*MAR Anesthesia and Pain Management (2024) 1:1*
*Research Article*

# Segmentary Cesarea: Postoperative Analgesic Efficacy of Intrathecal Morphine (75mcg Vs 100mcg): Comparative Study

Joseph Alejandro Veraza Almeida *[1], Mariam Alejandra Martínez Gutiérrez [2], Pedro Angulo [3]

*1,2,3. University Hospital of Caracas. Specialization Course in Anesthesiology*.

***Correspondence to:** Joseph Alejandro Veraza Almeida, Professor Emergency Medicine, KCGH, Bangalore.

## Copyright



Received: 01 February 2024

Published: 20 February 2024

## *Abstract*

*Postoperative analgesia provides faster rehabilitation, improves patient satisfaction, and reduces hospitalization time.*

***Objective**: To compare the analgesic efficacy of two doses of intrathecal morphine (75mcg vs 100mcg) for postoperative analgesia in segmental cesarean sections.*

***Methods:** An analytical, experimental, comparative, prospective, random and double-blind study in which the patients were divided into two groups A (75 mcg) and B (100 mcg) administered a mixture of bupivacaine 0.5% 7.5 mg plus morphine in an isobaric to perform a segmental cesarean section. Postoperative Pain (POP) was evaluated through the Visual Analogue Scale (VAS) at 0, 4, 8, 12 and 24 hours. We recorded rescues with NSAIDs and / or parenteral morphine as well as maternal- newborn.*

***Results:** in the evaluation of the POP all patients had a similar behavior with p> 0.05. In the rescue with NSAIDs group A merited 41% and in group B 37% with p> 0.5. There were no differences between groups as adverse effects and neonates were born without complications with shut down greater than 7 points at birth and at 5 minutes.*

***Conclusions**: intrathecal morphine 75mcg or 100mcg provides the same quality of analgesia with the same incidence of maternal adverse effects and No effects on the neonate.*


***Keywords:** segmental Caesarean, intrathecal morphine, postoperative pain.*

## Introduction

Postoperative analgesia provides faster rehabilitation, improves patient satisfaction, and reduces hospitalization time. In obstetrics, postoperative analgesia is important because postpartum women with pain have difficulty ambulating and may adopt analgesic positions that make it difficult to initiate breastfeeding. Furthermore, endocrine disturbances and stress resulting from pain can interfere with breastfeeding (1).

**Statement and delimitation of the problem**

Surgical pain after cesarean section interferes with the mother-child relationship in the first days of the baby's life, with negative consequences for this important couple, in addition to the effects of untreated postoperative pain having well-known harmful results, so that post-cesarean section analgesia is of great relevance. Experimental studies demonstrated that opioids had guaranteed potential as analgesia inducers when injected into the neuraxial space, basic and clinical research has appeared worldwide.

Opioids via the neuraxial route diametrically transformed the history of postoperative analgesia. Morphine, a pure μ receptor agonist, was introduced into the clinic more than 200 years ago. It is the opioid with which all analgesic drugs are compared, and it continues to be the most used narcotic in neuraxial postsurgical analgesia (2).

One of the areas that the anesthesiologist faces most frequently is obstetrics, which in addition to treating a large number of patients, is very controversial in terms of management lines. Advances in the area of anesthesiology have generated different innovative and safe techniques in this field; therefore, postoperative pain management should not be the exception.

Acute pain due to a surgical procedure must be viewed differently, since the use of analgesic drugs can have an impact on the maternal-fetal binomial and the newborn.

The control of postoperative pain in patients who have undergone a cesarean section is an important area, since an attempt has been made to implement an analgesic technique that causes minimal side effects but that provides good quality and duration, to have a rapid recovery. pain relief, good recovery and decreased hospitalization costs.

In the case of pain during a cesarean section, the surgical incision initiates the release of mediators, stimulating peripheral nociceptors and activating A delta and C afferent fibers. After surgery, uterine contractions activate mechanoreceptors, releasing mediators responsible for producing pain, including: potassium, hydrogen ions, lactic acid, bradykinin, histamine, prostaglandins E1 and E2, thromboxanes, cholinergic, adrenergic, dopaminergic, serotonergic systems; in addition to mediators of cellular immunity and the inflammatory process (3).

Postoperative pain relief after segmental cesarean section remains an unsolved problem (2). For this reason, the search is still underway for an effective drug for the management of postoperative pain, considering that drug that allows adequate analgesia, with minimal need for other medications for rescue analgesia, that

presents few adverse effects, and ideally favors to the recovery of the patients, in addition to being an accessible and economical drug.

It is currently known that the use of intrathecal morphine is the cornerstone to achieve effective analgesia; defining this term as that state where the patient has no pain or mild pain that allows carrying out daily activities with timely social reintegration after a surgical injury.

Consequently, the quality of analgesia and the incidence of side effects may vary according to the dose of intrathecal morphine used. In this sense, the research sought to resolve the following question: What is the effective dose of intrathecal morphine (75mcg vs 100mcg) for postoperative analgesia in patients undergoing segmental cesarean section? This study was carried out in the Anesthesiology Department of the University Hospital of Caracas (HUC) from January 1 to June 1, 2022. In charge of postgraduate residents of the Anesthesiology Department of the HUC, with obstetric patients undergoing cesarean section. segmental.

**Rationale and importance**

The treatment of postoperative pain in cesarean sections usually does not differ from pain management in open lower abdominal surgery procedures. Laparatomy constitutes a major aggression on the patient, which can translate into longer convalescence, and in many cases, increased morbidity derived from prolonged bed rest.

In the literature review, no major differences were found between pain treatment strategies in gynecological surgery and obstetric surgery, even between postoperative pain management strategies in general (4). However, it should be noted that among the postoperative pain strategies in patients undergoing segmental cesarean section, they may be a bit difficult due to the presence of the mother-neonate binomial, therefore an analgesic plan must be devised that is beneficial for the mother, but without affecting the well-being of the newborn.

Currently, morphine is the only opioid approved by the Food and Drug Administration (FDA) for intrathecal administration. In recent years, low-dose intrathecal morphine has become very popular for postoperative analgesia (5).

The application of low-dose intrathecal opioids is a safe, effective, and relatively inexpensive modality for the routine management of acute postoperative pain after a wide variety of surgeries. Intrathecal morphine

has been used for several surgical procedures, including major vascular surgery, hip arthroplasty, abdominal surgery, cholecystectomy, obstetric surgery, and normal childbirth.

This drug is a suitable selection as a neuraxial opioid because the duration of action of lipophilic opioids (sufentanil and fentanyl) is short, usually less than 6 hours, compared with 24 hours for morphine.

The peak of the analgesic effect of intrathecal morphine appears after 4 to 7 hours and therefore preoperative administration produces maximum analgesia during the period after surgery (5).

A single dose of intrathecal morphine administered at the time of surgery is easy to maintain and provides good neuraxial analgesia during the first postoperative day, and serves as an effective therapy until the patient can have oral analgesia. The analgesia produced by intrathecal morphine is suitable for pain relief after many different types of surgery at doses ranging from 0.025 to 20 mg. However, doses exceeding 0.5-1 mg are associated with a marked increase in adverse effects including respiratory depression. In an attempt to limit adverse effects, a low dose of opioids (approximately <0.3 mg intrathecal morphine) has been suggested (5).

The single dose is usually sufficient for postoperative analgesia, including major orthopedic surgery. When exploring the literature and the studies carried out, the advantages of using intrathecal morphine for postoperative pain management in urological surgeries, lower abdominal surgeries, cesarean sections and orthopedic surgeries are found with a low rate of secondary events at doses greater than 100 micrograms, however In Venezuela there are no conclusive data regarding the use of intrathecal doses of morphine evaluating its analgesic effectiveness in patients undergoing segmental cesarean section(5).

Due to the above, the researcher considered that this work is important and its performance was justified in view of the population of obstetric patients at the HUC, to whom the results obtained can be applied in daily anesthetic practice. Furthermore, it is a pioneering study, since there are no indexed publications at the institutional or national level, so it is expected to serve as a start and stimulus for future research and publications in the Anesthesiology Program of this healthcare center.

## Background

Cortes et al, in 2005 established that intrathecal morphine is an excellent choice to prevent or treat post-cesarean section pain in patients receiving subarachnoid anesthesia. Doses of 100 to 200 µg have been recommended in Caucasian women. However, it has been published that there are no clinical studies of

post-cesarean spinal analgesia with intrathecal morphine in Mexican women (2).

In turn, Vanegas et al. In a prospective descriptive study, they demonstrated that the administration of microdoses (50 mcg) of morphine shows acceptable control of postoperative pain, with a negligible incidence of side effects such as urinary retention, pruritus, nausea and vomiting (5).

Likewise, Egydio et al., in 2012, conducted a comparative study between doses of intrathecal morphine for analgesia after cesarean section and concluded that 50 µg of intrathecal morphine provided the same quality of analgesia as 100 µg, with a lower incidence of side effects. (1).

For their part, Bejar et al., in 2013 demonstrated that 100 µg of intrathecal morphine offers analgesic, obstetric and perinatological advantages compared to its systemic administration. Through an analytical, experimental, prospective, randomized, double-blind study with 152 ASA I and II patients, term pregnant women undergoing emergency and elective cesarean sections, divided into two groups. Group A: hyperbaric bupivacaine 0.5% 2 ml + intrathecal morphine 100 µg; Group B: hyperbaric bupivacaine 0.5% 2 ml + regulated IV morphine. Reason why they concluded that intrathecal morphine at low doses achieves better analgesic quality without major adverse reactions, becoming a valid and safe option (6).

In this order of ideas, Wong JY et al., presented in 2013 a retrospective review, with a sample of 241 patients who underwent elective cesarean section and received 100 or 200 µg of intrathecal morphine, in which the women who received morphine intrathecal doses of 200 µg had less pain compared to morphine at doses of 100 µg. The 200 µg group used fewer opioids in the first 24 hours after surgery. However, women who received intrathecal morphine 200 µg had more nausea and vomiting, which is why they needed to use more antiemetics. Once these results were obtained, the authors of this study concluded that the intrathecal morphine dose of 200 µg provides better analgesia, but with more nausea and vomiting compared to 100 µg of morphine (7).

Likewise, Sharma and Timalsena carried out a comparative study in 2013 at Lumbini Medical College in which a total of 60 cases of cesarean section of ASA classification I or II were performed. All patients received an intrathecal injection of 0.5% (2.5 ml) hyperbaric bupivacaine with 100 micrograms and 200 micrograms of preservative-free morphine. In which the duration of analgesia was prolonged with patients who had 200 µg of morphine and less with those who received 100 µg of morphine, a result that was not statistically significant ($p = 0.09$). The incidence of pruritus, nausea and vomiting was higher in the group receiving 200 µg of morphine, compared to those receiving 100 µg of morphine and was statistically non-

significant (p value 0.09 and 0.373 respectively). In this way, the authors concluded that intrathecal morphine provides satisfactory analgesia (8).

**Theoretical framework**

The International Association for the Study of Pain (IASP) defines pain as: "An unpleasant sensory and emotional experience associated with actual or potential tissue injury, or described as being caused by such injury."

This definition represented a change at the time with respect to the previous ones, by introducing two new concepts: firstly, it considers that pain is not a purely nociceptive experience, but is also made up of emotional and subjective components; Secondly, it can occur without a somatic cause that justifies it (9).

Emphasizing the aforementioned, it can be considered that pain is a multidimensional phenomenon, with sensory, physiological, cognitive, affective, behavioral and spiritual components. Emotions (affective component), behavioral responses to pain (behavioral component), beliefs, attitudes, and in particular spiritual and cultural attitudes regarding pain and its control (cognitive component) alter the way pain is suffered. (sensory component) modifying the transmission of harmful (unpleasant) stimuli to the brain (physiological component) (10).

**Pain classification**

According to pathophysiology, there are two main types of pain: nociceptive and neuropathic. The clinical distinction between one and the other is useful because the therapeutic approaches are different (11).

Nociceptive pain appears when tissue damage activates specific pain receptors, called nociceptors, which are sensitive to noxious stimuli. Nociceptors can respond to stimuli such as heat, cold, vibration or stretch, as well as chemicals released by tissues in response to lack of oxygen, tissue destruction or inflammation. This type of pain can be classified as somatic or visceral, depending on the location of the activated nociceptors.

Somatic pain is caused by the activation of nociceptors present in superficial tissues (skin, mucosa of the mouth, nose, urethra and anus) or in deep tissues, such as bones, joints, muscles or connective tissue. Visceral pain is caused by the activation of nociceptors located in the viscera (internal organs enclosed in

cavities, such as the thoracic and abdominal organs). It can be due to infections, distension from fluids or gases, stretching, or compression, usually from solid tumors.

Neuropathic pain is caused by structural damage and dysfunction of neurons in the Central Nervous System (CNS) or peripheral. Any process that damages the nerves, such as metabolic, traumatic, infectious, ischemic, toxic, or immunological conditions, can cause neuropathic pain. Additionally, neuropathic pain may be due to nerve compression or abnormal processing of pain signals by the brain or spinal cord (11).

According to the duration, acute pain: sudden in onset, felt immediately after the injury and intense, but generally short-lived. It appears as a result of tissue injuries that stimulate nociceptors and generally disappears when the injury heals (12). While chronic pain: is continuous or recurring pain that persists beyond the normal healing time. It may appear as acute pain and persist for a long time or reappear due to the persistence of noxious stimuli or repeated exacerbation of an injury.

**Pain induced by surgery**

After surgical stimulation, the afferents reach the spinal cord and magnify the response of the CNS to new stimuli. The response of spinal neurons is increased and prolonged, which in the absence of this sensitization, only generate small changes in spinal recordings.

There is an increase in neuronal excitability and cutaneous receptive fields, so normally innocuous stimuli are perceived as painful. Injury to peripheral nerve fibers also generates neuronal hyperexcitability and changes in the morphology of the spinal cord. Although activation of nociceptive neurons in the skin and other tissues is the final common pathway of nociception, direct stimulation of free endings is rarely the cause of postoperative pain. For painful transmission there must be an inflammatory process whose mediators facilitate nociceptive transmission (12).

In addition to this series of changes in the recently operated patient, pain usually occurs that may be induced by the surgery but not necessarily by the surgical incision. Damage to muscle fibers sensitizes the CNS, increasing and prolonging the excitability of spinal neuronal reflexes. Once this cycle begins, the neurons of the anterior horn are stimulated, which generates contraction and spasm with an increase in nociceptive afferent. Muscle spasm in stabilized peripheral limbs is almost nonexistent, but it is a common complication in abdominal or thoracic interventions.

These contractures are usually painless, but when frank spasms occur, they can generate pain of sufficient

magnitude to exceed the pain of the incision, and are refractory to treatment with opioids. The position of the patient during surgery, during transfers, in the recovery room or upon reaching his bed can aggravate muscle spasms (12).

Compression pain may occur at contact sites during surgery, and would be related to ischemia of the skin and underlying tissues. More important are pain due to intrasurgical neural compression or traction. Its best treatment is prevention, but if it occurs, the affected limb must be protected against further injuries until the sensory or motor deficit is recovered.

Compared to postsurgical somatic pain, which is usually well identified and located in a specific region of the body with defined characteristics, visceral pain is usually poorly defined temporally and spatially. “Referred” to regions other than the incision area and usually misdiagnosed. It is very common after abdominal and thoracic surgeries due to pleural or peritoneal irritation and poorly defined due to the lack of topographic segmentation of these structures; It adds to the effects and symptomatology of somatic pain, especially in the presence of abdominal or thoracic drainage tubes (12).

Currently there are a series of scales that are used to evaluate pain, including the Visual Analog Scale (VAS): In the visual analog scale, the intensity of pain is represented on a 10 cm line. At one end there is the phrase "no pain" and at the opposite end "the worst pain imaginable." The distance in centimeters from the point of "no pain" to that marked by the patient represents the intensity of the pain. It may or may not have marks every centimeter, although for some authors the presence of these marks reduces its precision (12).

The way it is presented to the patient, whether horizontal or vertical, does not affect the result. It is the most used scale, even in critically ill patients. For some authors it has advantages over others. The patient needs to have good motor and visual coordination, which is why it has limitations in the elderly patient and in the sedated patient (12). A value less than 4 on the VAS means mild or mild-moderate pain, a value between 4 and 6 implies the presence of moderate-severe pain, and a value greater than 6 implies the presence of very intense pain (12).

**Opioids**

Opioids act as agonists of the k receptors, closing voltage-dependent potassium channels and opening calcium-dependent potassium channels (agonists of the m and d receptors), which causes hyperpolarization and a reduction in the excitability of the neuron (13).

The binding of opiates to their receptors stimulates the exchange of guanosine triphosphate (GPT) of the G protein complex, releasing a subunit of said complex that acts on the effector system. In the case of analgesia induced by opioids, the effector system is adenylate cyclase and cyclic-AMP located in the internal part of the neuronal plasma membrane. In this way, opioids decrease intracellular cyclic-AMP by inhibiting adenylate cyclase, an enzyme that modulates the release of nociceptive neurotransmitters such as substance P, GABA or dopamine.

Opioids also act as modulators of the endocrine and immune systems. Thus, they inhibit the release of vasopressin, somatostatin, insulin and glucagon, all due to the blockade of the neurotransmitters GABA and acetylcholine. It is not well known how opiate agonists stimulate stimulatory and inhibitory processes at the same time (13).

From a clinical point of view, stimulation of m receptors produces analgesia, euphoria, circulatory depression, decreased peristalsis, miosis and dependence. The same effects are produced by the stimulation of k receptors, which also produce dysphoria and some psychomimetic effects (e.g. disorientation). Miosis is produced by an excitatory effect on the autonomic segment of the nucleus of the oculomotor nerve, while respiratory depression is due to a direct effect on the center that, in the brain, regulates respiration (13).

Opioid agonists increase the muscle tone of the antral portion of the stomach, the duodenum and large intestine, and the sphincters. At the same time, they reduce gastric, pancreatic and biliary secretions, all of which results in constipation and delayed digestion.

The tone of the urinary bladder also increases with opiate agonists, as does that of the detrusor muscle, ureters, and bladder sphincter, which may cause urinary retention. Other clinical effects that opiates can produce are cough suppression, hypotension, and nausea/vomiting (13).

Morphine is the most important alkaloid obtained from the seeds of the opium poppy or plant, Papaver somniferum. Morphine is the prototype of opiate agonists and is still extracted from opium due to the difficulty of its chemical synthesis. Morphine, in the form of sulfate or hydrochloride, can be administered by multiple routes of administration. Morphine sulfate is a powerful analgesic used for the relief of moderate or severe acute or chronic pain, and is also used as a pre-operative sedative and as a supplement to general anesthesia. Morphine is the drug of choice for the treatment of pain associated with myocardial infarction and cancer. It is also frequently used during childbirth, its effects on uterine contractions depending on the moment in which it is administered (13).

Regarding the mechanism of action, morphine is a potent agonist of μ-opioid receptors. Opioid receptors include μ (mu), k (kappa), and d (delta), all of which are coupled to G protein receptors and act as both positive and negative modulators of synaptic transmission that occurs through these receptors. proteins. Opioid-protein C systems include cyclic-AMP and phospholipase-3C-inositol-1,4,5-trisphosphate. Opioids do not alter the pain threshold of afferent nerve endings to nociceptive stimuli, nor do they affect the transmission of impulses along peripheral nerves. Analgesia is due to changes in the perception of pain at the spinal level caused by binding to the m2, d and k receptors, and at a higher level, to the m1 and k3 receptors. Morphine, like other opiates, does not show an analgesic "ceiling" effect.

Morphine sulfate is administered orally, parenterally, intrathecally, epidurally, and rectally. When administered orally it has between 16% and 33% of the potency seen when administered intravenously. This loss of activity is due to morphine undergoing significant first-pass hepatic metabolization after oral administration. It is absorbed very well through the intestine and, rectally, its absorption is even faster.

Food increases the absorption of morphine. Intrathecal morphine produces a high degree of analgesia in much lower doses than other analgesics, and its clearance is also slower. Thus, an intrathecal dose of 0.2 to 1 mg causes sustained analgesia for up to 24 hours. When intrathecal administration is used, the doses must be much lower: doses equivalent to 10% of epidurals are sufficient to achieve the same analgesic effects.

The analgesic effects of morphine cannot be predicted based on plasma levels, although for each patient there is a minimum analgesically effective plasma concentration. The response of patients to morphine depends on age, physical and mental status, and whether they have been medicated with opiates on other occasions (13).

Morphine is primarily metabolized in the liver by cytochrome P450 2D6 enzymes, but is also partially metabolized in the brain and kidneys. The main metabolites are 3-glucuronide, 6-glucuronide and 3,6-glucuronide. If very high doses of morphine are administered, the 3-glucuronide antagonizes the effects of morphine, producing hyperalgesia and myoclonus. This metabolite is believed to be responsible for the development of tolerance to morphine. In contrast, the 6-glucuronide metabolite is a more potent analgesic than morphine itself.

Likewise, it is eliminated in the form of the previous conjugates through the urinary and bile routes. 90% of the administered dose is eliminated in the urine within 24 hours, while 7-10% is eliminated in the feces. In patients with renal dysfunction, an accumulation of metabolites may occur with a corresponding increase

in toxic effects (13).

It is important to mention that the administration of intrathecal morphine is related to adverse effects, such as nausea, vomiting, pruritus, urinary retention, the most important and fearsome of which is respiratory depression. However, experiments in animals and humans indicate that hydrophilic opiates, such as hydromorphone or morphine, bind more strongly to specific receptors than lipophilic ones, such as alfentanil, fentanyl and sufentanil, which is explained by the selectivity of the spinal cord and the their bioavailability. These differences are attributable to pharmacokinetic and pharmacodynamic differences between the 2 groups of opioids; It is more difficult for lipophilics to reach and remain in sufficient concentrations at the site of action due to their sequestration by epidural fat and rapid plasma clearance from the epidural and intrathecal spaces. Likewise, its supraspinal effects are early. In contrast, the opposite properties of morphine make it the drug of choice for the treatment of acute postoperative pain. Progesterone and other steroid hormones act as chemical messengers in a wide range of target tissues, to produce a slow genomic response through the activation of nuclear receptors, or a rapid response through their action on cell membrane receptors. Pregnancy occurs with high levels of progesterone, which, by stimulating the respiratory center, increases minute ventilation, decreases PaCO2 and produces a slight respiratory alkalosis. Progesterone levels fall abruptly with the removal of the placenta and reach preconception levels on average by the fifth day postpartum. Experimental evidence suggests that progesterone and other steroid hormones may be involved in the central neural control of respiration by exerting their work on the respiratory rhythm-generating center, through a direct effect on GABA, and indirectly in the modulation of respiratory motor neurons, by acting on some neuromodulatory systems, particularly the serotonergic system (17).

Due to this, it is worth highlighting that a large number of studies have been carried out, with different doses, increasingly lower and in various scenarios, which allow us to affirm that with the low quantities (50 to 150µg) used today there is no difference in the incidence of respiratory depression when neuraxial opioids are compared with parenteral opioids; This is also mentioned in the guide of the American Society of Anesthesiology (ASA) on the subject. But there is a population of patients who could be "protected" from respiratory depression due to high levels of progesterone, a powerful stimulant of the respiratory center. These are obstetric patients, and in them anesthesia or analgesia, spinal or epidural, should be accompanied by the administration of morphine as a way to contribute to the solution of the problem of postpartum pain that affects more than a third of maternal women (17).

It is also important to mention that although exact descriptions of the anatomy of the spinal canal have been available since the 19th and early 20th centuries, the use of modern radiological imaging technology has provided some indication of new and important anatomical and pathophysiological aspects in intrathecal anesthesia. (5).

The spinal cord lies in the vertebral canal which is surrounded by pia mater, a highly vascularized membranous layer that closely covers the spinal cord and brain. The outermost layer is the dura mater and the innermost layer is the pia mater. Between these two layers is the arachnoid, which is a delicate avascular membrane that is attached to the dura mater.

The arachnoid currently represents the most important and active barrier, delineating the region of interest for intrathecal anesthesia (the subarachnoid space). It is made up of 2 portions: a compact and lamellar portion that covers the inner surface of the dural sac, and a trabecular portion that extends like a spider web around the pia mater. The arachnoid is not just a passive container for the cerebrospinal fluid; but it actively participates in the transport of anesthetic agents and neurotransmitters that are involved in the spinal block.

The subdural space contains the spinal nerves, spinal cord, and cerebrospinal fluid (CSF). The CSF is a crucial factor determining the effects of intrathecally administered agents, because all drugs injected into the subarachnoid space are diluted in the CSF before reaching their effector site in the spinal cord (5).

There is considerable interindividual variation in total CSF volume, demonstrated by MRI, with lumbosacral CSF volumes ranging from 28 to 81 milliliters. Lumbosacral CSF volume is the most important factor affecting peak sensory blockade and duration of spinal anesthesia. Although there is some correlation between body size and CSF volume, volume cannot be reliably estimated with simple anthropometric characteristics. Nevertheless, these findings support clinical evidence that the administration of intrathecal anesthesia is determined primarily by the amount of local anesthetic solution injected into the subarachnoid space.

On the contrary, if the total dose remains constant, the volume and concentration of the injected medication has no clinical significance of impact on the characteristics of the block, even the total injected dose influences the minimum effective concentration of the local anesthetic required. to produce surgical anesthesia (5).

The mechanism of action of local anesthetic solutions is based on their ability to produce conformational changes in voltage-gated sodium channels. This results in a reduction or blockage of passage through

sodium channels, blocking the conduction of the electrical impulse through the axon. The traditional explanation of the mechanism of nerve block induced by intrathecal injection is the complete blockade of the conduction of impulses from the periphery to the supraspinal nucleus. However, it is well demonstrated that intrathecal injection of local anesthetics also interferes with the function of other neurotransmitters such as substance P or gamma aminobutyric acid. It has also been shown that spinal anesthesia produces sedation, which is related to the maximum sensory level achieved (5).

During pregnancy, the movements of drugs and their clinical effects on the central nervous system (CNS) present alterations based on two main factors: hormonal and non-hormonal. Studies carried out in pregnant animals have shown a decrease in anesthetic and analgesic requirements in the face of painful stimuli. Different endogenous substances and possible mechanisms have been examined to explain the formation of an analgesic condition during pregnancy.

Progesterone for several decades has been identified as responsible for this phenomenon; it has a sedative effect and in large doses induces loss of consciousness in humans. One of its metabolites, 5-alpha-progesterone (5AP), administered intrathecally in rats, enhanced the analgesic effect of sufentanil, the possible analgesic route being through stimulation of opioid receptors. The plasma levels of progesterone during pregnancy are 53 times higher compared to non-pregnant women, while the increase in cerebrospinal fluid (CSF) is 10 to 20 times higher; this increase is less pronounced during the immediate postpartum period.

Among other substances associated with pain modulation during pregnancy, we have: beta-endorphins, enkephalins and serotonin. Until now, the mechanism of betaendorphins is not clear; its elevation during pregnancy is not related to progesterone levels, it is enhanced by the placenta and by pain during labor.

Subarachnoid administration of betaendorphins greater than physiological concentrations produces effective analgesia during labor. The data show the presence of a significant amount of substances to lower the pain threshold and adjust the doses of both analgesics and anesthetics, this last point establishes the other major cause of changes in pharmacodynamics during pregnancy. On the other hand, the subarachnoid space also undergoes modifications during pregnancy; a change in the density of the CSF that affects the dispersion and behavior of drugs is observed during pregnancy. The density values indicated for the CSF expressed in average standard deviation are 1.00030 ± 0.00004 g/mL (1.00049 ± 0.00004 g/mL in the non-pregnant woman), this effect is particularly attributed to high levels of estrogen and progesterone, which can be observed from the first trimester of pregnancy (14).

The mechanism is not well known, but it is thought that progesterone would physiologically alter the activity of potassium-ATPase and sodium in the choroid plexuses, modifying CSF production. This variation in density in the CSF determines other limits for terms such as hypobaricity and hyperbaricity, requiring a smaller amount of dextrose bound to the solution containing local anesthetics to raise it from isobaric to hyperbaric, or isobaric drugs that can behave discretely like hyperbaric drugs.

Although a correlation has not been achieved between CSF progesterone levels and dispersion of spinal anesthesia, the elevation of this hormone generates electrical and excitatory changes in both the central and peripheral nervous system, causing increased sensitivity to local anesthetics (LA) (14).

According to medical literature, cesarean section is an obstetric intervention in which the fetus is extracted abdominally (Laparotomy) through uterine opening (Hysterotomy), which causes high rates of postoperative pain in the range of the visual analogue scale. EVA 7/10, in small doses intrathecal morphine offers high rates of analgesia for up to 24 hours and more.

**Evaluation of neonatal depression – APGAR scale**

Until now, there is no indexed publication that reports a relationship between APGAR and the administration of intrathecal morphine. However, from an ethical point of view in the study it is important to evaluate to determine fetal well-being.

The APGAR test is a rapid and practical method to objectively and systematically evaluate the newborn immediately after birth, and its purpose is to help identify those who require resuscitation and predict their survival in the neonatal period. Sixty seconds after the baby is born (without considering the placenta), the 5 signs are evaluated, and each is assigned a score of 0, 1 or 2. These signs are heart rate which when absent the score is 0, when it is less than 100 the score is 1 and when it is greater than 100 the score is 2. The respiratory effort when the peak is absent is 0, when it is slow and irregular the score is 1 and when it is good and there is crying the score is 2. The muscle tone, when it is flaccid, is 0, when there is some flexion of the extremities the score is 1 and when there are active movements the score is 2. The color, when it is pale blue the score is 0, with the body pink but blue extremities the score is 1 and when the body is completely pink the score is 2. Finally, the response to probing through the nostrils is evaluated and when there is no response the score is 0, when there is a grimace to some gesture the score is 1 and when there is a cough or sneeze the score is 2 (15).

A total score of 10 indicates an infant in the best possible condition. Full-term newborns with normal cardiopulmonary adaptation should score 8-10 at 1 minute and 5 minutes. Scores of 4-7 require close attention and observation to determine if the baby's status will improve and to determine if any pathological conditions resulting from childbirth or intrinsic to the infant with which he or she was born are contributing to the low APGAR score. By definition a score of 0-3 requires immediate resuscitation. The APGAR score at one minute may then indicate the need for cardiopulmonary resuscitation. However, if the infant immediately shows signs of asphyxiation at birth, resuscitation will begin immediately at birth, since the first APGAR score is only obtained in the first minute of life. Traditionally, the test is always repeated after 5 minutes to follow the baby's situation, especially if any resuscitation maneuver has been required. Additional scores continue to be obtained at 10, 15 and 20 minutes at the pediatrician's discretion in case the newborn's condition is still not satisfactory at 5 minutes and successively. It is important to note that the APGAR test was not designed to predict a child's neurological development. For example, APGAR is normal in the majority of patients who have subsequently developed cerebral palsy; and the incidence of cerebral palsy is low in infants with scores of 0-3 at 5 minutes. The APGAR then helps us more to determine which infant requires resuscitation at birth and has value in predicting neonatal death, not subsequent neurological development (16).

**General Objective**

To compare the analgesic efficacy of two doses of intrathecal morphine (75 mcg vs 100 mcg) for postoperative analgesia in patients undergoing segmental cesarean section.

**Specific Objectives**

1. Determine the degree of pain through the VAS during the immediate postoperative period of segmental cesarean section in each group of patients.
2. Assess the need for rescue analgesia with NSAIDs and parenteral morphine in each group of patients.
3. Determine the incidence of urinary retention, pruritus, nausea, vomiting and other effects in the immediate postoperative period according to the patient group.
4. Record the incidence of neonatal depression at birth and at five minutes using the APGAR scale.

### Ethical Aspects

To comply with the legal requirements related to all research work, authorization was requested from the Bioethics Committee and the Department of Anesthesia of the University Hospital of Caracas. The patients of the Obstetrics Service of the University Hospital of Caracas who underwent segmental cesarean section and who met the inclusion criteria were informed and their informed consent was requested.

## Methods

### Type of study

An analytical study was carried out with an experimental, comparative, prospective, randomized and double-blind design.

### Population and sample

The population studied was represented by all those patients who attended the Obstetrics Service of the University Hospital of Caracas (HUC), scheduled for segmental cesarean section, during a period of 6 months between January and June 2022.

It is estimated that for the last half of 2020, approximately 700 patients underwent segmental cesarean section, according to data provided by the Obstetrics Service. Based on these data, a non-probabilistic, intentional sample was selected, made up of those patients undergoing segmental cesarean section, who agreed to participate voluntarily after signing the informed consent and who met the following inclusion criteria.

**Inclusion criteria were considered:**

- Older than 18 years
- ASA II - III patients.
- Patients undergoing segmental cesarean section
- Body mass index less than 30 Kg/m2.

**Patients with:**

- Patient with suspected or known allergy to the study drug or the drugs to be used during the anesthetic act.
- Patient's refusal to participate in the study
- Atopic patients
- Patients with maternal comorbidities: placenta previa, placental abruption, hypertensive disorders of pregnancy, heart disease, kidney disease, CNS diseases
- Pregnant patients with fetal pathologies

**Procedures**

Prior approval by the Academic Committee of the Chair of Anesthesiology and the Bioethics Committee of the University Hospital of Caracas, Coordination of Postgraduate Studies of the Faculty of Medicine of the Central University of Venezuela (UCV) and the signing of the written informed consent of the patients. , a pilot study was carried out whose objective was to compare the analgesic efficacy of two doses of intrathecal morphine (75mcg vs 100mcg) for postoperative analgesia in patients undergoing segmental cesarean sections.

The patients were evaluated 2 to 4 hours before the surgical procedure in the delivery room of the Obstetrics Service. Two peripheral lines were cannulated using an 18- to 20-gauge hypodermic needle. Pre-anesthetic medication was administered if they reported not being allergic to the following drugs: ketoprofen 100 mg, ranitidine 50 mg, metoclopramide 10 mg. The patients were divided into two groups shaped with the letters A and B.

To maintain double blinding, the anesthetic technique was performed by anesthesia residents who were not involved in the research study; they chose the dose at their discretion. The collection of the sample data was carried out by the researcher, who asked the residents to locate the copy of the anesthesia history and thus record the dose used. The letter A was assigned to the group that was administered 75 mcg and the letter B to the group that was administered 100 mcg.

The patient was transferred to the operating room, non-invasive blood pressure was monitored, continuous electrocardiogram with a three-lead cardioscope (EKG), pulse oximetry using a Datex Ohmeda Cardiocap/5

– multiparameter monitor (6061-0000-164- 01).

The anesthetic mixture was made based on 7.5 mg of 0.5% bupivacaine, plus the doses of morphine to be compared, said mixture was isobaric, subsequently a spinal neuraxial anesthetic technique was performed, sitting position, prior asepsis and antisepsis, placement From sterile fields, the L3-L4 intervertebral space was located taking the posterosuperior iliac spine as a reference, 1% lidocaine-type local anesthetic was infiltrated; To approach the subarachnoid space, a number 25 or 27 Gauge Quincke needle was used until the progressive outflow of CSF was evident with the subsequent instillation of the anesthetic mixture.

At the beginning of the surgical procedure, crystalloids of the physiological saline or ringer's lactate type were administered intravenously at 30 ml per kg of weight and blood losses were replaced with crystalloids, if the patient was not anemic (Hemoglobin less than 7g/dL) at 3ml. of crystalloids for each ml of blood lost.

Once the newborn was removed and the delivery had taken place, 30 international units of oxytocin diluted in 500 ml of physiological solution were administered intravenously.

Once the neonate was removed, the APGAR was jointly evaluated at minute 1 after birth and at 5 minutes and these data were recorded.

Once the surgical procedure was completed, the patient was transferred to the Post-anesthesia Care Room (PACU), where she was cared for by nursing staff, and monitored with non-invasive blood pressure, pulse oximetry and three-lead electrocardiogram with multiparameter monitor. Doctus – VI (M120583211).

Upon reaching the SCPA, variables such as pain were quantified (through the VAS) at 0 (zero), 4 (four), 8 (eight), 12 (twelve) and 24 (twenty-four) hours. The patient was discharged from the PACU at four hours once she met the criteria for discharge, with pain, nausea, vomiting, pruritus, acute urinary retention being monitored in the Obstetrics Service at eight, twelve and twenty-four hours. These data were collected by the author of the research and reported on the data collection sheet as well as the requirements for NSAIDs and/or morphine as rescue analgesia and the appearance of adverse effects. Analgesic rescue with NSAIDs (ketoprofen) was used when the patient had pain with VAS greater than or equal to 3 and less than or equal to 5; at a dose of 100mg/dose with a maximum dose of 300mg/day. While rescue with opioids (morphine) was performed when the patient had a VAS greater than or equal to 6 at doses of 0.05 mg/kg/dose as many doses were necessary to relieve pain.

**Statistical Analysis**

The data were processed with the PAST statistical program version 2.17c. The adjustment of age to the normal distribution was confirmed with the Kolmogorov-Smirnov test, which is why it is described with the mean ± standard deviation. The results of the VAS, as well as those of the Apagar scale, were described with the median and the interquartile range (difference between the 75th and 25th percentiles). Frequency distribution tables and comparisons between the study groups are presented. The means of the groups were compared with the Student's t test for independent samples or its non-parametric equivalent, the Mann-Whitney test. Proportions were compared with the Z test. All tests were considered significant with a value of $p < 0.05$.

**Human and material resources**

**A.- Materials:**

- Operating rooms, monitoring equipment, anesthesia machines and medical equipment at the University Hospital of Caracas.
- Anesthetic drugs supplied by the Pharmacy department of the HUC Anesthesiology Department.
- Computers.

**B.- Humans:**

- Patients from the Obstetrics Service who will undergo a segmental cesarean section.
- Attending and residents of the HUC Obstetrics Service.
- Residents of the HUC Chair-Service of Anesthesiology.
- Attached to the HUC Department of Anesthesiology.
- Adjuncts and residents of the HUC Neonatology Department.
- Nursing staff belonging to the operating room area.

**C.- Financing:**

- Own and institutional.

## Results

A sample of 240 pregnant patients was studied to whom postoperative analgesia was applied in segmental cesarean sections, distributed equally between the study groups (120 women each) and without statistically significant differences between the groups with respect to age (p>0. 89). All patients in the ASA classification were ASA II (Table 1).

In relation to the degree of pain according to the VAS taken at hours 0 (zero), 4 (four), 8 (eight), 12 (twelve) and 24 (twenty-four) hours of the postoperative period, the Mann U statistic was applied. Whitney by which it could be determined that patients in both groups had similar behavior, which was not statistically significant. 0 hours (p>0.33), 4 hours (p>0.26), 8 hours (p>0.29), 12 hours (p>0.99) and 24 hours (p>0.39). (Table2)

The frequency of mild pain according to the VAS at 0 hours was significantly higher among patients in group B (95.8%, 5 of 120) compared to that of group A (70.8%, 35 of 120), with Z = 1.94 and P = 0.02 (Table 3).

In group A, 50 patients (47%) needed rescue analgesia with NSAIDs and in group B, 45 women (37.5%) required it, without statistically significant differences (Table 4: Z = 0.0; P = 0.50). In none of the groups were there patients requiring rescue analgesia with opioids.

When comparing the incidence of undesirable effects according to the study group, no statistically significant differences were achieved when applying the Z test for comparison of proportions (Table 5).

The comparison of median scores on the APGAR scale at one minute and at 5 minutes did not report statistically significant differences when applying the Mann-Whitney test ($P \geq 0.05$).

The proportion of newborns with APGAR between 8 and 10 points was significantly higher in group B (87.5% versus 54.2%), with statistically significant differences (Table 6: Z =2.02; P = 0.01 ). All of the newborns (both group A and B) were in good condition 5 minutes after being born (Table 6).

| **Age** | **Group A: 75 mcg intratecal morphine (n = 120)** | | **Group B: 100 mcg intratecal morphine (n=120)** | | **P** |
|---|---|---|---|---|---|
| | Frequency | Percentage | Frequency | Percentage | |
| 18 a 19 | 20 | 16,7 | 5 | 4,2 | 0,12 |
| 20 a 29 | 50 | 41,7 | 65 | 54,2 | 0,28 |
| 30 a 43 | 50 | 41,7 | 50 | 41,7 | 0,38 |
| **Age (years) $\overline{X}$ ± D.E.** | 29,17 ± 7,28 | | 28,88 ± 7,15 | | 0,89 |
| **ASA** | Frequency | Percentage | Frequency | Percentage | P |
| ASA II | 120 | 100,0 | 120 | 100,0 | - |
| **Total** | 120 | 100,0 | 120 | 100,0 | - |

Source: Data collection instrument X ± S.A.: Media ± Standard deviation

**Table 1** Characterization of pregnant patients to whom postoperative analgesia was applied in segmental cesarean sections according to age and ASA classification, Anesthesiology Department of the University Hospital of Caracas (HUC), period January 2022-June 2022.

| Time of measurement | **Group A: 75 mcg intratecal morphine (n = 120)** | | | | **Group B: 100 mcg intratecal morphine (n = 120)** | | | | **P*** |
|---|---|---|---|---|---|---|---|---|---|
| | Mín | Máx | Md | RIC | Mín | Máx | Md | RIC | |
| VAS 0 hours | 0,0 | 7 | 1,5 | 2,0 | 0,0 | 4,0 | 1,0 | 3,0 | 0,33 |
| VAS 4 hours | 0,0 | 6 | 3,0 | 3,75 | 0,0 | 6,0 | 4,0 | 4,0 | 0,26 |
| VAS 8 hours | 0,0 | 7 | 2,0 | 3,0 | 0,0 | 9,0 | 1,0 | 3,0 | 0,29 |
| VAS 12 hours | 0,0 | 9 | 0,0 | 1,0 | 0,0 | 5,0 | 1,0 | 1,75 | 0,99 |
| VAS 24 hours | 0,0 | 6 | 0,0 | 0,0 | 0,0 | 4,0 | 0,0 | 1,0 | 0,39 |

*Source: Data collection instrument Min: Minimum. Max: Maximum. Md: Medium.*

*IQR: Interquartile Range = 75th Percentile – 25th Percentile.*

**Mann-Whitney non-parametric test for independent samples*

**Table 2** Comparison of median scores on the VAS at different measurement times, in pregnant patients to whom postoperative analgesia was applied in segmental cesarean sections, Anesthesiology Department of the University Hospital of Caracas (HUC), period January 2022-June 2022.

| Pain intensity | | **Group A: 75 mcg intratecal morphine (n = 120)** | | **Group B: 100 mcg intratecal morphine (n = 120)** | | **P*** |
|---|---|---|---|---|---|---|
| | | Frequency | Percentage | Frequency | Percentage | |
| VAS 0 hour | Mild | 85 | 70,8 | 115 | 95,8 | **0,02**** |
| | Moderate | 30 | 25,0 | 5 | 4,2 | 0,05 |
| | Severe | 5 | 4,2 | 0 | 0,0 | 0,50 |
| VAS 4 hours | Mild | 70 | 58,3 | 55 | 45,8 | 0,28 |
| | Moderate | 50 | 41,7 | 65 | 54,2 | 0,29 |
| | Severe | 0 | 0,0 | 0 | 0,0 | - |
| VAS 8 hours | Mild | 100 | 83,3 | 105 | 87,5 | 0,50 |
| | Moderate | 15 | 12,5 | 5 | 4,2 | 0,31 |
| | Severe | 5 | 4,2 | 10 | 8,3 | 0,50 |
| VAS 12 hours | Mild | 115 | 95,8 | 110 | 91,7 | 0,50 |
| | Moderate | 0 | 0,0 | 10 | 8,3 | 0,23 |
| | Severe | 5 | 4,2 | 0 | 0,0 | 0,50 |
| VAS 24 hours | Mild | 115 | 95,8 | 115 | 95,8 | 0,24 |
| | Moderate | 5 | 4,2 | 5 | 4,2 | 0,24 |
| | Severe | 0 | 0,0 | 0 | 0,0 | - |

*Source: Data collection instrument*

**Z test for comparison of proportions*

***Statistically significant*

**Table 3** Comparison of pain intensity according to the VAS scale at different measurement times, in pregnant patients to whom postoperative analgesia was applied in segmental cesarean sections, Anesthesiology Department of the University Hospital of Caracas (HUC), period January 2022-June 2022.

| Rescue with NSAIDs | **Group A: 75 mcg intratecal morphine (n = 120)** | | **Group B: 100 mcg intratecal morphine (n = 120)** | | **P*** |
|---|---|---|---|---|---|
| | Frequency | Percentage | Frequency | Percentage | |
| Yes | 50 | 41,7 | 45 | 37,5 | 0,5 |
| No | 70 | 58,3 | 75 | 62,5 | |
| Rescue with Opioids | Frequency | Percentage | Frequency | Percentage | P |
| Yes | 0 | 0,0 | 0 | 0,0 | - |
| No | 120 | 100,0 | 120 | 100,0 | |
| Total | 120 | 100,0 | 120 | 100,0 | - |

*Source: Data collection instrument*

**Z test for comparison of proportions*

**Table 4** Comparison of the need for rescue analgesia with NSAIDs and opioids, in pregnant patients who received postoperative analgesia in segmental cesarean sections, Anesthesiology Department of the University Hospital of Caracas (HUC), period January 2022-June 2022.

| Side effects | **Group A: 75 mcg intratecal morphine (n = 120)** | | **Group B: 100 mcg intratecal morphine (n = 120)** | | **P*** |
|---|---|---|---|---|---|
| | Frequency | Percentage | Frequency | Percentage | |
| Pruritus | 30 | 25,0 | 25 | 20,7 | 0,5 |
| Nauseas | 20 | 17,6 | 10 | 8,3 | 0,33 |
| Nauseas, Vomit | 5 | 4,2 | 0 | 0,0 | 0,5 |
| Nausea, Vomit, Pruritus | 5 | 4,2 | 0 | 0,0 | 0,5 |
| Vomits | 5 | 4,2 | 0 | 0,0 | 0,5 |
| Nauseas, Pruritus | 0 | 0,0 | 20 | 16,7 | 0,06 |
| Pruritus, Urine retention | 0 | 0,0 | 15 | 12,5 | 0,11 |
| Nauseas, Vomit, Pruritus, Urine retention | 0 | 0,0 | 5 | 4,2 | 0,5 |
| Vomits, Pruritus, Urine retention | 0 | 0,0 | 5 | 4,2 | 0,5 |
| Urine retention | 0 | 0,0 | 5 | 4,2 | 0,5 |
| None | 55 | 45,8 | 35 | 29,2 | 0,18 |

| Side effects frequency | Frequency | Percentage | Frequency | Percentage | P* |
|---|---|---|---|---|---|
| None | 55 | 45,8 | 35 | 29,2 | 0,18 |
| Mild (1 a 2 times) | 60 | 50,0 | 75 | 62,5 | 0,28 |
| Moderate (3 a 4 times) | 5 | 4,2 | 10 | 8,3 | 0,5 |
| Total | 120 | 100,0 | 120 | 100,0 | - |

*Source: Data collection instrument*

**Z test for comparison of proportions*

**Table 5** Comparison of the incidence of undesirable effects in the immediate postoperative period of pregnant patients to whom postoperative analgesia was applied in segmental cesarean sections, Anesthesiology Department of the University Hospital of Caracas (HUC), period January 2022-June 2022

| APGAR (Score) | **Group A: 75 mcg intratecal morphine (n = 120)** | | | | **Group B: 100 mcg intratecal morphine (n = 120)** | | | | **P*** |
|---|---|---|---|---|---|---|---|---|---|
| | Mín | Máx | Md | RIC | Mín | Máx | Md | RIC | |
| At minute | 7,0 | 9,0 | 8,0 | 1,0 | 6,0 | 8,0 | 8,0 | 0,0 | 0,05 |
| At 5 minutes | 8,0 | 10,0 | 9,5 | 1,0 | 8,0 | 10,0 | 10,0 | 0,75 | 0,09 |

| | **Group A: 75 mcg intratecal morphine (n = 120)** | | **Group B: 100 mcg intratecal morphine (n = 120)** | | |
|---|---|---|---|---|---|
| APGAR Classification | Frequency | Percentage | Frequency | Percentage | P** |
| Good conditions at minute (8 to 10 points) | 65 | 54,2 | 105 | 87,5 | **0,01*** ** |
| Continue assessment and stimulation at 1min (4 to 7 points) | 55 | 45,8 | 15 | 12,5 | |
| Good conditions within 5 minutes (8 to 10 points) | 120 | 100,0 | 120 | 100,0 | - |
| Total | 120 | 100,0 | 120 | 100,0 | - |

*Source: Data collection instrument Min: Minimum. Max: Maximum. Md: Medium.*

*IQR: Interquartile Range = 75th Percentile – 25th Percentile.*

**Table 6** Comparison of median scores on the APGAR scale at one minute and at 5 minutes, in the products of pregnant patients to whom postoperative analgesia was applied in segmental cesarean sections, Anesthesiology Department of University Hospital de Caracas (HUC), period January 2022 - June 2022.

## Discussion

In relation to the demographic variables of the sample, the statistical analysis determined that there were no statistically significant differences between the groups with respect to age. All patients in the ASA classification were ASA II, which was a homogeneous sample.

Regarding the score on the VAS scale, there were no statistically significant differences between the median scores on the VAS scale at the different measurement times. This finding corresponds to another previously published study, such as that of Egydio et al. (1) In 2012, these authors carried out a comparative study and concluded that 50 µg of intrathecal morphine provides the same quality of analgesia as 100 µg.

It was observed that in group A, 50 patients (47%) needed rescue analgesia with NSAIDs and in group B, 45 women (37.5%) required it, without statistically significant differences. In none of the groups were there patients requiring rescue analgesia with opioids. This corresponds to the study published by Wong JY et al (7), in 2013, where they did a retrospective review, with a sample of 241 patients who underwent elective cesarean delivery and received 100 or 200 µg of intrathecal morphine. In which women receiving intrathecal morphine 200 µg had less pain and opioid use was less compared to morphine 100 µg. The 200 µg group used fewer opioids in the first 24 hours after surgery.

When comparing the incidence of undesirable effects according to the study group, no statistically significant differences were achieved, this is similar to the works published by Egydio et al (1), in 2012 and Bejar et al (6), in 2013. Authors concluded respectively that 50 µg of intrathecal morphine provides the same quality of analgesia as 100 µg, with a lower incidence of side effects and that intrathecal morphine at low doses achieves better analgesic quality without major adverse reactions, becoming a valid and safe option.

All of the newborns (both group A and B) were in good condition 5 minutes after being born. At the time of carrying out this research work, there were no previous studies that evaluated the level of neonatal depression due to the use of intrathecal morphine in segmental cesarean section.

It was concluded that the administration of 75 µg of morphine intrathecally in patients undergoing segmental cesarean section provides the same analgesia efficacy as 100 µg with the same low incidence of adverse effects for both the mother and the neonate.

For the development of future studies inherent to this line of research, it is recommended:

1. Consider a larger study sample.
2. Assess hemodynamic variables
3. Evaluate intraoperative and postoperative behavior in terms of intensity of motor and/or sensory blockade.
4. Compare higher doses up to 200 µg to provide single intrathecal analgesia with few maternal-neonatal adverse effects.
5. Determine maternal ambulation and/or breastfeeding time.
6. Administer antiemetics, such as dexamethasone, or an antihistamine to counteract possible adverse effects.

## References

1. Egydio F.A.,Tenóriob S.Estudio comparativo entre dosis de morfina intratecal para analgesia después de la cesárea. Revista Brasileira Anestesiología [Internet] 10 de Enero 2012[citado2013;]. 63(6):492−9. Disponible en: http://www.sciencedirect.com/science/article/pii/S2255496313001128

2. Cortes-BlancoB., Segura-López F., Alba-Viesca H. Analgesia Post Cesárea con Morfina Intratecal: 100 µg versus 200 µg. Anestesia en México [Internet]. 2005 sep-diciembre. [citado 2005Vol.17, No.3, Septiembre - Diciembre]. Disponible en: http://www.anestesiaenmexico.org/RAM7/3/17-3-005.pdf

3. FerreiraL. Efectividad del tramadol por vía peridural o endovenosa para analgesia postoperatoria en pacientes obstétricas. Venezuela 2012

4. GarcíaI.M. Evaluation of the perceived quality regarding pain management after obstetric surgery in female undergoing caesarean operation. Madrid. 2004

5. Vanegas J., Montoya D. Morfina intratecal, un estudio descriptivo prospectivo en el Hospital Universitario Clínica San Rafael. Bogotá; 2012.

6. Bejar J., Santiago G., Enrique D. Comparative study of intrathecal morphine versus intravenous morphine for postoperative analgesia in cesarean section. Hospital Universitario de Maternidad y Neonatología Hospital Universitario de Maternidad y Neonatología. Actas PeruAnestesiol. [Internet]. 2013 julio [citado.

2013;21(1):18-26] Disponible. en: http://sisbib.unmsm.edu.pe/BVRevistas/actas_anestesiologia/v21n1/pdf/a04v21n1.pdf.

7. WongJ.Y., Carvalho B., RileyE.T.Intrathecal morphine 100 and 200 μg for post-cesarean delivery analgesia: a trade-off between analgesic efficacy and side effects. International Journal of Obstetric Anesthesia. [Internet]. 2013. [citado.January 2013; 22(1):36–41] Disponible en: http://www.obstetanesthesia.com/article/S0959-289X(12)00129-X/abstract

8. Sharma N.R., Timalsena P. Intrathecal morphine in combination with bupivacaine: a comparative study following caesarean section. Nepal Medical College Journal[Internet]. 2013. [citado. 2013; 15(1):37-39] Disponible.en: http://nmcth.edu/images/gallery/Original%20Articles/hJ3sqNR%20Sharma.pdf

9. International Association for the Study of Pain (IASP). Pain terms: a current list with definitions and notes on usage. Pain 1986; Suplemento 3: S215-S221.

10. Loeser J.D., Treedi R.D. El dolor en niños, clasificación y manejo. Consenso del dolor Organización Mundial de la Salud [internet]. 2008 julio. [citado abril 2015]; 137(16):17-26. Disponible en: http://www.who.int/medicines/areas/ quality_safety/3PedPain GLs_coverspanish.pdf

11. Jilian M.,Willem S.Estrategias farmacoterapeuticas para el dolor en población pediátrica. Consenso del dolor Organización Mundial de la Salud [internet]. 2008 julio. [citado abril 2015]; 137 (16): 60-76. Disponible en: http://www.who.int/medicines/areas/quality_safety/3PedPainGLs_coverspanish .pdf

12. Pardo C., Muñoz C., Chamorro A.Monitorización del dolor. Recomendaciones del grupo de trabajo de analgesia y sedación de la SEMICYUC. Medicina intensiva [internet]. 2008. [citado abril 20015]. 32 (1):.38-44..Disponible.en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=s0210-56912006000800004

13. P.R.VADEMÉCUM.[internet].Venezuela[citado.2015] Disponible en http://ve.prvademecum.com/index.php

14. Tejada P., Cohen A. Modificaciones fisiológicas de embarazo e implicaciones farmacológicas: maternas, fetales y neonatales. Revista Obstétrica Ginecológica Venezuela 2007; 67(4):246-276.

15. Golergant Davil. El Test de Apgar en el Recien Nacido. Revista de pediatría chilena [Internet] 2012; [Citado en agosto 2016]; 66(2): 220-229. Disponible en: http://www.drgolergant.com/movil/descarga/apgar.pdf

16. Peñaranda Avila Rosse. Atencion y evaluación del recién nacido. Revista de la Sociedad Española de Pediatria y Puericultura [Internet] 2015; [Citado e agosto 2016]; 10 (1): 112-123. Disponible en: http://www.ops.org.bo/textocompleto/nped26781.PDF

17. Pedro José Herrera Gómez y Juan Federico Garzón. Intrathecal opioids and respiratory depression: Is it myth in obstetrics? Revista Colombiana de Anestesiología.[Internet]2015;43(1):101–103..Disponible.en: http://www.revcolanest.com.co/en/opiaceos-intratecales-depresion-respiratoria-un/articulo/S2256208714001187