

## COMPARISON OF INTRATHECAL NEOSTIGMINE VERSUS FENTANYL AS ADJUVANTS TO SPINAL ANESTHESIA IN ELECTIVE SURGERIES

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*Submitted 18 July 2025; accepted 31 August 2025*

### ABSTRACT

**Background:** Spinal anesthesia is a widely employed method in elective surgeries due to its efficacy, and adjuvants such as fentanyl are commonly added to enhance analgesia. Although neostigmine (a cholinesterase inhibitor) has analgesic benefits when used as an adjuvant, less commonly used due to its perceived side effects. This study aimed to compare the efficacy and safety of intrathecal neostigmine with intrathecal fentanyl as adjuvants in patients undergoing elective lower abdominal surgery.

**Method:** A total of 184 were randomly assigned to receive either neostigmine (15µg) or fentanyl (15µg) intrathecally with 15mg of heavy bupivacaine. Patients' hemodynamic stability, vital signs, dermatomal level of the sensory block, motor block intensity, and duration of postoperative analgesia, mobility time, and post-spinal anesthesia complications were documented perioperatively.

**Result:** Our findings indicated no significant difference in hemodynamic stability or complications (including nausea and vomiting) between the fentanyl group and the neostigmine group. However, neostigmine significantly prolonged the duration of postoperative analgesia with early mobility (p-value < 0.0001 and 0.0002, respectively) and delayed the onset of spinal anesthesia (p-value < 0.0001), which may limit its use.

**Conclusion:** This study found that intrathecal neostigmine at 15 µg is a valid alternative to intrathecal fentanyl, since it offers a longer duration of postoperative analgesia and earlier mobilization with insignificant difference in terms of intra- and postoperative complications as compared to intrathecal fentanyl.

**Duhok Med J 2025; 19 (2): 111-123**

**Keywords:** Spinal anesthesia adjuvants, Intrathecal neostigmine, intrathecal fentanyl, hemodynamic stability.

Spinal anesthesia is a widely employed method due to its substantial contribution to enhancing recovery outcomes through optimal postoperative pain management, early mobilization, and reduced perioperative respiratory and cardiovascular complications<sup>[1]</sup>. Both opioid and non-. Opioid adjuvants can be utilized with spinal anesthesia to provide greater cardiovascular stability and extend the postoperative analgesic effect<sup>[2]</sup>.

Despite the association of intrathecal opioids with several complications, including early and late respiratory failure, pruritus, nausea, and urinary retention, their application remains prevalent in daily practice. However, neostigmine is seldom utilized in contemporary practice, primarily due to the heightened incidence of intraoperative nausea and vomiting linked to its administration, especially at higher dosages<sup>[3, 4]</sup>. At the same time, intrathecal

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fentanyl, specifically in small doses, has an antiemetic effect<sup>[5]</sup>. Fonseca et al. conducted a comprehensive meta-analysis encompassing 76 randomized controlled trials, which unveiled that the spinal administration of fentanyl and Sufentanil markedly alleviated postoperative pain while concurrently reducing opioid consumption and enhancing analgesia along with pruritus. Notably, fentanyl—unlike Sufentanil—demonstrated a significant reduction in both postoperative nausea and vomiting, as well as in postoperative shivering, when compared to local anesthetics administered in isolation. Moreover, the incidence of respiratory depression was documented at 0.7% following the administration of spinal fentanyl or Sufentanil, which is in stark contrast to a rate of 0.8% observed in the absence of such intervention. Finally, the studies analyzed found no instances of in-hospital mortality associated with the administration of spinal lipophilic opioids<sup>[6]</sup>. Neostigmine, classified as a cholinesterase inhibitor, exhibits an analgesic effect when administered intrathecally, resulting from the elevation of acetylcholine levels in the dorsal horn of the spinal cord. In previous

studies, Doses ranging from 1 microgram to 750 micrograms have been utilized. However, due to the significant incidence of nausea that correlates with increasing doses, as well as the occurrence of agitation, bradycardia, and fecal incontinence, its application is currently limited<sup>[4]</sup>.

**PATIENT AND METHOD:**

The current study was conducted in the hospitals of Duhok between October 2024 and March 2025, following approval from the Duhok Health Authority’s Ethical Committee, reference number 30102024-9-22, dated 30 October 2024. 200 patients who were scheduled to undergo elective lower abdominal surgeries under spinal anesthesia. Informed written consent was obtained from all participants. Additionally, a questionnaire form including the patient's code, age, weight, height, gender, type of surgery, and past medical history has been appropriately completed for all patients. At the same time, Body mass index (BMI) was calculated manually. Note that data were de-identified before analysis to maintain anonymity. Figure 1 shows the flow of patients.

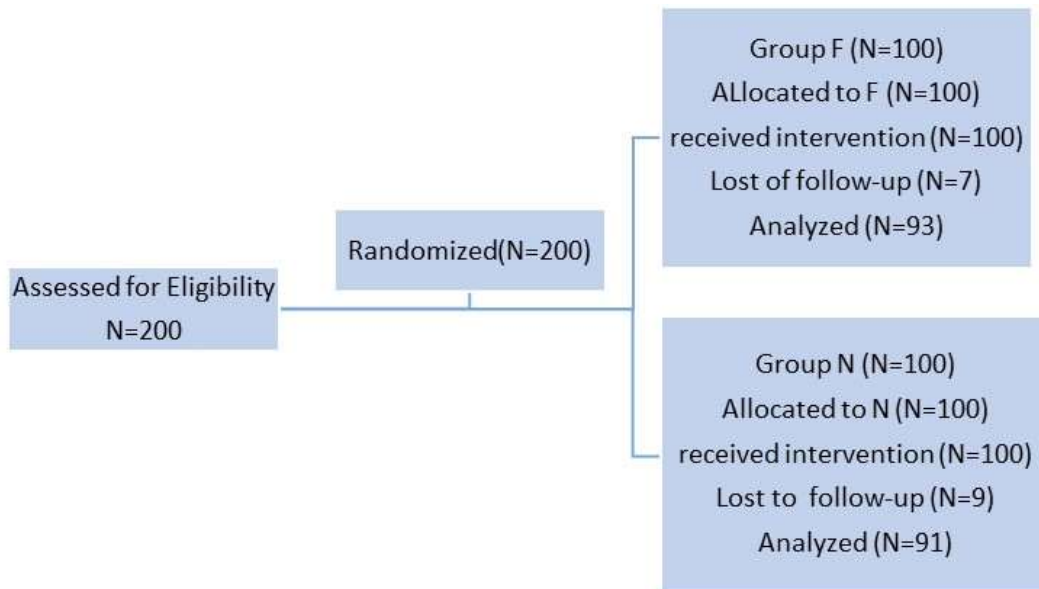


Figure 1: Patient Allocation into study groups (CONSORT chart)

The Inclusion Criteria comprise patients classified under the American Society of Anesthesiologists' (ASA) physical status classification, specifically those classified as I and II, including healthy patients and patients with mild, controlled disease<sup>[7]</sup>, aged between 18 and 64. Conversely, the Exclusion Criteria encompass conditions such as pregnancy, the necessity for emergency surgery, any contraindication to spinal anesthesia, allergies to neostigmine or fentanyl, body height of less than 150 cm, and the presence of any of the following medical conditions: epilepsy, asthma, hypothyroidism, peptic ulcer, arrhythmia, or ischemic heart disease.

This study was a prospective single-blinded simple randomized study where only the patient was unaware of their group allocation. Patients were randomly assigned in a 1:1 ratio to two groups based on the type of intrathecal adjuvant administered in the interspinous space at the L2-L3 or L3-L4 levels, using a 25-gauge Quincke spinal needle while the patient was in the sitting position. Neostigmine Group (group N) includes patients who received 15mg heavy bupivacaine in conjunction with 15µg of neostigmine intrathecally, whereas Fentanyl (group F) includes patients who received 15mg heavy bupivacaine along with 15µg of fentanyl intrathecally.

Following the administration of spinal anesthesia, the subsequent details were documented intraoperatively, which include the onset of the block, the dermatomal level of the sensory block (evaluated by cold sensation using alcohol-soaked cotton), the intensity of the motor block measured by the Bromage scale (grade I complete motor block, grade II almost complete motor block, grade III partial motor block, grade IV no motor block) [8]. Also, vital signs are recorded every five minutes, including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR). Hypotension is defined as mean arterial blood pressure less than

65mmHg, and bradycardia, a heart rate less than 60/ min, were registered and treated with bolus doses of ephedrine and atropine. Potential intraoperative complications may include nausea, vomiting, agitation, shivering, and early respiratory depression. Postoperatively, patients were monitored to ascertain the duration of postoperative analgesia (assessed by the time of the first analgesic administration, the Visual Analog Scale score (VAS score) during the initial analgesic requirement, and the total dose of analgesia provided over 24 hours), the timing of patient mobilization, and any delayed complications, which may encompass pruritus, late respiratory depression, postoperative nausea and vomiting, headache, and backache.

Statistical analyses

The statistical calculations were performed by the statistical software called JMP Pro, Version 18.0, SAS Institute Inc., Cary, NC, 1989–2023

(<https://www.jmp.com/en/software/predictive-analytics-software>). The general and medical characteristics of patients undergoing elective surgeries were presented as mean (SD) or number (%). The study groups were analyzed using the Chi-squared test. Physiological outcomes between study groups receiving elective surgeries were evaluated using an independent t-test. The Chi-squared test or one-way ANOVA was used to assess pain comparisons among and between study groups. A significance level of difference was determined with a p-value of 0.05.

## RESULT:

Among 200 patients with ASA risk status classification I or II, 16 cases were excluded due to lost follow-up after surgery. The F group consisted of 93 patients with an average age of 47.2 years, while the N group had 91 patients with an average age of 41.37 years. As shown in Table 1, there were statistically insignificant differences between the two groups in terms of gender and body mass index.

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**Table 1: General and medical characteristics of the patients under elective surgeries**

Characteristics	Study groups no (%)		p
	Fentanyl (N=93)	Neostigmine (N=91)	
	F group	N group	
Age mean ±SD	47.20 ±13.18	41.37 ±13.57	0.0035
Age groups			0.0049
18-45	39 (41.94)	57 (62.64)	
46 and over	54 (58.06)	34 (37.36)	
Gender			0.5652
Male	65 (69.89)	60 (65.93)	
Female	28 (30.11)	31 (34.07)	
BMI mean ±SD	27.19 ±3.87	27.52 ±3.52	0.5439
BMI			0.6554
Normal weight	30 (32.26)	24 (26.37)	
Overweight	38 (40.86)	42 (46.15)	
Obese	25 (26.88)	25 (27.47)	

Although there was a statistically significant difference in the age group, it didn't affect the result, as Tables 2 and 3

show, and the ASA classification, as it was within classes I and II, which wouldn't affect the clinical outcome.

**Table 2: Comparisons of the significant complications among different age groups**

	Age groups (Fentanyl)			Age groups (Neostigmine)		
	18-45	46 and over	p	18-45	46 and over	p
onset of block mean (SD)	88.38 (4.73)	94.91 (4.02)	0.2957	137.68 (74.26)	122.53 (50.66)	0.2958
duration of analgesia (hrs.) mean (SD)	19.97 (6.74)	22.15 (4.89)	0.0776	22.36 (4.10)	22.18 (4.02)	0.8386
Mobility time mean (SD)	7.57 (2.46)	7.76 (2.63)	0.7264	6.46 (1.01)	6.76 (1.16)	0.1984

Pearson Chi-squared test was performed for statistical analyses

**Table 3: Comparisons of the significant complications among different ASA groups**

Outcomes	Fentanyl		Neostigmine	
	ASA I	ASA II	ASA I	ASA II
nausea and vomiting				
no	43 (89.58)	40 (88.89)	63 (94.03)	23 (95.83)
yes	5 (10.42)	5 (11.11)	4 (5.97)	1 (4.17)
p	1.0000		1.0000	
duration of analgesia				
4-6 hrs.	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
7-12 hrs.	11 (23.91)	6 (13.33)	4 (5.97)	1 (4.35)
13-24 hrs.	35 (76.09)	39 (86.67)	63 (94.03)	22 (95.65)
p	0.1955		1.0000	
mobility time				
mean (SD)	7.91 (2.62)	7.44 (2.47)	6.48 (1.08)	6.87 (1.01)
p	0.3832		0.1304	
onset of block				
mean (SD)	87.85 (30.04)	96.78 (28.59)	140.37 (70.58)	108.71 (47.52)
p	0.1463		0.0548	

The neostigmine group exhibited a delayed onset with a mean of 132.02 ± 66.53 seconds.

In contrast, the onset of spinal anesthesia in the fentanyl group was 92.17 ± 29.53

seconds with a statistically significant p-value <0.0001. Furthermore, T8 and above had been blocked in the majority of both groups, and a complete or almost complete motor block was achieved in both groups.

The sensory block level and Bromage motor block score were statistically indistinguishable between the two groups, with a p-value greater than 0.05, as shown in Table 4.

**Table 4: Comparisons of the onset of blocks, level of sensory block, and the Bromage score between study groups**

Intra-operative outcomes	Study groups no (%)			Mean diff (95% CI) OR (95% CI)
	fentanyl (N=93)	neostigmine (N=91)	p	
onset of block	92.17 (29.53)	132.02 (66.53)	<0.0001	39.85 (24.93-54.77)
level of block				Ref
T6	35 (37.63)	35 (38.46)	0.3437	0.79 (0.31-1.97)
T7	14 (15.05)	11 (12.09)		0.88 (0.46-1.68)
T8	40 (43.01)	35 (38.46)		1.75 (0.47-6.52)
T9	4 (4.30)	7 (7.69)		2.91 (0.29-29.41)
T10	0 (0.00)	3 (3.30)		
Brombage				
I	88 (94.62)	84 (92.31)	0.5647	Ref
II	5 (5.38)	7 (7.69)		1.47 (0.45-4.8)

Intraoperatively, hemodynamic stability was shown in both groups with no statistically significant p value >0.05, as shown in Table 5. The only significant difference was the p-value of 0.0131, which corresponded to the heart rate. Still, both groups within a normal heart rate are clinically indifferent. The incidences of the hypotension and bradycardia were less in

neostigmine group, 13.19% versus 18.28% in the fentanyl group, as well as the bradycardia, 6.56% versus 12.90% and the same for corresponding doses of atropine and/or ephedrine required, but were also statistically insignificant differences as p value > 0.05, as Table 6 shows.

**Table 5: Physiological outcomes among and between study groups who received elective surgeries**

	Group mean (SD)		P
	Fentanyl (N=93)	Neostigmine (N=91)	
SBP			
pre	140.10 (20.71)	137.45 (18.03)	0.3569
5 min	130.04 (25.21)	133.74 (20.13)	0.2741
10 min	123.03 (21.35)	121.76 (19.67)	0.6745
15 min	120.76 (19.37)	118.67 (19.01)	0.4604
20 min	120.53 (19.39)	117.74 (18.92)	0.3246
25 min	119.96 (19.72)	117.66 (16.67)	0.3950
DBP			
pre	83.09 (12.40)	81.12 (12.48)	0.2854
5 min	75.73 (12.97)	76.82 (14.22)	0.5865
10 min	71.56 (12.44)	69.64 (12.10)	0.2896
15 min	70.92 (11.58)	67.92 (12.65)	0.0948
20 min	69.61 (11.53)	67.90 (12.66)	0.3388
25 min	69.49 (11.63)	67.56 (10.51)	0.2384
MAP			
Pre	102.16 (15.32)	101.11 (13.39)	0.6210
5 min	93.11 (16.13)	96.82 (14.21)	0.0992
10 min	88.08 (14.23)	88.93 (13.72)	0.6774
15 min	86.66 (13.30)	86.07 (13.36)	0.7644
20 min	85.42 (13.32)	86.34 (14.02)	0.6481
25 min	85.45 (13.90)	86.31 (11.63)	0.6515

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	Group mean (SD)		P
	Fentanyl (N=93)	Neostigmine (N=91)	
HR			
Pre	84.70 (15.51)	88.33 (11.94)	0.0772
5 min	81.78 (18.63)	88.38 (17.05)	0.0131
10 min	80.51 (16.38)	83.00 (15.07)	0.2841
15 min	78.84 (14.14)	80.84 (13.41)	0.3272
20 min	79.02 (14.36)	80.09 (12.92)	0.5973
25 min	78.66 (14.04)	80.33 (12.56)	0.3957

ANOVA one- test was performed for statistical analyses. The pairwise comparisons were performed using the Tukey test.

**Table 6: Intra-operative outcomes among and between study groups who received elective surgeries**

Intra-operative outcomes	Study groups no (%)		P value
	Fentanyl (N=93)	Neostigmine (N=91)	
number of hypotension			
0	76 (81.72)	79 (86.81)	
1	12 (12.90)	7 (7.69)	0.7568
2	2 (2.15)	3 (3.30)	
3	2 (2.15)	1 (1.10)	
4	1 (1.08)	1 (1.10)	
Hypotension			
no	76 (81.72)	79 (86.81)	0.3432
yes	17 (18.28)	12 (13.19)	
Bradycardia			
no	81 (87.10)	85 (93.41)	0.1497
yes	12 (12.90)	6 (6.59)	
ephedrine			
no	76 (81.72)	79 (86.81)	0.3432
yes	17 (18.28)	12 (13.19)	
Atropine			
no	81 (87.10)	85 (93.41)	0.1497
yes	12 (12.90)	6 (6.59)	

Pearson Chi-squared test was performed for statistical analyses.

Despite the lower incidence of intraoperative nausea and vomiting in group N (5.49%) compared to group F (10.75%), this discrepancy was found to be statistically insignificant, with a p-value of 0.2815. Neither group noted any agitation. However, Group F exhibited a 3.23% incidence of early respiratory failure, while Group N did not experience any cases of early respiratory failure. Furthermore, shivering, pruritus, and backache were less prevalent in group N than in group F, although these differences were similarly deemed statistically insignificant (p-value>0.05). Finally, postoperative nausea and vomiting, as well as delayed respiratory failure and headaches, were more frequently reported in the neostigmine

group, with these findings also remaining statistically insignificant p value 0.3712, 0.1689, respectively.

There were statistically insignificant differences between the two groups in terms of post-spinal anesthesia complications, including intra- and postoperative nausea and vomiting, agitation, shivering, pruritus, headache, backache, early and late respiratory depression, with a p-value > 0.05, as shown in Table 7.

**Table 7: Post-spinal outcomes among and between study groups who received elective surgeries**

Outcomes	Study groups no (%)		p
	Fentanyl (N=93)	Neostigmine (N=91)	
Intraoperative nausea and vomiting			
no	83 (89.25)	86 (94.51)	0.2815
yes	10 (10.75)	5 (5.49)	
Agitation			
no	93 (100)	91 (100)	Na.
Shivering			
no	80 (86.02)	82 (90.11)	0.3928
yes	13 (13.98)	9 (9.89)	
Early respiratory failure			
no	90 (96.77)	91 (100.00)	0.0841
yes	3 (3.23)	0 (0.00)	
Post OP nausea and vomiting			
no	75 (82.42)	72 (80.00)	0.6771
yes	16 (17.58)	18 (20.00)	
Nausea and vomiting score			
0	74 (81.32)	71 (78.89)	0.5638
1	13 (14.29)	11 (12.22)	
2	4 (4.40)	7 (7.78)	
3	0 (0.00)	1 (1.11)	
Pruritus			
no	89 (97.80)	89 (98.89)	1.0000
yes	2 (2.20)	1 (1.11)	
Delayed respiratory depression			
no	87 (95.60)	83 (92.22)	0.3712
yes	4 (4.40)	7 (7.78)	
Headache			
no	70 (76.92)	61 (67.78)	0.1689
yes	21 (23.08)	29 (32.22)	
severity of headache			
no	70 (76.92)	61 (67.78)	0.3298
mild	19 (20.88)	25 (27.78)	
moderate	0 (0.00)	2 (2.22)	
severe	2 (2.20)	2 (2.22)	
Backache			
no	70 (76.92)	72 (80.00)	0.6147
yes	21 (23.08)	18 (20.00)	

Pearson Chi-squared test was performed for statistical analyses.

Regarding the duration of postoperative analgesia, a statistically significant difference was observed, as indicated by a p-value of <0.0001 (CI 1.37-11.1), with prolonged analgesia duration exceeding 12 hours in the neostigmine group compared to the fentanyl group. Conversely, the VAS pain score and severity of pain when the analgesic effect diminished, along with the doses of analgesic agents required within 24 hours postoperatively, exhibited a statistically insignificant difference between the two groups. Also, a significant

delay in mobilization was observed in the fentanyl group, p-value 0.0002, CI ( -1.68 to -0.53), as Table 8 shows.

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**Table 8: Comparisons of pain among and between study groups who received elective surgeries**

Outcomes	Study groups no (%)		P value	Mean diff (95% CI) OR (95% CI)
	Fentanyl (N=93)	Neostigmine (N=91)		
Numerical pain score	2.48 (1.82)	2.48 (1.98)	0.9796	-0.01 (-0.56 to 0.55)
Pain score				
None	14 (15.38)	15 (16.67)		Ref
Mild	60 (65.93)	61 (67.78)	0.8047	0.95 (0.42-2.13)
Moderate	13 (14.29)	11 (12.22)		0.79 (0.27-2.34)
Severe	4 (4.40)	3 (3.33)		0.7 (0.13-3.7)
duration of analgesia				
7-12 hrs.	17 (18.68)	5 (5.56)	<0.0001	Ref
13-24 hrs.	74 (81.32)	85 (94.44)		3.91 (1.37-11.1)
mobilization time hr.	7.68 (2.55)	6.58 (1.07)	0.0002	-1.10 (-1.68 to -0.53)
Type of Analgesia				
no	74 (81.32)	76 (84.44)		
diclofenac	0 (0.00)	1 (1.11)	0.3170	
paracetamol	12 (13.19)	5 (5.56)		
pethidine	1 (1.10)	1 (1.11)		
tramadol	4 (4.40)	7 (7.78)		

a ANOVA one-way and b Pearson Chi-squared test were performed for statistical analyses.

**DISCUSSION:**

In the present study, we investigate whether 15 µg of intrathecal neostigmine is as effective as 15 µg of intrathecal fentanyl as an adjuvant in spinal anesthesia. Our findings reveal that both adjuvant doses are effective in producing efficient motor block and dermatomal sensory level block. There were no statistically significant differences between the two groups concerning post-spinal anesthesia complications, including hypotension, bradycardia, intra- and postoperative nausea and vomiting, agitation, shivering, pruritus, headache, backache, early and late respiratory depression (p-value > 0.05). Furthermore, the use of neostigmine prolonged analgesia duration and was associated with earlier mobility, with highly significant p-values of <0.0001 and 0.0002, respectively.

Although previous studies discourage the use of neostigmine due to its association with increased intraoperative nausea and vomiting, other risks include hemodynamic instability, higher incidence of bradycardia, increased anxiety, sedation, and delayed mobility linked to prolonged motor block [4]. However, the studies that suggest these

effects have all used doses of neostigmine higher than 15 µg, which is the dose that was used in the current study. The difference in dosage may explain the failure to maintain hemodynamic stability, among other complications, in previous studies compared with the current findings.

According to Ebrie, A.M., et al (2022), there is a lower incidence of post-spinal hypotension in patients receiving bupivacaine in conjunction with fentanyl (42.2%) compared to those who received bupivacaine alone (46.7%)<sup>[9]</sup>. This means that when used without an adjuvant or in high doses, Bupivacaine is more likely to cause post-spinal hypotension. In this study, the incidence of post-spinal hypotension was 18.28% with higher doses of bupivacaine (15 mg). In contrast, the incidence of hypotension in the neostigmine group within our study was recorded at 13.19%, accompanied by a statistically insignificant difference in ephedrine doses required to manage hypotension across both groups. These findings underscore the prophylactic role of incorporating neostigmine as an adjuvant in mitigating the incidence of post-spinal hypotension.

The incidence of bradycardia reaches 8% in certain studies employing 25 micrograms of neostigmine. In our study, a lower dose of 15 µg of neostigmine reduced this incidence to 6.59%, which is a statistically insignificant difference compared to the fentanyl group. Bradycardia caused by intrathecal neostigmine results from both acetylcholinesterase inhibition and direct activation of cardiac parasympathetic receptors. This risk is dose-dependent and can be managed effectively with appropriate interventions, such as anticholinergics. Nonetheless, this limits the use of neostigmine as a spinal adjuvant relative to alternatives like fentanyl<sup>[10]</sup>.

Intraoperative nausea and vomiting were the primary reasons for reducing the use of intrathecal neostigmine, with some studies reporting a high incidence of up to 30%<sup>[11]</sup>. This occurs via the cholinergic pathway in the medulla oblongata, where increased acetylcholine levels activate muscarinic receptors in the vomiting center. In our study, the incidence was lower in the neostigmine group at 5.49%, compared to 10.75% in the fentanyl group. The difference between the groups was not statistically significant, supporting the idea that the low dose of intrathecal neostigmine remains below the emetic threshold<sup>[12]</sup>.

Other complications associated with neostigmine include agitation and pruritus. Agitation caused by intrathecal neostigmine is a common and predictable complication, with an odds ratio exceeding 10 compared to placebo in a previous study. This occurs due to cholinergic overstimulation, which results in hyperexcitability of the central nervous system and negative emotional encoding<sup>[13]</sup>.

Neostigmine showed a delay in onset, while fentanyl showed a delay in mobility. The observed delay in mobility within the fentanyl group of our study aligns with findings from other research that demonstrate a dose-dependent delay in the regression of motor block<sup>[14]</sup>. The

mechanism underlying the synergistic effect of the lipophilic µ-opioid agonist, which extends the efficacy of local anesthetics by obstructing lower limb afferent pathways<sup>[15]</sup>. On the other hand, neostigmine significantly doubles the delay in spinal anesthesia onset (mean 132.02 sec) compared to fentanyl (mean 92.17 sec), with a p-value of <0.0001. This delay was observed in the motor block, as investigated in our study. Nonetheless, while inconsequential in contexts where rapid block is not needed, this delay may negatively affect operating room efficiency and patient comfort. It is necessary to examine further whether this delay in the onset of sensory block persists in future research.

Intrathecal neostigmine significantly extended the duration of analgesia by more than 12 hours in 94.44% of cases, p-value <0.0001, CI (1.37-11.1). This finding highlights the superiority of intrathecal neostigmine for pain management and enhancement of patient recovery, eliminating the need for additional interventions and surpassing the durations reported in other studies utilizing higher doses of intrathecal neostigmine—specifically, 150 mcg, which provided analgesia for up to 10 hours, and 50 mcg, which lasted approximately 6 hours<sup>[16,17]</sup>. Various pharmacological mechanisms, including receptor desensitization at high doses, the ceiling dose effect, and the bell-shaped response phenomenon, can explain this<sup>[18]</sup>.

The limitations of the study include being single-centered and only including ASA class I and II patients, with the exclusion of geriatric patients. Further research is needed to investigate the hemodynamic effects of intrathecal administration in ASA class III and IV patients, as well as in the geriatric population, particularly those with cardiovascular disease. The study utilized one-to-one simple randomization to decrease potential bias from participants. However, this study did not employ

blinding of anesthesiologists or outcome assessors, which introduces a potential risk of bias in intraoperative and postoperative outcome reporting. Double-blinded methods may eliminate this risk in future research. Furthermore, despite aiming to keep the study sample as close to those reported in previous literature, no formal sample size calculation was performed. This may be a concern in terms of overpowering the study or underpowering it, therefore the data should be validated.

### CONCLUSION:

Administering 15 µg of neostigmine during spinal anesthesia has been shown to be as effective as fentanyl in providing motor and sensory blockade, maintaining intraoperative hemodynamic stability, and preventing post-spinal complications, with no significant difference between the two ( $p > 0.05$ ). Additionally, intrathecal neostigmine significantly prolongs postoperative analgesia and enables early mobility ( $p < 0.0001$  and  $p < 0.0002$ , respectively). The only reported concern is a significantly delayed onset of spinal anesthesia with neostigmine ( $p$ -value  $< 0.0001$ ). This highlights the benefits of using intrathecal neostigmine for pain control and opioid-free anesthesia, supporting improved patient recovery without extra interventions.

Conflict of interest: none

Acknowledgment and Funding: none

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## پوخته

### بهرآوردکردنی نیوستیگمینی ناو بربره ی پشت له بهرامبهر فینتانیل و هک یارمهتیدر بو بیهوشکردنی بربره ی پشت له نهشتهرگهریبه ههلبژیردراوهکاندا

**پیشهکی و نارمانج:** بیهوشکردنی بربره ی پشت ریگهیهکی به شیوهیهکی بهر فراوان بهکاردههینریت له نهشتهرگهریبه ههلبژیردراوهکاندا بههوی کاریگهریبهکهمه، و یارمهتیدر هکانی و هک فینتانیل به شیوهیهکی باو زیاد دهکرتین بو بهر زکرنهوی نازار شکتین. ههچهنده نیوستیگمین (ریگریکریکی کولین نیستران) سوودی نازار شکتینی ههیه کاتیک و هک یارمهتیدر یک بهکاردههینریت، بهلام کهمتر بهکاردههینریت بههوی کاریگهریبه لاهکیه ههستینکراوهکانی. ئەم توژیینهویه نامانجی بهراوردکردنی کاریگهری و سهلامتی نیوستیگمینی ناو سک بو لهگهل فینتانیلی ناو سک و هک یارمهتیدر له نهخوشانی که نهشتهرگهری ههلبژیردراوی خواروهوی سکبان بو دهکرتیت.

**شینواز:** سهر جهه 184 کس به شیوهیهکی ههرمهکی دستنیشان کران بو و مرگرتنی یان نیوستیگمین (15 میکروگرام) یان فینتانیل (15 میکروگرام) له ریگهی ناو بربره ی پشت لهگهل 15 میلیگرام بوپیفاکاینی قورس. سهقامگیری هیموداینامیکی نهخوشهکان، نیشانه گرنهکان، ناستی پینستی بلوکی ههستیار، توندی بلوکی جوولهیی، و ماوهی نازار شکتینی دواي نهشتهرگهری، کاتی جووله، و نالوزیبهکانی دواي بیهوشکردنی بربره ی پشت له کاتی نهشتهرگهریدا بهلگهار کران.

**نهجام:** دۆزینهوهکانمان ناماز میان به ههچ جیاوازییهکی بهرچاو له سهقامگیری هیموداینامیک یان نالوزیبهکان (لهوانهش سکچوون و رشانهوه) له نیوان گروپی فینتانیل و گروپی نیوستیگمیندا نهکرد. بهلام، نیوستیگمین ماوهی نازار شکتینهکانی دواي نهشتهرگهری به شیوهیهکی بهرچاو دریزکردوه لهگهل جوولهی زوو (بههای  $p < 0.0002$  و دهستینکردنی دواخست (بههای  $p < 0.0001$ ) ههچهنده دواکوتتی دهستینکردن لهوانهیه بهکار هینانی له ههندیک سیناری یوی کلینیکیدا سنووردار بکات

**دهرهجام:** ئەم توژیینهویه دهریخت که نیوستیگمینی ناو بربره ی پشت به 15 میکروگرام بهدیلیکی دروسته بو فینتانیلی ناوبربره ی پشت، لهبهرئوهی ماوهی دریزتری نازار شکتینی دواي نهشتهرگهری و جوولاندنی زووتر پیشکەش دهکات لهگهل جیاوازییهکی کهم له روی نالوزیبهکانی ناو بربره ی پشت و دواي نهشتهرگهری به بهراورد لهگهل فینتانیلی ناو لولهی.

## الخلاصة

### مقارنة بين النيوستيغمين داخل القراب الشوكي والفتنانيل كمواد مساعدة للتخدير الشوكي في الجراحات الاختيارية

**الخلفية والأهداف:** يعد التخدير الشوكي طريقة واسعة الاستخدام في الجراحات الاختيارية نظرا لفعالته، وتضاف عادة مواد مساعدة مثل الفتنانيل لتعزيز التسكين. على الرغم من أن النيوستيغمين (مثبط الكولينستراز) له فوائد مسكنة عند استخدامه كعامل مساعد، إلا أنه أقل شيوعًا نظرا لآثاره الجانبية المحتملة. هدفت هذه الدراسة إلى مقارنة فعالية وسلامة النيوستيغمين داخل القراب مع الفتنانيل داخل القراب كعامل مساعد لدى المرضى الذين يخضعون لجراحة اختيارية في أسفل البطن.

**الطريقة:** تم توزيع 184 مريضًا عشوائيًا لتلقي إما النيوستيغمين (15 ميكروغرام) أو الفتنانيل (15 ميكروغرام) داخل القراب مع 15 ملغ من البوبيفاكين الثقيل. وُثِّقَت استقرار الدورة الدموية لدى المرضى، والعلامات الحيوية، ومستوى التخدير الحسي في الجلد، وشدة التخدير الحركي، ومدة التسكين بعد الجراحة، ووقت الحركة، ومضاعفات ما بعد التخدير الشوكي، وذلك خلال الفترة المحيطة بالجراحة.

**النتيجة:** لم تُشير نتائجنا إلى وجود فرق جوهري في استقرار ديناميكية الدم أو المضاعفات (بما في ذلك الغثيان والقيء) بين مجموعة الفتنانيل ومجموعة النيوستيغمين. ومع ذلك، أطال النيوستيغمين مدة تأثير التخدير بعد الجراحة بشكل ملحوظ مع الحركة المبكرة (القيمة الاحتمالية 0.0002) وأخر ظهوره (القيمة الاحتمالية >0.0001). مع أن تأخر ظهوره قد يحد من استخدامه في بعض الحالات السريرية.

**الخلاصة:** وجدت هذه الدراسة أن النيوستيغمين داخل القراب بجرعة 15 ميكروغرام يعد بديلا فعالا للفتنانيل داخل القراب، إذ يوفر مدة أطول لتسكين الألم بعد الجراحة وحركة أسرع مع اختلاف طفيف في المضاعفات أثناء وبعد الجراحة مقارنة بالفتنانيل داخل القراب.