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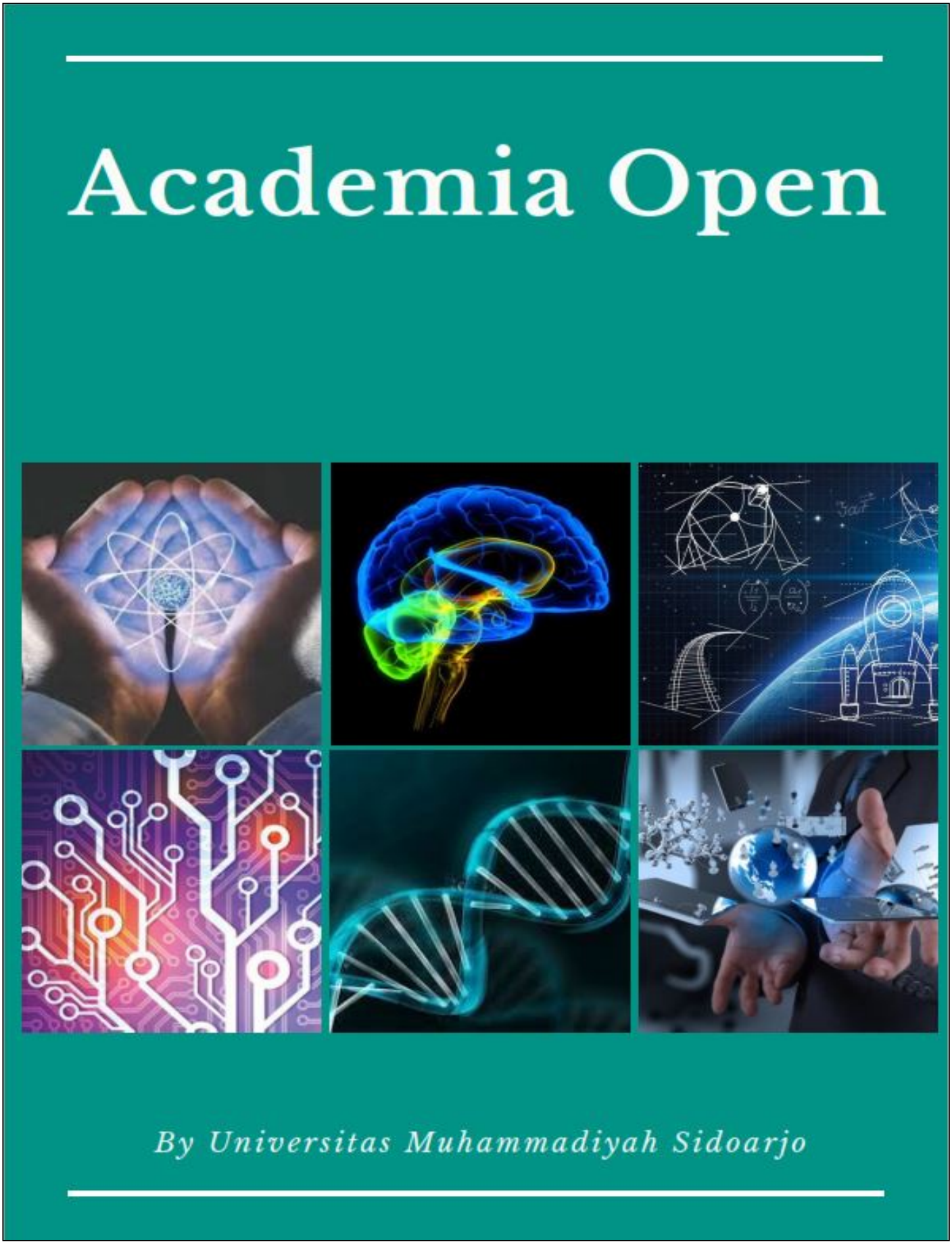

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Dexamethasone in Indonesian Surgery Lowers Post-Op Pain Medication Use

Deksametason dalam Pembedahan di Indonesia Menurunkan Penggunaan Obat Nyeri Pasca Operasi

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Abstract

Dexamethasone is commonly used to prevent postoperative nausea and vomiting, but its analgesic effects remain uncertain. This study aims to investigate the efficacy of intraoperative dexamethasone in reducing postoperative pain after inguinal hernia repair surgery. Methods: A randomized double-blind, placebo-controlled trial was conducted on eighty ASA class I patients aged 15–30 years at Al-Yarmouk Teaching Hospital in Baghdad, Iraq. Patients received varying intravenous doses of dexamethasone or normal saline during surgery. Pain levels were assessed using verbal analogue pain ratings, and the time to first analgesic consumption was recorded. Results: Analysis revealed that the dexamethasone group had significantly lower postoperative discomfort compared to the control group, with higher doses showing greater efficacy. Specifically, a single intravenous dose of dexamethasone administered at the onset of anesthesia significantly reduced the need for postoperative analgesia. Implications: This study highlights the potential of intraoperative dexamethasone as an effective adjunct for postoperative pain management in inguinal hernia repair surgery. Further research is warranted to optimize dosing strategies and confirm these findings in larger and more diverse patient populations.

Highlight:

1. Efficacy of Dexamethasone: Demonstrated significant reduction in postoperative pain.
2. Intraoperative Administration: Single dose at anesthesia onset proved effective.
3. Clinical Implications: Potential for dexamethasone as adjunct in pain management strategies.

Keyword: Dexamethasone, Postoperative Pain, Inguinal Hernia Repair, Analgesia, Randomized Controlled Trial

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INTRODUCTION

Dextamethasone is one kind of corticosteroid that is often used during the perioperative period. Its primary purpose is to lessen post-operative nausea and vomiting. It could also make postoperative pain management easier.To begin with.(1)

Multimodal analgesia

Multimodal analgesia was created over ten years ago with the goal of enhancing pain relief and lowering the frequency of opioid-related adverse effects (2). This tactic blends many analgesic medications that target various neural system regions and operate via various processes. In addition to producing a cumulative or cooperative pain reduction effect, this lowers the likelihood of adverse effects associated with taking a single medicine alone (2, 3). A comprehensive approach to pain management during the perioperative period is necessary due to the complicated response that surgical procedures induce in the brain and humeral systems (1, 4). Systematic studies have shown the effectiveness of many additional medications in lowering postoperative pain and/or the need for opioids. These treatments include nonsteroidal anti-inflammatory drugs, ketamine, gabapentin, and paracetamol (1). These drugs have shown to be useful components of multimodal pain treatment plans. The synergistic effects of several types of analgesics working together to lower the doses of individual medications permit adequate pain relief. This reduces the possibility of any specific medicine used for this purpose having negative side effects.

Multimodal analgesia techniques have been the subject of much research, with several trials demonstrating their advantages in postoperative pain control (1, 2, 4). The use of these techniques has been associated with a reduced risk of adverse effects and better pain management, which may lead to advantages including shorter hospital stays, enhanced postoperative functioning and recovery, and perhaps lower total healthcare expenditures (1,5,6,7). The American Society of Anesthesiologists Task Force on Acute Pain Management now strongly recommends the adoption of multimodal analgesic strategies to enhance both patient outcomes and the standard of perioperative care. According to current guidelines and best practices, multimodal analgesia is utilized to improve patient satisfaction, promote speedy recovery, and ultimately result in a more cost-effective healthcare system.

The action of opioid

Opioids bind to specific receptors in the central nervous system to elicit a range of pharmacological effects. They work by first blocking the spinal cord from receiving nociceptive signals from the periphery. This mechanism helps to lessen the impression of spinal pain.Second, opioids activate descending inhibitory pathways, which change the way pain signals are relayed inside the spinal cord, to further reduce pain.

- Third, opioids may alter limbic system activity, which is linked to emotional responses and aids in the processing of pain perception..

Indications and uses:

Opioids are often utilized in lieu of non-opioid medications when such medications are insufficient in treating moderate to severe pain. Since this synergistic approach has the dose-sparing effect, which permits the use of lower opioid doses, combining opioids with non-opioids is a common technique (3,8,9,10). While opioids may be used to treat a wide range of pain syndromes, nociceptive pain often reacts to opioids more favorably than neuropathic pain (3); hence, higher dosages of opioids may be needed to provide optimal pain relief.

The side effects:

Opiate use is associated with sedation, respiratory depression, mental fogging or confusion, nausea, vomiting, constipation, pruritus (itching), and urine retention (1). It's important to keep in mind that, other from constipation, the most of these side effects often disappear as the body adjusts to the medication. Because of the potential risks, individuals with liver failure, bronchial asthma, difficulty breathing, or high intracranial pressure should take opioids cautiously (1,3). This methodical approach lowers the risk of adverse events while ensuring safe and effective pain management.

Like other glucocorticoids, dexamethasone functions by binding to the nuclear receptor superfamily member known as the glucocorticoid receptor, specifically a member of subfamily 3C(4,8,6,7). Steroid binding to the receptor initiates a variety of signaling cascades, including direct interaction with DNA, which modifies gene transcription (11, 12, 13, 14,). This cascade of events ultimately impacts gluconeogenesis and results in significant alterations to protein, lipid, and carbohydrate metabolism (4,12,15). In the perioperative context, there is a substantial reduction in prostaglandin 1 production and suppression of bradykinin release, tumor necrosis factor, interleukin-1, interleukin-2, and interleukin-6 (6,12,16). Additionally, there is a decrease in impulse transmission in C fibers, highlighting the intricate ways in which dexamethasone affects physiological processes.

Although dexamethasone is often given intravenously by anesthetists, patients may start taking the medicine orally prior to surgery, indicating the drug's versatility in clinical settings (6,17,18). Despite having a three-hour

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biological half-life, the medication's actual duration of action may be substantially longer (9), demonstrating the medication's long-lasting effects. When compared to other glucocorticoids, dexamethasone exhibits much lower levels of binding to plasma proteins (10), which has an impact on the drug's pharmacokinetic properties and distribution. The liver breaks down dexamethasone by a variety of processes, such as glucuronidation and sulfation, which result in inactive metabolites that the body excretes. The body metabolizes dexamethasone extensively, as shown by the fact that less than 3% of the prescribed dosage remains unchanged after 24 hours and that a significant portion of the dose—roughly 65%—is eliminated in the urine (7). Furthermore, the rapid achievement of peak plasma concentrations after intramuscular injection of dexamethasone (within an hour) (16) suggests that the medication is well absorbed and dispersed throughout the body.

Dexamethasone's effects as an analgesic

The fact that dexamethasone's analgesic activity is multifactorial has been sufficiently shown by several research (8,11,6,17). This medication lowers inflammation by a variety of mechanisms, including blocking phospholipase-A2, slowing cytokine production, and reducing polymorphonuclear leucocyte activity. Additionally, it may prevent the production of free oxygen radicals and nitric oxide by endothelial cells, which lowers postoperative edema (19,13,14, 20). The anti-inflammatory characteristics of dexamethasone are thought to be crucial in lowering the clinical symptoms connected to airway morbidity. This is particularly true in circumstances when the development of postoperative sore throat after tracheal intubation operations is believed to be primarily caused by direct damage to the airway mucosa or acute inflammatory responses triggered by the presence of a tracheal tube (6,12,10,21).

Evidence suggests that among other markers of pain behavior, systemic glucocorticoid therapy lowers proinflammatory cytokine levels, total neuronal firing rate, incidence of bursting activity, and abnormal sympathetic sprouting in the dorsal root ganglia (2,9, 22). Proinflammatory cytokine production around a nerve injury site is recognized to have a major role in the initiation and maintenance of neuropathic pain and central sensitization (9, 22). Glucose corticoids exhibit their anti-inflammatory qualities by suppressing proinflammatory cytokines and promoting the synthesis of anti-inflammatory cytokines. They also inhibit phospholipase A2 and stop the synthesis of messenger RNA for cyclooxygenase-2, two processes involved in the creation of prostaglandins. Spinal glial cell activation triggers nuclear factor B, which in turn induces cyclooxygenase-2, releases prostaglandins, and produces other inflammatory mediators.

Several studies have shown strong evidence about the production of proinflammatory cytokines, growth factors, and excitatory amino acids that are involved in pathologic pain (2,7,23,18, 24). Through the reduction of nuclear factor B activation and glial activation, glucocorticoids have shown a good preventative activity against the development of neuropathic pain behavior in animal models (10,24,25). In addition, glucocorticoids reduce the release of neuropeptides from nerve terminals, inhibit signal transmission in nociceptive C fibers, and cause ectopic discharge from damaged neurons in order to achieve their analgesic effects. Additionally, glucocorticoids have been shown to improve nerve repair and regeneration, reduce mechanically induced dysesthesia after nerve injury, and rapidly and dose-dependently inhibit voltage-dependent calcium currents in dorsal root ganglion neurons (2,7, 18). Both in animal and human studies, the rapid antihyperalgesic actions of glucocorticoids have been successfully shown (4,5). The reduction in neuronal discharge that takes place in a matter of minutes or seconds is a significant discovery in these studies and is associated with the nongenomic steroid activities on membrane receptors (4). The rapid nongenomic effects of glucocorticoids are hypothesized to be associated with reduced and augmented release of glutamate, endocannabinoids, and β-aminobutyric acid, respectively. Because they control these neurotransmitters, glucocorticoids are crucial for decreasing pain and hyperalgesia in a range of situations (4,7,21). Moreover, the variety of ways in which glucocorticoids function contributes to their overall efficacy in the management of neuropathic pain and the symptoms that accompany it.

According to a number of publications, glucocorticoids would swiftly raise -aminobutyric acid levels, which would result in a significant decrease in nerve cell excitability. Steroids may theoretically influence analgesic and antihyperalgesic effects via both genetic and nongenomic pathways. Numerous papers state that whereas the genomic channels are expected to have a prolonged impact lasting hours or even days, the nongenomic routes are expected to give quick analgesic and antihyperalgesic effects in a matter of minutes.(26,27,28,13). Two glucocorticoids, dexamethasone or methylprednisolone, have been shown to provide long-lasting postoperative opioid sparing and pain relief for up to three days with a single dose. It seems unlikely that the about 36-hour duration of methylprednisolone's physiologically mediated anti-inflammatory activity is the only reason for this enduring effect. It is believed that a reduction in central sensitization, which in turn lowers postoperative hyperalgesia, is connected to the prolonged analgesic effect and reduced opioid intake after surgery(1,2).

Central opacity, hypertension, hyperglycemia, proximal myopathy, inadequate wound healing, and heightened susceptibility to infection are among the adverse effects of dexamethasone. These adverse effects must be considered while giving this medication.

METHODS

The research carried out at Al-Yarmouk Teaching Hospital in Baghdad, Iraq, was granted approval by the ethics

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committee of the Iraqi Board Council. Written informed consent was obtained from all 80 patients, aged 15-30, who were involved in this double-blind, placebo-controlled clinical trial. The trial commenced on October 1, 2011, and concluded in May 2012.

All of the patients were eligible for inguinal hernia surgery and were ASA I. A history of alcohol or drug abuse, morbid obesity or severe underweight, significant renal or hepatic disorders, opioid allergies, and patients with a common cold were among the patients excluded from the study. Neither were patients who had received psychoactive drugs, antiemetics, antihistamines, steroids, opioids, sedatives, or any kind of analgesics less than one week prior to the operation. The research did not include any patients who fulfilled the aforementioned exclusion criteria. Standard patient monitoring was commenced and intravenous cannulation was carried out. A 30 ml/kg/hr glucose 5% solution was given to each subject throughout the procedure. Dexamethasone was given to them in four dose groups at random:

Twenty patients in group one were given a modest dosage of 0.1 mg/kg.

1. An intermediate dosage of 0.2 mg/kg was given to group two (20 patients).

2. A high dosage of 0.25 mg/kg was given to group three (20 patients).

3. The control group, consisting of twenty patients, was given normal saline.

Following induction, each patient received 0.002 mg/kg of fentanyl, 4-6 mg/kg of sodium thiopental was used to induce anesthesia, and 0.5 mg/kg of atracurium was used to ease endotracheal intubation using a cuffed tube of the proper size. In order to maintain anesthesia, 100% oxygen, 1.5% halothane, and regulated breathing were used. Throughout the research period, there were no reports of instances of delayed recovery. Participants who were incompatible with the anesthetic drugs used in the research were not allowed to participate. When a patient could elevate their head for five seconds and obey spoken orders, they were extubated. After the mouth and throat were thoroughly suctioned, the patient was extubated. Following that, the patients were moved to the post-anesthesia care unit, where they were observed for two hours before being sent back to the ward for more monitoring. Vital sign monitoring was maintained throughout the procedure, and intravenous fluid delivery was continued at the same pace. The purpose of the research was to evaluate, while accounting for possible drug side effects, the effects of various Dexamethasone dosages on patients having inguinal hernia repair surgery.

In the recovery room following anesthesia, patients were asked to rate their pain during the first four hours using a numerical visual analogue pain scale (VAS) with 0 denoting no pain and 10 denoting the highest possible pain. This assessment was done upon initial arrival and then at regular intervals every thirty minutes. The pain ratings on the visual analogue scale (VAS) for both resting and moving discomfort, as well as the amount of time before the patient requested analgesic medicine for the first time, were scrupulously recorded by an unbiased observer. An anesthesiologist who was not engaged in direct supervision, data collection, patient recruitment, or evaluation procedures carefully prepared the drugs used in the trial according to a published protocol. The study medications were diluted in 10 milliliters of normal saline solution and put into syringes that were labeled with the patient's study number. The attending anesthesiologist administered the medications, not knowing what was specifically in the syringe. The chosen research medication was infused intravenously over the course of one minute after the endotracheal intubation process. The infusion's finish was chosen as the specified time zero for all evaluation and observation procedures that followed. Complete demographic data about the patients, such as the moment the patient reported pain for the first time, the length of the surgery, and the time the first analgesic was given, were all carefully recorded and kept for additional review and examination.

RESULT

Eighty patients were involved in the research, with ages ranging from 15 to 30 years. The investigation focused on the perioperative impact of dexamethasone following inguinal hernia repair. It was observed that there were no significant variations in the statistical characteristics of patients and the duration of surgical procedures among the four groups (G1 displaying 27 minutes, G2 displaying 29 minutes, G3 displaying 29 minutes, and G4 displaying 29 minutes) as illustrated in table 1.

Table 1 Comparison between different doses with time of operation

G1 (0.1mg/kg)	G2 (0.2mg/kg)	G3 (0.25mg/kg)Placebo	G4	
Time of operation (minute)	27.25±6.34(18.0-41.0)	29.35±5.72(22.0-40.0)	29.40±6.64(20.0-40.0)	29.45±4.38(24.0-39.0)
P value compared to 0.2mg	0.210	0.951	0.978	-
P value compared to 0.25mg	0.301	0.980	-	-

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P value compared to control	0.278	-	-	-
*p value less than 0.05 = significance				

Table 1.

The very significant correlation between the use of different dexamethasone doses and the pain score (pain score (0-10) in G1 6.6, G2 4.6, G3 4.3, and G4 8.1 is shown in Table 2.

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Table 3 Comparison between different doses of dexamethasone on the time for first analgesia admin				
DexamethasG1 (0.1mg/kg)	DexamethasG2 (0.2mg/kg)	DexamethasG3 (0.25mg/kg)	PlaceboG4	
Type of pain score (0-10) during the first hour.	6.65±1.09(5.0-8.0)	4.60±0.82(3.0-6.0)	4.35±1.04(2.0-6.0)	8.15±0.99(5.0-9.0)
P value compared to control	0.0001*	0.0001*	0.0001*	-
P value compared to 0.25mg	0.0001*	0.404	-	-
P value compared to 0.2mg	0.0001*	-	-	-
*p value less than 0.05 = significance				

Table 2.

DISCUSSION

The use of the corticosteroid Dexamethasone, which is often used perioperatively to lessen postoperative nausea and vomiting, is the subject of debate. Our comprehensive analysis has yielded some significant conclusions. Initially, 0.2 mg/kg of intermediate-dose dexamethasone was shown to exhibit considerable opioid-sparing advantages and to dramatically lower early and late pain levels in both stationary and moving individuals. Similarly, a high-dose of dexamethasone (0.25 mg/kg) reduced pain ratings and also showed similar opioid-sparing effects. The intraoperative administration of low-dose Dexamethasone, on the other hand, at 0.1 mg/kg did not significantly alter the requirement for opioids. The findings suggest that a complete pain treatment plan to reduce postoperative discomfort may include a single systemic dose of dexamethasone given prior to surgery.

Our findings have important clinical ramifications since lower dosages of dexamethasone are often given intraoperatively during anesthesia induction to lessen postoperative nausea and vomiting. Moderate doses of dexamethasone (i.e., 0.2 mg/kg) may be helpful in lowering the incidence of nausea and vomiting, decreasing the need for analgesics, and minimizing postoperative pain. These outcomes are in line with the typical half-hour to hour-long interval that dexamethasone requires to start working fully.

The high-dose Dexamethasone cohort did not demonstrate a statistically significant benefit in terms of opioid-sparing effects when compared to the intermediate-dose group. The low-dose group was unable to achieve statistical significance, despite the fact that all three Dexamethasone dosage groups had similar decreases in point estimates. Notably, our analysis provided compelling evidence that a single perioperative Dexamethasone dose did not seem to slow down wound healing or raise issues with dosage restrictions, such as wound infections.

The operations in Iraq required less time than those in Spain, as was evident when our research was compared with that of Dr. Oliver (1). This discrepancy could be explained by the fact that Iraq performs open surgery for repairs, whilst Spain employs laparoscopic techniques. Furthermore, an analysis of the various pain scales indicates that laparoscopic procedures result in more discomfort during the procedure because of the combination of the abdominal gas infusion (CO2) and the surgical approach (12).

The timing of the patient's first analgesic dose is very accurate, according to Dr. Oliver's research. This accuracy might be attributed to the patient-controlled analgesia (PCA) device, which has shown to be more accurate than our own practice's methodology. Note that Dr. Oliver's work raises the possibility that a decrease in postoperative pain might lead to a shorter hospital stay, even if our current study could not prove this point. Rather than how dexamethasone would impact pain management down the line, our focus was primarily on how it alleviated pain immediately. Our comprehensive analysis raises significant issues that need more research.

Above all, further study is needed to understand the effects of high and low preoperative dexamethasone doses on

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postoperative pain.

Second, it's critical to carefully consider high-dose dexamethasone side effects, such as wound infections and healing issues, particularly in open surgical procedures. These are significant aspects that need more examination to further our understanding of clinical pain treatment strategies.

Research into the effects of dexamethasone on chronic postoperative pain is considered relevant since acute pain may contribute to the development of chronic pain. More investigation into the effects of dexamethasone is required in order to comprehend its role in the long-term treatment of postoperative pain. In order to optimize patient care and recovery outcomes, it's also critical to look at the relationship between the length of hospital stay and the reduction in pain after surgery. By examining this link, medical practitioners may be able to discover strategies for lowering postoperative pain and raising the overall level of patient recovery.

In addition, it is crucial to stress in clinical practice that appropriate treatments, such dexamethasone injections, may lessen the negative effects of opioids. The investigation's findings provide significant new information on the potential benefits of dexamethasone in the management of postoperative pain and the avoidance of issues related to opiate usage. Extensive randomized clinical studies are necessary to establish the validity and generalizability of the results obtained from this work. To improve patient outcomes and evidence-based therapy, it is essential to validate the safety and efficacy of dexamethasone across a variety of dosage levels and demographics of patients.

CONCLUSION

The results suggest that low-dose intraoperative dexamethasone does not seem to have effects that spare opioids after surgery. On the other hand, high-dose dexamethasone at 0.25 mg/kg during surgery has benefits that reduce pain following surgery and save opioids. Nonetheless, the advantages of dexamethasone at a moderate dosage of 0.2 mg/kg seem to be on par with or even higher than those of large dosages. An intermediate dose of dexamethasone is recommended as a safe and effective multimodal pain management method for surgical patients. More research and clinical trials are required to confirm these findings and optimize the use of dexamethasone in postoperative pain control strategies.

Recommendation

We suggest enhancing the representativeness of the study sample through the selection of a larger dataset, increased number of patients, consideration of diverse average body weights among patients, utilization of various types of operations, documentation of both acute and chronic pain levels, and evaluation of the capacity to reduce discharge time from the hospital. These adjustments are crucial to obtaining more precise and reliable outcomes concerning the sensitivity and specificity of each pertinent factor.

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