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Dexmedetomidine and clonidine as adjuvants in epidural anaesthesia: A comparative evaluation

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Abstract
Introduction: Epidural administration of α-2 adrenergic agonist is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis. Clonidine has been used successfully over the last decade for the said purpose and the introduction of dexmedetomidine has further widened the scope of α-2 agonists in regional anaesthesia.
Objectives: The purpose of this study was to compare the clinical profile and efficacy of two alpha 2 agonists dexmedetomidine and clonidine when administered epidurally as an adjuvant to Bupivacaine in patients undergoing elective infraumbilical and lower limb surgeries.
Methods: A prospective randomized double blind controlled study was planned. 60 patients of ASA I & II physical status aged between 18-60 yrs who underwent elective infraumbilical and lower limb surgical surgery from 1st of January 2019 to 31st of November 2020 and satisfying all the inclusion criteria were enrolled in the study and were randomly allocated into two groups.
Group A (n=30) = patients received 0.5% isobaric bupivacaine 15 ml with dexmedetomidine 1µg/kg.
Group B (n=30) = patients received 0.5% isobaric bupivacaine 15ml with clonidine 2µg/kg.
Results: Addition of dexmedetomidine to bupivacaine as an adjuvant resulted in an earlier onset of sensory analgesia at T10 as compared to the addition of clonidine. Dexmedetomidine not only provided a higher dermatomal spread but also helped in achieving the maximum sensory anaesthetic level in a shorter period compared to clonidine Modified Bromage scale 3 was achieved earlier in patients who were administered dexmedetomidine as an adjuvant. All these initial block characteristics turned out to be statistically significant values on comparison. Dexmedetomidine is a popular sedative agent nowadays and similar findings were observed in our study as well. Mean sedation scores were significantly higher in Dexmedetomidine group compared to Clonidine group. Dexmedetomidine provided a smooth and prolonged post-operative analgesia as compared to clonidine. Time to two segmental dermatomal regression as well as return of motor power to Bromage 1 was significantly prolonged in dexmedetomidine group. As a result patients in clonidine group required rescue analgesia earlier than dexmedetomidine group.
Conclusion: Dexmedetomidine is a better adjuvant than clonidine in epidural anaesthesia because of better sedation, anxiolysis, superior intraoperative and postoperative analgesia and stable cardio-respiratory parameters.

Keywords: bupivacaine, dexmedetomidine, clonidine, sedation, epidural

Introduction
Epidural blockade is becoming one of the most useful and versatile procedures in modern anesthesiology. It is unique in that it can be placed at virtually any level of the spine, allowing more flexibility in its application to clinical practice. It is more versatile than spinal anaesthesia, giving the clinician the opportunity to provide anaesthesia and analgesia, as well as enabling chronic pain management. It can be used to supplement general anaesthesia, decreasing the need for deep levels of general anaesthesia, therefore providing a more haemodynamically stable operative course. It provides better postoperative pain control and more rapid recovery from surgery. For orthopedic surgery, the provision of pain relief enables early post operative mobilization, accelerates rehabilitation and return to normal function [1-3]. Surgical methods and the anaesthetic techniques have evolved and improved drastically over the last two decades. Many techniques and drug regimens, with partial or greater success, have been tried from time to time to calm the patients and to eliminate the anxiety component during regional anaesthesia [4-7].
The fear of surgery, the strange surroundings of the operation theatre, the sight and sound of sophisticated equipment, dynamicity of an 'operation' during regional anaesthesia and the masked faces of so many strange personal makes the patient panic to any extent [8, 9].

The intense sensory and motor block, continuous supine position for a prolonged duration and the inability to move the body during regional anaesthesia brings a feeling of discomfort and phobia in many of the patients [10]. The high cephalic spread of analgesia with local anaesthetics may be significant but still its quality sometimes may not correlate with the level of sensory analgesia [11].

Bupivacaine is a long acting amide local anaesthetic which has been in use for more than 40 years. Its introduction in 1957 is a very important step in the evolution of regional anaesthesia. It is commercially available as a racemic mixture containing equal proportions of the S(-) and R(+) isomers. It is widely used for subarachnoid block, epidural block, caudal block, nerve blocks, infiltration, post operative analgesia and labor analgesia [12].

α-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia. Dexmedetomidine is a highly selective α2Adrenergic agonist with an affinity of eight times greater than clonidine. There is no such study which has compared the dose equivalence of these drugs but the observations of various studies have stated that the dose of clonidine is 1.5–2 times higher than dexmedetomidine when used in epidural route keeping their pharmacologic interactions and other properties we planned a double blind prospective randomized clinically controlled study at our institute with an aim to compare the analgesic and sedative effects of both these drugs when used epidurally as an adjuvant to Bupivacaine in patients undergoing lower abdominal and lower limb surgeries. Very limited literature is available on the use of dexmedetomidine and clonidine as an adjuvant drug with bupivacaine in epidural analgesia. This study appears to be the first comparing these drugs in epidural analgesia.

Aim & Objectives

The purpose of this study was to compare the clinical profile of two alpha 2 agonists dexmedetomidine and clonidine when administered epidurally. The following parameters will be compared and studied.

- To compare the onset of analgesia.
- To compare the ability to provide smooth intraoperative and postoperative analgesia.
- To compare the sensory and motor block levels
- To compare the ability to provide sedation.
- To compare the duration of analgesia provided.
- To compare the side effects.

Materials and Methods

Source of data

Adult patients (18- 60yrs) of physical status ASA I & II who underwent elective lower limb surgical procedures under epidural anaesthesia from 1st of January 2019 to 31st of November 2020.

Methods of collection of data

A prospective randomized double blind controlled study was planned. 60 patients of ASA I & II physical status aged between 18-60 yrs who underwent infraumbilical and lower limb elective surgery and satisfying all the inclusion criteria were enrolled in the study and were randomly allocated into two groups.

Group A (n=30) = patients received 0.5% isobaric bupivacaine 15 ml with dexmedetomidine 1µg/kg.

Group B (n=30) = patients received 0.5% isobaric bupivacaine 15ml with clonidine 2µg/kg.

Inclusion criteria

1. ASA grade I & II status.
2. 18-60 years of age.
3. Patients giving informed written consent.
4. Patients scheduled to undergo elective below umbilical and lower limb surgical procedures under epidural anaesthesia.

Exclusion criteria

1. ASA III or greater.
2. Age more than 60 years and less than 18 years.
3. Pregnant and lactating women.
4. Any contraindication to epidural anaesthesia – uncooperative patients, hypotension, previous spinal surgeries, spine abnormalities, local site infection and coagulation abnormalities.
5. Poorly controlled hypertension, angina, and cardiopulmonary disease.
6. Patients with hematological disease, neurologic, psychiatric disease, severe renal or hepatic derangement.
7. Patients taking Tricyclic antidepressants, any anti psychotic drugs, alpha-2 ādrenergic agonists, opiods, anti-arrythmics, beta blockers, anticoagulants.

Method of study

- A prospective randomized double blind study was planned. The study solutions were prepared by an anaesthesiologist not involved in the patients care. Patient and anaesthesiologist who deliver the epidural anaesthesia were blinded by the study solutions.
- All pre-anaesthetic evaluation of the patients was performed by an anaesthesiologist a day before the surgery. All patients who belonged in the inclusion criteria, after being taken a written informed valid consent were randomly allocated into the following groups.

Group A (n=30) = patients receiving 0.5% isobaric bupivacaine 15 ml plus dexmedetomidine 1µg/kg.

Group B (n=30) =patients receiving 0.5% isobaric bupivacaine 15ml plus clonidine 2µg/kg.

In the operation theatre, a good peripheral intravenous access was secured using 18 gauge cannula.

Baseline non invasive blood pressure, pulse rate, electrocardiograph, pulse oximetry were recorded.

All patients received Ringer's lactate solution 20ml/kg as preloading solution before the block. Intravenous fluids were given as per body kg weight and operative loss requirement.

Patients were put in sitting position and skin over the desired site was infiltrated with 2% lignocaine 2ml.

Epidural spaces of L2-L3/L3-L4 interspaces was located using 18G Tuohy needle, midline approach, using loss of resistance technique and epidural catheter 18gauge was placed in space.

After exclusion of blood in the needle with negative aspiration, 3ml of lignocaine with adrenaline 1:200000 test dose was administered to exclude intrathecal or intravascular placement of the needle.

After 5minutes of administering test dose, patients in group A received 0.5% isobaric bupivacaine 15 ml plus dexmedetomidine 1µg/kg body weight and group B received 0.5% isobaric bupivacaine 15ml plus clonidine 2µg/kg body weight epidurally.

Parameters observed were

Baseline pulse rate, respiratory rate, noninvasive blood pressure was recorded. Cardio respiratory parameters were monitored continuously and recordings were made every 5 minute until 30 min and at 10 min interval, thereafter up to 60 minute and then at 15 minute interval for the next hour and finally at 30 minute in the 3rd hour.

Intraoperatively and postoperatively, incidence of bradycardia (heart rate<50beats per minute) was treated with 0.3mg of injection atropine and hypotension (systolic blood pressure falling more than 20% mm of Hg) was treated with injection Mephenteramine 3-6 mg in bolus.

Time to analgesic block at T10 dermatome i.e. time interval between the end of administration of anaesthetic and the onset of cutaneous analgesia at T10 was evaluated using midline bilateral pin prick every minute till complete loss of cutaneous sensation at T10 at which point surgery was proceeded. Maximum dermatome reached by analgesic block was recorded.

Degree of motor block was assessed when cutaneous sensation was lost at T10 using modified Bromage scale.

a) 0= No block
b) 1=Inability to raise extended leg
c) 2=inability to flex the knee
d) 3=inability to flex ankle and foot

- Sedation scores were recorded just before the initiation of surgery and every 20 minutes. Level of sedation was assessed using a 5 point scale.
- 1= alert and wide awake
- 2= arousable to verbal commands
- 3= arousable to gentle tactile stimulation
- 4= arousable to vigorous shaking
- 5= un arousable
- Duration of analgesia was recorded as time interval from the completion of anaesthesia to the time when the patient complains of pain.
- During surgical procedure adverse effects like anxiety, nausea, vomiting, dry mouth, dizziness, headache, respiratory depression, pruritis and shivering were recorded.
- Post operatively patients were assessed at 30 min, 2 hours,6 hours 24 hours.
- Intensity of post operative pain and quality of relief of pain was assessed using verbal analog scale,
- 0 = no pain
- 10 = maximum pain
- Rescue analgesia will be provided by intramuscular injection of diclofenac 75mg, when patient complains of pain or verbal analog score >4.
- The group allocation of the patient was revealed after the end of the study.

Observations

Table 1: Distribution of patients according to age groups in group A and group B

Age groups	Group A	%	Group B	%	Total	%
20-29yrs	12	40.00	13	43.33	25	41.67
30-39yrs	6	20.00	9	30.00	15	25.00
40-49yrs	9	30.00	5	16.67	14	23.33
50+yrs	3	10.00	3	10.00	6	10.00
Total	30	100.00	30	100.00	60	100.00
Mean age	35.17		33.87		34.52	
SD age	11.15		9.38		10.24	
Chi-square= 3.4073, df=3, p=0.3330						

The mean age in group A is 35.17±11.15 years and in group B is 33.87 ± 9.38 years. Age incidence between the two groups is comparable. (P>0.05)

Table 2: Distribution of male and female patients in group A and group B

Sex	Group A	%	Group B	%	Total	%
Male	18	60.00	17	56.67	35	58.33
Female	12	40.00	13	43.33	25	41.67
Total	30	100.00	30	100.00	60	100.00
Chi-square= 0.0699, df=1, p=0.7934						

Group A has 18 male patients (60%) and 12 female patients (40%), whereas group B has 17 male patients (56.6%) and 13 female patients (43.3%). The sex distribution in the two groups is comparable (P>0.05).

Table 3: Distribution of patients according to asa grades in group A and group B

ASA grade	Group A	%	Group B	%	Total	%
Grade I	26	86.67	27	90.00	53	88.33
Grade II	4	13.33	3	10.00	7	11.67
Total	30	100.00	30	100.00	60	100.00
Chi-square= 0.1623, df=1, p=0.6875						

Both group were comparable in regards to ASA grading, showed no statistical significance.

Table 4: Comparison of group a and group b with respect to total duration of surgery (in min) by t test

Group	Mean	SD	t-value	P-value
Group A	111.83	23.58	-0.1595	0.8739
Group B	112.67	16.23		

The mean duration in group A is 111.8±23.6 min and in group B is 112.7±16.2 min. Statistical analysis using students unpaired t test shows that there is no statistically significant difference between the groups. (t=0.17, P>0.05)

Table 5: Comparison of group a and group b with respect to onset time of sensory block at t 10 (in min) by t test

Group	Mean	SD	t-value	P-value
Group A	8.70	1.12	-7.8045	0.00001*
Group B	11.23	1.38		

*p<0.05

In group A the mean time of onset of sensory block was 8.7±1.12 min and in group B was 11.23±1.38 min. The statistical analysis done by students unpaired t-test shows that the difference is statistically significant. (P<0.05)`

Table 6: Comparison of group A and group B with respect to time to maximum sensory block by t test

Group	Mean	SD	t-value	P-value
Group A	12.87	1.04	-12.5265	0.00001*
Group B	17.13	1.55		

*p<0.05

In group A it was 12.87±1.04 min and in group B it was 17.13±1.55 min. The statistical analysis done by students unpaired t-test shows that the difference is statistically significant. (P<0.05)

Table 7: Comparison of group a and group b with respect to time in min for complete motor block / bromage 3 by t test

Group	Mean	SD	t-value	P-value
Group A	19.30	1.62	-13.5996	0.00001*
Group B	24.87	1.55		

*p<0.05

In group A it was 19±1.62 min and in group B it was 24±1.55 min. The statistical analysis done by students unpaired t-test shows that the difference is statistically significant. (P<0.05).

Table 8: Distribution of patients according to maximum sensory block levels in group A group B

Maximum sensory block level	Group A	%	Group B	%	Total	%
T5	0	0.00	1	3.33	1	1.67
T6	13	43.33	11	36.67	24	40.00
T7	8	26.67	6	20.00	14	23.33
T8	9	30.00	12	40.00	21	35.00
Total	30	100.00	30	100.00	60	100.00
Chi-square=1.8812, df=3, p=0.5974						

In group A, 13 patients (43.33%) had a maximum sensory block upto T6, 8 patients (26.66%) upto T7 and 9 patients (30%) upto T8. None of them in group A had a block level till T5. In group B, 11 patients (36.66%) had a maximum sensory block upto T6, 6 patients (20%) upto T7 and 12 patients (40%) upto T8 and one patient (3.33%) upto T5. Statistical analysis by Chi square test shows that the two groups are comparable. (X^2 =1.8, P>0.05)

Both groups were comparable in Mephenteramine requirement and p value was not statistically significant.

Table 9: Comparison of group A and group B with respect to mephenteramine requirement (in mg) by t test

Group	Mean	SD	t-value	P-value
Group A	0.80	1.75	0.0000	1.0000
Group B	0.80	1.92		

Table 10: Comparison of group A and group B with respect to sedation scores during surgery

Duration	Group A		Group B		t-value	P-value	P-value
	Mean	Std. Dev.	Mean	Std. Dev.			
Basal	1.00	0.00	1.00	0.00	--	--	NS
20 minutes	2.87	0.68	1.30	0.47	10.3937	0.00001*	S
40 minutes	2.27	0.45	1.00	0.00	15.4250	0.00001*	S
60 minutes	1.20	0.41	1.00	0.00	2.6926	0.0093*	S
80 minutes	1.00	0.00	1.00	0.00	--	--	NS
100 minutes	1.00	0.00	1.00	0.00	--	--	NS
120 minutes	1.00	0.00	1.00	0.00	--	--	NS
140 minutes	1.00	0.00	1.00	0.00	--	--	NS
160 minutes	1.00	0.00	1.00	0.00	--	--	NS
180 minutes	1.00	0.00	1.00	0.00	--	--	NS
200 minutes	1.00	0.00	1.00	0.00	--	--	NS

Mean sedation scores were significantly higher in dexmedetomidine group compared to Clonidine group (P<0.0001). Sedation scores were statistically significant at 20 min, 40 min, 60min in group A compared to group B. More patients group A achieved sedation scores of 3 when compared to group B.

Table 11: Comparison of group A and group B with respect to systolic BP (mm of hg) by t test

Time point	Group A		Group B		t-value	P-value	Significance.
	Mean	Std.dev.	Mean	Std.dev.			
Basal	125.20	13.39	125.40	12.74	-0.0593	0.9529	NS
1 minute	125.33	13.47	125.80	12.92	-0.1370	0.8915	NS
3 minutes	124.93	13.99	125.13	12.79	-0.0578	0.9541	NS
5 minutes	124.60	13.35	124.13	12.55	0.1395	0.8895	NS
10 minutes	122.00	12.81	121.87	12.41	0.0410	0.9675	NS
15 minutes	118.07	12.56	118.27	12.27	-0.0624	0.9505	NS
20 minutes	113.67	12.15	114.93	13.05	-0.3890	0.6987	NS
35 minutes	110.87	12.30	114.13	12.81	-1.0074	0.3180	NS
50 minutes	110.33	10.96	113.60	12.61	-1.0711	0.2886	NS
65 minutes	110.60	11.22	113.87	12.10	-1.0843	0.2827	NS
80 minutes	111.33	10.77	114.73	11.69	-1.1716	0.2461	NS
95 minutes	112.53	9.55	115.00	11.82	-0.8888	0.3778	NS
110 minutes	113.40	9.05	115.20	11.96	-0.6572	0.5136	NS
125 minutes	114.13	9.32	116.07	11.60	-0.7117	0.4795	NS
140 minutes	115.40	8.82	116.60	12.30	-0.4343	0.6657	NS
155 minutes	115.73	8.94	117.47	11.77	-0.6424	0.5231	NS
170 minutes	117.67	9.20	118.13	11.70	-0.1717	0.8642	NS
185 minutes	118.60	8.63	119.00	11.44	-0.1528	0.8791	NS
200 minutes	119.20	8.75	119.73	11.61	-0.2009	0.8415	NS
215 minutes	118.93	9.30	119.60	11.83	-0.2426	0.8092	NS
230 minutes	120.53	9.98	122.00	11.23	-0.5348	0.5948	NS
245 minutes	121.73	9.39	122.53	11.57	-0.2941	0.7697	NS
260 minutes	122.93	9.95	122.73	11.68	0.0714	0.9433	NS
275 minutes	123.07	10.28	123.27	11.16	-0.0722	0.9427	NS

Table 12: Comparison of group A and group B with respect to diastolic BP (mm hg) by t test

Time point	Group A		Group B		t-value	P-value	Significance.
	Mean	Std.dev.	Mean	Std.dev.			
Basal	80.73	8.40	79.87	7.10	0.4316	0.6676	NS
1 minute	81.13	8.56	79.93	7.34	0.5827	0.5623	NS
3 minutes	80.40	8.14	79.67	7.26	0.3682	0.7141	NS
5 minutes	79.80	8.54	79.67	7.79	0.0632	0.9498	NS
10 minutes	79.60	7.69	77.93	7.27	0.8627	0.3919	NS
15 minutes	77.33	7.83	76.13	6.58	0.6426	0.5230	NS
20 minutes	75.27	7.73	74.60	6.22	0.3681	0.7141	NS
35 minutes	73.73	7.93	73.33	6.13	0.2186	0.8277	NS
50 minutes	73.20	7.57	73.07	5.55	0.0778	0.9382	NS
65 minutes	74.00	6.95	73.20	5.37	0.4989	0.6197	NS
80 minutes	74.13	6.72	73.47	6.06	0.4035	0.6881	NS
95 minutes	75.67	6.89	74.13	6.56	0.8829	0.3809	NS
110 minutes	75.87	7.61	74.53	7.18	0.6980	0.4880	NS
125 minutes	76.73	7.00	74.60	7.05	1.1764	0.2442	NS
140 minutes	77.73	6.90	74.93	6.49	1.6185	0.1110	NS
155 minutes	78.40	7.53	75.33	6.50	1.6885	0.0967	NS
170 minutes	78.47	7.57	76.07	6.36	1.3299	0.1888	NS
185 minutes	78.33	7.26	76.13	6.41	1.2442	0.2184	NS
200 minutes	78.53	7.46	76.27	6.03	1.2940	0.2008	NS
215 minutes	79.00	7.50	76.87	6.70	1.1622	0.2499	NS
230 minutes	79.33	6.63	77.27	6.18	0.2167	1.2489	NS
245 minutes	80.07	7.15	78.27	6.12	0.2993	1.0473	NS
260 minutes	80.13	7.57	78.40	6.96	0.3597	0.9232	NS
275 minutes	80.07	7.69	78.33	6.43	0.3477	0.9467	NS

The above table and graph compares the mean diastolic blood pressure at different time intervals between the two groups. Statistical analysis using students t-test shows that there is no statistically significant difference between the baseline as well as subsequent readings of DBP between the two groups. (P>0.05)

Table 13: Comparison of group A and group B with respect to pulse rate by t test

Time point	Group A		Group B		t-value	P-value	Significance.
	Mean	Std. dev.	Mean	Std. dev.			
Basal	82.33	8.41	82.20	7.29	0.0656	0.9479	NS
1 minute	81.77	8.37	81.93	7.29	-0.0822	0.9348	NS
3 minutes	80.90	8.14	80.93	7.10	-0.0169	0.9866	NS
5 minutes	79.70	7.85	79.80	6.62	-0.0533	0.9576	NS
10 minutes	77.57	7.56	78.43	6.67	-0.4709	0.6395	NS
15 minutes	76.63	8.31	77.13	6.75	-0.2559	0.7990	NS
20 minutes	75.33	8.24	76.17	7.15	-0.4183	0.6773	NS
35 minutes	73.97	8.53	75.33	6.98	-0.6791	0.4998	NS
50 minutes	73.23	8.61	75.20	6.72	-0.9867	0.3279	NS
65 minutes	73.37	8.07	75.37	6.99	-1.0266	0.3089	NS
80 minutes	73.57	8.23	75.13	7.21	-0.7844	0.4360	NS
95 minutes	74.00	8.18	74.87	7.75	-0.4212	0.6752	NS
110 minutes	73.90	7.96	75.23	8.11	-0.6424	0.5232	NS
125 minutes	75.20	8.05	75.27	8.12	-0.0319	0.9746	NS
140 minutes	75.33	8.66	75.37	7.80	-0.0157	0.9876	NS
155 minutes	76.20	8.62	75.57	7.50	0.3036	0.7625	NS
170 minutes	75.90	8.73	75.33	7.25	0.2735	0.7855	NS
185 minutes	76.60	9.02	75.57	6.97	0.4965	0.6214	NS
200 minutes	76.43	9.29	75.90	6.89	0.2526	0.8015	NS
215 minutes	76.57	9.06	76.10	6.92	0.2243	0.8233	NS
230 minutes	76.50	8.75	74.00	14.69	0.8009	0.4265	NS
245 minutes	76.10	9.11	75.90	7.64	0.0922	0.9269	NS
260 minutes	76.37	8.91	76.23	7.46	0.0628	0.9501	NS
275 minutes	76.07	8.64	76.37	7.52	-0.1434	0.8865	NS
300 minutes	75.67	8.18	75.93	7.04	-0.1354	0.8928	NS

The above table and chart compares the mean pulse rate at different time intervals between the two groups. Statistical analysis using students t-test shows that there is no statistically significant difference between the baseline as well as subsequent readings of mean pulse rate between the two groups. (P>0.05).

Table 14: Comparison of group A and group B with respect to respiratory rate (min) by t test

Time point	Group A		Group B		t-value	P-value	Significance.
	Mean	Std. dev.	Mean	Std. dev.			
Basal	14.23	1.50	14.00	0.87	0.7363	0.4645	NS
1 minute	14.27	1.64	14.00	0.87	0.7871	0.4344	NS
3 minutes	14.17	1.44	13.97	0.93	0.6394	0.5251	NS
5 minutes	14.23	1.22	14.03	0.89	0.7243	0.4718	NS
10 minutes	14.20	1.13	14.17	0.87	0.1280	0.8986	NS
15 minutes	14.23	1.43	14.20	0.89	0.1085	0.9140	NS
20 minutes	14.33	1.21	14.23	0.86	0.3686	0.7138	NS
35 minutes	14.20	1.19	14.23	0.90	-0.1227	0.9027	NS
50 minutes	14.30	1.26	14.17	0.95	0.4620	0.6458	NS
65 minutes	14.50	1.25	14.10	0.84	1.4501	0.1524	NS
80 minutes	14.33	1.49	14.10	0.96	0.7200	0.4744	NS
95 minutes	14.23	1.10	14.23	0.82	0.0000	1.0000	NS
110 minutes	14.23	0.97	14.20	0.85	0.1417	0.8878	NS
125 minutes	14.27	1.23	14.20	0.89	0.2408	0.8105	NS
140 minutes	14.13	1.17	14.20	0.89	-0.2492	0.8041	NS
155 minutes	14.40	1.22	14.17	0.91	0.8385	0.4052	NS
170 minutes	14.57	1.19	14.17	0.79	1.5291	0.1317	NS
185 minutes	14.43	1.17	14.07	0.94	1.3390	0.1858	NS
200 minutes	14.47	1.41	14.20	0.81	0.9007	0.3715	NS
215 minutes	14.37	1.30	14.27	0.83	0.3555	0.7235	NS
230 minutes	14.20	1.16	14.17	0.91	0.1239	0.9018	NS
245 minutes	14.37	1.10	14.30	0.92	0.2554	0.7993	NS
260 minutes	14.17	1.18	14.07	0.94	0.3630	0.7179	NS
275 minutes	14.30	1.15	14.17	0.83	0.5143	0.6090	NS

The above table and chart compares the mean respiratory rate at different time intervals between the two groups. Statistical analysis using student t-test shows that there is no statistically significant difference between the baseline as well as subsequent readings of mean respiratory rate between the two groups. (P>0.05)

Table 15: Comparison of group A and group B with respect to time to two segment regression (in min) by t test

Variable	Group	Mean	SD	t-value	P-value
Mean time to two segment regression	Group A	136.00	6.86	6.3279	0.00001*
	Group B	124.97	6.65		

In group A the time for two segment regression is 136±6.86 min and in group B it is 124±6.65 min. Statistical analysis by students unpaired t-test shows that the difference is statistically significant. (P<0.05).

The time taken for regression of the sensory block to S1 in group A is 314.17±18.87 min and in group B is 298.73±20.26 min. Statistical analysis by students unpaired t- test shows that the difference is statistically significant. (P<0.05).

Table 16: Comparison of group A and group B with respect to time to regression to s1 in min by t test

Variable	Group	Mean	SD	t-value	P-value
Mean time to sensory regression to s1	Group A	314.17	18.87	3.0195	0.0038*
	Group B	298.73	20.68		

*p<0.05

Table 17: Comparison of group A and group B with respect to time to regression to bromage 1 (in min) by t test

Variable	Group	Mean	SD	t-value	P-value
Mean time to regression to bromage 1	Group A	240.93	16.54	13.7541	0.00001*
	Group B	160.17	27.58		

*p<0.05

In group A it is 240±16.54 min and in group B 160±27.58 min. Statistical analysis by students unpaired t-test shows that this difference is significant (P<0.001)

Table 18: Distribution of patients according to side effects in group A and group B

Side effects	Group A	%	Group B	%	Total	%
Dizziness	2	6.67	2	6.67	4	6.67
Headache	1	3.33	1	3.33	2	3.33
Nausea	4	13.33	3	10.00	7	11.67
Shivering	2	6.67	1	3.33	3	5.00
Vomiting	1	3.33	1	3.33	2	3.33
Dry mouth	6	20.00	7	23.33	13	21.67
Respiratory Depression	o	-	0	-	-	-

Comparative incidence of various side effects in both the groups which were observed in the intra-op and post-op period. The incidence of dry mouth was significantly higher in both the groups but it was statistically non-significant on comparison (P>0.05). The incidence of other side effects like nausea, vomiting, headache, shivering and dizziness were comparable in both the groups and statistically non-significant. We did not observe the respiratory depression in any patient from either group.

Discussion

Epidural anaesthesia and analgesia is considered by many as the gold standard technique for major surgery. It has the potential to provide complete analgesia for as long as the epidural is continued. Epidural techniques are particularly effective at providing dynamic analgesia, allowing the patient to mobilize and resume normal activities unlimited by pain. It also improves the postoperative outcome and attenuates the physiologic response to surgery, in particular, significant reduction in pulmonary infections, pulmonary embolism, ileus, acute renal failure and blood loss.

A prospective randomized double blind controlled study was planned with 60 patients of ASA I & II physical status aged between 18-60 yrs scheduled to undergo infraumbilical and lower limb elective surgery and satisfying all the inclusion criteria were be enrolled in the study. Patients were randomly divided into 30 groups each. Group A (n=30) patients received 0.5% isobaric bupivacaine 15 ml with dexmedetomidine 1µg/kg. Group B (n=30) patients received 0.5% isobaric bupivacaine 15ml with clonidine 2µg/kg.

Demographic profile

The demographic profile of the current study was comparable to similar other studies and did not show any statistical significance on comparison.

Age

All the patients were belonging to the age group of 18-60 years.12 patients in group A and 13 in group B were between 21-30 yrs, 6 in group A and 9 in group B were between 31-40 yrs, 9 in group A and 5 in group B were between 41-50 yrs and 3 in group A and 3 in group B were between 51-60 yrs. The mean age in group A was 35.16 ± 11.15 yrs and in group B was 33.83 ± 9.43 yrs. Age incidences between the groups were comparable.

Sex

Group A had 18 male patients (60%) and 12 female patients (40%), whereas group B has 17 male patients (56.6%) and 13 female patients (43.3%). The sex distribution between the two groups was comparable (P>0.05).

Height weight and BMI

Weight and Height of each patient was noted**.** The mean weight in group A was 56.73±7.52 kg and in group B was 58.93±8.22 kg. Mean weight between the two groups was comparable. (t=1.08, P>0.05). The mean height in group A

was 164.3±3.58 cm and group B was 165.3±3.40 cm. Mean height between the two groups is comparable. (t=1.10, *P*>0.05)**.** The mean BMI in group A was 21.02±2.77 and group B was 20.83±4.31. Mean BMI between the two groups was comparable.

Duration of surgery

The mean duration of surgery in group A was 111.8±23.6 min and in group B was 112.7±16.2 min.

ASA grading

In group A 26 patients belonged to ASA I and 4 patients belonged to ASA II. In group B 27 patients belonged to ASA I and 3 patients belonged to ASA II. Both group were comparable in regards to ASA grading, showed no statistical significance.

In the operation theatre, baseline blood pressure and pulse was recorded. 18 g IV canula was inserted and patients received 20ml/kg of ringers lactate solution. Patients were placed in sitting position and skin infiltration was done with 2ml of 2% lignocaine. Epidural space was located at L2-L3 interspace with a 18 g Touhy needle using the midline approach and loss of resistance technique. After negative aspiration for blood, 3 ml of lignocaine with 1:200000 adrenaline test dose was administered. Then after a 5 min period, the study drug was injected over 2 min. Patients in group A received 0.5% isobaric bupivacaine 15 ml plus dexmedetomidine 1µg/kg body weight and group B received 0.5% isobaric bupivacaine 15ml plus clonidine 2µg/kg body weight epidurally. The results of our study has shown that the addition of either 1µg/kg dexmedetomidine or 2 µg/kg clonidine as adjuvant to epidural bupivacaine not only prolongs the duration of analgesia but also provides a good sedation level during the surgical procedure. Dexmedetomidine has a visible edge over clonidine as it enables an earlier onset and establishment of sensory and motor block. Further, addition of these two adjuvants promotes faster onset compared to established time of onset of sensory analgesia with bupivacaine alone.

Initial block characteristics

Dexmedetomidine provided a smooth intra-operative analgesia as compared to clonidine which is evident from the following parameters observed.

The onset of sensory block

In our study, the onset of sensory block among group A patients was in the range of 8.7±1.12 min and in group B was 11.23±1.38 min. The statistical analysis done by students unpaired t-test shows that the difference is statistically significant (*P*<0.05).

Our findings correlate with a study conducted by Bajwa S.J et al. where they found that addition of dexmedetomidine to ropivacaine as an adjuvant resulted in an earlier onset (8.52 ± 2.36 min) of sensory analgesia at T10 as compared to the addition of clonidine (9.72 ± 3.44 min).

Similarly Babu M.S, Verma A.K, Agarwal A, Tyagi M.S.C, Upadhyay M, Tripathi S [13] found that addition of dexmedetomidine to ropivacaine as an adjuvant resulted in an earlier onset (7.33±1.76 min) of analgesia as compared to the addition of clonidine (8.40±1.61 min).

Jain A, Gupta V, Sehgal C, Kumar R [14] found that clonidine 2µ /kg when added to bupivacaine shortened the onset of analgesia significantly (11.13 ± 2.08 min) which is similar to our study.

Bajwa SJ, Arora V, Kaur J, Singh A,Parmar SS [15] administered 0.75% ropivacaine, 15 ml epidurally with addition of 1 µg/kg of dexmedetomidine in RD group and 1 µg/kg of fentanyl in RF group.Onset of sensory analgesia at T10 was (7.12±2.44 min)in RD group and (9.14±2.94min) RF group. The difference was statistically significant.

Paula F. et al. [16] found that Dexmedetomidine did not affect the latency of anaesthesia when administered with ropivacaine (11.5min) compared to ropivcaine alone (13.8 min). Gupta S, Raval D, Patel M, Patel N, Shah N [17] found that the onset of sensory anaesthesia was faster (493.8±31.66s) when clonidine was added to epidural bupivacaine compared to bupivacaine alone (686.4±47.42s).

Time to achieve maximum height of sensory block

In our study, time to achieve maximum height of sensory block was12.87±1.04 min in group A and 13±1.55 min in group B. The statistical analysis done by students unpaired t-test shows that the difference was statistically significant. (*P*<0.05)

Babu MS, Verma AK, Agarwal A, Tyagi MSC, Upadhyay M, Tripathi S [13] found that dexmedetomidine helped in achieving the peak analgesic level (VAS – 0) in a shorter period (11.66±2.05 min) compared with clonidine (13.20±2.90 min).

Our study also correlates with a study done by Bajwa S J *et al*. where they found that dexmedetomidine achieved the maximum sensory anaesthetic level in a shorter period (13.14 ± 3.96 min) compared to clonidine (15.80 ± 4.86 min). Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS [15] conducted a study using ropivacaine,

15 ml of 0.75%, epidurally in both the groups with addition of 1 µg/kg of dexmedetomidine in RD group and 1 µg/kg of fentanyl in RF group. Time to achieve

maximum sensory block was (13.38 ±4.48min) in RD group and (16.61± 4.36min) in RF group, these results are similar to our study.

Unlike our study Paula F. et al. [16] found no significant difference in time taken to attain maximum sensory block of T 6 when dexmedtomidine was administered with ropivacaine and ropivacaine alone.

Maximum sensory block achieved

In our study, among group A, 13 patients (43.33%) had a maximum sensory block upto T6, 8 patients (26.66%) upto T7 and 9 patients (30%) upto T8. None of them in group A had a block level till T5. In group B, 11 patients (36.66%) had a maximum sensory block upto T6, 6 patients (20%) upto T7 and 12 patients (40%) upto T8 and one patient (3.33%) upto T5. Statistical analysis by Chi square test showed that the two groups are comparable. (X^2 =1.8, *P*>0.05)

Paula F. et al. [16] found that epidural dexmedetomidine did not achieve a upper level of anaesthesia (*P*>0.05) when compared to ropivacaine alone.

Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS [15] administered Inj. Ropivacaine, 15 ml of 0.75%, epidurally in both the groups with addition of 1µg/kg of dexmedetomidine in RD group and 1µg/kg of fentanyl in RF group. They found statistical significance in level of anaesthesia provided, RD group achieving higher dermatomal spread.

Time to achieve bromage 3 (Table 11)

Degree of motor block was assessed when cutaneous sensations were lost at T10 using modified Bromage scale and every min thereafter.Bromage 3 motor block was achieved in all patients before the initiation of surgery.

Comparison of group A and group B with respect to time in min to achieve bromage 3 by t test in group A was19±1.62 min and in group B was 24±1.55 min. The statistical analysis done by students unpaired t-test shows that the difference is statistically significant (P<0.05).

Similar to our study Bajwa S J *et al*. found that Modified Bromage scale 3 was achieved earlier (17.24 ± 5.16 min) in patients who were administered dexmedetomidine as an adjuvant to ropivacaine compared to clonidine (19.52± 4.06 min).

Paula F. *et al*. found that the intensity of motor block was more pronounced in the dexmedetomidine group compared with the control group (p<0.05) of ropivacaine and time taken for bromage 3 was significantly shorter.

Similar to our study Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS used 0.75% 15 ml ropivacaine epidurally with addition of 1 µg/kg of dexmedetomidine in RD group and 1 µg/kg of fentanyl in RF group. They found that the establishment of complete motor blockade (18.16±4.52 vs 22.98±4.78) was significantly earlier in the RD group.

Bajwa SJ, Bajwa SK, Kaur [15] used ropivacaine 0.75% versus ropivacaine 0.75% with clonidine for caesarean sections. The establishment of complete motor blockade was much earlier in the RC group which was statistically significant (P<0.05)

Gupta S, Raval D, Patel M, Patel N, Shah N [17] found significant difference in the mean time for onset of motor anaesthesia (615.6±31.99s) in clonidine group and (808.0±54.39s) in bupivacaine group.

Sedation scores achieved (Table 14).

The results of our study clearly indicate the effectiveness of epidural dexmedetomidine as it produced profound sedation in majority of the patients, which is very essential in decreasing the peri-operative stress in regional anaesthesia. Throughout the surgery patients were calm and composed in both the groups but the sedation scores were highly significant statistically with administration of dexmedetomidine than clonidine.

Comparison of group A and group B with respect to sedation scores by t test revealed that Sedation scores were statistically significant at 20 min group A (2.87±0.68) group B (1.30± 0.47),40 min group A (2.27± 0.45) group B (1.00±0.00),60min group A (1.20±0.41) group B (1.00±0) in group A compared to group B.

In a study done by Bajwa S J *et al*., [15] mean sedation scores were significantly higher in dexmedetomidine group compared to clonidine group. 36% patients in group RD had a sedation score of 3 as compared 16% in group RC (P<0.0001). Only 16% of the patients in the dexmedetomidine group had sedation scores of 1 compared to 32% wide and awake patients in clonidine group, which was a highly significant statistical entity (P<0.0001).

Paula F *et al*. [16] found significant difference in the level of consciousness between groups (p<0.05), with patients who received dexmedetomidine than patients in the control group. There was significant difference between the groups, with 70% of patients in the control group and only 26% of patients in the dexmedetomidine group requiring supplemental sedation (p<0.05).

Post op block characteristics

Dexmedetomidine provided a smooth and prolonged post-operative analgesia as compared to clonidine which is evident from the following parameters observed. The Dexmedetomidine group showed visible superiority over Clonidine group in various post-operative block characteristics like the weaning of sensory and motor block, prolonged post-operative analgesia.

Time for two segment regression

In our study, the time for two segment regression in group A was 136±6.86 min and in group B was 124±6.65 min. Statistical analysis by students unpaired t-test showed that the difference is statistically significant (P<0.05)

In a study done by Bajwa S J et.al [15] there was significant prolongation of time to two segmental dermatomal regression (136.46 ± 8.12 min) in dexmedetomidine group when compared to clonidine group (128.08±7.54 min) when added to epidural ropivcaine.

Time taken for regression of the sensory block to S1

In our study the time taken for regression of the sensory block to S1 in group A was 314.17±18.87 min and in group B was 298.73±20.26 min. Statistical analysis by students unpaired t-test showed that the difference is statistically significant (P<0.05).

In a study done by Bajwa S J et.al [15] there was significant difference in time taken to segmental regression to S1 in the dexmedetomidine group (316.64 ± 40.36 min) when compared to clonidine group (296.72 ± 36.52) min p<0.05.

Time for mean regression to bromage 1

In our study time taken for mean regression to bromage 1 (in min) among group A was 240±16.54 min and in group B was 160±27.58 min. Statistical analysis by students unpaired t-test shows that this difference is significant (P<0.001)

In a study done by Bajwa S J *et al*. [15] there was significant prolongation of time taken to return of motor power to Bromage 1 in dexmedetomidine group (246.72 ± 30.46 min) when compared to clonidine group (228.44± 27.18) when used with ropivacaine. In a study done by Paula F *et al*. [16] the duration of motor block was significantly higher in the dexmedetomidine group (P>0.05), being on average 30% higher than that observed in the control bupivacaine group.

Paula F *et al*. found no difference in the scores of pain, assessed in the PACU in control group and dexmedetomidine group (P>0.05).

Time to rescue analgesia and duration of analgesia

In group A time taken to rescue analgesia was 342.97±18.03 min and in group B was 307.97±22.54 min. Statistical analysis by students unpaired t-test shows that this difference is significant (P<0.001)

In a study done by Bajwa S J *et al*. [15] the time for rescue analgesia was comparatively shorter (310.76 ± 23.75 min) in the patients who were administered clonidine (P<0.05) when compared to dexmedetomidine. (342.88±21.86 min).

In a study conducted by Gupta S, Raval D, Patel M, Patel N, Shah N [17] the duration of postoperative analgesia was very

much prolonged in Clonidine group (334.2 min) as compared to control bupivacaine group (161.4 min) p<0.05.
In a study conducted by Paula F *et al*. [16] the duration of postoperative analgesia was significantly different between groups (p<0.05), and dexmedetomidine group showed analgesia 33% higher than the control group.
In a study done by Bajwa S J, Arora V, Kaur J, Singh A, Parmar S [15] first rescue top requirement was (366.62 ±24.42 min) in dexmedetomidine group and (242.16± 23.86min)in clonidine group (P>0, 05).

Cardio respiratory parameters
The cardio-respiratory parameters, remained stable throughout the study period which reaffirms the established effects of α-2 agonists in providing a haemodynamically stable peri-operative and post-operative period.
The requirement of vasopressors for the maintenance of stable haemodynamic parameters did not reveal significant differences between the both groups on statistical comparison (table 13). In our study we monitored Pulse rate, blood pressure (systolic & diastolic) and respiratory rate of all the patients at base line, 1,3,5,10,15,20,35,50 min and thereafter every 15 min. In our study the mean baseline SBP was 125.20±13.39 mm Hg in group A and 125.40±12.74 in group B. The mean baseline DBP was 80.73±8.4in group A and 79.87±7.1 in group B.
We observed that there was a fall in the systolic and diastolic blood pressure below the baseline after epidural administration at various intervals in both the groups. But this difference was not statistically significant (P>0.05). six patients in group A and five patient in group B had clinically significant hypotension (SBP <30% baseline) which was corrected with IV mephentermine bolus. Mephenteramine dose consumption was comparable in both groups. The baseline mean pulse rate was 82.33±8.41 in group A and 82.2±7.29 in group B. Pulse rate was assessed at various intervals after the administration of epidural anaesthesia. We observed that there was a fall in the pulse rate after administration of epidural doses at various intervals in both the groups. But this difference was not statistically significant (P>0.05) and the change in mean pulse rate between the groups was not statistically significant (P>0.05).
it started to decrease as evident at 30 min post-injection, there was a fall in both groups. There was a decreasing trend of heart rate and mean arterial pressure post-injection in both groups and this decrease was significant in the RC group compared with RD group (P<0.05) but none of the patient showed bradycardia or hypotension at any time.
In a study conducted by Paula F *et al*. [16] the occurrence of hypotension and bradycardia in the intra-and postoperative time was similar between dexmedetomidine group and bupivacaine group, with no significant difference (P>0,05).
The baseline mean respiratory rate was 14.23±1.50/min in group A and 14±0.87/min in group B. There was no difference in the respiratory rate between the groups when measured at various intervals after administration of epidural anaesthesia. (P>0.05).
In a study conducted by Babu M S, Verma A K, Agarwal A, Tyagi MSC, Upadhyay M, Tripathi S [13] there was a decrease in mean respiratory rate in dexmedetomidine and clonidine groups after giving the drug and the difference between the groups was statistically not significant (P>0.05) at different time intervals. None of the patient showed respiratory depression (<10/min) at any time.

Side effect profile
The incidence of nausea (4 patients in group A and 3 patients in group B) and dry mouth (6 patients in group A and 7 patients in group B) was significantly higher in both the groups but it was statistically non-significant on comparison (P>0.05). The incidence of other side effects like vomiting, headache, shivering and dizziness were comparable in both the groups and statistically non-significant. We did not observe the respiratory depression in any patient from either group.
Similar to our study Bajwa S J *et al*. [15] found the incidence side effects to be statistically non-significant on comparison between dexmedetomidine group and clonidine group (P>0.05). El-Hennawy A M, Abd-Elwahab A M, Abd-Elmaksoud A M, A, El-Ozairy H S, Boulis S R [18] found no significant differences in incidence of side-effects between clonidine and dexmedetomidine group.

Conclusion
Our results allow us to conclude that addition of dexmedetomidine or clonidine to epidural bupivacaine significantly promoted analgesia in patients undergoing lower limb surgeries without increasing the incidence of side-effects.
Dexmedetomidine is a better neuraxial adjuvant to bupivacaine when compared to clonidine for early onset of analgesia, superior intraoperative analgesia, stable cardio respiratory parameters, prolonged post operative analgesia and providing patient comfort.
Overall the experience with dexmedetomidine was quite satisfactory as compared to clonidine because of its superior sedative and anxiolytic properties during the surgical procedure under epidural anaesthesia.

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Conflict of Interest
None

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References
1. Bailey, *et al*. Respiratory effects of clonidine alone and combined with morphine, in humans. Anaesthesiology. 1991;74:43-48.
2. Ooi, *et al*. The effects of IV clonidine on ventilation. Anaesthesia. 1991;46:632-33.
3. Admir Hadzic. Regional Anaesthesia and acute pain management. 1st Edn. McGraw- Hill Professional, 2006.
4. Höhener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. Br J Anaesth. 2008;100:8-16.
5. Helgeson LE. Sedation during regional anaesthesia: Inhalational versus intravenous. Curr Opin Anaesthesiol. 2005;18:534-9.
6. Nemethy M, Paroli L, Williams-Russo PC, Blanck TJ. Assessing sedation with regional anaesthesia: Inter-

rater agreement on a modified Wilson Sedation Scale. Anesth Analg. 2002;94:723-8.
7. Asehnoune K, Albaladejo P, Smail N, Heriche C, Sitbon P, Gueneron JP, *et al*. Information and anaesthesia: What does the patient desire? Ann Fr Anesth Reanim. 2000;19:577-81.
8. Badner NH, Nielson WR, Munk S, Kwiatkowska C, Gelb AW. Preoperative anxiety: Detection and contributing factors. Can J Anaesth. 1990;37:444-7.
9. Schnider TW, Minto CF. Predictors of onset and offset of drug effect. Eur J Anaesthesiol. 2001;23:26-31.
10. McNamee DA, Parks L, McClelland AM, Scott S, Milligan KR, Ahlén K, *et al*. Intrathecal ropivacaine for total hip arthroplasty: Double-blind comparative study with isobaric 7.5mg.ml -1 and 10mg.ml-1 solutions. Br J Anaesth. 2001;87:743-7.
11. Kamibayashi T, Maze M. Clinical uses of alpha-2 adrenergic agonists. Anaesthesiology. 2000;93:1345-9.
12. De Beer DAH, Thomas ML. Caudal additives in children – solutions or problems? Br J Anaesth. 2003;90(4):487-98.
13. Babu MS, Verma AK, Agarwal A, Tyagi MSC, Upadhyay M, Tripathi S. A comparative study in the post-operative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for post-operative analgesia. Indian J Anaesth. 2013;57:371-376.
14. Jain A, Gupta V, Sehgal C, Kumar R. Bupivacaine-clonidine mixture for epidural anaesthesia. Journal of evolution of medical and dental sciences. 2013 Jan;2(7):39-42.
15. Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Saudi J Anaesth. 2011 Oct-Dec;5(4):365-370.
16. Paula F, *et al*. Synergistic effect between dexmedetomidine and ropivacaine 0.75% in epidural anaesthesia. Rev Assoc Med Bras. 2008;54(2):110-115.
17. Gupta S, Raval D, Patel M, Patel N, Shah N. Addition of epidural Clonidine enhances postoperative analgesia: A double-blind study in total knee- replacement surgeries. Anesth Essays Res. 2010;4:70-4.
18. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth. 2009 Aug;103(2):268-74.