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Comparison of Ropivacaine Vs Ropivacaine + Dexmeditomidine as an Adjuvant in Post – Operative Epidural Analgesia in Abdominal Surgeries.

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ABSTRACT

The purpose of the study is to compare the hemodynamics and duration of post-operative motor and sensory blockade with ropivacaine + dexameditomidine as an adjuvant in post- operative in epidural analgesia in abdominal surgeries.

Keywords: ropivacaine, dexameditomidine, epidural analgesia.

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INTRODUCTION

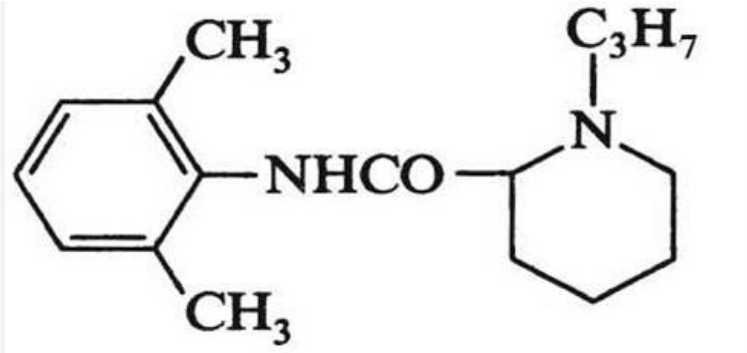
Epidural blockade is one of the most useful and versatile procedure in modern anesthesiology. It is unique in that it can be virtually placed at any level of the spine allowing more flexibility in anesthetic practice. It is more versatile than spinal anesthesia giving the anesthetist the opportunity to provide continuous surgical analgesia, anesthesia and post-operative pain control.

Epidural anesthesia can reduce the adverse physiologic responses to surgery such as autonomic hyperactivity, cardiovascular stress, increased metabolic rate, pulmonary dysfunction and immune system dysfunction. It also reduces the incidence of hyper coagulability, deep vein thrombosis(DVT), Pulmonary Embolism(PE) and also decreases intraoperative blood loss.

Abdominal surgeries are a challenge for every anesthetist. Post-operative pain management is one of the significant problems after abdominal surgeries. Epidural analgesia is preferred in these cases as it aids in the most comfortable positioning for the patient during the post-operative period. The special advantage of epidural adjuvant is the synergistic effect they exhibit with local anesthetic which allowed a marked decrease in the dose of both drugs to achieve the same level of analgesia.

Ropivacaine

Structural Formula



Ropivacaine is a long acting enantiomerically pure S-enantiomer amide local anesthetic. It is the propyl analogue of bupivacaine with high pKa and low lipid solubility.

Ropivacaine has significantly better sensory-motor differentiation due to lower lipid solubility and so blocks nerve fibers involved in pain transmission A delta and C fibers to a greater degree than those controlling motor function(A beta fibers). Its onset time and duration are comparable to bupivacaine but with less cardiotoxicity due to the fact that it dissociates from sodium channels more rapidly. Has mild intrinsic vasoconstricting properties, hence not suitable for infiltrating in tissues without collateral blood supply and is the reason for longer cutaneous anesthesia.

Dexmeditomedine

History

The α_2 adrenergic agonist provide sedation, anxiolysis, hypnosis, analgesis and sympatholysis. It is a more selective $\alpha_2$agonist with a 1600 greater selectivity for $\alpha_2$receptor compared with the α_1 receptor.

Physiochemical Characteristics

Dexmeditomidine is the d-enantiomer of meditomedine a substance that has been used for sedation and analgesia in veterinary medicine for many years. It 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. Dexmeditomidine belongs to the imidazole subclass of α_2 receptor agonist similar to clonidine.

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Effects on Central Nervous System

The $\alpha_2$agonist producetheir sedative hypnotic effect by the action on α_2 receptors within the locuscaeruleus and within the spinal cord. Despite sound levels of sedation there is limited respiratory depression providing wide safety margins. The advantage they have is that their effects can be readily reversed by α_2 adrenergic antagonist (e.g.,atipamezole). Dexmeditomidine reduces the catecholamine outflow during injury and resulted in less neural tissue damage with better neurologic outcome.

Effects on Respiratory System

Dexmeditomidine at concentrations producing significant sedation reduces minute ventilation, but retains the slope of the ventilator response to increasing carbon dioxide. Also exhibited a hyperbaric arousal phenomenon, which has been described during sleep and is a safety feature.

Effects on the Cardiovascular System

The basic effect of α_2 agonist on CVS are decrease in heart rate, decrease in systemic vascular resistance, and indirectly decreasing myocardial contractility, cardiac output and systemic blood pressure. Infusion of dexmeditomedine also has been shown to result in a compensated reduction in systemic sympathetic tone without change in baroreflex sensitivity.

Introduction to Clinical Study

α_2 agonist do have an analgesic effect when injected via the intrathecal or epidural route. Intrathecally injected dexmeditomidine in sheep reduces blood pressure in 1 minute. When dexmeditomedine is injected into the epidural space, it rapidly diffuses into the CSF (in one study, 22% of injected dose was identified in the CSF). The effects on the blood pressure are slower in onset with an epidural injection than with an intrathecal administration. Epidural effects are seen in 5 to 10 minutes.

In humans, dexmeditomedine was first administered epidurally in 1997 combined with lignocaine 1.5% in patients undergoing hystrectomy, prolonging post-operative anesthesia. Based on studies with clonidine we evaluated the synergism of dexmeditomedine with ropivacaine during epidural administration in improving the characteristics of anesthesia.

METHODOLOGY

After approval of the study protocol by the ethics committee and obtaining informed consent. It's a comparative, double blind, randomized, controlled and distribution study.

Inclusion Criteria	Exclusion Criteria
1. ASA I & II	1. Allergy to local anesthesia
2. Both sexes	2. Patient refusal
3. Age between 18-70	3. ASA III
4. All abdominal surgeries	

After shifting the patient to the operation theatre, after a period of absolute fasting without administering premedication. Venupuncture was performed with an 18G catheter for administration of Ringers lactate at 8ml/kg/hour.

Monitoring consists of Pulse-oximetry(SpO_2), NIBP, ECG.

Epidural puncture was performed with a 18G Tuohy needle, with patient in sitting position, through loss of resistance technique.

Patient is then induced and under General Anesthesia surgery is performed. Post surgerythe patients were referred to the recovery room where they remained for a period until they are completely recovered from general anesthesia.

Patients were administered the epidural bolus when they complained of pain. And from this time the hemodynamicparameters, drug onset time is recorded as per protocol.

Group R(n=30): 0.3% Ropivacaine 10ml

Group RD(n=30): 0.3% Ropivacaine + Dexmeditomidine 1mcg/Kg

Definition of Variables

Sensory Block Onset Time

Time interval between Epidural bolus and appearance of sensory analgesia

Duration Motor Block

Administration of epidural topup and attainment of grade 0 Bromage motor scale

Post-Operative Analgesic Duration

Duration of sensory analgesia from the time of epidural bolus

Statistical Analysis

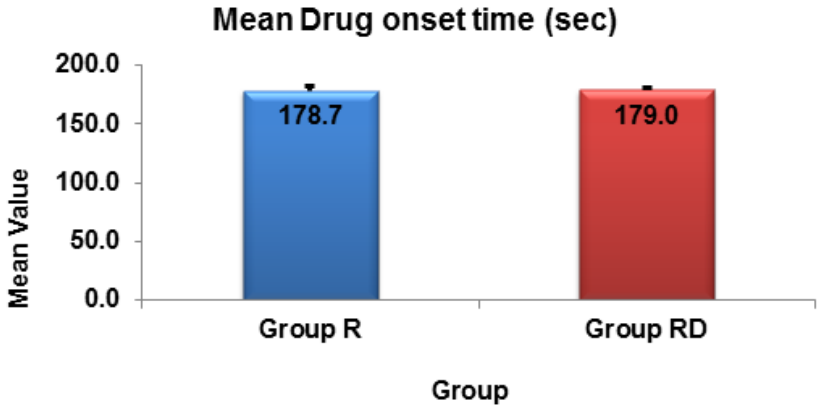
It's a double blind randomized controlled clinical study
Variables were analyzedwith 'T' test, Chi square test
Variables like Age, Gender, ASA status, onset & duration of motor and sensory block were compared
'P' value less than 0.05 taken as significant

RESULTS

There was no significant difference between groups in distributions of Age, Gender and ASA status. Regarding the drug onset time, there was not much difference between both the groups. The onset time of both the groups were almost the same.

Independent samples T-Test to compare the mean onset time (sec) between Group R and RD

Variable	Group	N	Mean	Std. Dev	P-Value
Drug Onset Time (sec)	Group R	30	178.67	3.377	0.655
	Group RD	30	179.00	2.274	



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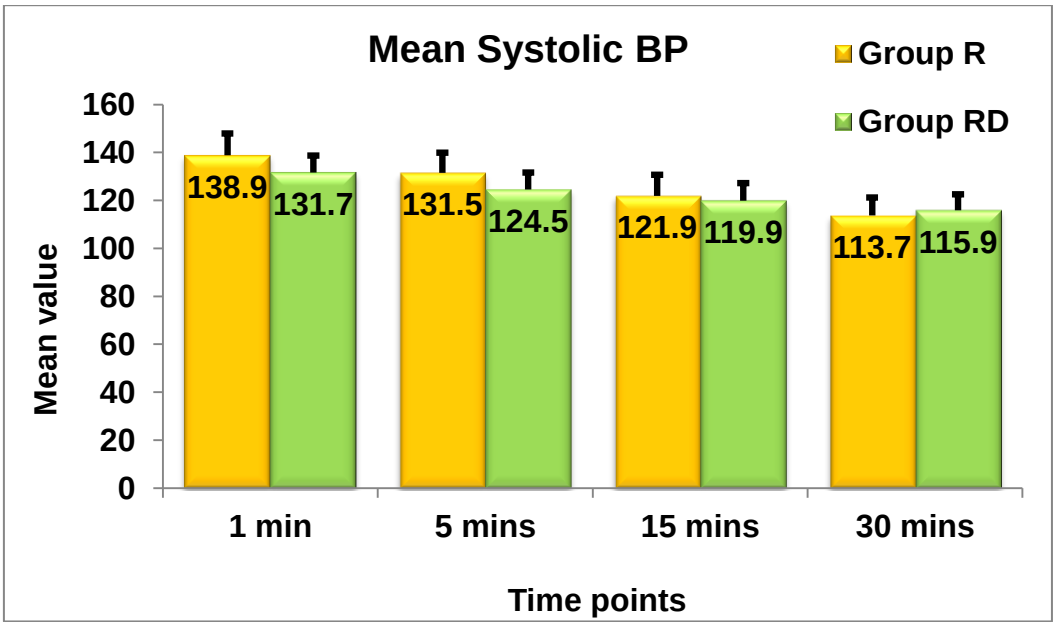
Regarding mean blood pressure, there was significant difference between both groups. Group RD had a stable heamodynamic compared to Group R clinically though not significant statistically.

Independent samples T-Test to compare the mean Blood Pressure between Group R and RD

Variable	Group	N	Mean	Std. Dev	P-Value
SBP at 1 min	Group R	30	138.87	9.031	0.001
	Group RD	30	131.67	6.989	
DBP at 1 min	Group R	30	84.53	7.333	0.061
	Group RD	30	81.27	5.813	
SBP at 5 mins	Group R	30	131.47	8.435	0.001
	Group RD	30	124.53	7.104	
DBP at 5 mins	Group R	30	78.20	4.824	0.603
	Group RD	30	78.80	4.021	
SBP at 15 mins	Group R	30	121.90	8.829	0.349
	Group RD	30	119.93	7.230	
DBP at 15 mins	Group R	30	74.07	5.741	0.921
	Group RD	30	73.93	4.502	
SBP at 30 mins	Group R	30	113.67	7.558	0.221
	Group RD	30	115.93	6.612	
DBP at 30 mins	Group R	30	71.67	5.307	0.844
	Group RD	30	71.93	5.159	



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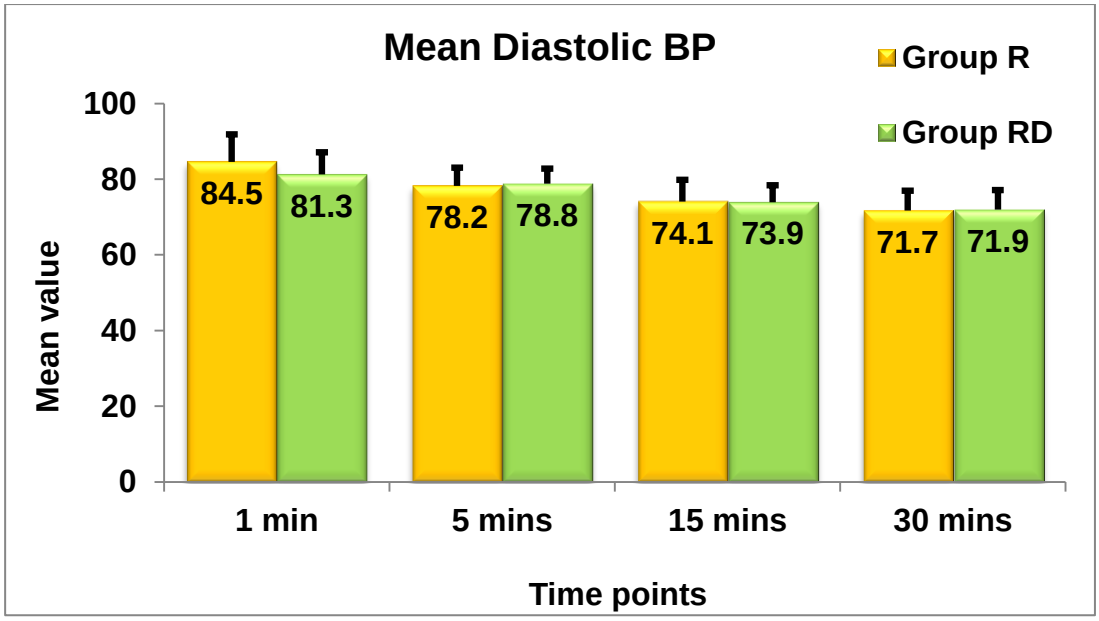
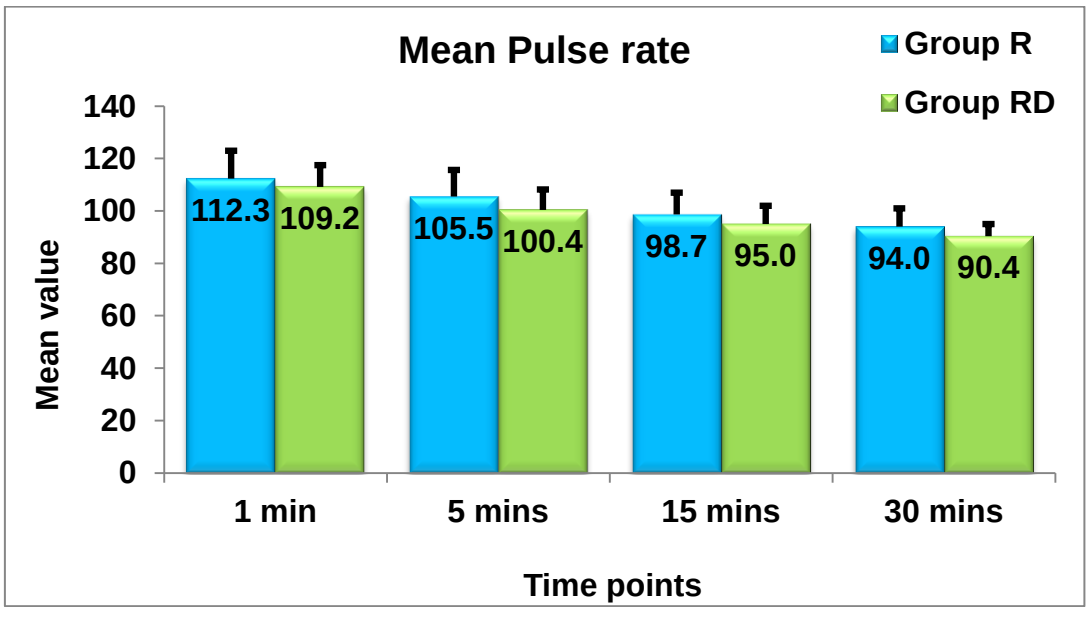


Independent samples T-Test to compare the mean Pulse rate between Group R and RD

Variable	Group	N	Mean	Std. Dev	P-Value
Pulse rate at 1 min	Group R	30	112.30	10.671	0.214
	Group RD	30	109.20	8.281	
Pulse rate at 5 min	Group R	30	105.53	10.058	0.030
	Group RD	30	100.37	7.770	
Pulse rate at 15 min	Group R	30	98.67	8.293	0.070
	Group RD	30	95.03	6.861	
Pulse rate at 30 min	Group R	30	94.00	7.027	0.022
	Group RD	30	90.40	4.530	



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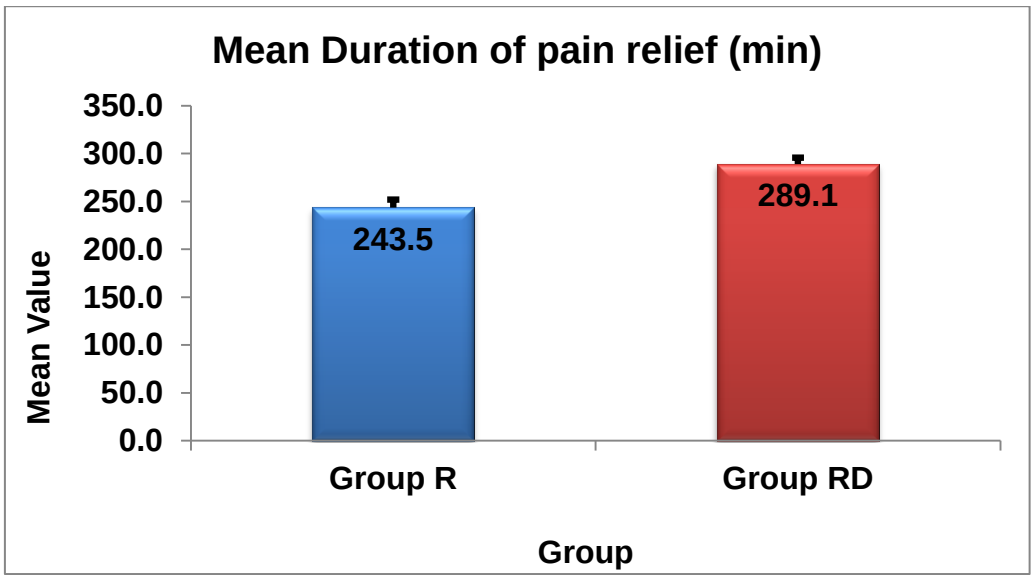
The duration of post-operative analgesia was significantly different between groups, P value (<0.001), and the Dexmeditomidine group had a duration of analgesia which is more than Ropivacaine group. Value in minutes as an average were 289.07minutes for the Dexmeditomidine group when compared to 243.53minutes for the Ropivacaine group.

Independent samples T-Test to compare the mean duration of pain relief (min) between Group R and RD

Variable	Group	N	Mean	Std. Dev	P-Value
Duration of pain relief (min)	Group R	30	243.53	8.452	<0.001
	Group RD	30	289.07	6.762	



DISCUSSION

In this study, the comparative effect of Ropivacaine vsDexmedetomidine added to epidural ropivacaine was evaluated. The results showed duration of post-operative analgesia, hemodynamic changes and motor block duration where there was a significant increase in post-operative analgesia duration. There exists a clear synergism between dexmedetomidine and ropivacaine when administered epidurally than with Ropivacaine alone when administered epidurally.

In our study we used Dexmeditomidine at the dose of 1mcg/kg along with Ropivacaine. The combination proved to be more potent in increasing the post-operative analgesic duration as well as in decreasing the incidence of shivering, nausea and vomiting associated in post-operative patients.Fukushima K, Nishime Y, Mori K, Kaneko I, Fukushima Y.- The pioneering use of dexmedetomidineepidurally in humans occurred in 1997, in which dexmedetomidine at a dose of 2 µg.kg-1 was combined with lidocaine 1.5% in total dose of 225 mg in patients anesthetized with isoflurane and underwent hysterectomy. The authors found that the duration of postoperative analgesia was doubled by dexmedetomidine, compared with only the administration of epidural lidocaine.

And also we found out that comparing both the groups, there wasn't much of a difference in heamodynamic parameters as well as difference in drug onset time. We did not notice bradycardia in any of our patients during the study. Ala-Kokko TI, Pienimaki P, Lampel And Hollmen AI, Pelkonen O, Vahakangas K.et al in their study, "Transfer of clonidine and dexmedetomidine across the isolated perfused humanplacenta",suggested that enhanced analgesic potency of dexmedetomidine compared with clonidine,

when injected epidurally, due not only to its greater selectivity for alpha 2 receptors , but probably also to higher lipid solubility and penetration into the meninges.

As we have established in our study, a similar result has been obtained by Saravana Babu MS, Verma AK, Agarwal A, Tyagi CM, Upadhyay M, Tripathi S. A comparative study postoperative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for post-operative analgesia and also reported in their study a stable cardiorespiratory and heamodynamic parameters with not less than 20% reduction in blood pressure in both groups from the baseline value. None of their patients had sedation or respiratory depression at the given epidural dose of 1µg/kgDexmeditomidine. And the Dexmeditomidine group had prolonged post-operative analgesic duration and effect due to their increased affinity for α_2 receptors. And none of their patients required rescue analgesic during the period of study. [1-34]

SUMMARY

This is a randomized double blinded study conducted in 30 patients of ASA I and II undergoing elective abdominal surgeries. Patients were allocated in two groups.

Group R (Ropivcaine)
Group RD (Ropivacaine + Dexmedetomidine 1 µg)

Parameters observed were time of onset of sensory block, duration of post-operative analgesia, haemodynamic changes and side effects.

- The post-operative analgesia was significantly prolonged in group RD was 289.07 minutes more than the group R 243.53 minutes.
- There was no drastic fall in blood pressure and the fall was within the 20 percentage of basal blood pressure.
- There was no significant fall in pulse rate in both the groups.
- No sedation were observed in both groups, and the patients were comfortable, co-operative, oriented and calm.
- Neither respiratory depression nor decrease in saturation was observed in any of the group.

CONCLUSION

We conclude that Group RD (Dexmeditomidine + Ropivacaine) action was prolonged in epidural post-operative analgesia than Group R(Ropivacaine) alone. The drug Dexmeditomidine acts synergistically with Ropivacaine in epidural analgesia andpost-operatively there were no shivering or vomiting episodes in any patients.

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