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Original Article

Effects of Addition of Clonidine to Bupivacaine in Spinal Anaesthesia for Abdominal Hysterectomy

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ABSTRACT
Hyperbaric bupivacaine is a commonly used local anaesthetic for subarachnoid blocks. Several additives are added to prolong the action of intrathecal bupivacaine. We evaluated the effects of addition of 60µgms clonidine to 0.5% hyperbaric bupivacaine on the quality of subarachnoid block and vital parameter changes. Hundred ASA l and ll patients aged between 30 and 60 years for elective abdominal hysterectomy were randomly allocated into two equal groups, Group B receiving 0.5% hyperbaric bupivacaine 3ml with 0.4ml Saline and Group B+C receiving 60µgms clonidine (0.4ml) with 3ml of 0.5% hyperbaric bupivacaine).Time of onset of sensory block ,Level of block ,Time to regression of sensory block to T10 level , Duration of motor block ,Duration of pain relief, Changes in blood pressure, heart rate and side effect profile of intrathecal clonidine were studied. The onset of sensory block to T6 and the highest sensory level were similar in both groups. Time to regression of sensory block to T10 (256.04±20.61vs 146.08±9.91 minutes, p<0.001) and duration of motor block (189.02±16.93 vs 141.66±10.78 minutes, p<0.001) were significantly prolonged in the clonidine group. Effective analgesic time was also significantly longer in patients given clonidine (330.16±25.07 vs 163.26±21.11 minutes, p<0.001). Clonidine group showed a significant decrease in systolic blood pressure, but incidence of bradycardia was unchanged. Addition of 60µgms of clonidine enhances the anaesthetic properties of intrathecal bupivacaine, prolongs the duration of sensory and motor block and improves early postoperative pain relief with minimum side effects and serves as a useful adjuvant in spinal anaesthesia.
Keywords: *Clonidine, Bupivacaine, Spinal anaesthesia, Abdominal hysterectomy.*

INTRODUCTION

Sub arachnoid blocks have been extensively used for lower abdominal However the drawbacks of shorter duration of block and the lack of post-operative analgesia have popularized the use of intrathecal adjuvants for spinal anaesthesia. Clonidine is a useful adjuvant to hyperbaric bupivacaine for subarachnoid block as it enhances the anaesthetic properties of bupivacaine and improves early postoperative pain relief, without causing any additional adverse effects[1].

Clonidine is an imidazoline derivative with predominantly α2 adrenergic agonist activities. The analgesic effect due to the intrathecal

administration of Clonidine is mediated spinally through activation of post-synaptic α2 receptors located in substantia gelatinosa of spinal cord. Clonidine suppresses the generation of action potentials in tonic-firing spinal dorsal horn neurons by an interaction with voltage-gated Na+ and K+ currents[2].

Clonidine enhances and prolongs the sensory and motor blockade of local anaesthetics. Addition of clonidine provides better intra operative conditions than using hyperbaric bupivacaine alone, quality of analgesia and satisfaction scores were also significantly better.

Unlike neuraxialopioids, Clonidine does not cause depression of ventilation, pruritis, vomiting, nausea, delayed gastric emptying or urinary retention. Hypotension, bradycardia, sedation and dryness of mouth may accompany use of neuraxial Clonidine in high doses. With small doses of intrathecal Clonidine, hemodynamic stability was maintained with no significant differences in sedation score. The present study was conducted to evaluate the effects of addition of 60 µgmsof clonidine to intrathecal bupivacaine in patients undergoing elective abdominal hysterectomy.

MATERIALS AND METHODS

Hundred ASA physical status I & II female patients aged between 30 and 60 years scheduled for elective abdominal hysterectomy were included for the study after obtaining written informed consent and approval from institutional ethics committee.

Patients were randomized into two groups before the intervention by a computer generated random table. Group I receiving 0.5% hyperbaric bupivacaine 3ml (15 mg) with 0.4 ml Saline (control group) and Group 2 receiving 60µgms clonidine (0.4 ml) with 3ml (15 mg) of 0.5% hyperbaric bupivacaine (clonidine group).The patients and investigator were blinded to the randomized groups. The clonidine preparation used contained preservative free clonidine hydrochloride in a concentration of 150 µgms/ml. Both the dosage and volume of bupivacaine were kept identical in the two groups.

After pre anaesthetic evaluation, on arrival to the operating room, patients were monitored with electrocardiogram (ECG), pulse oximetry (spo_2) and non-invasive blood measure monitoring (NIBP) and lactated ringers solution was started. A lumbar subarachnoid block was performed under strict aseptic precautions with the patient in the lateral position. The lumbar tap was made in L3-L4 interspace in the midline using a 23 gauge quincke needle. After obtaining a clear flow of cerebrospinal fluid; the drug was injected slowly (0.2 ml/sec). The patient was made supine immediately after completion of injection. Oxygen was given through simple face mask. Heart rate and oxygen saturation were continuously monitored and blood pressure was recorded every 5 minutes until the end of surgery.

Time of administration of the drug was noted and the time of loss of pinprick sensation at T6 level bilaterally was noted every minute. This was taken as the latency of onset. The loss of sensation to pinprick was tested bilaterally to note the highest dermatome of block. Time in minutes from onset of sensory block (loss of pinprick sensation at T6 level) to time of return of pinprick sensation at T10 level (checked every 15 minutes, one hour after onset of block) was recorded. This time was noted as the time to regression to T10. Time from onset of sensory block to time of first analgesic (effective analgesia time) was also noted.

Motor block was assessed using Bromage scale. These measurements were performed at 1 min interval for first 10 minutes and then every 15 minutes after surgery. Time from onset of motor block (Bromage score more than or equal to 2) to regression of motor block (Bromage score ≤ 1) was noted. Bromage score; Grade 1 is free movement of legs and feet, Grade II where the patient is just able to flex knee with free movement of feet, Grade III where patient is unable to flex knees, but with free movement of feet and Grade IV Unable to move legs or feet.

A fall in blood pressure more than 20% was recorded as hypotension and rapid infusion of

fluid boluses were given followed by incremental doses of 6 mg intravenous mephentermine.

Sedation levels were assessed every 15 min using a four point scale; Score 1 is awake, 2 is a drowsy patient but responsive to verbal command, 3 is a drowsy patient but responsive to physical stimulus and 4 is unresponsive to verbal or physical stimulus. The highest score was noted. After surgery, patients were shifted to post anaesthesia care unit and monitored till the time to regression of sensory block to T10. Thereafter the patient was monitored for 24 hours in the post-operative care unit. Postoperative analgesia was assessed using a verbal numerical rating scale (NRS) from 0 to 10 (0 =no pain at all, 10 =maximum imaginable pain) recorded hourly for the first 8 hours and then at 12 and 24 hrs. Rescue analgesic was given on patient's demand, and consisted of intravenous tramadol 50mg with intravenous metoclopramide 10 mg and intramuscular diclofenac 75mg. The patients were monitored for complications like nausea and vomiting, shivering, pruritis, cardiovascular complications like hypotension or bradycardia, respiratory depression, postdural puncture headache, neurological symptoms and dry mouth.

Data were analyzed using computer software, Statistical Package for Social Sciences (SPSS) version 10. Data are expressed in its frequency and percentage. To elucidate the associations and comparisons between different parameters, Chi square ($\chi 2$) test was used as nonparametric test. Student's t test was used to compare two groups parametrically. For all statistical evaluations, a two-tailed probability value, < 0.05 was considered significant.

OBSERVATION & ANALYSIS

The demographic profile which include the age, height, weight& ASA classification were comparable and no significant differences ($p>0.05$) were observed between the two groups (Table 1).

Table 1: Demographic profile

Parameters	Group 1 (B)	Group II (B+C)	P value
Age (yrs.)	44.92 ± 5.85	44.94 ± 5.96	> 0.05
Height (cm)	159.28 ± 4.92	159.06 ± 4.75	> 0.05
Weight (kg)	62.66 ±6.40	62.96 ± 6.18	> 0.05

Time of onset of sensory block (latency) as well as the maximum level of block assessed by loss of pinprick sensation bilaterally was also identical in both groups (Table 2). Maximum height of block ranged between T2 to T6 in both groups. Majority of patients of both groups showed sensory block up to T4.Time of regression of sensory block to T10 was 256.04 minutes in the clonidine group as compared to 146.08 minutes in bupivacaine group. This was found to be very highly significant ($p<0.001$).The duration of motor block, was prolonged in the clonidine group as compared to bupivacaine group (141.66 minutes in control as against 189.02 minutes in clonidine group). This again was statistically very highly significant ($P < 0.001$). The time to first rescue analgesic in the clonidine group was 330.16 minutes compared to 163.26 minutes in control group. Duration of analgesia was significantly prolonged in clonidine group. This was found to be very highly significant ($P< 0.001$).

Table 2: Characteristics of spinal block

Parameters	**Group 1 (B)**	**Group II (B+C)**	**T value**	**P value**
Latency (minutes)	3.27 + 1.07	3.24 + 1.01	0.144	> 0.05
Sensory Maximum (Thoracic)	4.02 + 0.94	4.26 + 0.99	-1.248	> 0.05
Regression to T10 (minutes)	146.08 + 9.91	256.04 + 20.61	-33.996	< 0.001
Duration of motor block (minutes)	141.66 + 10.78	189.02 + 16.93	-16.686	< 0.001
Surgery duration (minutes)	97.86 + 14.24	104.62 + 13.71	- 1.419	> 0.05
Effective analgesia (minutes)	163.26 + 21.11	330.16 + 25.07	-36.009	< 0.001

Postoperative analgesia was assessed using a verbal numerical rating scale (NRS) from 0 to 10 (0 = no pain at all, 10 = maximum imaginable pain) recorded hourly for the first 8 hours and then at 12 and 24 hrs. Numerical pain scores at 2 hours, 3 hours and 4 hours(Table 3) were significantly lower with addition of clonidine when compared to bupivacaine alone ($p<0.001$).

Table 3: Distribution of numerical rating pain score

Parameters	Group 1 (B)	Group II (B+C)	T value	P value
Numerical pain score at 2 hr	2.62 ± 1.03	1.06 ± 1.15	7.151	< 0.001
Numerical pain score at 3 hr	4.67 ± 0.98	3.03 ± 1.01	6.907	< 0.001
Numerical pain score at 4 hr	5.24 ± 0.92	3.65 ± 0.89	9.879	< 0.001

Patients in both groups had similar sedation scores. Majority of patients were awake. 5 patients in control group and 5 patients in clonidine group were mildly sedated. Incidence of bradycardia, dry mouth, emesis and shivering were comparable among both groups.

Haemodynamic effects of addition of Clonidine was also observed. 30 patients in Group I(60%) and 35 in Group II(70%) had hypotension. Addition of clonidine 60µgms caused a reduction in systolic blood pressure, the decrease starting at 10-15 minutes and normalizing at 3 hours after intrathecal injection. The most significant difference in blood pressure between groups was observed at 45-60 minutes after intrathecal injection. The mean pulse rate was comparable among both groups.

Figure 1

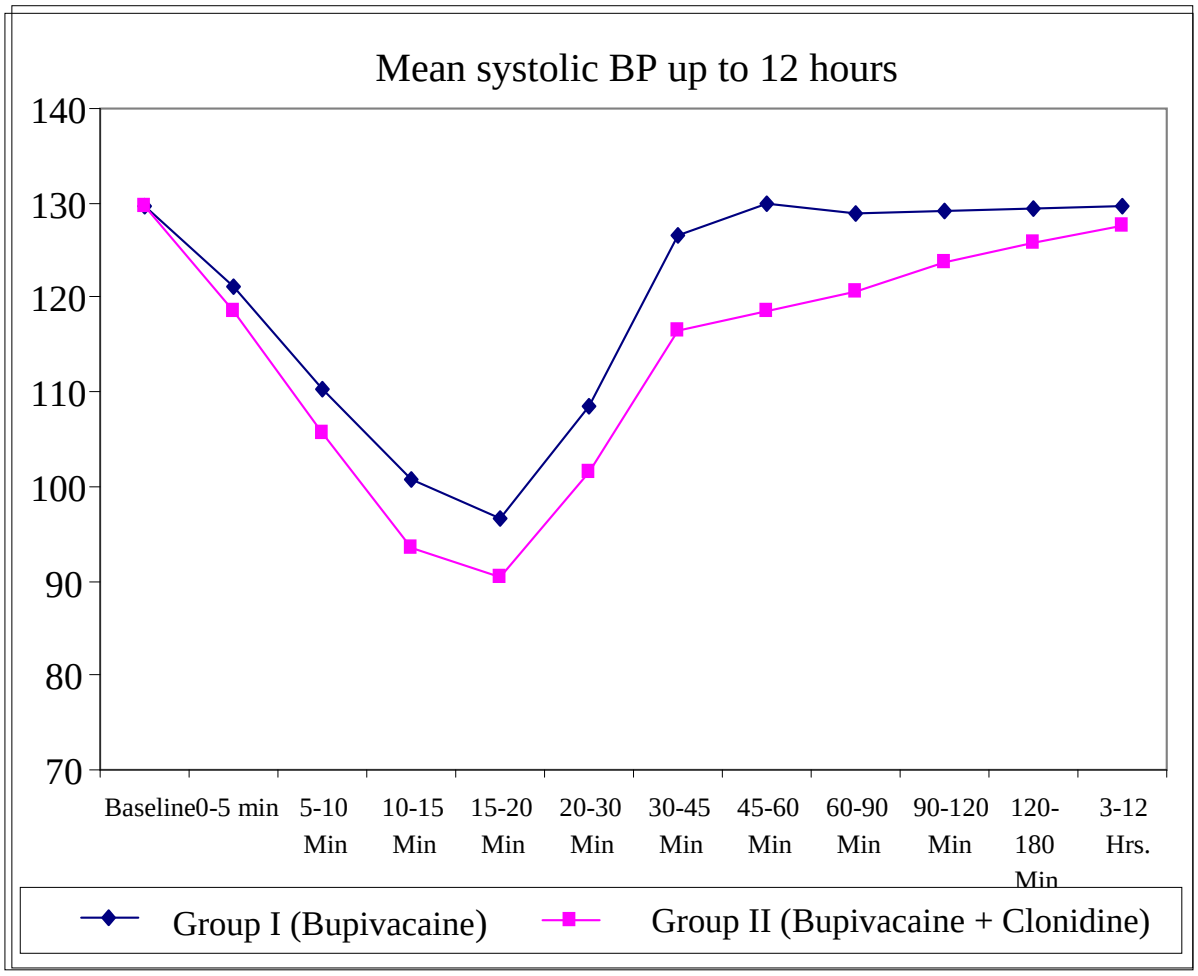
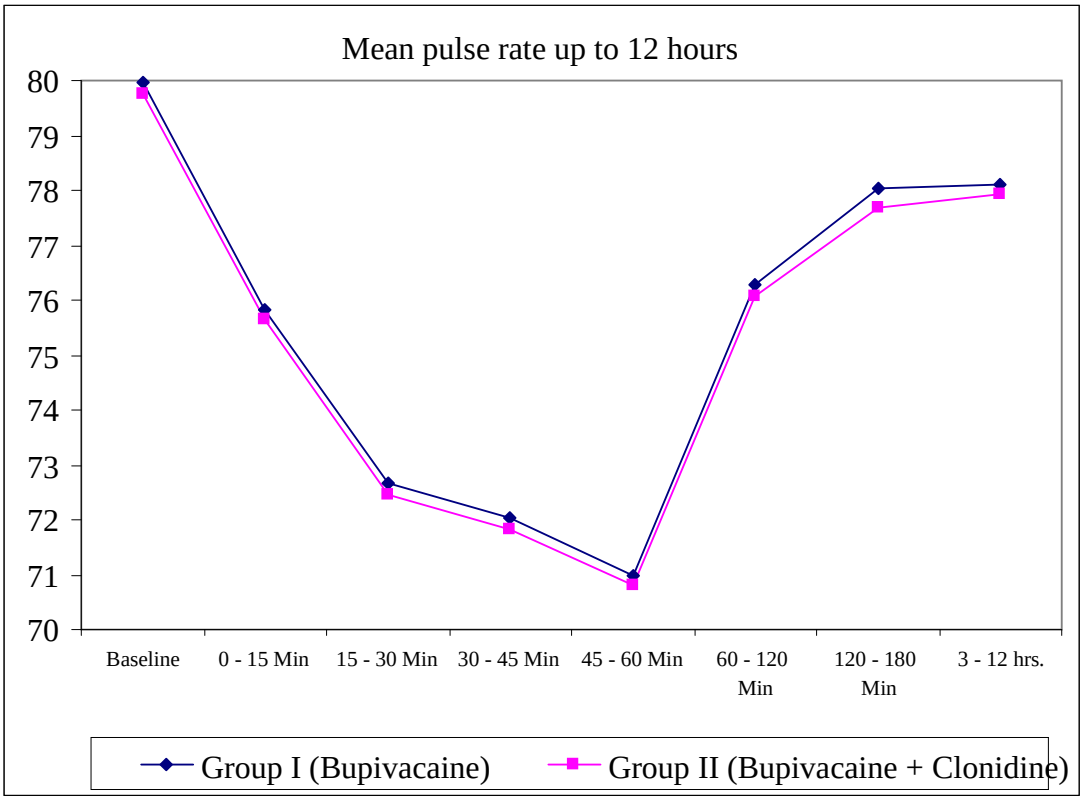


Figure 2



DISCUSSION

The study was done to compare the effects of intrathecal clonidine as an additive to bupivacaine for elective abdominal hysterectomies. The anaesthetic effects of adding 60µgms of clonidine to 0.5% hyperbaric bupivacaine were studied which included time of onset of block, level of block, duration of sensory block, duration of motor block, duration of pain relief, sedation levels and changes in blood pressure, heart rate, respiratory rate and arterial oxygen saturation. The addition of clonidine to bupivacaine was found to prolong the duration of sensory and motor block. Duration of sensory block in clonidine group was 256.04 minutes as compared to 146.08 minutes in control group. This was found to be very highly significant with a p value of <0.001.

In a similar study, Kaabachi Oet al[3] demonstrated significant prolongation of sensory block using intrathecal clonidine 1 µgms/kg in conjunction to 0.5% isobaric bupivacaine in spinal anaesthesia for orthopedic surgery without severe adverse events.

The present study has also supported the findings of B.S Sethi et al[4]who hasalso demonstrated significant prolongation of sensory block on addition of 1µgm/kg of clonidine to 12.5mg hyperbaric bupivacaine for gynaecological surgeries, time to two segment regression of sensory block was 218 minutes as against 136 minutes for the control group in their study (P <0.001).

The duration of motor block was studied by noting the time from onset of motor block (Bromage score ≥2) to regression of motor block (Bromage score ≤1). Clonidine group showed statistically significant prolongation of motor block. Duration of motor block was 189.02 minutes in the clonidine group as against 141.66 minutes in the control group. Our findings correlated with different studies [5, 6,7].

Strebel et al[8] in a study using intrathecal clonidine in doses from 37.5 µgms to 150 µgms in combination with bupivacaine for orthopaedic surgeries, had demonstrated a prolonged motor block with clonidine; potentially allowing longer orthopedic procedures such as one stage bilateral arthroplasties or complex prosthesis replacements. They reported that in elderly orthopedic patients undergoing lower extremity arthroplasties,

alternative techniques to prolong anaesthesia, such as epidural or combined spinal epidural techniques, may be technically difficult and time consuming.

Time to first analgesic was 330.16 minutes in the clonidine group compared to 163.26 minutes in the control group. Clonidine was found to significantly prolong the duration of analgesia when administered intrathecally (P<0.001).

Dobrydnjov I et al[9] has also found a pain free period of 337 ± 29 minutes vs. 236 ± 27 minutes in the control group (p<0.01) using clonidine for spinal anaesthesia with bupivacaine in patients undergoing orthopaedic procedures. However Dobrydnjov I et al[6]used 150µgms of clonidine whereas similar results were obtained in the current study with the use of 60 µgms of clonidine.

The findings of the present study also supports that of Van Tuijl I, Van Klei et al[10]whoon studying the effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after Caesarean section found out that the addition of clonidine (75 µgms) to hyperbaric bupivacaine prolongs spinal anaesthesia after caesarean section and improved early analgesia with no clinically relevant maternal or neonatal side-effects.

The current study has supported the findings of Elia Net al[11]who conducted a systematic review of randomized trials to quantify beneficial and harmful effects of clonidine when used as an adjuvant to intrathecal local anaesthetics for surgery. They included data from 22 randomized trials (1,445 patients) testing a large variety of doses of clonidine from 15 to 150 µgms. However they could not detect the optimal dose of clonidine.

Pain scores were recorded using numerical rating pain score. Pain scores at 2 hours, 3 hours and 4 hours were significantly lower in the clonidine group when compared with the bupivacaine group. Numerical rating pain scores were 1.06, 3.03 and 3.65 at 2 hours, 3 hours and 4 hours respectively with addition of clonidine; whereas the scores were 2.62, 4.67 and 5.24 when bupivacaine alone was used. This was both statistically significant (P<0.001) and clinically successful. This may be favourably compared with findings of Van Tujilet al[10]where addition of clonidine 75 µgms provided significant early postoperative analgesia.

Intraoperatively blood pressure, heart rate, respiratory rate and oxygen saturation were monitored to assess the hemodynamic and respiratory effects of intrathecal clonidine. Addition of clonidine caused a significant reduction in systolic blood pressure, the decrease starting at 10-15 minutes and normalizing at 3 hours after intrathecal injection. The most significant difference in blood pressure between groups was observed at 45-60 minutes after intrathecal injection. The hypotensive effect was rapidly and effectively correctable with i.v fluids and inj. Mephentermine.

B.S.Sethi et al[4]while studying the analgesic effects of intrathecal clonidine (1 µg/kg) as adjuvant to bupivacaine for gynaecological surgery, found that patients in the clonidine group had a significant fall in mean arterial pressure than in Control group. The decrease in mean arterial pressure from 45 minutes until the end of 6 hours was greater in clonidine group than in the control group (P<0.001). Even though a statistically significant decrease in MAP was noted in the clonidine group compared to the control group, none of the patients required any therapeutic intervention for either.My findings are in agreement with that of Santiveri X et al[12] who studied the effects of clonidine 75 µgms for subarachnoid anaesthesia for transurethral resection of urinary bladder tumours and have observed that although it provided excellent analgesia for about 8 hours, arterial pressure decreased significantly in the clonidine group 75-135 min after the block.

Incidence of bradycardia was also studied. 1 patient in the control group developed bradycardia but none in the study group. The difference was not statistically significant. Filos et al[13] reported significant decrease in arterial BP after administration of 150 µg of clonidine, but heart

rate was unaffected in their study performed on caesarean section patients. A study by Dobrydnjov[14] using intrathecal clonidine has also reported that the risk of bradycardia was unchanged. Interestingly, B S Sethiet al[4] who studied the effects of intrathecal clonidine in gynaecological surgeries had noted a decrease in mean heart rate in the clonidine group but did not require any therapeutic intervention.

Findings of the current study are in consonance with the study by L Niemi[15] in which 3 µg/kg of clonidine was added to 15 mg of 0.5% bupivacaine intrathecally in patients undergoing knee arthroscopy. However it should be mentioned that Niemi used thrice the amount of clonidine as compared to the current study. Despite that, the mean time to administration of first analgesic from test drug administration was similar to our study and 3 patients in his study required intervention for hypotension and 1 patient for bradycardia. Our study thus implies that it is possible to achieve equally good analgesia without side effects when clonidine is used in dosages as low as 60 µg.

CONCLUSION

The addition of clonidine to bupivacaine in subarachnoid block prolonged the duration of sensory and motor block and also prolonged the duration of effective analgesia without associated significant hemodynamic changes. Clonidine is a useful adjuvant to hyperbaric bupivacaine for subarachnoid block as it enhances the anaesthetic properties of bupivacaine and improves early postoperative pain relief, without any additional adverse effects.

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REFERENCES

1. Maze M, Tranqilli W. Alpha 2 adrenoceptor agonists: defining the role in clinical anaesthesia. Anesthesiology 1991; 74: 581-605.
2. Wolff M, Heugel P, Hempelmann G, Scholz A, Mühling J, Olschewski A. Clonidine reduces the excitability of spinal dorsal horn neurons: Br J Anaesth. 2007 Mar;98(3):353-61
3. Kaabachi O, Zarghouni A, Ouezini R, Abdelaziz AB, Chattaoui O, Kokki H.Clonidine 1 µgm/kg is a safe and effective adjuvant to plain bupivacaine in spinal anesthesia in adolescents. AnesthAnalg. 2007 Aug; 105(2):516-9.
4. 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
5. Sites BD, Beach M, Biggs R, Rohan C, Wiley C, Rassias A, Gregory J, Fanciullo G Intrathecal clonidine added to a bupivacaine-morphine spinal anesthetic improves postoperative analgesia for total knee arthroplasty.AnesthAnalg. 2003 Apr;96(4):1083-8
6. van Tuijl I, Giezeman MJ, Braithwaite SA, Hennis PJ, Kalkman CJ, van Klei WA Intrathecal low-dose hyperbaric bupivacaine-clonidine combination in outpatient knee arthroscopy: a randomized controlled trial.ActaAnaesthesiol Scand. 2008 Mar;52(3):343-9
7. Boico O, Bonnet F, Mazoit JX. Effects of epinephrine and clonidine on plasma concentrations of spinal bupivacaine. ActaAnaesthesiol Scand. 1992 Oct;36(7):684-8
8. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH.Small-dose intrathecal clonidine and isobaric bupivacaine for orthopaedic surgery: a dose-response study. AnesthAnalg. 2004 Oct; 99(4):1231-8.
9. Dobrydnjov I, Axelsson K, Thörn SE, Matthiesen P, Klockhoff H, Holmström B, Gupta A. Clonidine combined with small-dose bupivacaine during spinal anesthesia for inguinal herniorrhaphy: a randomized double-blinded study.AnesthAnalg. 2003 May;96(5):1496-503

10. Van Tuijl, W. A. van Klei, D. B. M. van der Werff and C. J. Kalkman The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements afterCaesarean section: a randomized controlled trial. British Journal of Anaesthesia 2006 97(3):365-370.
11. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: systematic review of randomized trials.RegAnesth Pain Med. 2008 Mar-Apr; 33(2):159-67.
12. Santiveri X, Arxer A, Plaja I, Metje MT, Martínez B, Villalonga A, López M.Anaesthetic and postoperative analgesic effects of spinal clonidine as an additive to prilocaine in the transurethral resection of urinary bladder tumours Eur J Anaesthesiol. 2002 Aug; 19(8):589-93.
13. Filos KS, Goudas LC, Patroni O, Polyzou V. Hemodynamic and analgesic profile after intrathecal clonidine in humans. A dose-response study.Anaesthesiology. 1994 Sep; 81(3):591-601.
14. Dobrydnjov I, Axelsson K, Gupta A, Lundin A, Holmström B, Granath B. Improved analgesia with clonidine when added to local anesthetic during combined spinal-epidural anesthesia for hip arthroplasty: a double-blind, randomized and placebo-controlled study. Acta Anaesthesiol Scand. 2005 Apr;49(4):538-45.
15. Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamic, and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anaesthesiol Scand. 1994 Oct;38(7):724-8.