Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(9): 1541-1547
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5918.18

Synergestic Effect between Dexmedetomidine and 0.75% Ropivacaine in Epidural

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Abstract

Objective: The aim of this study is to evaluate and compare the clinical effects of added dexmedetomidine to epidural ropivacaine 0.75% for lower limb orthopedic procedures. *Methods:* 40 patients undergoing elective lower limb orthopedic procedures under epidural anesthesia were selected and divided into two groups of 20 each and assigned into Control Group (N=20): Epidural ropivacaine 0.75% 20ml (150mg)+1ml NS, Dexmedetomidine Group (N=20): Epidural ropivacaine 0.75% 20ml (150mg)+ Dexmedetomidine 1µg/kg+NS to complete 1ml. Variables studied include: Block onset time, maximum dermatomal level of anesthesia, duration of sensory and motor blockade, motor block intensityassessed by bromage motor scale, sensory block assessed by sensory scale, level of sedation assessed by ramsay sedation scale, hemodynamics, duration post operative analgesia-vas score *Results:* Duration of analgesia was prolonged in Dex group, level of significance ($p<0.05$), Motor block duration was prolonged in Dex group, level of significance ($p<0.05$), Intensity of motor block slightly increased in dex group, but without significance ($p<0.37$), need for Supplemental sedation was reduced need in Dex group, level of significance ($p<0.05$), Duration of post-op analgesia was significantly prolonged in Dex group when compared to control group, level of significance ($p<0.001$). *Conclusion:* There was a clear synergism between epidural dexmedetomidine and ropivacaine. Dexmedetomidine increases sensory and motor block duration during epidural anesthesia with ropivacaine, prolongs postoperative analgesia and does not cause hemodynamic instability.

Keywords: Synergestic Effect Between Dexmedetomidine and 0.75% Ropivacaine in Epidural.

How to cite this article:

Rajaram J. & Punidha Vardhani R. Synergestic Effect between Dexmedetomidine and 0.75% Ropivacaine in Epidural. Indian J Anesth Analg. 2018;5(9):1541-47.

Introduction

The α_2-adrenergic agonists provide sedation, anxiolysis, hypnosis, analgesia, and sympatholysis. Dexmedetomidine shows a high ratio of specificity for the α_2 receptor (α_2/α_1 1600:1) compared with clonidine (α_2/α_1 200: 1), making it a complete α_2 agonist [27].

Alpha$_2$ agonists do have an analgesic effect when injected via the intrathecal or epidural route [4,5,6]. Intrathecally injected dexmedetomidine in sheep reduces blood pressure in 1 minute. When dexmedetomidine is injected into the epidural space, it rapidly diffuses into the CSF (in one study, 22% of the injected dose was identified in the CSF). The effects on blood pressure are slower in onset with an epidural injection than with an intrathecal administration. Epidural effects are seen in 5 to 20 minutes. The primary site of analgesic action is thought to be the spinal cord [5,6].

In humans, dexmedetomidine was first administered

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Received on 25.05.2018, **Accepted on** 09.06.2018

epidurally in 1997, combined with lidocaine 1.5 % in patients undergoing hysterectomy, prolonging postoperative analgesia [6].

Based on studies with clonidine [7,8], We evaluated the synergism of dexmedetomidine with ropivacaine during epidural administration, in improving the characteristics of anesthesia. The aim of this study was to evaluate the clinical effects of Dexmedetomidine added to ropivacaine on the characteristics of epidural anesthesia.

Methods

After approval of the study protocol by the Ethics committe and obtaining informed consent. It was a comparative, double blind, randomized, controlled study and distribution by means of a draw with a sealed envelope.

Inclusion Criteria

1. ASA I & II
2. Both Sexes
3. Age Between 18-70 yrs
4. Elective Orthopedic Procedure
5. Under Epidural Anesthesia
6. Withaout Comorbid Illness

Exclusion Criteria

1. Allergy to Local Anesthetics
2. NM Diseases
3. Alpha 2 Antagonist
4. Weight More than 120kg

Patients were admitted to the hospital, after a period of absolute fasting at least 8 hours, without administering premedication. venipuncture was performed with an 18G catheter for administration of Ringer's lactate, 8 $ml.kg^{-1}. h^{-1}$.

Monitoring consists of, Pulse oximetry (SpO_2), NIBP, ECG. persons not directly involved in the anesthetic prepared dexmedetomidine or sodium chloride 0.9%, 1 ml syringe.

Epidural puncture was performed with a 16G Tuohy needle, through the lumbar epidural space, with patients in sitting position, through loss of resistance technique. Patients were sedated on demand basis with pentazocine or midazolam.

All patients received an epidural 20ml of 0.75% Ropivacaine along with etiher:

Control group (n=20) +1ml normal saline

or

Dexmedetomidine Group (n = 20): $1\mu g.kg^{-1}$ + dexmedetomidine solution of sodium chloride 0.9 %, so that the volume was completed in 1ml syringe.

Immediately after the injection of the study drug, all patients were administered 20 ml of 0.75% (150 mg), the rate of 1 ml every three seconds.

After the surgery, patients were referred to the recovery room, where they remained for a period, until there was complete recovery of sensory and motor block. All were monitored with Pulse oximetry (SpO_2), NIBP, ECG. Patients who complained of pain were given rescue post-operative analgesia with 10ml of 0.2% Ropivacaine through epidural route.

Definition of Variables

Sensory Block Onset Time

Time interval between end of anesthetic injection and appearance of cutaneous analgesia in dermatomes T-12, T-10, T-8, T-6.

Duration of Motor Block

Administration of anesthetic and attainment of grade 0 in Bromage motor scale.

Duration of Analgesia

Administration of anesthetic and disappearance of cutaneous level at each dermatomal level.

Post-Op Analgesia Duration

Administration of anesthetic and time of analgesic usage in PACU.

Supplemental Sedation

If patient felt pain or uncomfortable, Sedated with pentazocine 0.3mg/kg and or midazolam 0.02mg I.V If there were hypotension (measured as systolic blood pressure less than 30% of its initial value or below 90 mmHg) during anesthesia , it was treated with administration of ephedrine, 6 to 12 mg and increased administration of intravenous fluids. Bradycardia (heart rate<45) were treated with atropine, 0.6 mg , and administration of oxygen via face mask ($4\ l.min^{-1}$), if SpO_2 was < 94%.

Statistical Analysis

Variables were analysed with Student 't' test, Chi Square test. Variables like age, sex, weight, height

were compared using Levene's test for equality of variance.

Sample size obtained according to previous background study 'p' value less than 0.05 was taken as significant

Results

One patient in the control group excluded for failure of epidural and need for general anesthesia. There was no significant difference between groups in distributions of age, weight, height and sex, type of surgery or duration of surgery.

Regarding block onset time(time to attain analgesia at T12, T10, T8, T6), dex group has slightly shortented onset time with less significance when compared to control group (13.90mins vs 12.45mins) $p<0.08$.

Regarding the upper level of analgesia, examined after an hour after epidural, all patients did attain T6 level without any significance between groups

Table 1:

Variables		Control	DEX
Age		42.25	39.1
Sex	Female	3	4
	Male	17	16
Height (cm)		169.4	163.2
Weight (kg)		69.95	66.75
Level Of Epidural	L1-L2	2	2
	L2-L3	10	10
	L3-L4	8	8
Cathetar Length (cm)		6.5	6.85
Surgery	IM / IL Nailing	10	9
	Illizarao ring fixation	4	2
	DHS	2	5
	TKR	1	1
	THR	1	0
	DCS	0	1
	Encirclage / TBW L Patella	1	0
	Plate & Screw fixation	0	2
	Hemiarthroplasty	1	0
ASA	I	12	15
	II	8	5
Duration of Surgery (mins)		158.3	177

Table 2:

Independent Samples Test

		t-test for Equality of Means		
		DF	Sig. (2-tailed)	Mean Difference
Analgesia duration minutes	Equal variances assumed	38	.000	-67.900
	Equal variances not assumed	37.821	.000	-67.900

		Levene's Test for Equality of Variances		t-test for Equality of Means
		F	Sig.	t
Regression Time T6-T10 Minutes	Equal variances assumed	1.614	.212	-12.787
	Equal variances not assumed			-12.787
Regression Time T10-12 Minutes	Equal variances assumed	4.076	.051	-.394
	Equal variances not assumed			-.394

Regarding the duration of analgesia, the group receiving dexmedetomidine had significantly higher compared to the control group.in dex group it is 304.25mins compared to 236.35 in control group ($p<0.02$) and two segment regression time was prolonged in dex group.

Regarding motor block duration, dex group showed significant prolongation in duration (248mins) when compared to control group (204.65mins), level of significance $p<0.04$, slightly increased intensity of blockade assessed by bromage motor scale was observed with dex group, but without much significance $p<0.37$. The duration of postoperative analgesia was significantly different between groups ($p<0.001$), and the dexmedetomidine group had a duration of analgesia which is 60% more than control group. Values in minutes as an average were 496.95mins for dex group when compared to 309mins in control group

The occurrence of hypotension and the need for vasopressors in the intra- and post-operatively was similar between groups, with no significant difference $p>0.13$. Both groups showed excellent

Table 3:

Independent Samples Test

		t-test for Equality of Means		
		DF	Sig. (2-tailed)	Mean Difference
Post of Analgesis in Minutes.	Equal variances assumed	38	.000	-187.450
	Equal variances not assumed	32.091	.000	-187.450

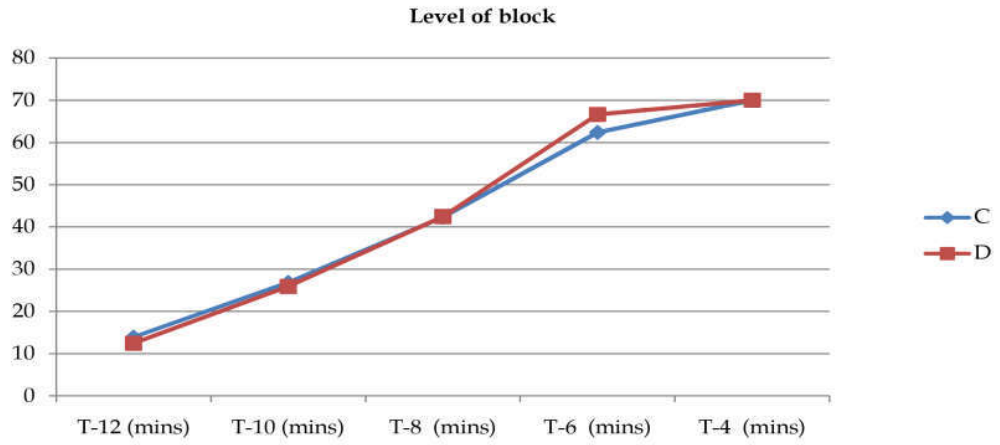

Fig. 1:

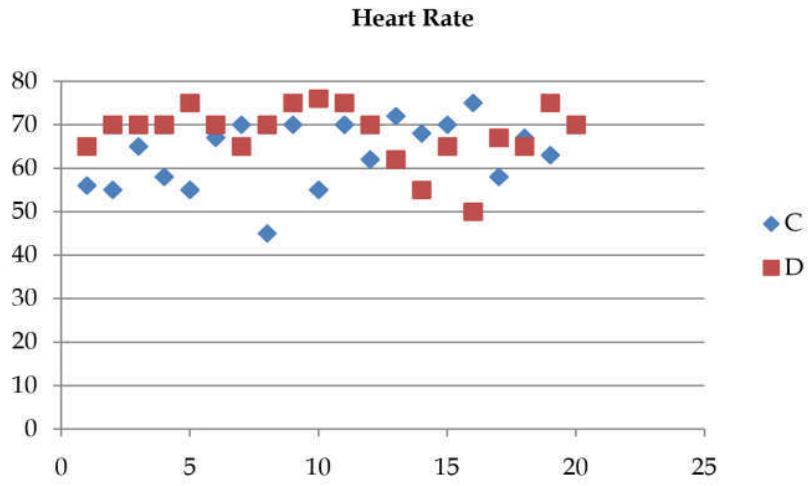

Fig. 2:

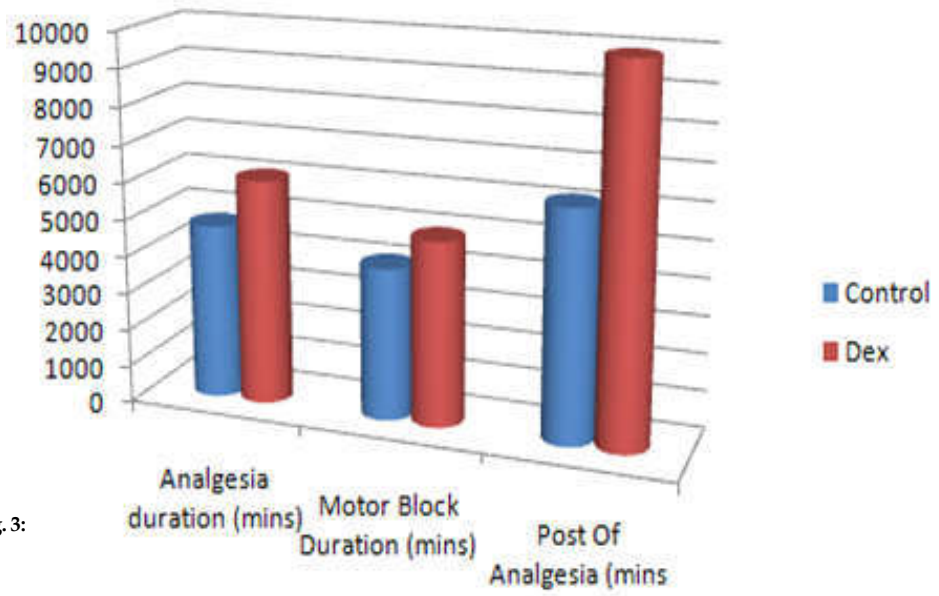

Fig. 3:

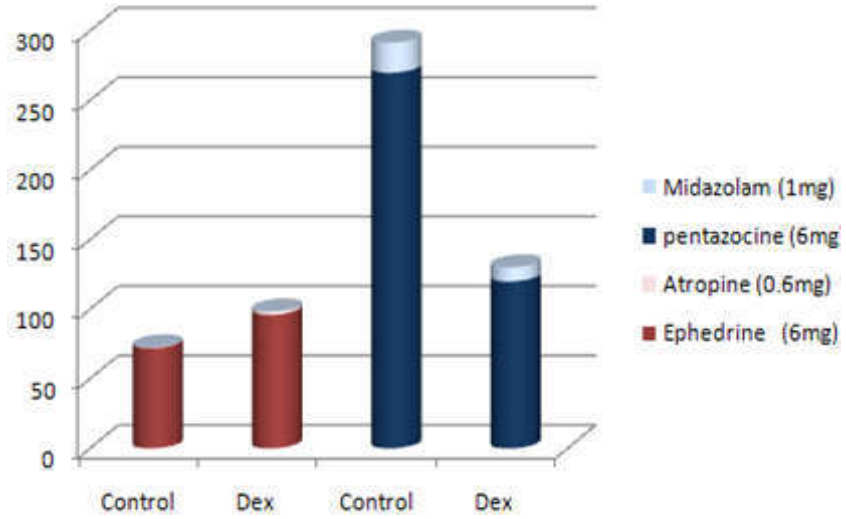

Fig. 4:

hemodynamic stability with less incidence of hypotension or bradycardia. The need for sedation was decreased in dex group when compared to control groups.

Discussion

In this study, the effect of added dexmedetomidine to epidural ropivacaine was evaluated. The results showed duration of analgesia,motor block block duration and postoperative analgesia were significantly increased and there is clear synergism between dexmedetomidine and ropivacaine when administered epidurally. Previous studies evaluated the effect of α_2 agonist added with various local anesthetics.This study conducted based on previous studies with epidural clonidine [8,10,11], which prolongs post operative analgesia [12,14,15]. Dexmedetomidine is a nonselective α_2 agonist. Three subtypes of α_2 adrenoreceptors have been described in humans: α_{2A}, α_{2B}, and α_{2C} [27,30]. The α_{2A} adrenoreceptors are primarily distributed in the periphery, whereas α_{2B} and α_{2C} are in the brain and spinal cord. Postsynaptic located α_2 adrenoreceptors in peripheral blood vessels produce vasoconstriction, whereas presynaptic α_2 adrenoreceptors inhibit the release of norepinephrine, potentially attenuating the vasoconstriction. The overall response to α_2

adrenoreceptors agonists is related to the stimulation of α_2 adrenoreceptors located in the CNS and spinal cord. These receptors are involved in the sympatholysis, sedation, and antinociception effects of α_2 adrenoreceptors. Ropivacaine is a long acting amide local anesthetics and 'S' isomer of the propyl analogue of mepivacaine and bupivacaine. It has similar properties to bupivacaine , but with better cadiotoxicity profile because it dissociates from Na+channels more rapidly and produces less accumulation of Na+channel block. Significantly better sensory-motor differentiation, due to lower lipid solubility than bupivacaine Has mild intrinsic vasoconstricting properties and so unsuitable for infiltration in tissues without collateral blood supply and is the reason for longer cutaneous anesthesia. Ropivacaine pKa is 8.07, Protein binding is 94%, Partition co-efficient is 11, CC:CNS ratio is 5:1, Potency 4. Dexmedetomidine is an agonist of α_2 adrenergic receptor – agonist where ratio among α_2:α_1 is 1600:1.Dex epidural effect is dose dependent and superior than I.V due to its high affinity for α_2 adrenergic receptors in spinal cord. After epidural administration of Dex , it is rapidly detected in CSF within five mins, however only 22% is absorbed into intra thecal space [19,31,33]. Its anti-nociceptive effect is dose dependent and is related to affinity of located α_2 adrenergic receptors in spinal cord and higher lipid solubility and penetration of meninges [5,20]. Prolonged analgesic action of local anesthetics in epidural space is due to reduced systemic absorbtion caused by local vasoconstriction mediated by α_{2C} adrenergic receptors in smooth muscle of epidural venous plexus [11,21,27].

The α_2 agonists produce their sedative-hypnotic effect by an action on α_2 receptors in the locus caeruleus and an analgesic action at α_2 receptors within the locus caeruleus and within the spinal cord [28,33,34]. During epidural administration cephalad spread of the drug into meninges may be responsible for sedation [16,22]. The α_2 agonists act through the endogenous sleep-promoting pathways to exert their sedative effect . Dexmedetomidine produces a decrease in activity of the projections of the locus caeruleus to the ventrolateral preoptic nucleus. This increases GABAergic and galanin release in the tuberomammillary nucleus, producing a decrease in histamine release in cortical and subcortical projections. Dexmedetomidine at concentrations producing significant sedation reduces minute ventilation, but retains the slope of the ventilatory response to increasing carbon dioxide. Dexmedetomidine also exhibited a hypercarbic arousal phenomenon, which has been described during normal sleep and is a safety feature. IV or inhaled dexmedetomidine has been implicated in blocking histamine-induced bronchoconstriction in dogs [22]. Another advantage is that their effects are easily reversible with alpha-2-adrenergic agonists such as atipamazole (with an affinity for the receptors of 60:1, compared to dexmedetomidine), which is the dependent dose, it rapidly reverses the sedation and cardiovascular effects at doses from 15 to 150 micg/kg [29]. The basic effects of α_2 agonists on the cardiovascular system are decreased heart rate; decreased systemic vascular resistance; and indirectly decreased myocardial contractility, cardiac output, and systemic blood pressure. Bradycardia and hypotension with administration of dexmedetomidine is dose dependent and occurs in epidural if level is higher [19,21,22,24]. Shivering incidence may be reduced with α_2 agonists due to central inhibition of thermoregulatory centre [23,25,26].

Conclusion

We conclude that dexmedetomidine at a dose of 1 $\mu g.kg^{-1}$ acts synergistically with ropivacaine 0.75% in epidural anesthesia. The drug increases the duration of analgesia, motor block duration, prolongs the duration of postoperative analgesia and decreases sedative usage and shivering episodes.

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