Original Article

A clinical comparative study between dexmedetomidine v/s clonidine with bupivacaine intrathecally in major orthopaedic lower limb surgery

Dipak L. Raval*, Minaxi Chaudhary*

*Additional Professor, Anesthesiology dept., Shri M.P. Shah Government Medical College, Jamnagar, Gujarat, India

DOI: 10.5455/jrmds.20142114

ABSTRACT

Background: We compared intrathecal Bupivacaine with either Dexmedetomidine or Clonidine.

Aims: 1. To review the literature 2. Sensory and Motor Characteristics and 3. Total duration of Post-op analgesia

Material and Methods: 90 patients of either sex, age 20-50 years, ASA grade I or II undergoing orthopedic lower limb surgery were randomly divided in group D (0.5%Bupivacaine15mg+Dexmedetomidine3µg) and group C (0.5%Bupivacaine15mg+Clonidine30µg) intrathecally. All parameters were recorded.

Results: Mean time for onset of sensory block at shin of tibia and onset of motor block were comparable. The mean time to achieve T10 sensory blockade was 5.822 ±2.38 minutes in group D while 6.5 ±2.33minutes in Group C. With regard to the highest sensory level attained, both groups were comparable. Mean time to achieve complete motor block was 8.177 ±2.124 minutes in group D while 9±2.044 minutes in group C. The time for two segment regression was also comparable in both the groups. The mean of total duration of motor block in group D was 254.44±40.65minutes compared to 262.22±34.23 minutes in clonidine group. The time for sensory block was 296.889±38.3063 minutes in group D and 306.22±35.63 minutes in group C. Total duration of postoperative analgesia was also same in both groups. Haemodynamic stability was maintained and side effects were comparable.

Conclusion: We conclude that both Dexmedetomidine and Clonidine when used as an adjuvant to intrathecal hyperbaric Bupivacaine cause early onset of motor and sensory block, increases two segment regression time, prolonged motor, sensory blockade and post-operative analgesia with hemodynamic stability and no side-effects.

Keywords: Dexmedetomidine, Clonidine, Bupivacaine, Intrathecal

INTRODUCTION

In rural and semi urban area of our country, because of lacking of sophisticated anaesthetic equipment and anaesthetic gases for general anaesthesia as well as for economic reasons, simple technique of spinal anaesthesia has got a useful and definite role.

Spinal anaesthesia is widely used regional anaesthetic technique specially for lower limb orthopaedic surgeries as it is very economical & easy to administer, however post-operative analgesia is a major problem associated with relatively short duration of action of spinal anaesthetics so early analgesic intervention is needed in post-operative period.

Recently, use of intrathecal adjuvant has gained popularity with the aim of prolonging duration of post-operative analgesia, better success rate, patient satisfaction, decreased resources utilization etc. Intrathecally as well as epidurally administered opioids provides the perceived benefits of selective analgesia without sensory or motor blockade, however dangerous side effect i.e. delayed respiratory depression have prompted further research to develop non opioid analgesic with less side effect [1].

Alpha-2 adrenergic agonists are used intrathecally as adjuvant drugs to local anaesthetic [2-4]. Alpha-2 agonists possess analgesic properties and augmentation of local anaesthetic effects. Peri-operative anaesthetic and analgesic requirement get

reduced to a huge extent by adding these two adjuvants [5-9].

Clonidine, a partial alpha-2 adrenoreceptor agonist has long been used to treat hypertension. In general anaesthesia clonidine given systemically has been found to decrease perioperative anaesthetic and analgesic requirement while, addition of clonidine to local anaesthetics during spinal anaesthesia, prolongs the duration of both motor and sensory blockadge [2-4].

A newer highly selective alpha-2 adrenergic agonist Dexmedetomidine is under study as a intrathecal and epidural adjuvant as it provide stable haemodynamic condition, better quality of intra-operative and prolonged duration of post-operative analgesia with less side effects [10-12]. Other uses like premedicant and as an adjunct to general anaesthesia as well as sedative agent in the intensive care unit have made it wonder drugs in anaesthesia [13]. It has eight times higher alpha-2/alpha-1 selectivity ratio than that of clonidine [14].

MATERIAL AND METHODS

Hospital Ethical Committee had approved the study protocol and ethical clearance certificate was obtained. 90 Patients aged between 20 -50 years, of either sex belonging to ASA grade I or II undergoing major orthopedic lower limb surgery were randomnly divided into two groups, Group(gr) D patients had received 0.5% Bupivacaine 15mg + Dexmedetomidine 3µg while gr C patients had received 0.5% Bupivacaine 15 mg + Clonidine 30µg intrathecally. Patients who had contraindication to spinal anaesthesia, i.e. allergy to drug, known case of labile hypertension, evidence of cardiac arrhythmia and heart block were excluded from the study.

Pre-anaesthetic check-up was done on the day before surgery. The procedure of subarachnoid block explained to the patient and informed written consent was obtained.

On the day of operation, all the patients were re-assessed in pre-operative anaesthesia room and basal vital data like temperature (T), Heart Rate (HR), Blood Pressure (BP), Respiration Rate (RR) and SpO_2 were recorded. A suitable IV (intravenous) line was secured with 18 G cannula and inj. Ringer's Lactate(RL) (500ml) started. On operation table, all monitors were attached including ECG in Std. Lead II, non invasive BP, pulse oximeter and baseline HR, BP, RR and SpO_2 recorded. Patients were premedicated with Inj. Glycopyrrolate 0.2 mg IV. After proper pre-loading with RL, with strict aseptic and antiseptic precautions, lumber puncture was performed in sitting position with 25 gauge Quincke needle, at L3-L4 intervertebral space using midline approach. Following free flow of CSF, drugs were injected slowly over 10 seconds. Patients were positioned supine immediately after the administration of intrathecal agents. Fluid therapy was maintained with RL and other appropriate iv fluids. The level of sensory block was evaluated by loss of pinprick sensation bilaterally along the mid clavicular line. We used T2- as baseline point for normal sensation. The test was performed every 5seconds (sec) till onset of sensory block on shin of tibia. Then every 1 minutes (min) till it reaches T10 dermetome. Onset of sensory block was taken as time interval between the complete injections of local anaesthetic solution to the achievement of complete loss of sensation at shin of tibia (L4). Maximum sensory level achieved as well as two segment regression times was also noted. Total duration of sensory block was taken from onset of sensory block to return of pin prick to heel of feet (S1).

The motor blockade was assessed using modified Bromage scale [15].

0=Free movement of legs, feet, with ability to raise extended legs.
1=Inability to raise extended leg and hip flexion is decreased but full flexion to feet and knee present.
2=Inability to raise leg or flex knees, flexion of ankle and feet present.
3=Inability to raise legs, flex knees ankle or move toes.

Onset of motor block (Bromage score 1) and time to achieve maximum motor block (Bromage score 3) were recorded.

After the subarachnoid blockade, all the patients were monitored for HR, BP, RR and SpO_2 at 1, 2, 5, 10, 15, 30, 45, 60, 90, and 120 min then every 30 min till 5^{th} hour and at 6^{th}, 8^{th}, 12^{th} and 24^{th} hour. Any untoward effects like bradycardia, hypotension, nausea, vomiting and shivering were noted and treated appropriately. HR less than 60 beats per min was considered as bradycardia and, if any, was treated with inj. atropine 0.6 mg iv. Systolic BP of less than 90 mmHg was considered as hypotension and was corrected with rapid infusion of IV fluids, oxygen with facemask, foot end elevation and inj. Mephentermine 9mg IV as and when needed, in incremental doses.

Post operatively, the pain score was recorded by using visual analog pain scale (VAS) between 0 & 10 (0= no pain, 5 = moderate pain, 10 = severe pain). Rescue analgesia (inj. Tramadol 50mg IV) was given when VAS ≥ 5.

Statistical analysis

The data were collected and comparison of variables between two groups was done by using unpaired student 't' test. P value of < 0.05 was considered to be statistically significant(S). Data analysis was carried out using MedCalc software package.

RESULTS

Demographic profile

The demographic profiles are comparable in both groups and total number, type and duration of surgical procedures are comparable in both groups (Table 1).

Table 1: Demographic profile

		No. of patients			
		Dexmede-tomidine	Cloni-dine	'P' Value	Infere-nce
Age group	Mean	36.8	32.75	0.0721	NS
	SD	10.04	11.039		
Weight	Mean	59.4	57.24	0.077	NS
	SD	5.84	5.62		
Sex	Male	34	37		
	Female	11	8		
Surgical procedure					
Tibia CRIF		7	9		
Tibia ORIF		7	6		
Tibia I/R		7	5		
Femure CRIF		9	8		
Femure ORIF		8	6		
Femure I/R		2	3		
HRA Hip		3	4		
Knee Arthroscopy		2	3		

NS : Not Significant
CRIF : Closed reduction and internal fixation
ORIF : Open reduction and internal fixation
I/R : Implant removal
HRA : Hemi replacement arthroplasty

The result regarding characteristic of sensory block, motor block and post-operative analgesia are summarised in Table II. Chart I shows onset of

Chart 1: Onset of sensory and motor block in seconds

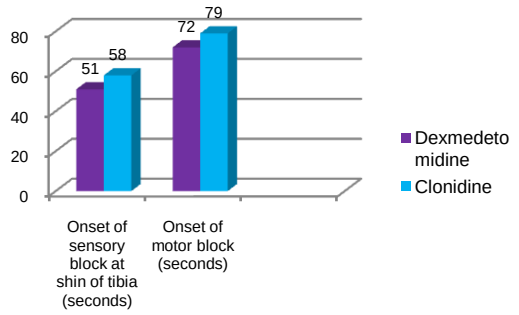


Chart 2: Total duration of sensory block, motor block and post operative analgesia

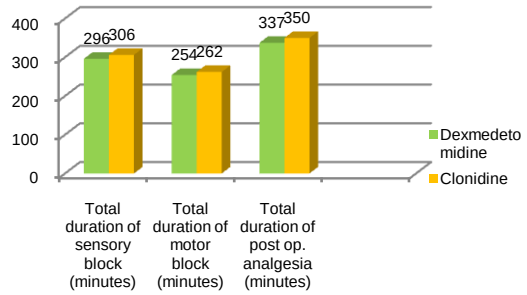
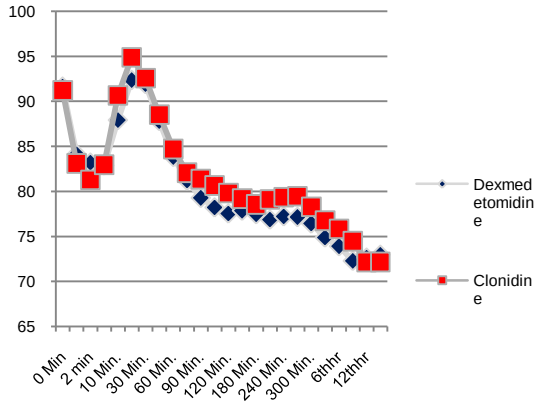


Chart 3: Mean pulse rate changes



sensory and motor block in both groups. While comparing both groups, the results were statistically not significant. Chart II shows total duration of sensory block, motor block and post-operative analgesia in both groups were found to be comparable and the

Chart 4: Mean arterial pressure changes

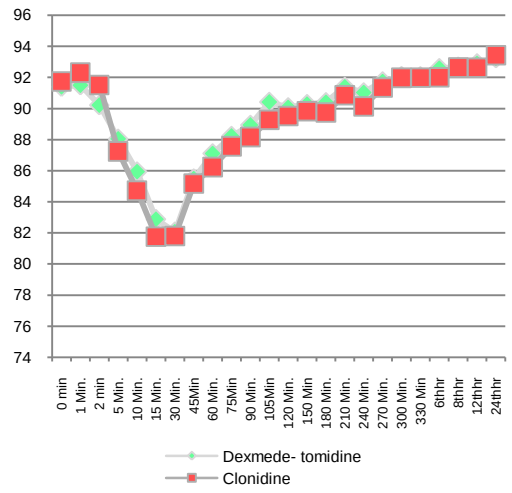


Table 2: Summary of results

Characteristics	Group d	Group c	P value
Onset of sensory block at shin of tibia (sec)	51.77±18.59	58±18.51	0.115
Time to reach T10 sensory dermatome (min)	58.22±2.38	65.33 ±2.33	0.156
Two segment regression time (min)	110.44±21.63	118.67±25.55	0.103
Total duration of sensory block(min)	296.88±38.30	306.22 ±35.63	0.235
Onset of motor block(sec)	72.11±21.67	79.22 ±21.53	0.122
Time to achieve motor blockade bromage score 3(min)	8.17 ±2.12	9 ±2.045	0.065
Total duration of motor blockade(min)	254.44±40.65	262.22±34.23	0.329
Total duration of surgery(min)	74.11 ±16.83	75.33 ±18.25	0.74
Total duration of post-operative analgesia(min)	337.33±35.31	350.44±34.37	0.07

difference is statistically not significant. Chart III shows that both groups were comparable regarding mean pulse rate after spinal anaesthesia at 0, 1, 2, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, 240, 270, 300, 330, 360 min and 6^{th}, 8^{th}, 12^{th} & 24^{th} hours. There were no significant differences. Chart IV shows that both groups were comparable regarding mean arterial pressure after spinal anaesthesia at 0, 1, 2, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210, 240, 270, 300, 330, 360 min and 6^{th}, 8^{th}, 12^{th} & 24^{th} hours. There were no significant differences.

Hypotension occurred in both groups after 5, 10, 15 min but difference was not significant. 3 patients of Dexmedetomidine gr required injection mephentermine compared with 5 patients in Clonidine gr. Intra-operative or post-operative nausea and vomiting did not occurred in any of two gr compared. We did not observe any incidence of shivering in both the groups. None of the patients in either group had any degree of respiratory depression. All patients had peripheral oxygen saturation greater than 95% at all times and did not require supplemental oxygen.

DISCUSSION

Orthopedic lower limb surgeries are very painful and dreadful condition. Various techniques like local infiltration block, spinal, epidural or general anaesthesia can be used. Because of rapid onset, less failure, technically easy administration and economical than general anaesthesia as well as epidural, spinal anaesthesia is most commonly used technique in developing country like India.

Various drugs like neostigmine [16], ketamine [17], morphine [18], midazolam [19], and magnesium sulphate [20] have been tried intrathecally to improve quality of spinal anaesthesia in the form of faster onset and prolonged duration of sensory and motor block with post-operative analgesia.

Local anaesthetic agents act by blocking sodium channel whereas alpha-2 adreno receptor agonist act by binding to pre-synaptic c fibers and post-synaptic dorsal horn neurons and shows analgesic action by depressing release of c fibers transmitter and hyperpolarising post-synaptic dorsal horn neuron [21]. The prolongation of effect may result from synergism between local anaesthetic and alpha-2 adreno receptor agonist.

Yaksh [22] has shown that alpha-2 adrenoreceptor when given intrathecally causes dose dependent

decrease in motor strength in animals. Alpha-2 adreno receptor agonists administered intrathecally have been found to have antinocicepive action for both somatic and visceral pain [10]. Dexmedetomidine when used intrathecally in combination with bupivacaine found no postoperative neurological deficit [10-12].

Kalso et al [23] reported that Dexmedetomidine has 10 times more affinity to alpha-2 adrenoreceptor than clonidine. On the basis of this hypothesis we compared sensory and motor characteristics, post-operative analgesia and haemodynamic changes between Dexmedetomidine 3µg or Clonidine 30µg.

In our study we found no statistically significant difference with regard to onset of sensory and motor block between the groups.

G.E Kanazi et al [12] compared the low dose of Dexmedetomidine 3µg and Clonidine 30 µg with Bupivacaine 12mg intrathecally and observed that, mean time to reach T10 sensory block was 9.7 ± 4.2 min in gr bupivacaine alone (B) whereas 7.6 ±4.4 min in Clonidine gr (C) and 8.6 ±3.7 min in Dexmedetomidine gr (D). The median and range of the peak sensory level reached were T6 (T4-T10) in gr B, T6.5 (T3-T9) in gr C and T6 (T2-T10) in gr D, without significant differences between the groups. In their study done by Al-Mustafa MM et al.[11], Dexmedetomidine added to spinal bupivacaine for urological procedures, they observed that the mean time of sensory block to reach the T10 dermatome was 4.7 ± 2.0 min in D10 (dexmedetomidine10µg) gr, 6.3±2.7min in D5 (dexmedetomidine5µg) gr, and 9.5 ± 3.0 min in gr N (normal saline). Subhi M. Al-Ghanem et al. [10] compared the effect of Dexmedetomidine 5µg (D) or fentanyl 25µg (f) given intrathecally with plain 0.5% Bupivacaine for spinal anaesthesia and they found that time to reach T10 sensory block level was7.5± 7.4min for gr D and 7.4±3.3 min for gr F and the peak sensory level was T_6 (T4-T9) in gr D and T6 (T3-T8) in gr F, without significant difference between the groups. In our study, the mean time to achieve T_{10} sensory blockade was 5.822 ±2.386 min in gr D and 6.5 ± 2.3316 min in gr C. There was no significant difference regarding time to achieve T_{10} sensory dermatome and highest level of sensory block between gr D and gr C.

G.E Kanazi et al [12] found that all patients achieved bromage 3 motor block. However, the time to reach bromage 3 motor block was significantly shorter in gr D (13.2 ± 5.6 min) and gr C (11.7 ±5.9 min) than in gr B (20.7 ±10.3 min). These values were not significantly different between groups C and D, and the sensory regression of two dermatomes were 80 ±28 min in gr B, 101 ± 37min in gr C and 122 ± 37 min in gr D. The regression times of the two dermatomes were significantly different between groups B and D.

In reference to recovery parameters like time for complete sensory and motor recovery G.E Kanazi et al [12] found that sensory regression times were comparable between gr C and D. Sensory regression to S1 segment for gr B, C and D were 190 ± 48 min, 272 ± 38 min and 303 ± 75 min respectively and regression to Bromage score 0 for gr B, C and D were 163 ±47 min, 216 ±35 min and 250 ± 76 min respectively. In one study Al-Mustafa MM et al [11] observed that sensory regression to S1 segment in gr N (12.5mg Bupivacaine + normal saline), gr D5 (Dexmedetomidine 5ug) and gr D10 (Dexmedetomidine 10 ug) were 165.5±32.9min, 277.1±23.2 min and 338.9±44.8 min respectively and duration of motor block were 140.1±32.3 min, 246.4±25.7 min and 302.9±36.7 min respectively. In another study Subhi M. Al-Ghanem et al [10] observed that the regression time to reach modified Bromage 0 in gr D (240±64min.) were significantly longer than that for gr F (155±46 min), and also the time reach S1 segment were significantly longer in gr D (274.8±73.4 min) than in gr F (179.5±47.4 min).

Regarding post-operative analgesia Suchita A. Joshi et al [19] observed that mean duration of analgesia in BM gr (Bupivacaine + Midazolam, intrathecally) were 391.64 (132.98) min longer than BC (Bupivacaine + Clonidine, intrathecally) gr 296.60 (52.77) min. In our study, total duration of post-operative analgesia was 337.333±35.31 min in gr D and 350.444±34.37 min in gr C. The difference is not significant (p=0.07). All the above mentioned studies support our results.

In view of hemodynamics, G.E Kanazi et al [12] found that, addition of Dexmedetomidine or Clonidine to Bupivacaine did not cause a significant decrease in the BP either intra-operatively or post-operatively. The mean values of MAP and HR were comparable between the three groups. In our study, the two groups D and C did not differ significantly with respect to HR at any interval. There was no any bradycardia in either of groups. Incidence of Hypotension occur in both the groups but it was less and comparable. In both the groups hemodynamic stability was maintained and side effects were comparable.

CONCLUSION

After study of 90 patients in lower limb orthopedic surgeries we conclude that both Dexmedetomidine 3µg and Clonidine 30µg when used as an adjuvant to intrathecal hyperbaric Bupivacaine 0.5% 15mg provides early onset of both motor and sensory block, increases two segment regression time and delayed motor and sensory blockade as well as prolonged postoperative analgesia. The both groups Dexmedetomidine and Clonidine were similar with respect to all parameters mentioned in aims of the study as there were no any statastical significant differences. Both the groups showed hemodynamic stability without any significant side-effects.

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How to cite this article: Raval DL, Chaudhary M. A clinical comparative study between dexmedetomidine v/s clonidine with bupivacaine intrathecally in major orthopaedic lower limb surgery. J Res Med Den Sci 2014;2(1):77-83

Source of Support: None
Conflict of Interest: None declared

Corresponding Author:

Dr. Dipak L. Raval,
Axar Vatika "AUM",
Near halar house and forest office,
Nagnath gate,
Jamnagar- 361001, Gujarat, India
Email: dr.dipakraval@gmail.com

Date of Submission: 02/02/2014
Date of Acceptance: 22/03/2014