

A Study to Compare the Effect of Fentanyl 25 µg vs. Clonidine 30µg on Intra-Operative Analgesia

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ABSTRACT

Introduction: There is well known clinical aphorism that when pain is treated prophylactically the amount of drug required is considerably less than that which would be required if treatment were to be delayed until pain became severe. Objective of the research was to compare the effect of Fentanyl 25 µg vs. Clonidine 30µg on intra-operative analgesia

Material and Methods: Randomized double blind controlled study. Patients were Co-loaded with 10ml/kg Ringers Lactate 15 minutes prior to surgery. Patient's baseline rate were noted. Equipment's and drugs necessary for resuscitation and general anaesthesia administration were kept ready. Subarachnoid block was achieved with 25 G Quinke's Spinal needle in L3-L4 lumbar space in lateral decubitus position. Study groups received spinal anaesthesia with Group I: 3 ml of 0.75% Ropivacaine (22.5 mg) + 0.5 ml of Fentanyl (25 µg) (total vol. - 3.5 ml). Group II: 3 ml of 0.75% Ropivacaine (22.5 mg) + 0.2 ml of Clonidine diluted to 0.5 ml with normal saline (30 µg) (total vol.- 3.5ml).

Results: Thus duration of Post - operative analgesia was statistically significant ($p=0.000$) in Group II as compared to Group I with Clonidine having longer total duration of Post - operative analgesia. The baseline systolic blood pressure, diastolic blood pressure and heart rate were comparable in both groups. Similarly incidence of shivering was statistically insignificant in both groups the percentage being 15.00% and 12.50% in group I and II respectively.

Conclusion: Incidence of hypotension and bradycardia was more with Clonidine as compared to Fentanyl. There was no significant difference in incidence of nausea, vomiting and shivering in both groups.

Key words: Hypotension, Bradycardia, Clonidine

INTRODUCTION

The ASA "Practice guidelines for acute pain management in the peri-operative setting"¹ stresses on multimodal therapy with two or more analgesic agents or techniques used in combination for control of postoperative pain.

The final aim of this aspect of therapy would be seen as the complete relief of postoperative pain with no treatment related side effects.

There is well known clinical aphorism that when pain is treated prophylactically the amount of drug required is considerably less than that which would be required if treatment were to be delayed until pain became severe.

Adjuvant drugs are pharmacological agents possessing little pharmacological effect by themselves, but enhance or potentiate the action of other drugs when given at the same time. Adjuvant drugs modify LA effects and reduce side effects.

Peri-operatively these drugs affect:

- Latency i.e. time of onset of LA block
- Duration of analgesia i.e. duration of sensory and motor

block

- Quality of analgesia i.e. complete, incomplete (partial or patchy analgesia requiring supplemental drugs)
- Postoperatively adjuvant drugs affect:
- Analgesic gap i.e. time interval between subsequent doses administered
- Quality of analgesia i.e. patient satisfaction, care provider's impression of pain relief

• Side effects i.e. reduction of untoward effects of LA drugs
Knowledge and use of adjuvant drug therapy has rendered neuraxial analgesia more effective in the management of both acute and chronic pain conditions.

Spinal opioids along with LA drugs are the mainstay of post-operative acute pain treatment. They are also helpful in painful conditions alone or in combination with other drugs. Analgesia is dose-related, and is specific for visceral pain, not somatic pain. Opioids cause analgesia by acting on opioid receptors which are abundant throughout the CNS including lamina II or substantia gelatinosa of the dorsal horn. These receptors belong to a subfamily of G protein coupled receptors. Four types of opioid receptors mu (M), kappa (K), sigma (S), and delta (D) have been described. The endogenous opioid system acts via enkephalins, endorphins and dynorphin. Neuraxial opioids produce analgesia by directly acting on the opioid receptors of the CNS.² They may also inhibit release of other excitatory neurotransmitters. Not all opioids administered neuraxially acts at the level of the spinal cord. Opioids administered intrathecally eventually reach the plasma by absorption and thereby reach different areas of the cerebral cortex. Consequently, their effects are produced at the post central gyrus, nucleus raphe magna, reticular activating system, and medulla. However opioids have few side effects such as respiratory depression, urinary retention, vomiting and itching which prompted a search for other non-opioid agent which can be used intrathecally.

The analgesic effect following its intrathecal administration is mediated spinally through activation of postsynaptic alpha - 2 receptors in substantia gelatinosa of spinal cord. The rationale behind intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of alpha - 2 adreno-

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How to cite this article: Mohammed N. Ali, Pradeep P. A study to compare the effect of fentanyl 25 µg vs. clonidine 30µg on intra-operative analgesia. International Journal of Contemporary Medical Research 2016;3(3):819-821.

Variable	Group I	Group II	P Value
	Mean ± SD	Mean ± SD	
Time for Two Segment Regression(In Min)	111.625 ± 15.897	116.525 ± 7.494	0.080
Duration of Surgery (In Min)	62.875 ± 33.862	71.125 ± 40.088	0.322
Duration of Sensory Block (In Min)	259.125 ± 16.904	427.850 ± 19.732	0.000
Duration of Motor Block (In Min)	110.625 ± 16.725	322.425 ± 34.446	0.000
Duration of Post-op Analgesia (In Min)	228.250 ± 19.400	314.125 ± 21.747	0.000

Table-1: Comparison of two groups in various parameters

Sr No.	SBP	Group I	Group II	SEM	P value
		Mean	Mean		
1.	Baseline	127.2	129.3	2.046	0.470
2.	5 min	122.7	123.4	1.905	0.796
3.	10 min	120.9	118.95	1.819	0.451
4.	15 min	120.4	115.95	1.823	0.088
5.	20 min	121.05	113.4	1.810	0.004
6.	25 min	121.7	111.9	1.749	0.000
7.	30 min	121.75	112.3	1.695	0.000

Table-2: Comparison of two groups in terms of systolic blood pressure

Sr No.	DBP	Group I	Group II	SEM	P value
		Mean	Mean		
1.	Baseline	77.100	77.050	1389	0.980
2.	5 min	74.750	72.800	1.292	0.289
3.	10 min	73.850	70.800	1.268	0.093
4.	15 min	73.900	68.800	1.316	0.008
5.	20 min	74.300	67.750	1.270	0.000
6.	25 min	74.600	66.550	1.252	0.000
7.	30 min	73.450	68.800	1.202	0.000

Table 3: Comparison of two groups for diastolic blood pressure

Sr No.	Heart Rate	Group I	Group II	SEM	P value
		Mean	Mean		
1.	Baseline	76.300	76.100	1.187	0.905
2.	5 min	75.300	72.400	1.159	0.081
3.	10 min	74.850	69.300	1.254	0.002
4.	15 min	74.250	67.500	1.234	0.000
5.	20 min	74.800	65.450	1.233	0.000
6.	25 min	75.350	64.550	1.202	0.000
7.	30 min	75.150	65.200	1.083	0.000

Table-4: Comparison of two groups in terms of heart rate

ceptors in the spinal cord and its work by blocking the conduction of C and A delta fibres, increases potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics. Thus clonidine is now acceptable adjuvant to local anaesthetics in spinal route.

The present study was undertaken to evaluate clinical effects of adding fentanyl or clonidine to intrathecal Isobaric Ropivacaine 0.75% to study the characteristics of the block, hemodynamic and postoperative pain relief in patients undergoing lower abdominal surgeries.

MATERIALS AND METHODS

Study Design: Randomized double blind controlled study.

Inclusion Criteria

1. Patients of either sex in age group of 20-60 yrs.

2. Height > 140 cms and Weight less than 120 kgs.
3. American Society of Anaesthesiology (ASA) physical status 1 and 2.
4. Posted for lower abdominal surgeries like TURP, TUR-BT, Cystolithotripsy/Lithotomy, Genitourinary surgeries, Hernioplasty, Hydrocelectomy, Hysterectomy (Open/Vaginal) etc.
5. Elective or Emergency Procedure.

Exclusion Criteria

1. Age < 18 or > 60 yrs.
2. American Society of Anaesthesiology (ASA) physical status other than 1 and 2.
3. Those with known allergies/ contraindications to drugs being used in studies.
4. Those with Height < 140 cms or Weight >120 kgs.
5. Contraindication to spinal anaesthesia

Inside O.T.

Patients were Co-loaded with 10ml/kg Ringers Lactate 15 minutes prior to surgery. All standard monitors (NIBP, ECG, pulse oximeter) attached. Patient’s baseline systolic/diastolic/mean BP, heart rate, SpO₂ along with respiratory rate were noted. Equipment’s and drugs necessary for resuscitation and general anaesthesia administration were kept ready. Subarachnoid block was achieved with 25 G Quinke’s Spinal needle in L3-L4 lumbar space in lateral decubitus position.

Study groups received spinal anaesthesia with

Group I: 3 ml of 0.75% Ropivacaine (22.5 mg) + 0.5 ml of Fentanyl (25 µg) (total vol. – 3.5 ml).

Group II: 3 ml of 0.75% Ropivacaine (22.5 mg) + 0.2 ml of Clonidine diluted to 0.5 ml with normal saline (30 µg) (total vol.- 3.5ml).

The total volume injected was 3.5 ml in all groups. The person giving the spinal and the person who was observing intra-operative and postoperative parameters was unaware of the drug given. The time of injection of drug was noted.

Onset of sensory block (by pin prick sensation), onset of motor block (by modified Bromage scale) were noted in all patients. The parameters like Sensory blockade, Motor blockade, Cardiovascular stability, Central effects were observed.

RESULTS

In our study the mean Time required for two segment regressions in sensory level in group I was 111.625 ± 15.897 min while in group II this time was 116.525 ± 7.494 min. The P value was 0.080 which was statistically insignificant. The total duration of surgery was also comparable in both groups. Duration of sensory block, total duration of post operative analgesia and motor block is statistically significant (p = 0.000) in Group II as compared to Group I.

So in our study the baseline systolic blood pressure was com-

parable in both groups with no significant difference till 15 min. Then there was a significant fall in blood pressure in Clonidine group as compared to Fentanyl group.

So in our study the baseline diastolic blood pressure was comparable in both groups with no significant difference till 10mins. Then there was a significant fall in blood pressure in Clonidine group as compared to Fentanyl group.

So in our study the baseline Heart rate was comparable in both groups with no significant difference at 05 min. Then there was a significant decrease in Heart rate in Clonidine group as compared to Fentanyl group.

The incidence of nausea and vomiting in group I and II was 17.50% and 15.00% respectively. The difference was statistically insignificant.

Similarly incidence of shivering was statistically insignificant in both groups the percentage being 15.00% and 12.50% in group I and II respectively.

DISCUSSION

CemileÖztinÖğün et al³ concluded that, intrathecal 17.5 mg 0.5% isobaric ropivacaine provides efficient and safe anaesthesia for caesarean section delivery.

SukhminderJit Singh Bajwa et al⁴ concluded that analgesic properties of clonidine and fentanyl when used as adjuvant to ropivacaine in epidural anaesthesia are almost comparable and both can be used in combination at lower doses without impairing the pharmacodynamic profile of the drugs as well as with a significant reduction in side effects.

Benhamou D et al⁵ concluded that adding a small dose of intrathecal clonidine to bupivacaine increase the quality of intraoperative analgesia and decreases pain during caesarean section.

SangeetaVarun et al⁶ concluded that intrathecal administration of ropivacaine-fentanyl has faster onset and regression of sensory block, delayed onset but comparable regression of motor block and shorter duration of analgesia as compared to intrathecal bupivacaine-fentanyl.

B.S.Sethi et al⁷ concluded that addition of clonidine to bupivacaine in the dose of 1 µg/kg significantly increases the duration of analgesia as compared to bupivacaine alone. Though these doses have an effect of sedation level, heart rate and mean arterial pressure that does not require any therapeutic intervention.

Un Canan et al in 2013⁸ concluded that in elective cesarean delivery, the combinations of bupivacaine + fentanyl or ropivacaine + fentanyl exhibited similar anesthetic efficacy, and fetal and maternal effects.

Jack W. van Heef et al⁹ concluded that subarachnoid injection of glucose-free ropivacaine solutions results in a variable spread of analgesia, mostly accompanied by a good quality of motor block, in particular with the 0.75% solution.

Gonul Sagiroglu et al¹⁰ concluded that addition of clonidine to intrathecally administered ropivacaine increased the duration of sensory and motor block. However, when clonidine was added, careful monitoring of hypotension, bradycardia and sedation was necessary.

De Kock et al¹¹ concluded the association of low-dose clonidine (15 µg) with 8 mg ropivacaine for ambulatory knee arthroscopy significantly improves the subjective parameters that reflect the quality of intra-operative analgesia and without compromising early mobilization or inferring systemic side

effects. The benefits of this association in cases of ambulatory surgery must be weighed against the potential drawbacks that can result from mixing different drugs for intrathecal administration.

CONCLUSION

Incidence of hypotension and bradycardia was more with Clonidine as compared to Fentanyl. There was no significant difference in incidence of nausea, vomiting and shivering in both groups.

REFERENCES

1. American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116:248-73.
2. Zhou Hy, Chen SR, Chen H, Pan HL. Opioid-induced long-term potentiation in the spinal cord is a pre synaptic event. *J Neuroscience*. 2010;30: 4460-6.
3. Cemile. Ötzin, E.N. Kirgiz, A. Duman, I. Kara, S. Ökesli: The Comparison of Intrathecal Isobaric Ropivacaine and Isobaric Ropivacaine-Clonidine for Caesarean Delivery. *The Internet Journal of Anesthesiology*. 2007:15.
4. Sukhminder Jit Singh Bajwa, Sukhwinder Kaur Bajwa, Jasbir Kaur, Amarjit Singh, Geetika Bakshi, Kanwalpreet Singh, Aparajita Panda. Admixture of clonidine and fentanyl to ropivacaine in epidural anesthesia for lower abdominal surgery. *Anaesthesia essays and researches*. 2010:4
5. Benhamou D, Thorin D, Brichtant JF, Dailland P, Milon D, Schneider M. Intrathecal clonidine and Fentanyl with hyperbaric bupivacaine improves analgesia during caesarean section. *Anaesthesia and Analgesia*. 1998:2
6. Sangeeta Varun, Mridul Srivastava, Indubala Maurya, Rakesh Garg, Vipin Dhama, Yogesh Kumar Manik. A clinical prospective, randomized study to compare intrathecal isobaric bupivacaine – fentanyl and isobaric ropivacaine – fentanyl for lower abdominal and lower limb surgeries. *Anaesthesia, pain and Intensive care*. 2012:2
7. B.S.Sethi, Mary Samuel, Deepak Sreevastava, Efficacy of Analgesic Effects of Low Dose Intrathecal Clonidine as Adjuvant to Bupivacaine. *Indian Journal of Anaesthesia*. 2007;51:415-419.
8. Un Canan, D Örnek, O Kilci, F Dönmez, M Gamli, B Dikmen. Comparison of the maternal and neonatal effects of bupivacaine plus fentanyl and ropivacaine plus fentanyl during cesarean delivery. 2013;16:195-200.
9. Jack W. van Heef, Bernadette Th. Veering, and Anton G. L. Burm. Spinal Anesthesia with Ropivacaine: A Double-Blind Study on the Efficacy and Safety of 0.5% and 0.75% Solutions in Patients Undergoing Minor Lower Limb Surgery. *Anesthesia and Analgesia*. 1994;78: 1125-30
10. Gonul Sagiroglu, Tamer Sagiroglu, Burhan Meydan. The Effects of Adding Various Doses of Clonidine to Ropivacaine in Spinal Anesthesia. *The Eurasian journal of Medicine*. 2009;41:149-153.
11. De Kock M, Gautier P, Fanard L, Hody JL, Lavand'homme P. Intrathecal ropivacaine and clonidine for ambulatory knee arthroscopy: A dose-response study. *Anesthesiol*. 2001;94:574.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 28-01-2016; **Published online:** 19-02-2016