ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS: Bupivacaine, Clonidine, Fentanyl.

COMPARISON OF EFFICACY OF INTRATHECAL FENTANYL, CLONIDINE AND FENTANYL-CLONIDINE COMBINATION AS ADJUVANT TO BUPIVACAINE FOR LOWER LIMB ORTHOPAEDIC SURGERIES

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ABSTRACT

INTRODUCTION: The aim of my study was to assess block duration, analgesic consumption, time from block insertion until first administration of analgesic, visual analogue scores for assessment of pain, and block-related and analgesic related complications.

MATERIALS AND METHODOLOGY:

This is a prospective randomized doubled blinded study consisting of 90 patients of ASA physical status I-III of both sexes, aged between 18 and 70 years and weighing 40-70kgs, scheduled for lower limb orthopaedic surgeries under sub-arachnoid block. Patients were randomly divided into 3 groups of 30 patients each as:-

- Group BC – Inj 0.5% Bupivacaine heavy 2.5ml+ Inj Clonidine 30mcg.
- Group BF - Inj 0.5% Bupivacaine heavy 2.5ml + Inj Fentanyl 25mcg.
- Group BCF – Inj 0.5% Bupivacaine heavy 2.5ml + Inj Fentanyl 12.5mcg + Inj Clonidine 15mcg.

Onset and duration of sensory and motor blockade, haemodynamic parameters, total duration of post-operative analgesia for 24hrs using VAS score, time of first analgesic requirement and side effects were recorded.

RESULTS:

In our study we found that the duration of motor blockade was superior in Group BCF compared to Group BC and Group BF with stable haemodynamic parameters and the requirement of post-operative analgesia in the first 24hrs significantly lower with group BCF when compared to group BC and group BF.

CONCLUSION:

Ultralow doses of Fentanyl and Clonidine when added as adjuvants to intra-thecal 0.5% Bupivacaine was superior to either drug added alone in prolonging the duration of sensory and motor blockade and maintaining better haemodynamic stability and reduced side effects.

INTRODUCTION

Spinal anaesthesia is the preferred anaesthetic technique in lower extremity and lower abdominal surgeries. It is very economical, easy to administer, produces rapid onset of anaesthesia and complete muscle relaxation. It offers the advantages of reduced incidence of deep venous thrombosis, decreased intra-operative blood loss, and continued postoperative analgesia.

Hyperbaric bupivacaine is the most commonly used intra-thecal local anaesthetic. However, post-operative pain control is a major problem because spinal anaesthesia using local anaesthetics alone is associated with relatively short duration of action and thus early analgesic intervention is needed in post-operative period. To overcome this, addition of an adjuvant drug intra-thecally which will increase the efficacy of neuraxial block is a logical choice. A number of drugs have been used as an adjuvant to spinal local anesthetics e.g., opioids like morphine, buprenorphine, pethidine, fentanyl, sufentanil, and tramadol. Other adjuvants like clonidine, ketamine, neostigmine and dexmeditomedine have also been used.

Fentanyl acts primarily as an agonist at μ-opioid receptors to produce analgesia allowing dose reduction of local anesthetic but causes side effects such as pruritus, nausea, vomiting, urinary retention and respiratory depression.

Clonidine is a centrally acting selective partial α2 adrenergic agonist and prolongs the duration of sensory and motor blockade by virtue of its ability to decrease sympathetic nervous system outflow but may cause hypotension, brady cardia and sedation.

By using low dose clonidine and fentanyl combination we hypothesised that the incidence of adverse effects could be reduced and duration of post-operative analgesia could be prolonged.

MATERIALS AND METHODS

After obtaining the Ethical committee clearance and taking written informed consent, 90 patients of ASA physical status I-III of both sexes, aged between 18 and 70 years and weighing 40-70kgs, scheduled for lower limb orthopaedic surgeries under sub-arachnoid block were included in the study.

A detailed preanaesthetic check up was done. Patients were kept nil per oral for 6hrs for solids and 2hrs for clear fluids.

PATIENTS WERE RANDOMLY DIVIDED INTO 3 GROUPS OF 30 PATIENTS EACH AS:-

- Group BC – Inj 0.5% Bupivacaine heavy 2.5ml+ Inj Clonidine 30mcg.
- Group BF - Inj 0.5% Bupivacaine heavy 2.5ml + Inj Fentanyl 25mcg.
- Group BCF – Inj 0.5% Bupivacaine heavy 2.5ml + Inj Fentanyl 12.5mcg + Inj Clonidine 15mcg.

Total volume was made to 3ml in all the groups by adding Normal Saline.

The person doing the study was blind regarding the patient group and the drug injected.

The solutions were prepared by another anaesthesiologist, the co-investigator 1 who was not involved in the study without mentioning its content in the case proforma and another anaesthesiologist, the co-investigator 2 entered the patient group in the case proforma and the data in softcopy or hard copy.

In operation theatre baseline heart rate, blood pressure, respiratory rate and SpO_2 were recorded. A good IV access achieved and ringer lactate was started. Under strict aseptic precautions, a midline spinal puncture was performed at L3-L4 or L4-L5 level in sitting position using a 23gauge Quincke spinal needle after prior local infiltration with 2% lignocaine. All injections were given at a rate of 1 ml over 4-5s and then the

patients were positioned in supine position for surgery.

THE FOLLOWING PARAMETERSWERE STUDIED:-

- Onset and duration of sensory and motor blockade by pinprick test and modified Bromage scale respectively.
- Haemodynamic parameters like HR and NIBP were monitored throughout the procedure.
- Total duration of post-operative analgesia for 24hrs using VAS score.
- Time of first analgesic requirement.
- Side effects like nausea, vomiting, pruritis and sedation were noted.
- Patient satisfaction was assessed on a 4-point Likert scale (3-complete satisfaction, 2-partial satisfaction, 1-dissatisfaction, 0-not applicable)[11].

A decrease in systolic BP of more than 20% (as compared to the baseline) or < 90 mm Hg systolic, whichever was low, was treated with incremental doses of 6mg I.V Mephentermine and heart rate <50 beats/min was treated I.V atropine 0.6mg.

RESULTS

The results was analysed by using Kruskal Wallis Test and p < 0.05 was considered to be statistically significant.

p value of ASA physical status was 0.513 which was >0.05, thus statistically insignificant.

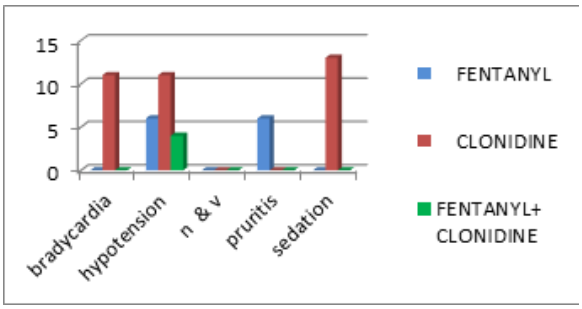
The Group BCF had faster time of onset of sensory and motor blockade, prolonged duration of action and good post-operative analgesia when compared to the other two groups which was statistically significant.

Table-1

Basic Characteristics	Fentanyl		Clonidine		Fentanyl+ Clonidine		p-VALUE
	Mean	SD	Mean	SD	Mean	SD	
ASA status	1.67	0.606	1.77	0.626	1.87	0.681	.513
OSB(MINS)	3.10	0.960	2.60	0.515	2.42	0.543	.012
OMB(MINS)	7.60	1.133	3.13	0.490	2.88	0.583	<0.001
DSB(MINS)	156.67	24.612	261.17	39.253	287.67	29.645	<0.001
DMB(MINS)	181.67	24.081	294.67	41.125	321.17	30.729	<0.001
1ST ANALGESIC TIME(MINS)	203.33	24.612	315.33	37.827	360.17	28.752	<0.001
VAS-2HRS	0.00	0.000	0.00	0.000	0.00	0.000	1.000
VAS-3HRS	0.00	0.000	0.00	0.000	0.00	0.000	1.000
VAS-4HRS	2.67	1.516	0.00	0.000	0.00	0.000	<0.001

With the VAS scores at 2hrs and 3hrs there is no significant difference between the three groups, however the VAS score at 4hrs was better with Group BCF and Group BC which was statistically significant.

COMPARISON OF INCIDENCE OF SIDE EFFECTS AM ONG THE THREE GROUPS



Graph 1 The occurance of side effects was significantly minimum with Group BCF when compared to Group BC and Group BF.

DISCUSSION

Table 2

Author And Year	Drug And Dosages	Duration Of Sesnsory Block (mins)	Duration Of Motor Block (mins)	Duration Of Effective Analgesia (mins)
Milin Raju Shah et al 2018	GROUP BCF (2.6ml+30µg+20µg)	208.5±22.1	236.7 ± 21.7	407 ± 131.5
	GROUP BC (2.6ml + 30µg)	176.7±29.6	201.2 ± 30.2	320 ± 96.2
	GROUP BF (2.6ml + 20µg)	144 ±12.3	165.5 ± 12.9	180 ±45.6
Sweety Rana et al, 2018	GROUP BCF (2.6ml+45µg+15µg)	195.33±34.11	277.67±26.90	424.50 ± 45.95
	GROUP BC (2.6ml + 45µg)	192.33±36.55	207.17±32.61	323 ± 57.98
	GROUP BF (2.6ml + 15µg)	124.66±29.48	160.83±25.63	240.83 ± 31.62
Ravanjit Singh et al, 2015	GROUP BCF (1.5ml+37.5µg+12.5µg)	137.80±11.09	112.40±10.32	208.00±26.58
	GROUP BC (1.5ml + 75µg)	128.20±14.85	111.60±9.80	209.80±26.32
	GROUP BF (1.5ml + 25µg)	89.00±9.68	88.20±7.48	199.20±21.92
	GROUP BS (1.5ml+0.5ml saline)	80.00±11.55	72.80±11.37	135.20±12.70
Marilyn Nazareth et al, 2013	GROUP BCF (2.4ml+30µg+20µg)	350.6	318.2	774.4 ± 59.59
	GROUP BC (2.4ml + 30µg)	335.9	308.4	524.6 ± 32.21
Present study	GROUP BCF (2.5ml+15µg+12.5µg)	287.67±29.645	321.17±30.729	360.17±28.752
	GROUP BC (2.5ml + 30µg)	261.17±39.253	294±41.125	315.33±37.827
	GROUP BF (2.5ml + 25µg)	156.67±24.612	181.67±24.081	203.33±24.612

B – 0.5% Hyperbaric Bupivacaine, C-Clonidine, F-Fentanyl, S-Saline.

In our study we found that addition of 12.5μg fentanyl + 15 g of clonidine to 0.5% hyperbaric bupivacaine significantly prolongs the duration of the sensory and motor block (321.12±30.729mins) and duration of effective analgesia (360.17±28.752mins) as compared to the bupivacaine + clonidine and bupivacaine + fentanyl combinations ($p<0.001$) with stable haemodynamics. The incidence of bradycardia was 36.6%in Group BC and nil in other two groups. Significant hypotension requiring treatment occurred in 20% in Group BF, 36.6% in Group BC and 13.3% in Group BCF. Side effects like pruritis was observed in 20% of the patients in Group BF and sedation was seen in 13% with Group BC. None of the patients in the three groups had nausea and vomiting.

Milin Raju Shah et al, in 2018 did a study on 90 patients undergoing orthopaedic surgery obtained similar results of prolonged duration of sensory block, motor block and effective analgesia with 30 g of clonidine added to bupivancaine and fentanyl combination as compared to bupivacaine + clonidine and bupivacaine + fentanyl combinations.

Marilyn Naza et al in 2013 showed that addition of 20 g fentanyl to intrathecal 30 g clonidine and 12 mg bupivacaine enhanced the duration of post-operative analgesia in Group BCF and BC with moderately increased sedation and higher incidence of pruritis in Group BCF.

CONCLUSION

This prospective randomised double blind study done on 90 patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia concluded that Ultralow doses of Fentanyl and Clonidine when added as adjuvants to intra-thecal 0.5% Bupivacaine was superior to either drug added alone in prolonging the duration of sensory and motor blockade and maintaining better haemodynamic stability and reduced side effects.

REFERENCES

1. Abdul Hakim, Arif Amin Bhat, Masrat Jan. Effect of Clonidine and/or Fentanyl in Combination with Intrathecal Bupivacaine for Lower Limb Orthopedic Surgeries in Spinal Anaesthesia. Journal of medical science and clinical research, 2017 Nov;(5):31085-31093.
2. Singh R, Kundra S, Gupta S, Grewal A, Tewari A. Effect of clonidine and/or fentanyl in combination with intrathecal bupivacaine for lower limb surgery. Journal of anaesthesiology, clinical pharmacology. 2015 Oct;31(4):485.
3. Nazareth M, Ghoshal P, Namshikar V, Gaude Y. Addition of intrathecal fentanyl to bupivacaine clonidine mixture effect on quality of subarachnoid block and postoperative analgesia. Anesthesia, essays and researches. 2013 Jan;7(1):76.
4. Shah MR, Diwan G. Comparison of Effect of Clonidine Added to Bupivacaine-Fentanyl Mixture on the Quality of Spinal Anaesthesia and Peri-Op Analgesia with Bupivacaine-Fentanyl or Bupivacaine-Clonidine Mixture in Major Orthopaedic Lower Limb Surgeries. MVP Journal of Medical Sciences. 2018 Aug 17;5(1):69-74.
5. Rana S, Singh SP, Asad M, Bakshi V. Comparative Evaluation of the Efficacy of Intrathecal Fentanyl, Clonidine and Fentanyl-Clonidine Combination as an Adjuvant to Bupivacaine for Infra-Umblical Surgery. Journal of Case Reports. 2018 May 13;8(1):67-71.
6. Routray SS, Raut K, Pradhan A, Dash A, Soren M. Comparison of intrathecal clonidine and fentanyl as adjuvant to hyperbaric bupivacaine in subarachnoid block for lower limb orthopedic surgery. Anesthesia, essays and researches. 2017 Jul;11(3):589.
7. Diwakaran R, Parthasarathy S, Krishnaveni N. Comparative evaluation of addition of either fentanyl or clonidine to bupivacaine in spinal anesthesia–a randomized controlled trial. Anaesthesia, Pain & Intensive Care. 2019 Jan 20:223-7.
8. Tilkar Y, Bansal SA, Agnihotri GS. Effect of adding clonidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in orthopedic procedures: A double blind controlled study. Int J Med Sci Public Health. 2015 Apr 1;4:458-62.
9. Madhava R, Prasad N, Shankar R. Spinal anaesthesia for single level spine surgery: comparison between bupivacaine with fentanyl and bupivacaine with clonidine. Sri Lankan Journal of Anaesthesiology. 2019 Feb 6;27(1).
10. Singh RB, Chopra N, Choubey S, Tripathi RK. Role of Clonidine as adjuvant to intrathecal bupivacaine in patients undergoing lower abdominal surgery: A randomized control study. Anesthesia, essays and researches. 2014 Sep;8(3):307.
11. Neuprez A, Delcour JP, Fatemi F, Gillet P, Crielaard JM, Bruyère O, Reginster JY. Patients' expectations impact their satisfaction following total hip or knee arthroplasty. PLoS One. 2016 Dec 15;11(12):e0167911.