

# A Comparative Study to Assess the Effectiveness of Intrathecal Clonidine Alone Versus Clonidine Combined with Fentanyl for Laparoscopic Surgeries Under General Anesthesia

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KEYWORDS	Abstract: Background: Laparoscopic surgeries, although minimally invasive, can lead to
hemodynamic,	hemodynamic changes due to the creation of pneumoperitoneum [1], [2]. Several research studies
pneumoperitoneum,	have been conducted to reduce these hemodynamic effects during laparoscopic procedures. Material
clonidine.	and methods: A randomized, double-blind study was conducted involving 40 patients of both genders,
	with American Society of Anesthesiologists Grade I and II classifications, aged between 20 and 50
	years, who were scheduled for laparoscopic surgeries. In this study, Group CL (comprising 20
	patients) received an intrathecal dose of 140 micrograms of clonidine, while Group CF (also with 20
	patients) received intrathecal clonidine at a dosage of 70 micrograms followed by intrathecal fentanyl
	at 25 micrograms before the administration of general anesthesia. The evaluation parameters
	encompassed hemodynamic measurements, postoperative pain relief, and sedation scores. Results:
	During the surgical procedure, Group CL exhibited a noteworthy decrease in intraoperative heart
	rate, as well as systolic, diastolic, and mean arterial blood pressures at intubation, during
	pneumoperitoneum, and at extubation when compared to Group CF $(p < 0.05)$ [3]. Additionally, the
	average duration of postoperative pain relief was significantly longer in Group CL (10.20
	$\pm$ 1.24 hours, $p < 0.001$ ) compared to Group CF (5.23 $\pm$ 1.11 hours). Furthermore, Group CL had a
	notably higher mean sedation score (2.06 $\pm$ 0.25) compared to Group CF (1.90 $\pm$ 0.31; $p = 0.025$ ).
	Importantly, no adverse effects were reported during the study. Conclusion: The administration of
	intrathecal clonidine at a dosage of 150 micrograms has demonstrated remarkable efficacy in
	preserving stable intraoperative hemodynamics in the context of laparoscopic surgeries performed
	under general anesthesia. Furthermore, this approach offers extended postoperative pain relief when
	compared to the combination of intrathecal clonidine at 70 micrograms with fentanyl at 20
	micrograms.

### I. INTRODUCTION

Minimally invasive procedures, such as laparoscopic surg- eries, provide patients with the benefits of reduced trauma and shorter hospital stays. Typically, laparoscopic surgeries involve the introduction of gases like carbon dioxide into the abdominal cavity for various purposes [4]. Nevertheless, the establishment of pneumoperitoneum, coupled with the frequent repositioning of patients during laparoscopic procedures, can lead to substantial pathophysiological These changes encompass significant changes. cardiovascular and res- piratory effects. Intrathecal clonidine, a partial  $\alpha^2$  receptor agonist, has been observed to diminish the hemodynamic stress response and reduce anesthetic requirements in laparo- scopic surgeries while also extending postoperative pain relief. [5] However, it's worth noting that clonidine can poten- tially induce hypotension and bradycardia. On the other hand, fentanyl, a synthetic opioid agonist, offers robust analgesic effects without significant motor blockade. Combining opi- oid and  $\alpha^2$  adrenoreceptor agonist therapies, despite a sub- stantial body of evidence indicating their synergistic effects

,has been relatively underutilized in clinical practice.



Con- sequently, we embarked on an endeavor to merge these two medications, hypothesizing that this approach yield fewer side effects and reduced would hemodynamic disturbances while preserving the quality of postoperative pain relief. To explore this hypothesis, we conducted a comparative study between a single dose of clonidine at 150 micrograms and a half-dose of clonidine at 70 micrograms in combination with an opioid like fentanyl at 20 micrograms [6]. Our objective was to determine if this combination would offer improved hemodynamic stability alongside a prolonged duration of postoperative analgesia. The primary objectives of this studywere to assess and compare various intraoperative hemody- namic parameters, as well as the hemodynamic responses during intubation and extubation. Additionally, we examined the duration of postoperative pain relief and evaluated postoperative sedation levels as part of our research. [7]

### **II. MATERIAL AND METHODS**

Following approval from the Institutional Ethics Committee, we carried out a prospective double-blinded randomized study involving 40 patients [8]. These patients, aged between 20 and 50 years, could be of any gender and had a Body Mass Index (BMI) ranging from 18 to 30 kg/ $m^2$ . They were classified under American Society of Anesthesiologists Grade I and II and were scheduled for elective laparoscopic general surgeries with a duration of two hours or less. Patient selection was carried out, and they were divided into two groups, each consisting of 20 individuals, using a computergenerated randomization table. We excluded patients from our study if they had contraindications to spinal techniques, a known allergy to clonidine, or significant cardiovascular and respiratory diseases. Group 'CL' comprised 20 patients who were administered intrathecal clonidine at a dosage of 150 micrograms, followed by the application of conventional general anesthesia. Before enrolling patients in the study, a thorough preanesthetic assessment was conducted, which included a detailed medical history, systemic examination, and an evaluation of the airway. Patients were provided with a comprehensive explanation of the anesthesia technique, and informed written consent was obtained from them. Ad- ditionally, all patients received premedication in the form of Tablet Ranitidine 150 mg and Tablet Anxit 0.5 mg on the evening preceding the surgery. Furthermore, the selected patients were instructed to maintain an overnight fast for a duration of eight hours. An 18-gauge intravenous line was established on either upper limb for the patients. Prior to the surgery, patients were preloaded with 500 milliliters (ml) of Ringer's lactate solution. Upon transportation to the operating theater, various monitors were affixed, including an electrocardiogram, a noninvasive blood pressure monitor, and a pulse oximeter. Baseline measurements were taken and recorded for heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation, and end-tidal carbon dioxide. Under strict aseptic measures, lumbar punctures were carried out on patients placed in the left lateral position [9]. A 25-gauge Quincke-type spinal needle was used, targeting the L3-L4 intervertebral space through a midline approach to obtain clear and freely flow- ing cerebrospinal fluid. In Group CL, patients received an intrathecal injection of clonidine totaling 150 micrograms (1 ml), which was loaded in two separate syringes, each con- taining 70 micrograms (0.5 ml), and administered sequen- tially. Conversely, patients in Group CF were administered an intrathecal injection consisting of 75 micrograms (0.5 ml) of clonidine followed by 25 micrograms (0.5 ml) of fentanyl, with both injections being administered sequentially. In both groups, an anesthesiologist, different from the one perform- ing the lumbar puncture, loaded the injections for intrathe- cal administration into two separate syringes to maintain proper blinding. We employed the volatile inhalational agent, isoflurane, at the lowest effective concentration required to maintain mean arterial pressure and heart rate within a 20% range of their baseline values, while simultaneously ensur- ing that the bispectral index remained within the range of 40 to 60. Upon completion of the surgical procedure, any residual neuromuscular blockade was effectively reversed, and patients were extubated once they had sufficiently re- covered. Throughout the process, we diligently monitored various vital parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, end-tidal carbon dioxide levels, and oxygen saturation. We recorded these parameters at key points, such as during intubation, at appropriate intervals during the surgery, and during the extubation phase. Additionally, any instances of hypotension, hypertension, bradycardia, or tachycardia were carefully noted and documented.



### III. RESULTS

A total of 40 patients were randomly divided into two groups, each consisting of 20 individuals. Notably, none of the pa- tients were excluded from the study. In terms of patient characteristics, the mean age was  $38.9 \pm 8.2$ years in Group CL and  $37.5 \pm 9.5$  years in Group CF, with no statistically significant difference (p = 0.5). Additionally, there were 8 males and 12 females in Group CL and an equal distribution of 10 males and 10 females in Group CF (p = 0.6). The duration of surgery was quite similar between the two groups, with 60.5  $\pm$ 10.1 minutes in Group CL and  $61.25 \pm 10.8$  minutes in Group CF (p = 0.96). Mean body mass index (BMI) was 20.8  $\pm$  1.9 kilograms per square meter (kg/m<sup>2</sup>) in Group CL and 24.0  $\pm$  1.6 kg/m<sup>2</sup> in Group CF (p = 0.6). Baseline hemodynamic data were collected in both groups. Overall, the demographic characteristics were wellmatched between the two groups, with no statistically significant differences observed. Following intubation, Group CL dis- played a median decrease of 6 beats per minute in heart rate, whereas Group CF exhibited a median increase of 4 beats per minute. This difference was statistically significant (p < 0.001). During pneumoperitoneum, both Group CL and Group CF experienced median decreases in heart rate, with 11 beats per minute for Group CL and 10 beats per minute for Group CF. However, this difference was not statistically significant. Similarly, at the time of extubation, Group CL showed a median decrease of 6 beats per minute in heart rate, while Group CF had a median increase of 11.5 beats per minute, and this difference was statistically significant (p < 0.001).

Following intubation, there was a notable difference in mean arterial pressure values. Group CL displayed a median decrease of 9 mm Hg, while Group CF exhibited a median increase of 8.5 mm Hg. This difference was statistically sig- nificant (p < 0.001). Conversely, at the time of extubation, Group CL had a median decrease of 10 mm Hg in mean arte-





groups. rial pressure, whereas Group CF showed a median increase of 10.5 mm Hg. These changes were also statistically significant

(p < 0.001).

### IV. DISCUSSION

The establishment of pneumoperitoneum in laparoscopic surgery leads to an increase in systemic vascular resistance and blood pressure, resulting in significant hemodynamic shifts and increased perception of pain. Various classes of drugs, such as opioids, beta-blockers, dexmedetomidine, and nitroglycerine, have been explored to mitigate these changes. However, it's important to note that each of these drug classes has its own drawbacks and limitations [10]. Clonidine, as an  $\alpha^2$  adrenoreceptor agonist, is recognized for its ability to reduce sympathetic nervous system activity. Additionally,  $\alpha^2$  agonists like clonidine induce analgesic effects by acting on various sites within the body, including the brain, brain stem, spinal cord, and peripheral nerves (reference 7). It's worth noting that clonidine can be administered through different routes, including oral, intramuscular, intravenous, epidural, intrathecal, and others, depending on the specific clinical requirements. Indeed, clonidine is associated with potential side effects such as bradycardia, hypotension, and sedation. As a result, your study sought to compare the use of a com- bination of two drugs, intrathecal fentanyl with clonidine, against the administration of intrathecal clonidine alone. This comparison aimed to determine whether the addition of fentanyl could allow for a reduction in the clonidine dosage, potentially limiting its side effects, all while maintaining intraoperative hemodynamic stability and ensuring adequate postoperative pain relief. This study involved 40 patients who were scheduled for elective laparoscopic surgeries under gen- eral anesthesia, divided into two groups. Group 'CL' received intrathecal clonidine at a dose of 150 micrograms, while Group 'CF' received a combination of intrathecal clonidine at 70 micrograms and intrathecal fentanyl at 20 micrograms, followed by conventional general anesthesia [11]. It's inter- esting to note that a similar study conducted by Mohamed AA et al. in 2012, which was a double-blind randomized trial involving 80 patients undergoing major abdominal cancer surgery, assessed the safety and analgesic efficacy of intrathecally administered dexmedetomidine alone and in

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combi- nation with fentanyl. Their findings indicated that intrathe- cal dexmedetomidine improved the quality and duration of postoperative pain relief while also reducing the need for additional analgesics in patients undergoing major abdominal cancer surgery. Interestingly, they observed that the addition of fentanyl did not provide significant clinical benefits. In your study, you similarly found that intrathecal clonidine at a dose of 150 micrograms alone was superior in maintaining hemodynamic stability and offering prolonged postoperative pain relief. You noted that the addition of fentanyl did not eliminate the response to intubation and extubation but did help maintain hemodynamic stability during pneumoperi- toneum. These findings suggest a consistent trend in the efficacy of intrathecal  $\alpha^2$  receptor agonists like clonidine and dexmedetomidine in providing analgesia and stabilizing hemodynamics during surgery. Your study's observation that there were no statistically significant differences between the two groups, one receiving the combination of intrathecal clonidine and fentanyl and the other receiving intrathecal clonidine alone, in terms of heart rate, mean arterial pres- sure, systolic blood pressure, and diastolic blood pressure during pneumoperitoneum is noteworthy. This suggests that the combination of intrathecal clonidine and fentanyl is ef- fective in attenuating the hemodynamic responses to pneumoperitoneum in laparoscopic surgeries, even though it may not completely eliminate the hemodynamic response during intubation and extubation. These findings provide valuable insights into the potential use of this combination to manage hemodynamic stability in such surgical procedures.

### V. CONCLUSION

The results of your study indicate that a single dosage of intrathecal clonidine at 150 micrograms offers superior hemodynamic stability during the entire intraoperative pe- riod and provides prolonged postoperative pain relief when compared to the combination of clonidine at 70 micrograms and fentanyl at 20 micrograms. This suggests that the higher clonidine dosage may be a more effective approach for man- aging both intraoperative hemodynamics and postoperative analgesia in laparoscopic surgeries.

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# **CONFLICTS OF INTEREST**

The authors declared no conflict of interest.

# **AUTHORS' CONTRIBUTIONS**

All authors equally contributed to preparing this article.

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