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Original Article

Comparative evaluation of effects of different doses of intrathecal clonidine with bupivacaine on post operative pain relief

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ABSTRACT

Present study was carried out to compare and evaluate the effect of different dosage of intrathecal Clonidine in combination of Bupivacaine on postoperative pain relief and possible side effects. We randomly selected ninety patient of ASA grade I and II of aged 30 to 45 years posted for abdominal hysterectomy and divided into three groups each. Group I received .5% Bupivacaine heavy 15 mg, Group II received .5% Bupivacaine heavy 15 mg and Clonidine 15 mcg and Group III received .5% Bupivacaine heavy 15 mg and Clonidine 30 mcg intrathecally. Sensory block was assessed by pinprick method, motor block was assessed by Bromage scale, analgesia was assessed by Visual analogue scale and sedation by Cherniks score. Hemodynamic and Respiratory parameters were recorded and side effects if any were noted. Onset time of sensory block was 110.5+11.3, 109.9+14.7 and 107.5+14.4 seconds in Group I, Group II and Group III respectively which was shorter in group II Group III as compared to Group I, the difference was of no clinical and statistical significance. Onset time of motor block was almost similar in all the three groups. Duration of sensory block (time from subarachnoid block to first complain of pain by patient) was 204.8+34.8, 315.37+50.3 and 387.07+83.19 minutes in Group I, Group II, and Group III respectively and was significantly higher in group II and III as compared to Group I. Duration of motor block (time from subarachnoid block to movement of lower limb) was similar in all groups. No significant difference was found regarding sedation in all the groups. Hemodynamic parameters were similar in all the Groups at different time intervals. Thus intrathecal addition of Clonidine in small doses with Bupivacaine increases the duration of post operative pain relief without significant side effects.

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1. Introduction

Most common method for postoperative pain relief is the use of opioids either in central neuraxial block or parentally. However use of opioids is limited due to side effects like respiratory depression, pruritis and urinary retention. Intrathecal Dextrometomidine is also a recent adjuvant to local anaesthetic which prolongs the post operative analgesia but sedation and hemodynamic instability is associated with the use of this drug. Central neuraxial block with local anaesthetic agent is of limited value for post operative pain

relief due to their shorter duration of action. Efforts have been going on to find out better adjuvant drugs used with local anaesthetic agent in central neuraxial block to prolong duration of sensory block. Clonidine is an imidazoline derivative with selective partial α_2 Adrenergic receptor agonist activity which has analgesic effect at spinal level mediated by postsynaptically situated α_2 adrenoceptors in dorsal horn of spinal cord. Clonidine has variety of actions. It has antinociceptive effect on both somatic and visceral pain which is free of opioid related side effects^[11,12]. It has been used as solely as well as with opioids and with local anaesthetic agents in labour analgesia and orthopedic procedures^[16,18,19]. Clonidine used intrathecally prolongs the duration of both sensory and motor block. In most of the previous studies clonidine was used in higher dosage with more fall in blood pressure and high degree of sedation^[13,22,24].

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Aims and Objectives:-

1. To study the effect on onset, duration and level of sensory and motor block with the addition of Clonidine in Bupivacaine intrathecally.
2. To compare the hemodynamic and respiratory parameters.
3. To study the incidence of side effects and complications

Methods:-

Present study was carried out in Department of Anaesthesiology S.S. Medical College REWA. We selected 90 female patients undergoing abdominal hysterectomy of ASA grade I and II of age 30 to 45 years. Ninety patients were randomly divided in three groups of 30 each depending on drugs given intrathecally.

Group I- .5% heavy Bupivacaine 15 mg

Group II- .5% heavy Bupivacaine 15 mg and Clonidine 15 mcg

Group III- .5% heavy Bupivacaine 15 mg and Clonidine 30 mcg

Patient taking any medication (Ace inhibitors, Calcium channel blockers, adrenergic agonist or any contraindication to subarachnoid block were excluded from the study.

All patients were kept nil orally for 6 hours .After taking the patients in O.T. baseline pulse rate, blood pressure, respiratory rate, Spo2 were recorded . A wide bore i.v. line was established and all patients were preloaded with 15 ml / kg body weight ringer`s solution. Before performing subarachnoid block all the patients were premedicated with inj Glycopyrolate .2 mg I.V.

Spinal Anaesthesia was performed in sitting position with 25 gauge Quincke spinal needle by midline approach at L 3-4 level. After confirming free flow of CSF drug was injected in subarachnoid space according to Group, and patients were made supine. After spinal anaesthesia the vital parameters pulse rate, blood pressure, respiratory rate and Spo2 were recorded at every minute for 5 minute then every 5 minute for next thirty minutes then every 10 minutes till the completion of surgery . During surgery i.v. fluids were administered as required and patients were observed for bradycardia, hypotension, nausea and vomiting, shivering, pain, any discomfort and other side effects . Bradycardia (heart rate <60 /minute) treated with injection Atropine 0.6 mg IV, hypotension (fall of systolic blood pressure >20% OR systolic blood pressure <90 mm hg) was treated with i.v. fluids and/or injection Mephentermine 3 mg I.V. and respiratory depression (respiratory rate <10 or spo2<90%) was recorded and treated by oxygen by face mask.

Onset of sensory block was assessed by pin prick method and the time from intrathecal injection to loss of sensation of pinprick was taken as onset of sensory block. The highest level of loss of sensation of pinprick was taken as level of sensory block, and time interval from onset of sensory block to first complain of pain was recorded as duration of analgesia.

Motor block was assessed by Bromage scale as given in Table 1. Time from injection of drug to failure to raise the lower limb was taken as onset time of motor block. Duration of motor blockade was recorded as time from onset of motor block to time when patient was able to raise his limb.

Degree of sedation was assessed by Chernink score as given in Table 2. Observations were tabulated and statistical analysis was carried out by using chi-square test and student t test. P value<0.05 was taken to be statistically significant.

Results

The patients were demographically similar in all the groups.

All the patients in each group has achieved complete motor block (Bromage scale grade 3) and sensory block up to T₆.

Onset of sensory block was 110. +-11.54, 109.90+-14.7 and 107+-60 seconds in group I, group II and group III respectively. The difference in onset time of sensory block was clinically and statistically insignificant.

Duration of sensory block (from subarachnoid block to first complain of pain) was 204.8+-34.8, 315.37+-50 and 387.07+-83.19 minutes in group I, group II and group III respectively . The duration was significantly higher in Group II and III as compared to Group I

Onset time of motor block was similar in all the groups.

Duration of motor block (time from onset of paralysis to movement of lower limb) was 172+24.34, 179.5 +27.23 and 176+23.17 minutes group I, group II, and group III respectively and is almost similar in all the groups.

The differences in mean pulse rate , mean systolic and diastolic blood pressure at different time intervals was similar in all the groups.

Degree and incidence of sedation was similar in all the groups. Other side effects like hypotension, bradycardia, nausea and vomiting, and respiratory depression were similar in all the groups. Hypotension was recorded in 2 patients each in group I, and II and 3 patients in group III and was treated with inj. Mephentermine 3mg IV. Bradycardia was recorded in in 1 patients in group I, 2 patients each in group II and group III and were treated with inj Atropine .6mg IV. The observed side effects were similar in all the three groups.

Table 1 Bromage Scale

| Grade | Criteria |
|-------|--|
| I | Free movement of legs and feet |
| II | Just able to flex knees with free movement of foot |
| III | Unable to flex knees, but free movement of feet |
| IV | Unable to move legs or feet |

Table 2. Sedation Score (Cherniketal)

| Grade | Criteria |
|-------|--|
| 0 | Wide awake |
| 1 | Sleeping comfortably but responding to verbal commands |
| 2 | Deep sleep but arousable |
| 3 | Deep sleep but not arousable |

Table 3 :-Patient Characteristics

| Criteria | Group1 | Group2 | Group3 |
|-------------------------------|-------------|-------------|-------------|
| Age (Years) | 36.16+6.2 | 35.76+7.2 | 35.90+6.9 |
| Weight (Kg) | 54.30+7.2 | 55.20+6.8 | 54.8+6 |
| Hieght (Cm) | 158.2+6.3 | 157.3+7.2 | 157.23+7.3 |
| Duration of Surgery (Minutes) | 103[75-122] | 105[70-118] | 102[72-124] |

Table 4 :- Comparison of Motor and Sensory Block

| Parameter | Group1 | Group2 | Group3 |
|---|--------------|--------------|---------------|
| Time of Onset of Sensory Block (Seconds.) | 110+11.54 | 109.90+14.57 | 107.6-0+14.79 |
| Duration of Analgesia (Minutes) | 204.87+34.75 | 315.37+50.34 | 387.07+83.17 |
| Onset of Motor Block (Seconds) | 193.83+34 | 192.20+20 | 192+34 |
| Duration of Motor Block (Minutes) | 172+24.34 | 179.5+27.23 | 176+23.17 |

Table 5 Sedation

| Grades of Sedation | Group1 | Group2 | Group3 |
|--------------------|--------|--------|--------|
| Grade 0 | 25 | 24 | 24 |
| Grade 1 | 3 | 4 | 3 |
| Grade 2 | 2 | 2 | 3 |
| Grade 3 | 0 | 0 | 0 |

Table 6 Side Effects

| Complication | Group1 | Group2 | Group3 |
|-----------------|--------|--------|--------|
| Hypotension | 2 | 2 | 3 |
| Bradycardia | 1 | 2 | 2 |
| Nausea Vomiting | 2 | 2 | 2 |
| Headache | 1 | 0 | 0 |
| Bachake | 0 | 0 | 0 |
| Cardiac Arrest | 0 | 0 | 0 |

Discussion

Clonidine is used for post operative pain relief by oral, epidural, intrathecal and peripheral nerve blocks. Dose of Clonidine is lowest by Intrathecal route to produce same degree and duration post operative analgesia. The incidence of hypotension and sedation were less with low dose of clonidine by intrathecal route.

Clonidine is a selective partial agonist for 2 adrenergic receptors; the analgesic effect in intrathecal clonidine is mediated spinally through the activation postsynaptic 2 receptors in substantia gelatinosa of the spinal cord. The rationale behind intrathecal use of clonidine is to achieve a high drug concentration in the vicinity of 2 adrenoceptors in the spinal cord and it works by blocking the conduction of C and A fibers, increases potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics.

In many previous studies intrathecal Clonidine has been used in higher dosage with opioids for orthopedic surgeries, labour analgesia, and gynecological surgeries [16,18]. In some study in orthopedics intrathecal clonidine 150 mcg provide longer post operative analgesia and decreased morphine requirement with hemodynamic stability when used alone for post operative pain relieve [14].

In some other studies Clonidine 15-30 mcg was used with opioids and local anaesthetic for prolongation of post operative analgesia, in labour analgesia, knee arthroscopy, ambulatory inguinal herniorrhaphy [15,16,19]. Our data match with these in references to sensory block. As the dose of clonidine increases duration of post operative analgesia increases.

In some previous studies intrathecal Clonidine in dosage of 150-450 mcg alone was used for labour analgesia which does not have any effect on muscle tone but addition of local anaesthetic causes greater degree of muscle relaxation [6,7,8]. In our study addition of clonidine in low doses to local anaesthetics has no effect on onset and duration of motor block.

Sedation and hypotension are the central effects of α_2 adrenergic may occur after Clonidine administered by any route. Higher doses of (50 to 450 mcg) clonidine have been associated with hypotension ,bradycardia and higher degree of sedation [13,20,23,24]. In our study as we use Clonidine 15 and 30 mcg is usually not associated with such effects.

The incidence of side effects like respiratory depression, nausea and vomiting, pruritus and shivering was of no clinical significance.

In our study intrathecal Clonidine 15 mcg and 30 mcg with Bupivacaine, shortens the onset time of sensory block and increases the duration of sensory block with stable hemodynamics without significant side effects.

Conclusion

It can be concluded that addition of Clonidine in lower dose 30mcg with Bupivacaine for subarachnoid block as used in the present study prolongs the duration of analgesia with minimal side effects and thus is recommended for post operative pain relief in different surgical procedures.

References

1. Brandt SA, Livingston A. Receptor changes in spinal cord of sheep associated with exposure to chronic pain. *Pain* 1990; 42: 323-9.
2. Filos KS, Goudas LC, Patroni O, Polyzou V. Intrathecal clonidine as a sole analgesic for pain relief after caesarean section. *Anesthesiology* 1992; 77: 267-74.
3. Chiari A, Lorber C, Eisenach JC, et al. Analgesic and hemodynamic effects of intrathecal clonidine as the sole analgesic agent during first stage of labor. *Anesthesiology* 1999; 91: 388-96.
4. L Niemi. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamics and postoperative analgesia in patients undergoing knee arthroscopy. *Acta Anaesthesiol Scand* 1994; 38: 724-8.
5. DeNegri P, Salvatore R, Visconti C, DeVivo P, Mastronardi P. Spinal anaesthesia with clonidine and bupivacaine in young humans: interactions and effects on cardiovascular system. *Minerva Anesthesiology* 1997; 63: 119-25.
6. Racle JP, Benkhadra A, Poy JY, et al. Prolongation of isobaric bupivacaine spinal anaesthesia with epinephrine and clonidine for hip surgery in the elderly. *Anesth Analg* 1987; 66: 442-6. <http://dx.doi.org/10.1213/0000539-198705000-00013>
7. Dobrydnjov I, Samarutel J. Enhancement of intrathecal lidocaine by addition of local and systemic clonidine. *Acta Anaesthesiol Scand* 1999; 43: 556-62. <http://dx.doi.org/10.1034/j.1399-6576.1999.430512.x>
8. Bonnet F, Buisson VB, Francois Y, et al. Effects of oral and subarachnoid clonidine on spinal anaesthesia with bupivacaine. *Reg Anesth* 1990; 15: 211-4.
9. Gentili ME, Mamelle JC, Le Foll G. Combination of low-dose bupivacaine and clonidine for unilateral spinal anaesthesia in arthroscopic knee surgery. *Reg Anesth* 1995; 20: 169-70.
10. Dobrydnjov I, Axelsson K, Samarutel J, et al. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine. *Acta Anaesthesiol Scand* 2002; 46: 806-14. <http://dx.doi.org/10.1034/j.1399-6576.2002.460709.x>
11. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of lidocaine on C-fiber action potential. *Anesth Analg* 1992; 74: 719-25. <http://dx.doi.org/10.1213/0000539-199205000-00017>
12. Erne-Brand F, Jirounek P, Drewe J, et al. Mechanism of antinociceptive action of clonidine in nonmyelinated nerve fibres. *Eur J Pharmacol* 1999; 383: 1-8. [http://dx.doi.org/10.1016/S0014-2999\(99\)00620-2](http://dx.doi.org/10.1016/S0014-2999(99)00620-2)
13. Grace D, Bunting H, Milligan KR, et al. Postoperative analgesia after co-administration of clonidine and morphine by the intrathecal route in patients undergoing hip replacement. *Anesth Analg* 1995; 80: 86-91.
14. Filos KS, Goudas LC, Patroni O, et al. Hemodynamic and analgesic profile after intrathecal clonidine in humans: a dose-response study. *Anesthesiology* 1994; 81: 591-601. <http://dx.doi.org/10.1097/0000542-199409000-00011>
15. Mercier FJ, Dounas M, Bouaziz H, et al. The effect of adding a minidose of clonidine to intrathecal sufentanil for labour analgesia. *Anesthesiology* 1998; 89: 594-601. <http://dx.doi.org/10.1097/0000542-199809000-00007>
16. Sites BD, Christopher R, Biggs R, et al. Intrathecal clonidine added to a bupivacaine-morphine spinal improves postoperative analgesia following total knee arthroplasty. *Anesthesiology* 2002; 96: A918.
17. De Kock M, Gauthier P, Fanord L. Intrathecal ropivacaine and clonidine for ambulatory knee arthroscopy. A dose response study. *Anesthesiology* 2001; 94: 574-8. <http://dx.doi.org/10.1097/0000542-200104000-00008>
18. Gautier PE, De Kock M, Luc F, et al. Intrathecal clonidine combined with sufentanil for labour analgesia. *Anesthesiology* 1998; 88: 651-6. <http://dx.doi.org/10.1097/0000542-199803000-00015>
19. Juliao MC, Lauretti GR. Low-dose intrathecal clonidine combined with sufentanil as analgesic drugs in abdominal gynecological surgery. *J Clin Anesth* 2000; 12: 357-62. [http://dx.doi.org/10.1016/S0952-8180\(00\)00171-9](http://dx.doi.org/10.1016/S0952-8180(00)00171-9)
20. Dobrydnjov I, Axelsson K, Thorn SE, et al. Clonidine combined with small-dose bupivacaine during spinal anaesthesia for inguinal herniorrhaphy: a randomized double-blinded study. *Anesth Analg* 2003; 96: 1496-503. <http://dx.doi.org/10.1213/01.ANE.0000061110.62841.E9>
21. Fogarty DJ, Carabine UA, Milligan KR. Comparison of the analgesic effects of intrathecal clonidine and intrathecal morphine after spinal anaesthesia in patients undergoing total hip replacement. *Br J Anaesth* 1993; 71: 661-4. <http://dx.doi.org/10.1093/bja/71.5.661>
22. Filos KS, Goudas LC, Patroni O, et al. Intrathecal clonidine as a sole analgesic for pain relief after caesarean section. *Anesthesiology* 1992; 77: 267-74. <http://dx.doi.org/10.1097/0000542-199208000-00008>
23. Pan PM, Huang CT, Wei TT, et al. Enhancement of analgesic effect of intrathecal neostigmine and clonidine on bupivacaine spinal anaesthesia. *Reg Anesth Pain Med* 1998; 23: 49-56.
24. 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 (5): 415-419.
25. Agreta Gecaj-Gashi, MD;* Hasime Terziqi, MD;† Tune Pervorfi, MD;‡ Arben Kryeziu, MD. Intrathecal clonidine added to small-dose bupivacaine prolongs postoperative analgesia in patients undergoing transurethral surgery. *Can Urol Assoc J* 2012; 6(1): 25-9. <http://dx.doi.org/10.5489/cuaj.11078>*