفسه والطاقم الطبي والتمريضي المسؤول عن تقديم العناية الخاصة بك. إن جميع البيانات الطبية والتمريضية سوف تسجل بالملف الخاص بك وسوف لن يذكر اسمك الشخصي في الدراسة وسوف تكون هذه البيانات مشفرة بنمط خاص.

إذا كان لديك أي استفسار بخصوص هذه الدراسة أو لديك أي مشكله متعلقة بالدراسة بإمكانك التواصل مع الباحث محمد أبو رجب –طالب تمريض تخدير- كلية الطب وعلوم الصحة

جوال: 0599872820

بريد الكتروني: mud88@yahoo.com

وفي حال رغبت بالاستفسار من لجنة تراعي سلامة المشاركين بالبحث لا علاقة لها بالقائمين على البحث يمكنك ارسال بريد الكتروني الى irb@najah.edu

نموذج الموافقة

لقد قمت بقراءة نموذج الموافقة وقد أعطيت الفرصة الكاملة لطرح الأسئلة, وعليه فإنني أوفق على المشاركة في هذه الدراسة.

الاسم الرباعي:..... التوقيع:.....

التاريخ:.....

- سوف يتم تسليمك نسخة من هذا النموذج وأخرى تحفظ في ملف البحث.

شاكرين لكم حسن تعاونكم

نموذج موافقة طوعية للمشاركة في بحث علمي

بعنوان

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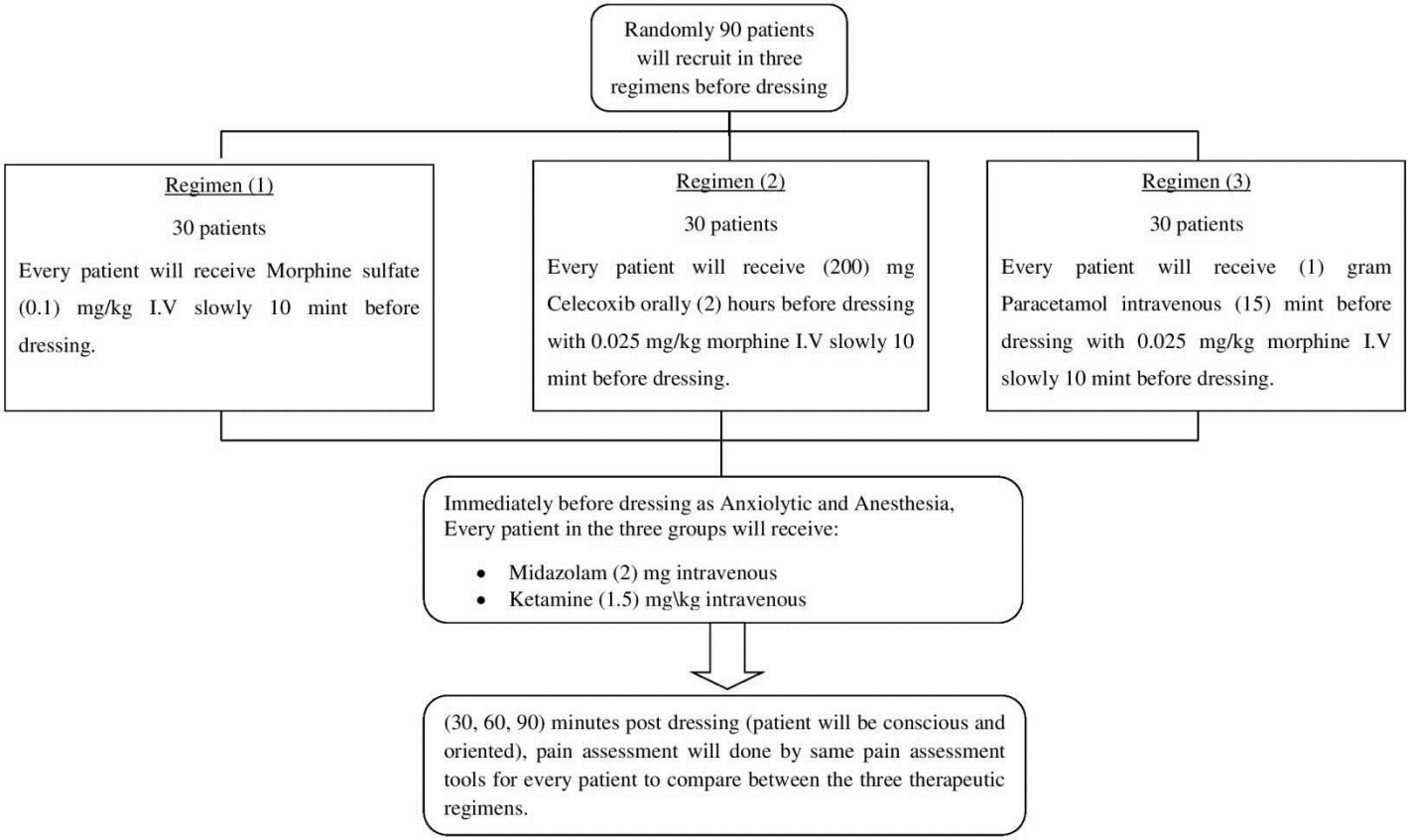
Research Protocol



AN-NAJAH NATIONAL UNIVERSITY

PAIN ASSESSMENT QUESTIONNAIRE

Comparison of different therapeutic regimens in pain management during dressing among burn patients, study at Rafidia hospital

Submitted by: Muhammad Abu Rajab
Supervised by: Dr. Waleed Sweileh

-2015-

TO BE COMPLETED BY PATIENT AND NURSE

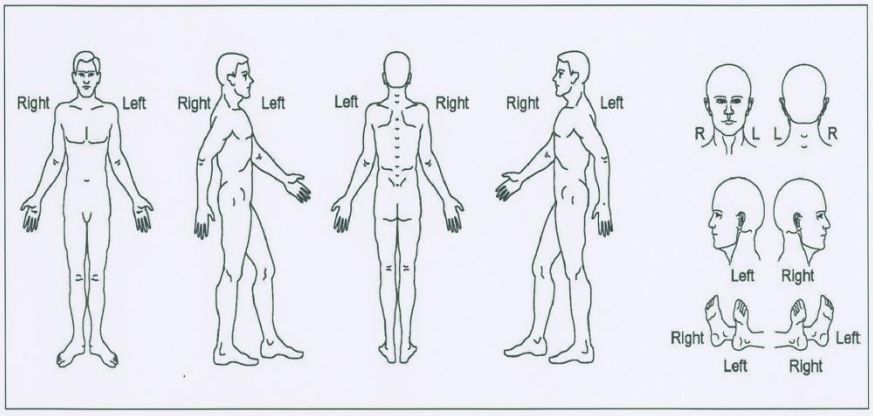
PT NAME: …… MEDICAL RECORD NUMBER: ……..

AGE: ……. GENDER: …….. PT WEIGHT: …… (Kg) INJURY DATE: ……..

DRESSING DATE: …… DRESSING TIME: …… DRESSING NO: ……..

TYPE OF BURN: ……..…… SITE OF BURN: ……. TBSA %: ……..

SIGNIFICANT MEDICAL / SURGICAL HISTORY: ……



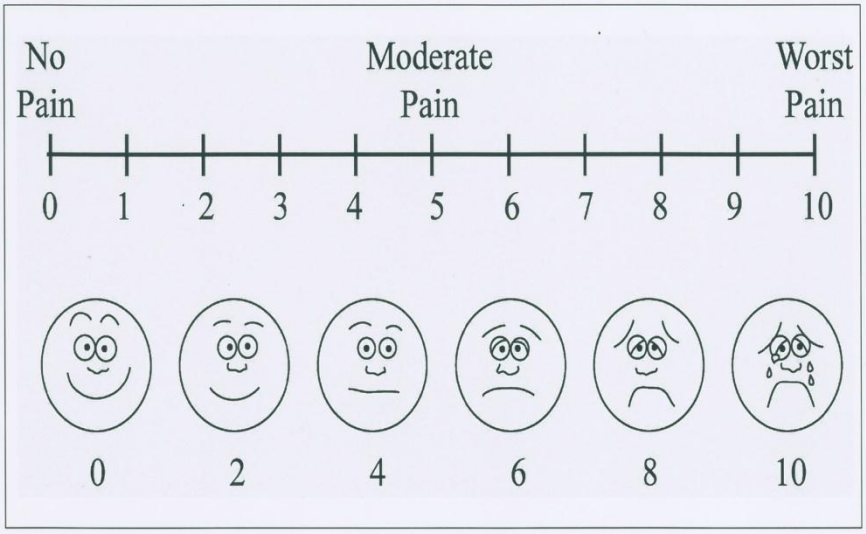
ANESTHESIA & ANALGESIA DRUGS WITH DOSES:

	DRUG	ROUT	1st DOSE	TIME OF 1st DOSE BEFORE DRESSING	2ed DOSE IF NEED	TIME OF 2ed DOSE
	MIDAZOLAM	I.V				
	KETAMINE	I.V				
	MORPHINE	I.V				
	PARACETAMOL	I.V				

VITAL SIGNS AND PAIN SCORE:

Vital Signs	Prior Analgesia	Prior Anesthesia	Prior start of dressing	During dressing	Recovery			
BP(mmHg)								
PULSE(b/m)								
RR(B/m)								
TEM(c)								
O_2 sat (%)								
PAIN SCORE								

VISUAL ANALOG SCALE:



Are you experiencing any of the following symptoms associated with pain?

☐Vision problems ☐Numbness ☐Weakness ☐Nausea ☐Fear

☐Spasm of muscle ☐Dizziness ☐Confusion ☐Vomiting ☐Anxiety

جامعة النجاح الوطنية
كلية الدراسات العليا

مقارنة أفضلية الأدوية المسكنة للألم لمرضى الحروق لفترة ما بعد عملية الغيار

اعداد
محمد أبو رجب

اشراف
أ.د. وليد صويلح
د. نور الدين المصري

قدمت هذه الاطروحة استكمالا لمتطلبات الحصول على درجة الماجستير، تخصص تمريض التخدير، بكلية الدراسات العليا في جامعة النجاح الوطنية، نابلس- فلسطين.

2016

مقارنة أفضلية الأدوية المسكنة للألم لمرضى الحروق لفترة ما بعد عملية الغيار

إعداد

محمد عطا أبو رجب

أشراف

البروفسور وليد صويلح

د. نور الدين المصري

الملخص

الخلفية: يعتبر الألم من أكثر المشاكل التي تواجه مرضى الحروق وأن كانت تعالج من خلال جرعات عالية من الادوية الافيونية، ولذلك فقد تم التركيز في هذه الدراسة على تأثير استخدام أنواع مختلفة من المسكنات في تخفيف الالم الناتج خلال الاجراء الطبي لمرضى الحروق.

الأهداف: تهدف هذه الدراسة الى تقييم فاعلية أكثر الانماط السائدة في علاج الالم عند مرضى الحروق وخاصة ما بعد الاجراء الطبي (غيار مكان الاصابة)، وتقييم نجاعة البدائل المقترحة في تخفيف ذلك الالم وتقليل الاثار الجانبية والمضاعفات المتوقعة.

منهج البحث: تم إجراء دراسة تجريبية عشوائية في وحدة الحروق الموجودة في مستشفى رفيديا الحكومي في شمال غرب فلسطين، وتم جمع البيانات والمعلومات السريرية والديمغرافية للمرضى الذين تنطبق عليهم شروط الدراسة وذلك باستخدام ملف المريض الطبي، ومن خلال مراقبة المرضى خلال الاجراء الطبي من خلال طاقم مدرب وأجهزة طبية وبإستخدام أداة تقييم للألم معتمدة عالمياً، وتم التحليل الوصفي والإحصائي باستخدام الرزم الإحصائية للعلوم الاجتماعية (SPSS – 19).

النتائج: اشارت نتائج الدراسة التي أجريت على (90) من مرضى قسم الحروق في مستشفى رفيديا الى أن متوسط أعمارهم كان من (29.69 ± 14.96) عاما. وكان أكثر من نصف المرضى الخاضعين للدراسة من الذكور (55.8٪). وبلغ متوسط النسبة المئوية لمساحة المنطقة المصابة من مجموع مساحة سطح الجسم 19.54± 10.85. وكانت أكثر أماكن الاصابة شيوعاً

بين المرضى الخاضعين للدراسة هي الطرف السفلي تليها الطرف العلوي (21.1٪ و18.9٪ على التوالي). وكانت الغالبية العظمى من المرضى الخاضعين للدراسة هم من حروق الدرجة الثانية (57.9٪).هذا وكانت الغالبية العظمى من المرضى الخاضعين للدراسة ممن كانوا قد اصيبوا نتيجة سوائل ساخنة (46.3٪) ويليها ممن أصيبوا نتيجة لهب ناري (38.9٪). وكان غالبية المرضى ممن لا يعانون من اي أمراض مزمنة (77.9%)، ويبين الجدول (4.1) الخصائص الديموغرافية والسريرية للمرضى الين تم إجراء الدراسة عليهم.

تم دراسة وتقييم كل مريض من خلال إجراء ثلاث غيارت طبية متتالية وباستخدام ثلاثة أنماط من الادوية المسكنة. وتبع ذلك تقييم ومراقبة المريض في الفترة ما بعد الغيار الطبي باستخدام اداة قياس الالم (VAS)، وكانت النتائج كما ظهر بالجدول رقم(4.2) والشكل (1). وأشار تحليل ANOVA أن هناك فرقا كبيرا بين انماط العلاج الثلاثة في النتيجة ($F=22.36$, $p<0.001$, $df=2$). وأشار تحليل Post–huc وباستخدام اختبار Tuckey أن كلا من العلاج رقم واحد واثنين لم تكن تختلف كثيرا عن بعضها البعض. من حيث قدرتها على تقليل الالم، وكانت قدرة النمط الثالث أقل بكثير على تقليل الالم، ويظهر ذلك بالشكل رقم (2).

وأخيرا، لم يكن هناك أي ارتباط بين الجنس أو درجة الحروق أو نوع الحروق أو وجود مرض مزمن مع درجة الالم باستخدام الانماط المختلفة من العلاج، ويتضح ذلك في الجدول (4.3).

المناقشة والاستنتاجات: لقد أشارت نتائج الدراسة إلى أنه يمكن تقليل جرعات المسكنات الافيونية المستخدمة في علاج الالم عند مرضى الحروق الى (25%) من الجرعة الموصى بها وذلك بأستبدالها بمسكن أخر من نوع (Celecoxib)، الامر الذي من شأنه أن يقلل من الاثار الجانبية والمضاعفات المترتبة على استعمال جرعات عالية من المسكنات الافيونية.