A COMPARISON BETWEEN THREE DOSES OF BOLUS AND CONTINUOUS INFUSION OF EPIDURAL NEOSTIGMINE VERSUS FENTANYL AS ADJUVANT ANALGESICS IN ADULTS

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ABSTRACT

Background: The cholinergic system has attracted new interest as a pharmacological target to accomplish effective analgesia without the limitations of opioid-induced side effects. **Objective:** the purpose of this prospective study was a comparison between three doses of bolus and continuous infusion of epidural neostigmine versus fentanyl as an adjuvant analgesic in adults. **Patients and methods:** In a prospective study of 160 adult patients undergoing lower half of the body surgeries using epidural anesthesia at Zagazig University Hospitals form May 2010 to May 2013 for comparing three doses of bolus and continuous infusion of epidural neostigmine versus fentanyl as an adjuvant analgesic. **Result(s):** The highest neostigmine dose used in this study 200 µg bolus or 125 µg/hour infusion showed significant better pain relief parameters than lower doses regarding duration of analgesia, postoperative VAS, number of diclophenac ampoules consumed in first postoperative 24 hours and patient satisfaction score with no significant different side effects. Neostigmine showed significant lower nausea/vomiting and no pruritis with no significant difference postoperative VAS,total number of diclophenac ampoules consumed in first postoperative 24 hours and patient satisfaction score in comparison to fentanyl but fentanyl showed significant longer duration of analgesia. **Conclusion(s):** The highest does of neostigmine either bolus or continuous infusion is better than lower doses and fentanyl showed longer duration of analgesia with more side effects than neostigmine doses with similar postoperative VAS, number of diclophenac ampoules consumption in first postoperative 24 hours and patient satisfaction score as highest dose neostigmine either infusion or bolus.

Key Words: epidural anesthesia, bupivacaine, neostigmine, fentanyl

INTRODUCTION

One of the methods for pain management is preemptive analgesia. A meta-analysis assessed the ability of preemptive analgesic interventions to attenuate postoperative pain scores, decrease supplemental postoperative analgesic requirements, and prolong the time to first rescue analgesia. One of the most important technique for operative pain control involves the use of an epidural catheter**(1)**.

Narcotic agents are frequently preferred analgesia; however, because of the well-known side effects of those agents such as respiratory depression, urinary retention, nausea/vomiting and pruritis. New agents are needed**(2)**.

Neostigmine is a parasympathomimetic agent reversible anticholinesterase which inhibits breakdown of Ach. Ach is considered to be one of t he major inhibitory neurotransmitters in pain modulation establish its analgesic effect by stimulating the muscarinic receptors of acetylcholine across the spinal cord, particularly in the substantia gelatinosa (lamina I, II)**(3)**.

Epidural neostigmine provides analgesia without the severe GIT side effects (nausea/vomiting and diarrhea) consecutive to its intrathecal injection. Furthermore, neostigmine does not induce respiratory depression, hypotension, or motor blockade. Hence, the characteristics of epidural neostigmine seem to meet those requested to achieve selective analgesia **(4)**.

PATIENTS AND METHODS

After approval of Local Ethical Committee, and taking informed consent. This prospective study was carried out on one hundred and sixty adult patients (16-65 years old),of American Society of Anaesthesiologists status I and II scheduled for elective surgery in lower half of the body (below or at level of T_{10}) under supervision of Anesthesia Department, Faculty of Medicine, Zagazig University from May 2010 to May 2013 in order to compare three bolus doses of epidural neostigmine and infusion versus fentanyl as an adjuvant analgesic. Patients with a history of back surgery, mental retardation, infection at injection sites, coagulopathy hypersensitivity to local anaesthetics or opioids were excluded form the study.

The patients were divided randomly into four main groups. All of them received epidural bupivacaine.

- **Group I:**
  - **Ia:** Epidural bolus neostigmine 100 µg.
  - **Ib:** Epidural bolus neostigmine 150 µ**g.**
  - **Ic:** Epidural bolus neostigmine 200 µg.

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bupivacaine 10 ml 0.5%. Each subgroup contained 20 patients.

- **Group II:** Epidural bolus fentanyl 50 µg plus bupivacaine 10 ml 0.5%. This group contained 20 patients.
- **Group III:**
  - **IIIa:** Epidural infusion neostigmine 75 µg/hour.
  - **IIIb:** Epidural infusion neostigmine 100 µg/hour.

- **IIIc:** Epidural infusion neostigmine 125 µg/hour.

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Bupivacaine loading dose 10 ml 0.5% then 10 ml 0.25% / hour, mixed with neostigmine infusion and started after complete motor block. each subgroup contained 20 patients.

- **Group IV:** Epidural infusion fentanyl 50 µg/hour plus bupivacaine same as group III. This group contained 20 patients.

Preoperative evaluation of VAS **(5)** to all patients for pain assessment and no patient received sedation or opioid premedication before arrival at operating room. In operating room, after intravenous access preloading with 10 ml/kg intravenous infusion ringer lactate and application of monitors, epidural catheterization was performed under strict aseptic condition at L_2-L_3 or L_{3-4} interspace in sitting position. A test dose of 3 ml injection of lignocaine (2%) containing 1:200,000 epinephrine was given through epidural catheter to confirm proper placement. Then, after 15 minutes, lumbar epidural bolus or loading doses were given and the somatosensory blockade was evaluated by pinprick test.

Preoperative measurement:

The onset time of sensory blockade with maximal cephalad spread was assessed by bilateral pinprick method along the mid-clavicular line. It was defined as the time form epidural injection to the occurrence of sensory block at dermatome level T_{10}. The motor blockade was assessed using a modified Bromage scale (0-3) **(6)**, the time of complete motor blockade was defined as the time from epidural injection to achieve bromage scale 3. The surgical anesthesia was considered effective when T_{10} dermatome was anesthetized. Preoperative assessment of HR, BP, RR and SpO_2 was done.

Intraoperative measurement:

1- **Haemodynamic changes:** Hypotension, bradycardia and decrease SpO_2.
2- **Sedation score** according to Ramsay sedation scale (7).
3- **Two-segment regression time.**
4- **First dose failure** in different types of surgery.
5- **Side effects;** nausea/vomiting and pruritis.

Postoperative measurements:

1- Postoperative VAS by 10 cm scale (0 cm = no pain to 10 cm = the worst possible pain)of over all 24h.patient's impression.
2- Time before first call for diclophenac as systemic analgesic.
3- Total numbers of diclophenac ampoules consumed during first postoperative 24 hours.
4- Overall postoperative 24h. patient satisfaction using a 1-3 verbal scale(8).
5- Side effects; ileus and urine retention.

Statistical analysis:

At the end of study, all data were checked, entered and analyzed by using Special Package for Social Science) (SPSS) version 17. Data were expressed as mean ± standard deviation for quantitative continuous variables.

Number and percentage for categorical variables, chi-square (X^2), Fisher exact test, ANOVA (F) test, paired t test were used when appropriate, post hoc test for comparison in between the groups.

$p < 0.05$ was considered statistically significant.

RESULTS

There were no significant difference regarding patient age, sex, weight, height, type of surgery, duration of surgery and preoperative VAS between groups of epidural bolus doses (groups I and II) and also between groups of epidural infusion doses (groups III and IV).

There were no significant difference across the three bolus doses of neostigmine (groups Ia, Ib and Ic) relative to sensory block onset time and time to complete motor block, but there were significant correlations between fentanyl group (II) and rapid onset of analgesia and time to complete motor block (table 1).

In our study, there were no significant differences between the groups regarding hypotension and bradycardia, (table 1).

In our study, we found that there was a significant sedation with increasing the dose of neostigmine (dose dependent)and with fentanyl dose. There was no significant difference between the group Ic and group II regarding patient sedation(table 1).

The current study established that addition of epidural neostigmine 100 µg, 150 µg and 200 µg to bupivacaine increases the duration of analgesia in dose-dependent manner through prolonged duration for first call for diclophenac. Also, there was a significant prolonged duration before first call for diclophenac with fentanyl group in comparison with neostigmine group. There were no significant differences between the highest dose neostigmine (group Ic) and fentanyl dose regarding postoperative VAS, total number of diclophenac ampoule consumption in first 24 hours and patient satisfaction score(table 1).

In our study, we found significant lower nausea/vomiting with neostigmine groups in comparison to fentanyl group. There were no significant ileus side effect difference between the groups. Also, neostigmine groups showed no pruritis or urine retention side effects (table 2).

In our study, we found that first dose failure was significant with lower neostigmine doses. orthopedic and vascular surgeries showed significant high first dose failure with the groups of lower neostigmine doses than highest dose neostigmien (group Ic) or fentanyl group (group II) (table 3).

In our study, we found no significant difference between the groups of epidural infusion regarding hypotension or bradycardia. Cases of bradypnea or hypoxemia were not reported in our study (table 4).

In our study, there were a significant sedation with the highest dose of neostigmine infusion (group IIIc) and fentanyl group (group IV). There were no significant difference between the other two groups (groups IIIa and IIIb) and also no significant difference between highest dose of neostigmien (group IIIc) and fentanly (group IV) regarding sedation (table 4).

In our study, the neostigmine infusion groups showed a significant short duration to two-segment regression in comparison to fentanyl group and we found also that there was a significant correlation between the lowest dose of neostigmine and short duration to two-segment regression(table 4).

In our study, we found that there were significant correlation between lower neostigmine doses (groups IIIa and IIIb) regarding short duration for first call for diclophenac (duration of analgesia), high total numbers of diclophenac ampoule consumption in postoperative 24 hours, high postoperative VAS and lower patient satisfaction score in comparison to the highest dose of neostigmine (group IIIc) and fentanyl dose (group IV)(table 4).

There were significant prolonged duration of analgesia in group IIIc compared to the other groups of neostigmine reflected by prolonged duration before first call for diclophenac, but highest neostigmine dose showed significant short duration of analgesia in comparison to fentanyl(groupIV), but no significant difference between highest neostigmine group and fentanyl group was found regarding total numbers of diclophenac ampoules consumption, postoperative VAS and patient satisfaction score(table 4).

In our study, we found that there were significant lower nausea-vomiting in neostigmine groups in comparison to fentanyl. Neostigmien groups showed no urine retention or purities side effects.

Table (1): Assessment of epidural bolus doses.

	Group Ia (n=20)	Group Ib (n=20)	Group Ic (n=20)	Group II (n=20)	F	p
Preoperative assessment						
Time of onset of sensory block (minutes)	27.2 ±4.9**	26.8±2.1**	25.2±2.3**	18.4 ± 3.2	20.6	0.02
Time of complete motor block (minutes)	37.5 ±4.8**	38 ± 4.8**	36 ±3.3**	25.6 ± 3.8	37.2	0.01
Intraoperative assessment						
Haemodynamic changes						
Hypotension	5(25.0)	4 (20.0)	3 (15.0)	4(20.0)	X^2 = 0.62	0.89
Bradycardia	1(5.0)	2 (10.0)	3(15.0)	3(15.0)	X^2 = 0.78	0.86
Bradypnea	0 (0%)	0 (0%)	0 (0%)	0 (0%)	X^2 = 0	0
Decreased saturation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	X^2 = 0	0
Sedation score	2.6 ± 0.5**	2.8± 0.5**	3.5 ±0.5	3.6 ± 0.5	18.48	0.000*
Postoperative assessment						
First call for diclophenac from complete block (minutes)	88.8±8.8**	107.5±8.4**	145.6±25.4	212.8±32.7	70.0	0.00*
Postoperative VAS	3.6±0.5**	2±0.7**	1.6±0.7	1.4 ±0.5	23.0	0.000*
Total number of diclophenac in 24 hours	2.8±0.5*	1.2±0.8	1.2±0.4	1.2 ±0.3	11.29	0.000*
Patient satisfaction score	1.1±0.3**	1.2±0.4**	2.2±0.6	2.6±0.5	27.56	0.000*

Data are expressed as mean ± SD.
Ftest=(ANOVA=analysis of variance).
*significant ($p<0.05$)
**post hoc test in comparison between groups.

Table (2): Side effects of epidural bolus doses

Bolus	Group Ia (n=20)	Group Ib (n=20)	Group Ic (n=20)	Group II (n=20)	x^2	P
Nausea/vomiting	2(10%)*	1(5%)*	1(5%)*	6(30%)	9.59	0.02*
Pruritus	0 (0%)*	0(0%)*	0(0%)*	3(15%)	9.23	0.026*
Illeus	0 (0%)	1 (5%)	1 (5%)	2(10%)	4	0.2
Urine Retention	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0

Data are expressed as number(percentage).
X^2= chai squer test.
*significant ($p<0.05$).

Table (3): Relation between types of surgery and epidural first bolus dose failure

	Group Ia (n=20)	Group Ib (n=20)	Group Ic (n=20)	Group II (n=20)	x^2	P
Orthopedic	5 (25%)*	3(15%)*	1(5%)	1(5%)	10.2	0.016*
Urology	1 (5%)	1 (5%)	0 (0%)	0 (0%)	5	0.18
Vascular	5 (25%)*	3(15%)*	2(10%)	1(5%)	9.6	0.019*
Gynaecology	1 (5%)	1 (5%)	0 (0%)	0 (0%)	5	0.18
First dose failure	12 (60%)*	8 (40%)*	3 (15%)	2 (10%)	8.6	0.01*

Data are experssed as number (percentage).
X^2 = chi squer test.
*significant ($p<0.05$).

Table (4): Assessment of epidural infusion doses

	Group Ia (n=20)	Group Ib (n=20)	Group Ic (n=20)	Group II (n=20)	F	p
Intraoperative assessment						
Haemodynamic changes						
Hypotension	2(10.0)	3(15.0)	2(10.0)	6(30.0)	X^2 = 3.9	0.27
Bradycardia	1(5.0)	3(15.0)	3(15.0)	4(20.0)	X^2 = 1.98	0.58
Bradypnea	0 (0%)	0 (0%)	0 (0%)	0 (0%)	X^2 = 0	0
Decreased saturation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	X^2 = 0	0
Sedation score	2.3 ± 0.5**	2.4 ± 0.5**	3.1 ± 0.6	3.2 ±0.6	18.48	0.000*
Time to two-segment regression from complete block in minutes	90 ± 4.7*	100 ± 4.2**	100 ± 5.5**	120 ± 6.1	118.17	0.000*
Postoperative assessment						
First call for diclophenac from complete block (minutes)	131.3±8.5**	131.1±7.8**	140±8.2	170±12.0	31.06	0.000*
Postoperative VAS	3±0**	2.6 ±0.4**	1.7±0.5	1.5±0.6	9.80	0.000*
Total number of diclophenac ampules in 24 hours	2.3±0.5**	2.4±0.5**	1.8±0.5	1.7±0.6	4.05	0.015*
Patient satisfaction score	1.8±1.0**	1.8±0.7**	2.6±0.5	2.5±0.6	4.22	0.012*

Data are expressed as mean ± SD,number(percentage).
F test (ANOVA=analysis of variance).
X^2= chi squer test.
*significant ($p<0.05$)
**post hoc test in comparison between groups.

Table (5): Side effects of epidural infusion doses

Infusion	Group IIIa (n=20)	Group IIIb (n=20)	Group IIIc (n=20)	Group IV (n=20)	X^2	P
Nausea/vomiting	1 (5%)*	1(5%)*	2(10%)*	8(40%)	13.33	0.004*
Pruritus	0 (0%)*	0(0%)*	0 (0%)*	3(15%)	9.23	0.026*
Ileus	0(0%)	1 (5%)	1(5%)	2 (10%)	4	0.2
Urine Retention	0 (0%)	0(0%)	0 (0%)	1(5%)	4.16	0.25

Data are expressed as number(percentage).
X^2= chai square.
*significant ($p<0.05$).

DISCUSSION

Epidural anesthesia is a safe and inexpensive technique with the advantage of providing surgical anesthesia and postoperative pain relief. Neostigmine is an acetylcholinesterase inhibitor used as adjuvant analgesia epidurally **(9)**.

In this study, we found that no significant difference across the three bolus doses of neostigmine (groups Ia, Ib and Ic) relative to sensory block onset time and time to complete motor block, but there were correlations between fentanyl group and rapid onset of analgesia and time to complete motor block.

Taspinar et al. (10) found that 4 µg/kg or 8 µg/kg epidural bolus neostigmine shows no significant difference across two groups relative to sensory block onset time and time to complete block in comparison to each other.

Tekin et al. (11) compared bupivacaine plus neostigmine 4 µg/kg and bupivacaine plus 1 µg/kg fentanyl using Patient-Controlled Epidural Analgesia (PCEA) and reported that analgesia begins faster and lasts longer in patient receiving low does of local anesthetic and opioid in patients after abdominal hysterectomy.

In this study, there were no significant differences between the bolus groups regarding hypotension and bradycardia.

Harjai et al. (12) reported that mean arterial blood pressure and heart rate showed no significant changes between groups after injection of epidural neostigmine 100 µg and 200 µg in patients undergoing lower extremity surgery.

Tawfik et al. (13) found no significant difference between neostigmine 50 µg and fentanyl after intrathecal injection as regard changes in mean blood pressure or heart rate.

In our study, there were no significant differences among the bolus dose groups regard bradypnea or decreased oxyhemoglobin saturation (SpO_2) (these complications were not recorded in our study at all).

Taspinar et al. (10) found that no difference between group received 4 µg/kg or group 8 µg/kg epidural neostigmine for lower extremity surgery as regard intraoperative oxyhemoglobin saturation changes.

Bajwa et al. (14) did not observe a single case of respiratory depression when comparing group of ropivacaine 0.75% plus fentanyl 75 µg and group of ropivacaine plus 75 µg clonidine group and they explained that probably due to smaller dose of fentanyl given in their study.

These results were matched with our findings as low absorption of epidural neostigmine and low dose of used fentanyl.

In our study, we foun that there was a significant sedation with increasing the dose of bolus neostigmine (dose dependent) and with fentanyl dose. There was no significant difference between the highest dose of neostigmine and fentanyl dose regarding patient sedation.

Harjai et al. (12) reported that the addition of epidural neostigmine produced mild sedation in both neostigmine group (100 µg and 200 µg), but sedation was statistically significant with high dose of neostigmine (200 µg) (dose-dependent). This matches with our study.

Bajwa et al. (14) found that there were a significant sedation with the group receiving ropivacaine plus fentanyl 75 µg alone than the group receiving ropivacaine-clonidine or ropivacaine-clonidine-fentanyl in epidural anesthesia for lower abdominal surgery.

In our study, we found that there were significant lower nausea/vomiting with neostigmine groups in comparison to fentanyl group.

Nausea/vomiting is seen less frequently in epidural neostigmine studies of **(15) (16)**.

Kawai et al. (17) concluded that patient-controlled epidural analgesia with ropivacaine alone resulted in a significantly lower incidence of nausea and vomiting than ropivacaine-fentanyl group.

Tawfik et al. (13) concluded that sedation and nausea were the causes of delayed discharge in the neostigmine group while pruritis and respiratory monitoring were the main concern in fentanyl group.

The current study established that addition of epidural neostigmine 100 µg, 150 µg and 200 µg to bupivacaine increases the duration of analgesia in dose-dependent manner through prolonged duration for first call for diclophenac. Also, there was a significant short duration before first call for diclophenac with neostigmine groups in comparison to fentanyl group.

Nakayama et al. (18) concluded that 10 µg/kg of epidural neostigmine in bupivacaine provides a longer duration of analgesia than bupivcaine alone or with 5 µg/kg of neostigmine after abdominal hysterectomy.

Tekin et al. (11) reported that analgesia begins faster and lasts longer in patients receiving low doses of local anesthetics and opioids in comparing analgesic activity of neostigmine 4 µg/kg to fentanyl 1 µg/kg using patient-controlled epidural analgesia.

Tawfik et al. (13) found that spinal neostigmine was as effective as fentanyl and significantly prolonged the time to the first analgesic administration compared to the saline group. Both neostigmine and fentanyl groups differed significantly from the saline group ($p = 0.05$ and $p< 0.001$ respectively).

In this study, there was a significant correlation between high-bolus neostigmine dose and low postoperative VAS (dose dependent) and also there were significant correlations between high VAS with neostigmine groups in comparison to fentanyl group.

Göktug et al. (19) concluded that 300 µg and 450 µg epidural neostigmine administered before anesthesia provides effective postoperative pain relief than saline and 150 µg epidural neostigmine after open cholycystectomy reducing intra- and post-operative opioid requirement.

Tekin et al. (11) stated that that visual analog scale scores were lower in the group receiving bupivacaine plus fentanyl significantly than the other groups receiving bupivacaine plus neostigmine or bupivacaine alone.

In our study, there were a significant correlation between the lowest dose of neostigmine (100 µg) and the high total number of diclophenac ampules received during first postoperative 24 hours, but no significant difference between the other two doses of neostigmine (150 µg and 200 µg) or fentanyl dose (50 µg) groups.

Taspinar et al. (10) has shown lower analgesic consumption at 12 and 24 hours in the 8 µg/kg neostigmine group than 4 µg/kg neostigmine and saline group.

Tekin et al. (11) found that during the following 24 hours, total analgesic consumption was significantly lower in the group receiving bupivacaine plus fentanyl than the other groups receiving bupivacaine plus neostigmine or bupivacaine alone.

In this study, there were a significant correlation between the highest dose of neostigmine (200 µg) and high patient satisfaction score and also a significant correlation between fentanyl group and high patient satisfaction score.

Tekin et al. (11) recorded that there was a significant decrase in group bupivacaine according to the comparison of satisfaction scores of other fentanyl or neostigmine groups at the end of 24 hours.

In our study, we found that first bolus dose failure was significant with lower neostigmine doses, orthopedic and vascular surgeries showed significant high first dose failure with the groups of lower doses of neostigmine than the highest dose of neostigmine or fentanly group.

Taspinar et al. (10) reported that the number of delivered bolus doses was lower in the 8 µg/kg neostigmine group compared to the saline and 4 µg/kg neostigmine group**.**

There is discrepancy about the effective dose of epidural neostigmine which may partly be explained by the type of surgery, the dose being larger for more extensive and painful surgical procedure than for minor ones **(15)**.

However, in patient who underwent abdominal hysterectomy, coadministration of epidural neostigmine 5 µg/kg neostigmine plus bupivacaine did not produce effective analgesia postoperatively, whereas coadministration of epidural neostigmine 10 µg/kg neostigmine plus bupivacaine provided effective analgesia **(18)**.

In our study, we found no significant difference between the infusion dose groups regarding hypotension and bradycardia, matched with **(20)(8)**

In this study, there were a significant sedation with the highest dose of neostigmine infusion and fentanyl infusion groups. There were no significant difference between the other two doses of neostigmine and also no significant difference between the highest dose of neostigmine and fentanyl regarding patient sedation.

Ross et al. (8) observed an increase in incidence of sedation when neostigmine infusion was added to bupivacaine and also the sedative effect of low dose of epidural neostigmine infusion to be very minimal if any.

Tan et al. (21) reported that epidural opioid can be associated with dose-dependent adverse effects for sedation, pruritis, nausea and respiratory depression.

In our study, the neostigmine infusion groups showed a significant short duration to two-segment regression in comparison to fentanyl group and we found also that there was a significant correlation between the lowest dose of neostigmine and short duration to two-segment regression.

Bhat et al. (22) found that the time of two-segment regression was statistically significantly different among group A receiving bupivacaine alone, group B receiving bupivacaine plus 50 µg neostigmine and group C receiving bupivacaine plus 150 µg neostigmine with group C more prolonged time than the other two groups in spinal anesthesia for lower abdominal and lower limb surgery.

Bajwa et al. (14) reported that the regression of block height was slightly prolonged in ropivacaine plus fentanyl group than the group of ropivacaine-clonidine and the group of ropivacaine-clonidine-fentanyl in epidural anesthesia for lower abdominal surgery.

In our study, we found that there were significant lower nausea-vomiting with neostigmine infusion groups in comparison to fentanyl group.

Chia et al. (20) stated that thoracic infusion of epidural neostigmine was not associated with an increased incidence of postoperative nausea and vomiting.

Eisenach (23) noted that neostigmine does not produce respiratory depression or pruritis in comparison to fentanyl during epidural infusions.

In our study, we found that there were significant correlation between the lower neostigmine doses (group IIIa,IIIb) regarding short duration for first call for diclophenac(duration of analgesia) , high total number of diclophenac ampoules consumption in postoperative 24 hours, high postoperative VAS and low patient satisfaction scorein comparison to the highest dose neostigmine(IIIc) and fentanyl dose(IV).

there were significant prolonged duration of analgesia in group IIIc compared to the other groups of neostigmine reflected by prolonged duration before 1st call for diclophenac, but fentanyl group still has upper hand in prolonged duration of analgesia in comparison to the highest dose of neostigmine significantly. No significant difference between highest neostigmine group and fentanyl group was found regarding total number of diclophenac in first postoperative 24h., postoperative VAS and patient satisfaction score.

Chia et al. (20) concluded that continuous thoracic epidural neostigmine started before anesthesia provided preemptive, preventive analagesia and analgesic-sparing effect that improved postoperative analgesia for these patients and that 125 µg/hour continuous epidural neostigmine infusion was effective for thoracotomy which is one of extensive and painful surgical procedures.

Ross et al. (8) concluded that adding neostigmine (4 µg/ml) instead of opioids can improve the quality of epidural pain relief for women in labor while decreasing the hourly bupivacaine requirement by 19%-23% and produced maternal satisfaction with analgesia.

Roelants et al. (24) concluded that epidural combination of neostigmine 500 micrograms (6-7 micgorams/kilogram) with sufentanil 10 micrograms provides similar duration of analgesia as epidural-sufentanil 20 micrograms allowing effective and selective analgesia devoid of side effects.

CONCLUSION

The highest doses of epidural bolus or infusion neostigmine used in this study showed significant better analgesic effects than lower doses with no significant different side effects. Fentanyl drug showed significant longer duration of analgesia than neostigmine drug with similar postoperative VAS, number of diclophenac ampoules consumed in first postoperative 24 hours, and patient satisfaction score but more significant side effects than neostigmine drug.

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المقارنة بين إعطاء ثلاث جرعات من النيوستجمين بالضغط أو التنقيط أعلى الأم الجافية للعمود الفقرى والفنتانيل كمسكنات مساعدة للبالغين

أجريت هذه الدراسة بمستشفيات كلية الطب البشرى جامعة الزقازيق على ١٦٠ مريض تراوحت أعمارهم ما بين ١٦ عام و ٦٥ عام خضعوا للتخدير لعمل جراحات بالجزء السفلى من الجسم فى الفترة ما بين مايو ٢٠١٠ إلى مايو ٢٠١٣ .

تهدف هذه الدراسة إلى المقارنة بين إعطاء ثلاث جرعات من النيوستجمين بالضغط أو بالتنقيط أعلى الأم الجافية للعمود الفقرى والفنتانيل كمسكنات مساعدة للبالغين.

تم تقسيم المرضى إلى مجموعات كالآتى :

١. المجموعة الأولى : تم إعطاؤها جرعات انضغاطية من النيوستجمين أعلى الأم الجافية للعمود الفقرى (١٠٠ ميكروجرام ، ١٥٠ ميكروجرام ، ٢٠٠ ميكروجرام) مع المخدر الموضعى بيبيفاكين ١٠ مليمتر بتركيز ٠.٥% وكان عدد المرضى ٢٠ مريض لكل جرعة من النيوستجمين .

٢. المجموعة الثانية : تم اعطاؤها جرعة انضغاطية من الفنتانيل أعلى الأم الجافية للعمود الفقرى (٥٠ ميكروجرام) مع المخدر الموضعى بيبيفاكين ١٠ مليمتر بتركيز ٠.٥% وكان عدد المرضى ٢٠ مريض .

٣. المجموعة الثالثة : تم إعطاؤها جرعات تنقيطية من النيوستجمين أعلى الأم الجافية للعمود الفقرى (٧٥ ميكروجرام لكل ساعة ، ١٠٠ ميكروجرام لكل ساعة ، ١٢٥ ميكروجرام لكل ساعة) مع المخدر الموضعى بيبيفاكين حيث تم إعطاؤه بجرعة أولية انضغاطية ١٠ مليمتر بتركيز ٠.٥% ثم بالتنقيط ١٠ مليمتر بتركيز ٠.٢٥% لكل ساعة وكان عدد المرضى ٢٠ مريض لكل جرعة من النيوستجمين .

٤- المجموعة الرابعة : تم إعطاؤها جرعة تنقيطية من الفنتانيل أعلى الأم الجافية للعمود الفقرى (٥٠ ميكروجرام لكل ساعة) مع المخدر الموضعى بيبيفاكين حيث تم إعطاؤه جرعة أولية انضغاطية ١٠ مليمتر بتركيز ٠.٥% ثم بالتنقيط ١٠ مليمتر بتركيز ٠.٢٥% لكل ساعة وكان عدد المرضى ٢٠ مريض .

تم أخذ التاريخ الطبى والجراحى للمرضى وعمل فحص طبى ومعملى لهم لاستبعاد من لا يمكن إعطاؤه حقن أعلى الأم الجافية بالعمود الفقرى وقد تم قياس النتائج بقياس عدة عوامل :

١. بداية الإنسداد الحسى واكتمال الانسداد الحركى .
٢. شدة الألم باستخدام المقياس البصرى للألم .
٣. درجة التسكين باستخدام مقياس رمزى للتسكين .
٤. الارتداد الحسى بمستويين دون العصب الصدرى العاشر لقياس الجرعات التنقيطية .
٥. التغيرات فى العلامات الحيوية من الهبوط فى مستوى ضغط الدم وبطء القلب وبطء معدل التنفس ونقص تشبع الهيموجلوبين بالأكسجين .
٦. المضاعفات الناتجة من غثيان وقئ والحكة واحتباس البول والعلوص أو مضاعفات أخرى .
٧. الطلب لأولى لمسكن الديكلوفيناك .
٨. عدد الأمبولات لمسكن الديكلوفيناك التى تم إعطاؤها خلال ٢٤ ساعة بعد الجراحه.
٩. قياس مدى إرضاء المريض .

فى هذه الدراسة لم توجد اختلافات ذات دلالة إحصائية بين مجموعات الحقن الانضغاطى أو التنقيطى فيما يخص عمر المريض – الجنس – الوزن – الطول – نوع الجراحات – الزمن القياسى للجراحات وشدة الألم بمقياس البصرى للألم ما قبل الجراحة .

طبقاً لأهداف هذه الدراسة تم محاولة التوصل إلى إمكانية استبدال عقار الفنتنيل أعلى الأم الجافية كمسكن مساعد للبالغين بعقار النيوستجمين ومعرفة الجرعة الأكثر فعالية من الجرعات المستخدمة لعقار النيوستجمين بهذه الدراسة وبعد البحث فى المراجع والأبحاث العلمية المختلفة ودراسة الحالات التى شملتها هذه الدراسة وجدنا ما يلى :

١. عوامل اختيار الجرعة الأكثر فعالية من عقار النيوستجمين :
   ١. لم نجد اختلافات ذات دلالة إحصائية بين الجرعات المستخدمة من عقار النيوستجمين وبداية الإنسداد الحسى أو اكتمال الانسداد الحركى (مع الجرعات الانضغاطية)
   ٢. لم نجد اختلاف ذات دلالة إحصائية بين الجرعات المستخدمة من عقار النيوستجمين والمضاعفات الناتجة عنه (مع الجرعات الانضغاطية والتنقيطية) .
   ٣. وجدنا علاقة ذات دلالة إحصائية بين الجرعة الأعلى من عقار النيوستجمين وطول المدة قبل طلب المسكن وقلة شدة الألم بعد الجراحة بالمقياس البصرى وقلة عدد أمبولات المسكن المستخدمة خلال ٢٤ ساعة بعد الجراحة وكذلك ارتفاع قياس إرضاء المريض بعد الجراحة (مع الجرعات الانضغاطية والتنقيطية) .
   ٤. وجدنا علاقة ذات دلالة إحصائية بين الجرعة الأعلى من عقار النيوستجمين المستخدم ونجاح التسكين أثناء الجراحة بالجرعة الأولية (مع الجرعات الانضغاطية)
   ٥. وجدنا علاقة ذات دلالة إحصائية بين الجرعة الأقل من عقار النيوستجمين المستخدم وقصر المدة لحدوث الارتداد الحسى بمستويين دون العصب الصدرى العاشر (مع الجرعات التنقيطية)

   ومما سبق فنفضل استخدام الجرعات الأعلى المستخدمة فى هذه الدراسة سواء الجرعة الانضغاطية أو الجرعة التنقيطية .

٢. عوامل تفضيل عقار النيوستجمين عن عقار الفنتانيل
   ١. كان هناك علاقة ذات دلالة إحصائية بين استخدام عقار الفنتانيل وحدوث الحكة والقئ والغثيان (مع الجرعات الانضغاطية والتنقيطية) .
   ٢. لم يكن هناك حالات مع استخدام عقار النيوستجمين تعانى من الحكة أو احتباس البول أو التاثير على التنفس أثر استخدام العقار (مع الجرعات الانضغاطية أو التنقيطية) .

٣. لم يكن هناك اختلاف ذات دلالة إحصائية بين عقار الفنتانيل وعقار النيوستجمين فيما يخص شدة الألم بعد الجراحة بالمقياس البصرى وعدد أمبولات المسكن خلال ٢٤ ساعة بعد الجراحة ودرجة إرضاء المريض بعد الجراحة (مع الجرعات الانضغاطية والتنقيطية) .

٤. لم يكن هناك اختلاف ذات دلالة احصائية بين نجاح الجراحة بالجرعة الأولية الانضغاطية بين عقار النيوستجمين والفنتانيل .

ومما سبق فنفضل استخدام الجرعات الأعلى المستخدمة فى هذه الدراسة سواء الجرعة الانضغاطية أو الجرعة التنقيطية كبديل لعقار الفنتانيل.

٣. عوامل تمانع استبدال عقار الفنتانيل بعقار النيوستجمين :

١. وجد أن هناك علاقة ذات دلالة إحصائية بين عقار الفنتانيل وبداية الانسداد الحسى أو اكتمال الانسداد الحركى مقارنة بعقار النيوستجمين (مع الجرعات الانضغاطية)

٢. وجد أن هناك علاقة ذات دلالة إحصائية بين عقار الفنتانيل وطول المدة قبل طلب المسكن مقارنة بعقار النيوستجمين (مع الجرعات الانضغاطية والتنقيطية)

٣. وجدنا علاقة ذات دلالة احصائية بين عقار الفنتانيل وطول المدة قبل الارتداد الحسى بمستويين دون العصب الصدرى العاشر (مع الجرعات التنقيطية).

ومما سبق يتضح أن عقار الفنتانيل ما زال له مميزات ولذلك نوصى بدراسات أخرى لاستخدام عقار النيوستجمين بجرعات أعلى نظراً لفاعليته الثابتة وقلة المضاعفات الناتجة عن استخدام أعلى الأم الجافية للعمود الفقرى سواء بالتنقيط أو الانضغاط .

على الرغم من وجود تطور كبير فى مجال التخدير بأنواعه إلا أننا ما زلنا نحاول أن نصل للأفضل وتحدى الغد أن تحاول وإن لم نستطيع الوصول إلى أفضل العقارات واقلها ضرراً على المرضى .