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RESEARCH ARTICLE

COMPARISON BETWEEN DEXMEDETOMIDINE AND NALBUPHINE AS AN ADJUVANT TO BUPIVACAINE IN SPINAL ANAESTHESIA

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Abstract

Introduction:-

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Acute postoperative pain management is not only a human feeling, but it is a key aspect of postoperative care, as acute pain, regardless of its site, can adversely affect nearly every organ function, and so affects the postoperative morbidity and mortality[1].The sole essence of anaesthesia is pain relief in peri- operative period. Regional anaesthesia has emerged as an important technique, with simplicity, effectiveness and safety as its added advantages. Neuraxial block for abdominal and lower abdominal surgeries are becoming popular as it has many advantages over general anaesthesia. Spinal anaesthesia consists of temporary interruption of nerve transmission in the subarachnoid space produced by the injection of a local anaesthetic solution in the subarachnoid space. Spinal anaesthesia has many advantages like easy to perform, rapid onset of action and good muscle relaxation and early recovery. One of the main disadvantages is its limited duration of action and hence lack of postoperative analgesia. Spinal anaesthesia with hyperbaric bupivacaine is commonly used in abdominal and lower abdominal surgeries[2] .

Spinal anesthesia with hyperbaric bupivacaine 0.5% is a popular method. Addition of opioids to local anesthetics is very commonly practiced. Though the opioids reduce the toxicity and cardiovascular effects of local anesthetics this type of combinations may bring about additional undesirable problems like itching, nausea and vomiting and / or respiratory depression.Various other drugs in small quantities are now being used as an adjuvant to hyperbaric bupivacaine to produce analgesia that is faster, more intense and prolonged sensory & motor blockade.

Nalbuphine, a drug with mixed μ antagonist and κ agonist properties, is related chemically to oxymorphone and naloxone. It is equal in potency as analgesic to morphine, and one-fourth as potent as nalorphine as an antagonist. Nalbuphine has the potential to maintain or even enhance μ-opioid based analgesia while simultaneously mitigating the μ-opioid side effect [3]. Nalbuphine and other κ agonists have provided potent analgesia in certain models of visceral nociception [4] . They demonstrate complicated interactions with μ opiates that suggest dose-dependent synergies and significant antagonisms at larger doses [5], but they have a short duration of action, consistent with their lipid solubility and rapid clearance. Initially, the advantage of such drugs given systemically was considered to be a reduced likelihood of respiratory depression. Later, their utility as adjuvant therapy was considered in terms of their ability to produce an antagonism of the side effects attendant to spinal opiates, e.g. respiratory depression,

pruritus and urinary retention—events that were considered to be reflective of the actions of spinal μ-opioids [6-8]. More recently, the exciting possibility has been offered that κ agonists may show an unexpected activity in female patients, suggesting a clinically relevant sex difference toward efficacy [9].

Nalbuphine is a potent analgesic. Its analgesic potency is essentially equivalent to that of morphine on a milligram basis based on relative potency studies using intramuscular administration [10] . The plasma half-life of nalbuphine is 5 hours and in clinical studies the duration of analgesic activity has been reported to range from 3 to 6 hours. Studies have shown that the addition of intrathecal nalbuphine 0.4 mg to hyperbaric tetracaine for spinal anaesthesia improved the quality of intra operative and postoperative analgesia[11], with minimal pruritis and respiratory depression[12].

Alpha-2(α_2) adrenergic receptor (AR) agonists have been the focus of interest due to sedative, analgesic, perioperative sympatholytic and hemodynamic stabilizing properties.Alpha2-receptors are found in many sites throughout the body. Alpha2 - adrenoceptors are found in peripheral and central nervous systems, in effector organs such as the liver, kidney, pancreas, and eye vascular smooth muscles and platelets [13]. Physiologic responses mediated by alpha2-adrenoceptors vary with location and can account for the diversity of their effects.

Dexmedetomidine - Dexmedetomidine is a new alpha2-agonist that received FDA approval in 1999 for use as a short-term (less than 24 h) sedative, analgesic in the intensive care unit. [14] It causes sedation without causing respiratory depression. It has sedative, analgesic, sympatholytic and anxiolytic effect that blunt many CVS responses in perioperative period. [15] It is an S- enantiomer of medetomidine used in veterinary medicine. The elimination half life is 2 hours and therefore discontinuing the infusion rapidly leads to a state of consciousness. Drug cannot be given as bolus due to concerns about peripheral alpha – 2 receptor stimulation with resulting hypertension and bradycardia. [16,17] It is also used in treatment of deleterious CVS effect for acute cocaine intoxication and overdose. [18] It is used in treatment of symptoms of distress (intractable pain, agitation and delirium). It is thought that intrathecal dexmedetomidine produces its analgesic effect by inhibiting the release of C fibers transmitters and by hyperpolarization of post-synaptic dorsal horn neurons [19]. The prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneurons [20]. Alpha 2 agonists produce sedative effect by acting on alpha 2-adrenergic receptors in locus ceruleus **.** Alpha 2 adrenoreceptors do not have an active role in the respiratory center , therefore, dexmedetomidine throughout a broad range of plasma concentration , has minimal effects on the respiratory system[21].

Dexmedetomidine has been used in the epidural space in humans without any reports of neurological deficits[22] . Small doses of dexmedetomidine (3μg) used in combination with bupivacaine, in humans, for spinal anesthesia, has been shown to produce a shorter onset of motor block and a prolongation in the duration of motor and sensory block with preserved hemodynamic stability and lack of sedation[23]. Dexmedetomidine has a dose dependent effect on the onset and regression of sensory and motor block when used as an adjuvant to bupivacaine in spinal anaesthesia. Intrathecal α2-adrenargic agonist produce analgesia by depressing the release of c-fibre transmitters and by hyper polarization of dorsal horn neurons. This antinociceptive effect explain the prolongation of sensory block when added to spinal anesthesia.

This study is designed to compare dexmedetomidine and nalbuphine as an adjuvant to bupivacaine in spinal anaesthesia .

Materials and methodology:-

After receiving approval from the ethical committee on 01/02/2014, this study was conducted in the Department of Anaesthesiology, S.B.K.S. Medical Institute and Research Centre, Dhiraj General Hospital, Piparia, Vadodara.

60 patients of ASA grade 1 & 2 classification, between the age of 20 and 55 years posted for lower abdominal and lower limb surgeries were selected for this study. The study was prospective , interventional and randomized controlled in nature, The patients were allocated randomly into two equal groups according to type of adjuvant added to local anesthetic. All the patients participating in the study was explained clearly about the purpose and nature of the study in the language they could understand. They were included in the study only after obtaining a written informed consent. We collected the data for 1 1/2year and analyzed the data statistically after clearance from the ethical committee.

Allocation of patients:-
Group D - Patients in this group were given Inj. Bupivacaine (15mg) + Inj. Dexmedetomidine (10µg) intrathecally.

Group N - Patients in this group were given Inj. Bupivacaine (15mg) + Inj. Nalbuphine (0.4mg) intrathecally.

Inclusion criteria:-
- ASA I & ASA II patients.
- Patients in the age range 25-55 years.
- No known history of allergy, sensitivity or other form of reaction to local anesthetics.
- Patient willing to sign informed consent

Exclusion criteria:-
- Patients with medical complications like anaemia, heart disease, severe hypovolemia, shock, septicaemia, hypertension.
- Patients with coagulation disorders or on anticoagulant therapy.
- Local infection at the site of proposed puncture for spinal anaesthesia, spinal deformities
- Known allergy to the trial drug
- Patient refusal.

Methods:-
General and Systemic examination:-
The patients were visited preoperatively and history was taken for:
- Hypertension, Ischaemic heart disease or any other cardiac problem.
- Diabetes Mellitus or any endocardial disorders.
- Asthama,COPD,smoking and alcohol.
- Bleeding tendency,antiplatelet drugs or anticoagulants.
- Hepatic or renal impairment.
- Convulsions or any neurogical disease.
- History of drug intake, history of allergy and sensitivity to any drug and previous anaesthetic experiences.
- Clinical examination of the cardiovascular system.
- Vital data including temperature, pulse, blood pressure
- Back Examination(spines)
- Investigations:
    - Complete blood count
    - Coagulation profile.
    - Liver and kidney function tests.
    - ECG, random blood sugar.
    - Chest x ray PA view
- All patients were kept nil by mouth for 8 hrs.

Preparation of equipments & drugs:-
- Premedication: Inj. Ondansetron 4mg i.v. Inj. Glycopyrrolate 0.2mg I.V
- Spinal needle (25 gauge).
- Inj.Bupivacaine (Hyperbaric) is available as 0.5% ampule; each 1 ml contains 5 mg.
- Inj.Nalbuphine
- Inj.Dexmedetomidine Preservative free

- 18 gauge intravenous cannula.
- Ringers lactate solution .

ANESTHETIC TECHNIQUE:-

The patient's consent was taken for agreement to accept spinal anesthesia. On the day of surgery, the patient was shifted to the operating room earlier than the expected time of surgery by about 20 minutes.

On arrival of patient in the operating room standard monitoring was applied; ECG limb lead II, non invasive arterial blood pressure and peripheral oxygen saturation was monitored via BPL monitor. An 18 gauge intravenous cannula was inserted and secured.

Pre-medication as Inj.Ondensetron 4mg and Inj. Glycopyrrolate 0.2mg was given intravenously and Ringer lactate solution was given as pre-load at 10mg/kg. 30 patients in group D will receive 10µg dexmedetomidine with 3ml of 0.5% hyperbaric bupivacaine . The other 30 patients in group N will receive 0.4mg nalbuphine with 3ml of 0.5% hyperbaric bupivacaine.

The spinal technique used:-

After pre-loading: the spinal anesthesia was performed

- Patients were positioned in the sitting position
- Painting & Draping of patients back was done with betadine solution and spirit.
- Identification of the level was done using intercrestal line which pass through L3- L4 intervertebral space.
- 25 G spinal needle was inserted in the midline at L3-4 or L4-5 inter-space.After penetration of ligamentum fllavum, dura and arachanoid matter, correct needle placement was identified by free flow of cerebrospinal fluid.
- The appropriate local anesthetic solution was injected over 10-15seconds.
- The patient was placed supine immediately after injection for 15 minutes.

INTRA OPERATIVE:-

All patients of both groups were monitored for:

- Heart rate (HR).
- Systolic blood pressure
- Diastolic blood pressure
- Sensory block: Onset and duration
- Motor block: Onset and density of block using modified Bromage scale.
- Sedation score

Assessment of Sensory block:-

The upper and lower spread of sensory block was determined bilaterally using pin prick test . The dermatomes were identified by reference to a standard diagram. To assess the height of the block; sensory block was assessed every minute post-injection, for five minutes and at 5-min intervals thereafter until two consecutive levels of sensory block were identical (i.e fixation of the level), after which assessment was done every 30 minutes.

Assessment of Motor block:-

Tested by Bromage scale, time of onset, degree of motor blockade and duration of motor blockade were recorded.

Bromage scale:

- Bromage 0: the patient is able to move the hip, knee and ankle.
- Bromage 1: the patient is unable to move the hip, but is able to move the knee and ankle.
- Bromage 2: the patient is unable to move the hip and knee, but is able to move the ankle.
- Bromage 3: the patient is unable to move the hip, knee and ankle.

- *Hemodynamic Changes:* Pulse rate, Systolic blood pressure, Diastolic blood pressure were monitored at: 0,1,3,5,10,15,20,25,30,35,40,45,60,75,90,105,120,135,150,165,180 minutes.

- *Duration of Complete Analgesia :* It was assessed using visual analogue scale. Visual Linear Analogue Scale was explained one day prior to the surgery to the selected patients taken for the study to determine the analgesia in the post operative period. This will be carried out with a 10 cm line. The 1st end mark '0' means 'no pain' and end marked '10' means 'severe pain'. The patients will be asked to mark the severity of pain experienced at that time in the post operative period.

The severity of pain will be evaluated as follows:

0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
No pain	**Mild pain**			**Moderate pain**			**Severe pain**			

- *Sedation :* Was assessed by Ramsay Sedation Scale:

Score	Response
1	Anxious or restless or both
2	Cooperative, oriented and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

- Side effects and complications if any were noted

- Data were collected, tabulated, coded then analyzed using SPSS ® computer software version 12.0.

- Numerical variables were presented as mean & standard deviation (SD) .

- As regard numerical variables; unpaired student – t test was done.

- p value

>0.05	Non Significant
<0.05	Significant
<0.001	Highly Significant

Observations and results:-

Sixty patients of ASA grade-I and II of American Society Of Anesthesiologists' (ASA) classification was taken for study in lower abdominal and lower limb surgeries. They were allocated randomly to two equal groups (Group D - 0.5% Hyperbaric Bupivacaine (15 mg) + Dexmedetomidine (10 µg)) and (Group N - 0.5% Hyperbaric Bupivacaine (15 mg) + Nalbuphine (0.4 mg))

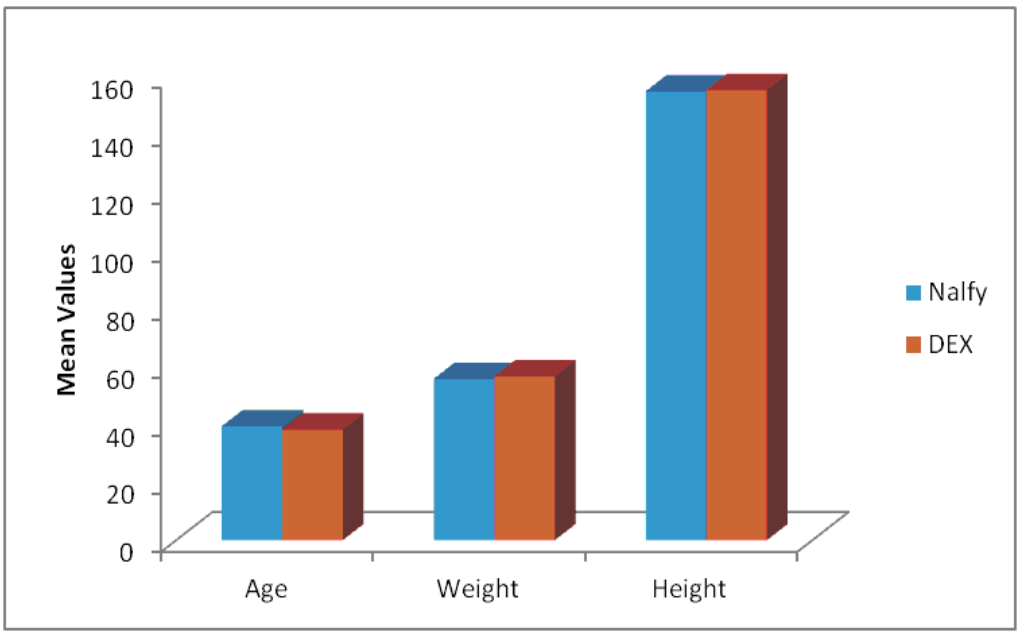
Comparison was done on the basis of onset of sensory and motor blockade, duration of analgesia, two segment regression, intraoperative haemodynamics, sedation score and complications if any.

The various observations were summarized as follows :-

Demographic data:-

Table 1: Comparison of the study groups according to mean age, weight and height

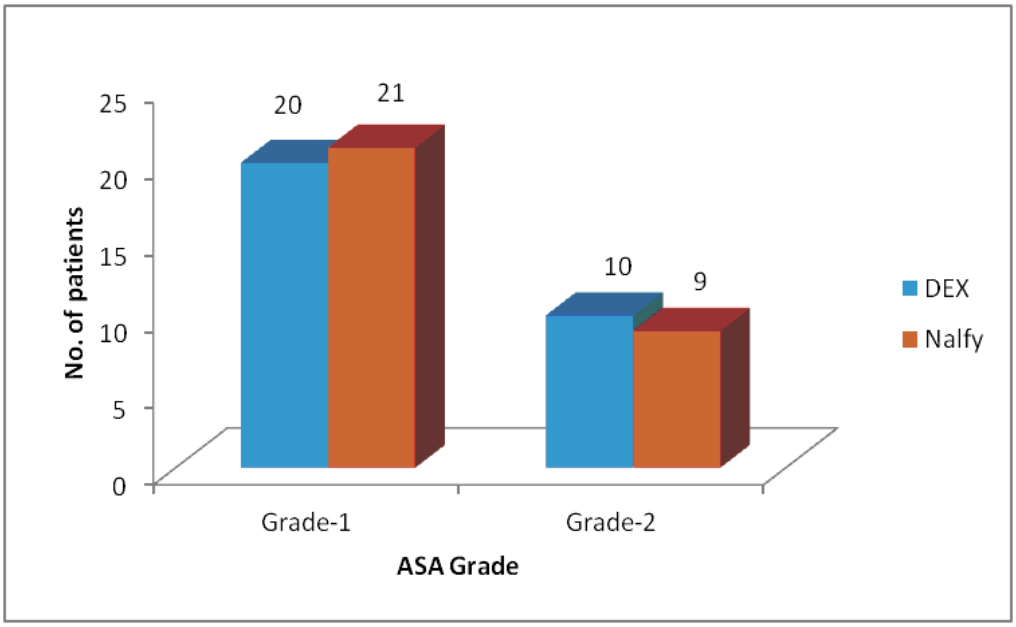
Variable	Group N (n=30)		Group D (n=30)		p value
Age (years)	Mean	SD	Mean	SD	0.694
	39.27	9.54	38.23	10.67	
Height (cms)	154.77	4.43	155.23	4.79	0.697
Weight (kgs)	55.63	6.145	56.5	4.462	0.534



The mean age in Group N was 39.27 years while in Group D it was 38.23 years. The mean height in Group N was 154.77 centimetres whereas in Group D was 155.23 centimetres. The mean weight in Group N was 55.63 kilograms and in Group D it was 56.5 kilograms. There was no significant difference between the groups with respect to the above parameters.
(p > 0.05)

Table 2 : American Society of Anaesthesia (ASA) Grade

ASA Grade	Group D (n=30)		Group N (n=30)		p-value
	N	%	N	%	
1	20	66.7	21	70.0	0.781
2	10	33.3	9	30.0	



Difference in ASA grading in both the groups was statistically non significant (p > 0.05).

Table 3 – Mean onset of Sensory block in both the groups

Time	Group N (n = 30)		Group D (n = 30)		p value
Onset of sensory block (minutes)	Mean	SD	Mean	SD	<0.001
	6.3	1.643	3.5	1.106	

The onset of sensory blockade was achieved early with a mean time of 3.5 minutes in Group D which showed very significant difference from Group N, where the mean time for onset of sensory blockade was found to be 6. 3 minutes. (p < 0.001)

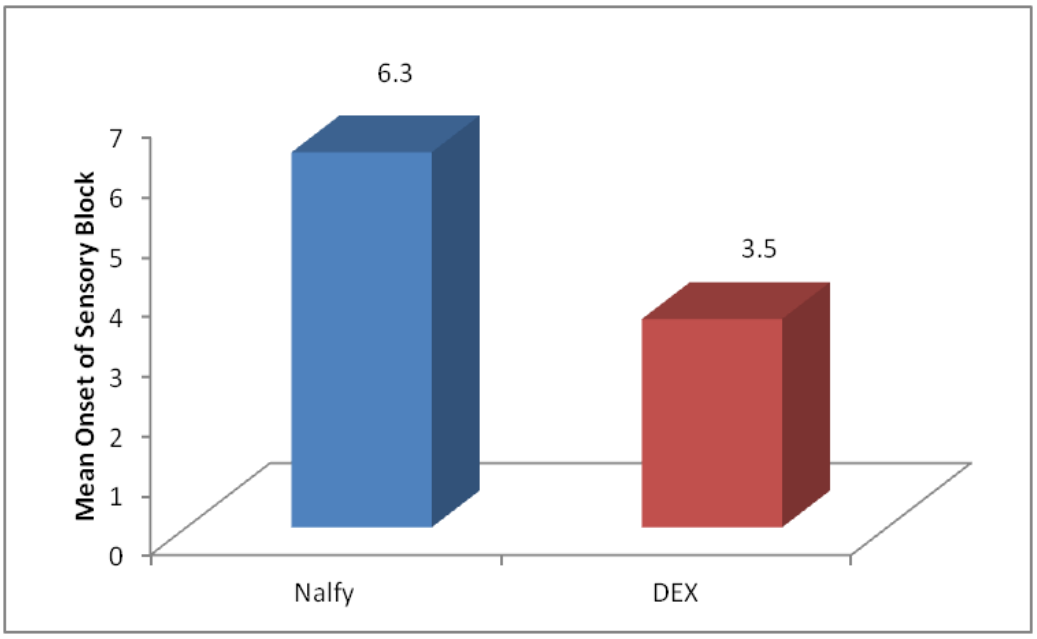


Table 4 – Mean duration of Sensory block in both the groups

Time	Group N (n = 30)		Group D (n = 30)		p value
Duration of sensory block (minutes)	Mean	SD	Mean	SD	<0.001
	200.67	22.118	276.07	31.287	

The mean duration of sensory block was statistically highly significantly prolonged in Group D, with a mean time of 276.07 minutes as compared to only 200.67 minutes in Group N, the results being statistically highly significant. ($p < 0.001$)

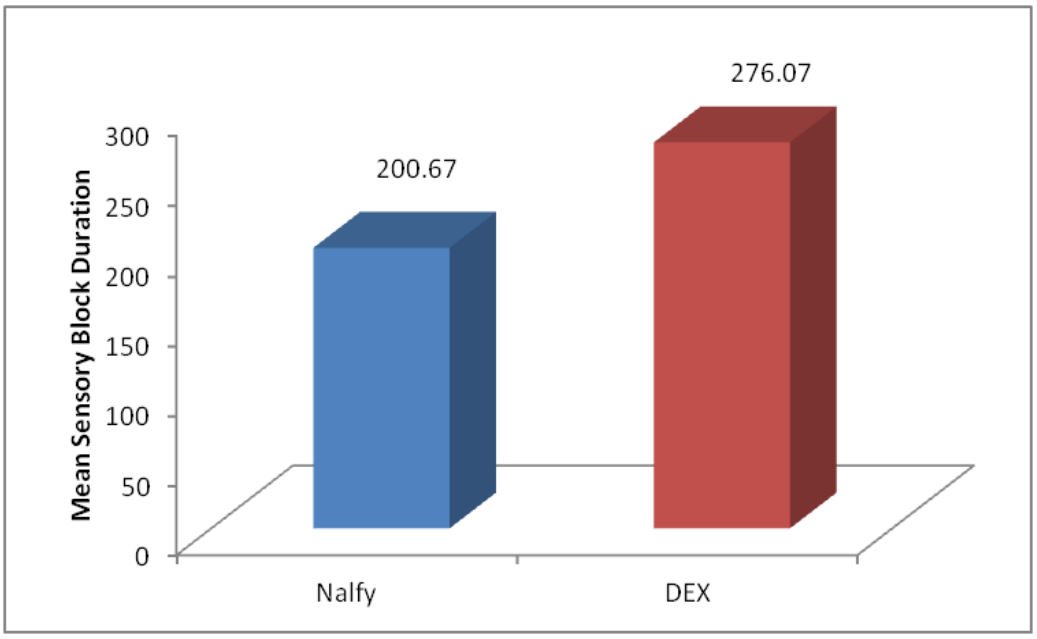


Table 5 – Mean onset of Motor block in both the groups

Time	Group N (n = 30)		Group D (n = 30)		p value
Onset of motor block (minutes)	Mean	SD	Mean	SD	<0.001
	8.73	1.874	6.23	1.382	

The onset of motor blockade was significantly faster in Group D, with a mean time of 6.23 minutes as compared to Group N, having a mean time of 8.73 minutes. (p < 0.001)

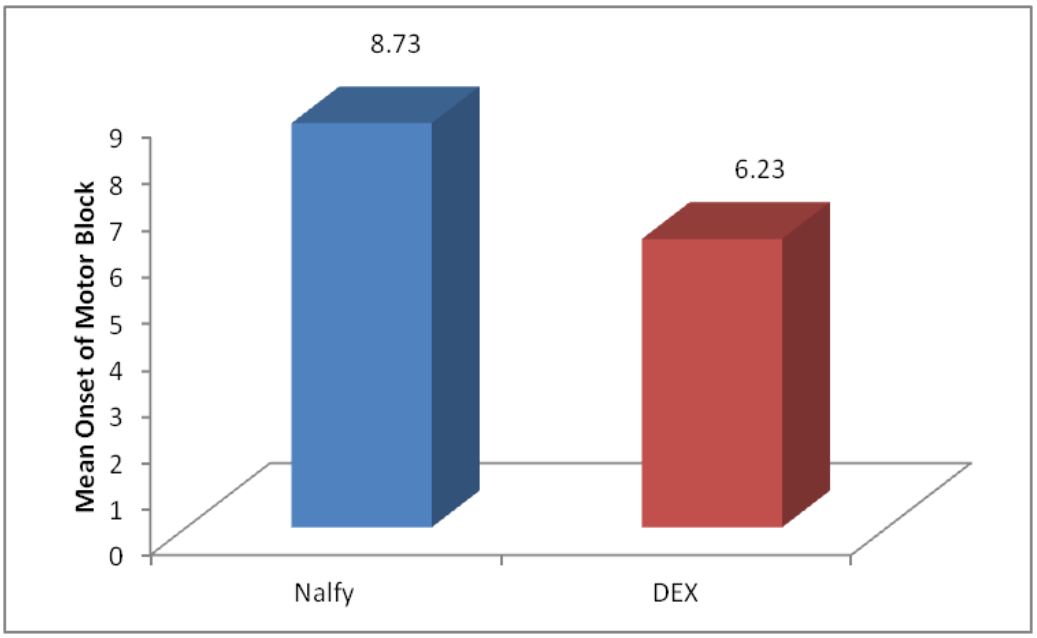


Table 6 – Mean duration of Motor block in both the groups

Time	Group N(n=30)		Group D(n=30)		p Value
Duration of motor block (minutes)	Mean	SD	Mean	SD	<0.001
	184.17	27.104	247.43	28.538	

The mean duration of motor blockade was 184.17 minutes in Group N, while it was 247.43 minutes in Group D which was highly significantly prolonged . (p value < 0.001)

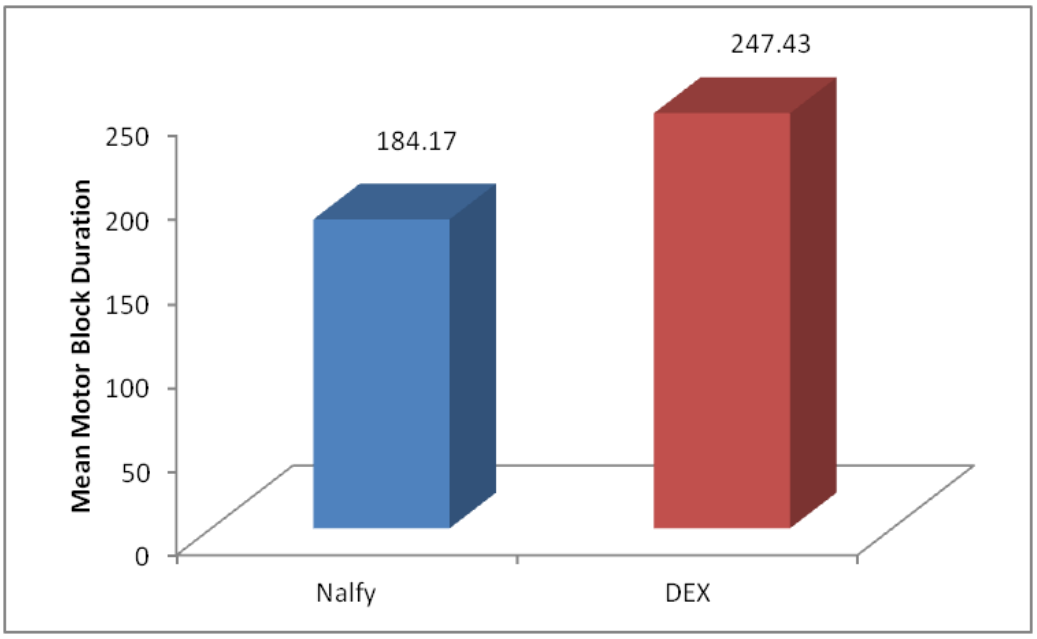


Table 7 – Mean two segment regression time

Time	Group N (n = 30)		Group D (n = 30)		p value
Two segment regression (minutes)	Mean	SD	Mean	SD	<0.001
	106.13	19.475	122.47	18.627	

The mean time of two segment regression was found to be 106.13 minutes in Group N, while it was 122.47 minutes, in Group D which was significantly longer. (p<0.001)

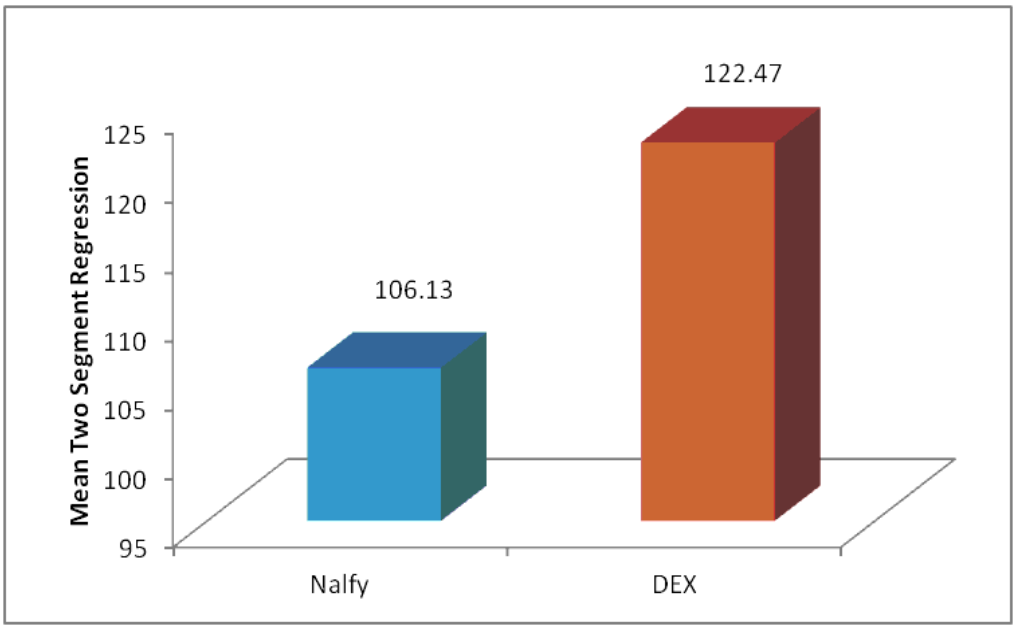


Table 8 – Mean duration of Analgesia in both groups

Time	Group N (n = 30)		Group D (n = 30)		p value
Duration of analgesia (minutes)	Mean	SD	Mean	SD	<0.001
	86.73	17.956	110.97	20.775	

The mean duration of analgesia in Group N was 86.73 minutes, as compared to 110.97 minutes in Group D which was found to be statistically significantly higher (p value < 0.001).

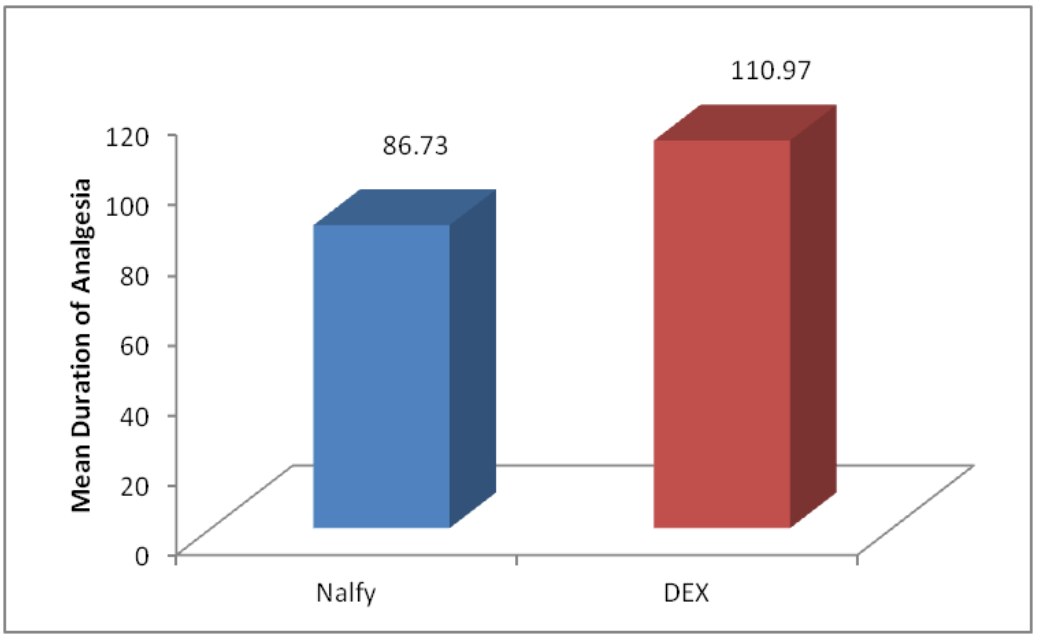


Table 9 – Mean pulse rate at different time intervals in both the groups

Time interval	Group N (n = 30)	Group D (n = 30)	p-value
Baseline	96.47±11.001	98.6±12.984	0.495
1 min	97.33±10.496	98.47±11.587	0.693
3 mins	98.13±10.75	97.27±10.948	0.758
5 mins	95.87±9.895	96.87±11.2	0.715
10 mins	93.27±9.089	95.6±8.427	0.307
15 mins	91.27±7.746	93.47±8.253	0.291
20 mins	89.07±7.552	92.53±8.136	0.093
25 mins	87.8±6.31	91±9.766	0.137
30 mins	85.93±6.136	90.07±9.165	0.045
45 mins	83.73±6.384	85.87±7.123	0.227
60 mins	83.6±7.744	84.93±7.311	0.496
75 mins	84.14±6.653	86.4±8.557	0.263
90 mins	83.66±5.32	85.47±7.718	0.300
105 mins	83.67±4.958	84.92±7.413	0.496
120 mins	83±5.369	83.25±6.234	0.901
135 mins	81.33±6.022	83.33±6.653	0.597
150 mins	83±4.243	84±0	0.212

Throughout the study the pulse of the patients in both groups remained below the baseline value except non significant increase in pulse rate upto 3 minutes in Nalbuphine group. No significant changes were noted between the groups at any intervals during the study period. (p > 0.05)

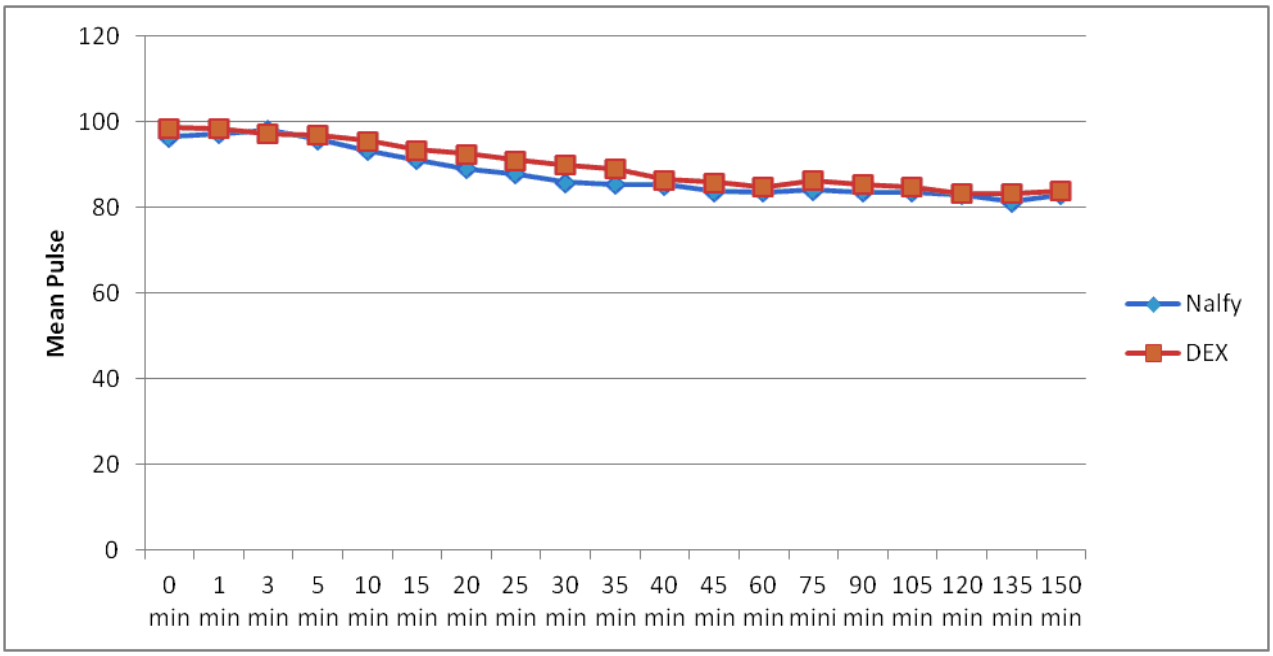


Table 10 – Mean systolic blood pressure at different time intervals in both the groups

Time interval	Group N (n = 30)	Group D (n = 30)	p-value
Baseline	125.53±4.447	128.13±5.063	0.039
1 mins	123±4.127	125.4±4.583	0.037
3 mins	118.8±5.108	120±5.608	0.390
5 mins	117.13±3.989	118.33±4.929	0.304
10 mins	116.33±4.787	116.87±6.004	0.705
15 mins	116.67±5.155	117.73±5.842	0.456
20 mins	117.93±5.078	118.07±5.42	0.922
25 mins	119.2±4.475	120.4±6.044	0.386
30 mins	120±4.102	120.8±4.597	0.480
45 mins	123±3.629	120.93±5.085	0.075
60 mins	122.53±3.821	121.6±4.248	0.375
75 mins	122.07±4.391	122.47±2.862	0.681
90 mins	121.52±3.879	121.67±3.527	0.877
105 mins	122.42±3.488	121.25±4.523	0.322
120 mins	121.89±2.867	123.38±4.113	0.226
135 mins	122±2.53	126.33±3.445	0.032
150 mins	122±2.828	126±0	0.454

The systolic blood pressure remained below the baseline during the study period in both the groups and there was no significant difference in systolic blood pressure between the groups. (p > 0.05).

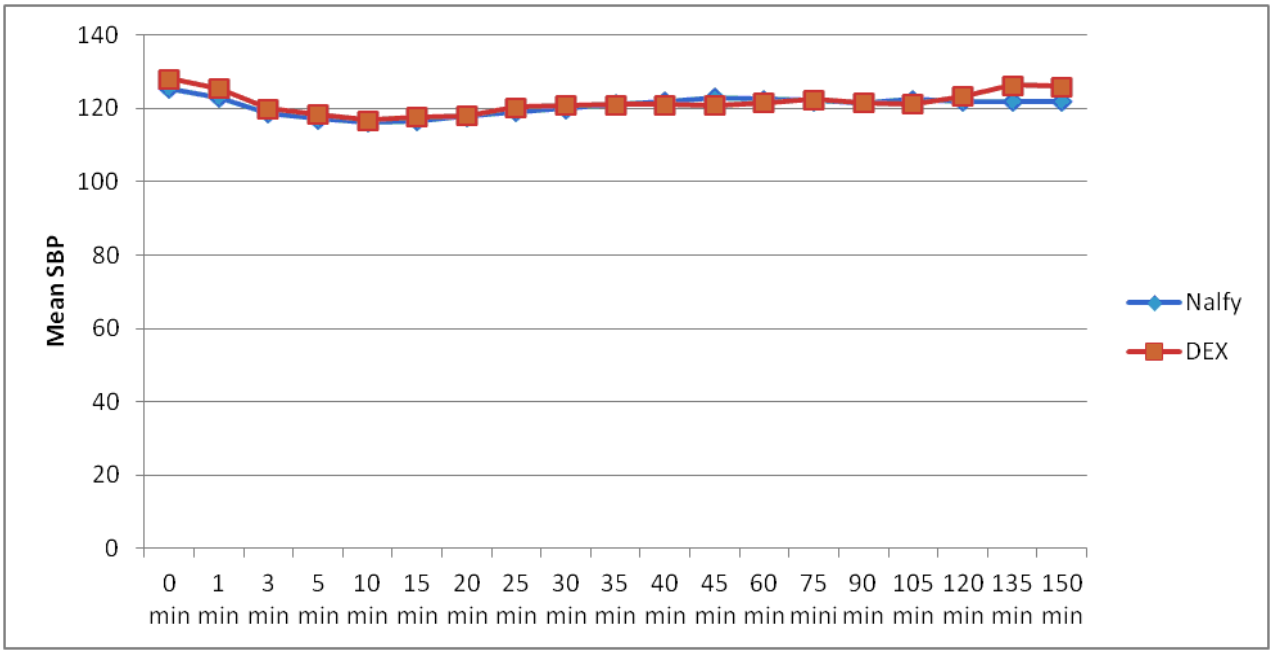


Table 11 – Mean diastolic blood pressure at different time intervals in both the groups

Time interval	Group N (n = 30)	Group D (n = 30)	p-value
Baseline	79.07±5.003	80.87±6.318	0.226
1 min	77.47±4.297	79.47±6.124	0.149
3 mins	77.2±5.215	78.27±6.186	0.473
5 mins	77.33±4.113	77.73±6.863	0.785
10 mins	77.4±4.673	76.8±5.933	0.665
15 mins	78.2±3.908	76.53±6.538	0.236
20 mins	78.27±5.577	77.13±7.215	0.499
25 mins	79.4±5.587	77.07±6.741	0.150
30 mins	77.83±5.226	77.47±5.431	0.791
35 mins	77.07±4.127	76.6±6.542	0.742
40 mins	77.93±3.581	77.8±6.31	0.920
45 mins	76.53±3.674	77.33±5.101	0.489
60 mins	77.13±3.665	78.53±6.235	0.293
75 mins	78.14±4.533	77.33±6.31	0.577
90 mins	77.1±4.195	77.2±4.972	0.936
105 mins	77.67±5.49	76.17±5.206	0.337
120 mins	78.22±4.596	78.38±3.117	0.912
135 mins	80.67±2.733	79±3.521	0.381
150 mins	78±2.828	74±0	0.454

There was non significant difference in diastolic blood pressure between the groups throughout the course of sudy and diastolic blood pressure remained below base line values. ($p > 0.05$)

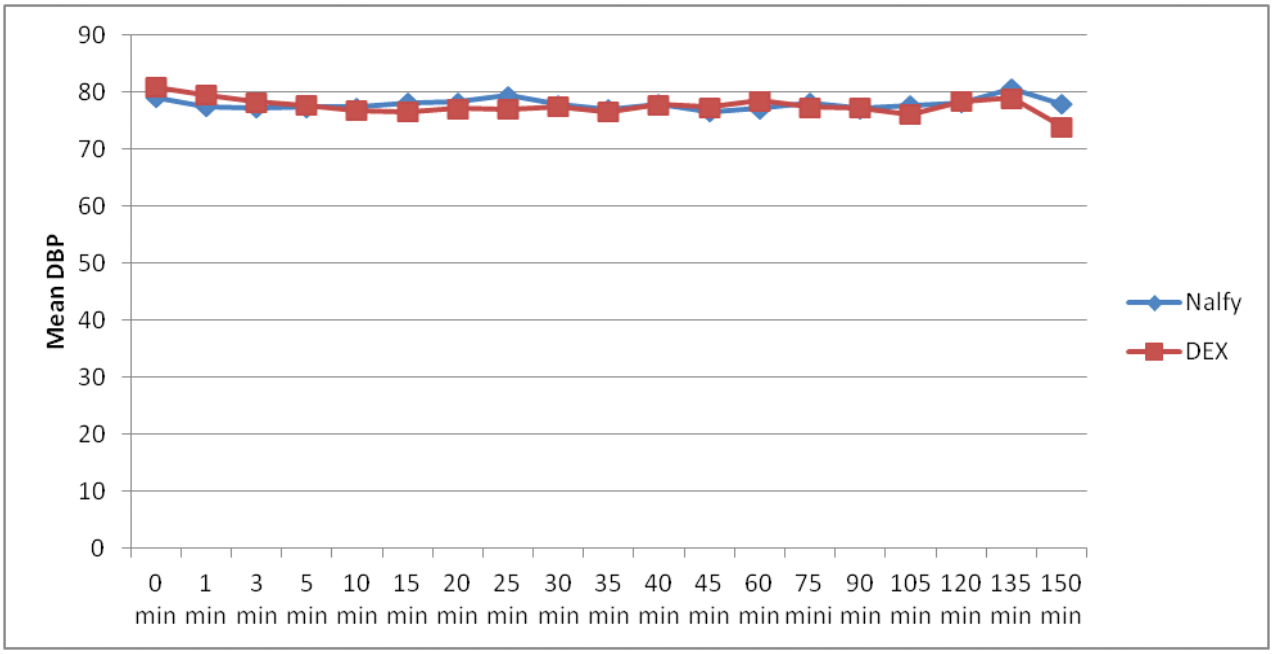


Table 12 - Mean sedation scores at different time intervals in both the groups

Time interval	Group N (n = 30)	Group D (n = 30)	p-value
Baseline	2±0	2±0	NA
1 min	2±0	2±0	NA
3 mins	2.03±0.18	2±0	0.321
5 mins	2.03±0.18	2±0	0.321
10 mins	2.03±0.18	2±0	0.321
15 mins	2.03±0.18	2±0	0.321
20 mins	2.03±0.18	2±0	0.321
25 mins	2.03±0.18	2.03±0.18	1.000
30 mins	2.3±0.466	2.13±0.346	0.121
35 mins	2.33±0.479	2.13±0.346	0.069
40 mins	2.33±0.479	2.13±0.346	0.069
45 mins	2.33±0.479	2.13±0.346	0.069
60 mins	2.3±0.466	2.17±0.379	0.229
75 mins	2.34±0.484	2.2±0.407	0.218
90 mins	2.24±0.435	2.25±0.442	0.943
105 mins	2.21±0.415	2.25±0.447	0.765
120 mins	2.22±0.428	2.5±0.548	0.211
135 mins	2.17±0.408	2	0.721
150 mins	2±0	2±0	NA

The difference in the sedation score of both the groups was not significant ($p > 0.05$)

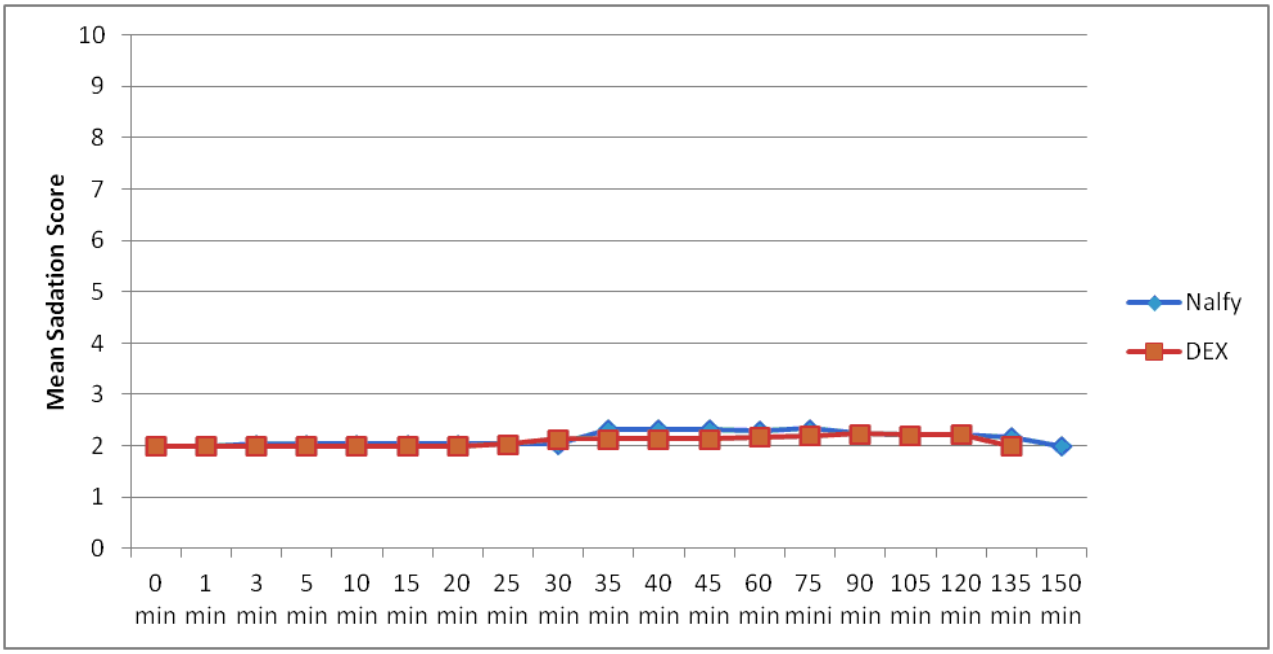


Table 13 - Incidence of side effects

Complications	Group		P Value
	N(n=30)	D(n=30)	
Nausea	0	0	-
Vomiting	0	0	-
Hypertension	0	0	-
Hypotension	0	0	-
Tachycardia	0	0	-
Post dural punctural headache	0	0	-

No complications were observed in either of the groups during the course of the study.

Discussion:-

Spinal anaesthesia has been commonly used for lower abdomen and lower limb surgeries because of its simplicity, speed, reliability and minimal exposure to depressant drugs. The aim of good postoperative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. Adding, an intrathecal adjuvant to local anaesthetics forms a reliable method to prolong the duration of anaesthesia. A number of adjuvants to local anesthetics for spinal anaesthesia like opioids (fentanyl and buprenorphine), benzodiazepines (midazolam), ketamine and neostigmine have been used. However intrathecal opioids can produce a number of side effects like nausea, vomiting, pruritis and respiratory depression depending on the dose used. Hence in our study, we decided to compare the effects of Nalbuphine (opioid) with Dexmedetomidine (α_2 adrenergic agonist), when used intrathecally as an adjuvant to Bupivacaine in spinal anaesthesia.

60 patients, of age between 20 and 55 years, were divided into two groups of 30 each. Group D was given Inj. Dexmedetomidine 10µg with Inj. Bupivacaine 15 mg intrathecally; and Group N was given Inj. Nalbuphine 0.4 mg with Inj. Bupivacaine 15 mg intrathecally.

Lin et al (1992)[11], found that the addition of intrathecal nalbuphine 0.4 mg to hyperbaric tetracaine, compared with intrathecal morphine 0.4 mg , improved the quality of intraoperative and postoperative analgesia, with minimal side-effects.

Al Mustafa MM and Halaweh Abu et al (2009)[24], did a randomized control study to compare 5 and 10 µg of intrathecal dexmedetomidine with bupivacaine and concluded that dexmedetomidine has a dose dependant effect on the onset and regression of sensory and motor block when used as an adjuvant to bupivacaine in spinal anesthesia.

Hala E A Eid MD, Mohamed A Shafie MD et al (2011)[25], conducted a randomized controlled study and concluded that intrathecal dexmedetomidine in doses of 10 µg and 15 µg significantly prolong the anesthetic effects of spinal hyperbaric bupivacaine in a dose-dependent manner.

A prospective randomized double blind study was conducted by Shukla Deepika and Varma Anil (2011)[26], to compare intrathecal dexmedetomidine and magnesium sulphate as adjuvants to bupivacaine and it was concluded that 10 µg of dexmedetomidine as adjuvant to spinal bupivacaine in surgical procedures of long duration has minimal side-effects, and provides excellent quality of postoperative analgesia.

Xavier et al, in 2000[57], performed a comparative study to evaluate analgesia and adverse effects after using three doses, 0.2mg, 0.8mg, 1.6mg of intrathecal nalbuphine and morphine 0.2mg given for caesarean section along with bupivacaine. They concluded that 0.8mg of intrathecal nalbuphine improves intraoperative analgesia and prolongs early postoperative analgesia.

Mukherjee et al (2011)[28], performed a study by comparing different doses of intrathecal nalbuphine, ie 0.2, 0.4 and 0.8mg to find out which dose prolonged post operative analgesia without increased side effects. It was observed that effective analgesia increased with increase in concentration and the final observation was 0.4mg of nalbuphine with 0.5% hyperbaric bupivacaine intrathecally prolonged analgesia, without any side effects.

In view of the above mentioned studies, we have chosen 10 µg dexmedetomidine to be used intrathecally, which was the minimal and safe dose used. We formulated our study to compare the same with intrathecal nalbuphine 0.4mg, as it was found to prolong analgesia with minimal side effects.

The main objectives of this study was to compare the two drugs on the following parameters :-

- Onset and duration of sensory blockade.
- Onset and duration of motor blockade.
- Time of two segment regression.
- Duration of analgesia
- Rescue analgesia, if required
- Haemodynamic changes in heart rate, systolic blood pressure and diastolic blood pressure.
- Sedation
- Side effects/complications.

The ratio of patients in both the groups depending on age, weight, height and ASA grading were similar and statistically not significant. ($p > 0.05$)

The onset of sensory blockade was highly significantly early in Group D, as compared to Group N. ($p < 0.001$).
The onset of motor blockade was significantly faster in Group D as compared to Group N. ($p < 0.001$)

Kanazi et al (2006)[23] showed that the combination of 12 mg of intrathecal bupivacaine with 3µg of dexmedetomidine significantly shortened the onset of sensory block and motor block, in comparison with bupivacaine alone. ($p <0.001$)

Subhi M Al- Ghanem et al (2009)[58] studied the supplementation of spinal bupivacaine with 5µg Dexmedetomidine intrathecally and found that the onset time of sensory block and motor block was significantly reduced.($p<0.001$)

Eid MD et al (2011)[25] studied the combination of 15 mg of bupivacaine with different doses of dexmedetomidine (10µg and 15µg) and concluded that there was a faster onset of sensory and motor blockade seen.($p<0.001$)

The mean duration of sensory block was statistically highly significantly prolonged in Group D, as compared to Group N ($p < 0.001$)

The mean duration of motor blockade in Group D which was highly significantly prolonged in comparison with Group N. ($p < 0.001$)

Yaksh et al (1985)[59], has showed that the intrathecal alpha 2 adrenoreceptor agonist can cause dose dependent decrease in motor strength in animals and prolongation of motor block of spinal anaesthetics due to addition of alpha 2 agonists, may result from their binding to motor neurons in dorsal horn.

Kanazi et al (2006)[23], showed that the combination of 12 mg of intrathecal bupivacaine with dexmedetomidine significantly prolonged the mean duration of sensory and motor block, in comparison with bupivacaine alone.($p < 0.001$)

Subhi M Al- Ghanem et al (2009)[58], showed that the supplementation of spinal bupivacaine with 5µg dexmedetomidine significantly prolonged mean duration of sensory blockade and motor blockade in comparison with intrathecal fentanyl 25µg and bupivacaine.
($p < 0.001$)

Eid MD et al (2011)[25], studied the combination of 15 mg bupivacaine with 10 and 15µg of dexmedetomidine using normal saline as a control group. It was found that, there was a dose dependent prolongation in mean duration of sensory and motor blockade with dexmedetomidine, in comparison with normal saline, when used as an adjuvant.($p < 0.001$)

Halder S and Das A (2014)[33], compared 5µg and 10µg of dexmedetomidine, intrathecally as an adjuvant to 15 mg bupivacaine and concluded that dose dependent intrathecal dexmedetomidine increases the sensory, motor block duration and time to first analgesic use, and decreases analgesic consumption in a dose-dependent manner.

Dubey Rashmi and Bisht Swati (2014)[32], conducted a randomized study and concluded that Nalbuphine provides better quality of block as compared to bupivacaine alone. It also prolongs postoperative analgesia when used as adjuvant to spinal bupivacaine in elderly patients.($p < 0.001$)

The results of our study was corresponding to the above mentioned studies reiterating the fact that Dexmedetomidine when used as an adjuvant to Bupivacaine decreases mean onset of sensory and motor block, but prolongs the mean duration of sensory and motor block.

The mean time of two segment regression was significantly longer in Group D as compared to Group N.The mean duration of analgesia was found to be statistically significantly higher in Group D, as compared to Group N. ($p < 0.001$)

Pain signals from the nociceptors may result in sensitization of secondary nociceptive neurons in the dorsal horn. This is mediated by a decrease in inhibitory input or an increase in synaptic efficiency or membrane excitability triggered by wind up neurokinin and NMDA receptor mechanism. Subsequently activity in nociceptors and non-nociceptors A- beta fibres will be amplified, which leads to increased pain and allodynia. Local anaesthetic bupivacaine, acts mainly by blockage of voltage gated sodium channels in the axonal membrane. It can also interfere with synaptic transmission by a presynaptic inhibition of calcium channels in addition to their effect on nerve conduction.

Dexmedetomidine is a novel alpha- 2 agonist and is being commonly used as an additive to local anaesthetic agent in subarachnoid block. As a neuraxial adjuvant $\alpha 2$ agonists can activate a number of antinociceptive mechanisms depending on the dose; however, the main site for their antinociceptive effect in physiological pain conditions seems

to be the spinal dorsal horn. They produce analgesia by depressing release of C-fiber transmitters and by hyperpolarization of post synaptic dorsal horn neurons. Thus both dexmedetomidine and local anaesthetic have similar action with different mechanism , enhancing and prolonging the effect of spinal anaesthesia when given in combination intrathecally.

Intra thecal opioids have the ability to produce extensive analgesia, when used as adjuvants and has an advantage of allowing early ambulation of patients because of their sympathetic and motor nerve-sparing activities. Nalbuphine is an opioid, structurally related to oxy-morphone. It is a highly lipid-soluble opioid with an agonist action at the k opioid receptor and an antagonist activity at the mu opioid receptor. Nalbuphine and other k agonists had provided reasonably potent analgesia in certain models of visceral nociception. They have a short duration of action, consistent with their lipid solubility and rapid clearance compared with other opioids like morphine.

No statistically significant changes were seen in pulse rate , systolic or diastolic blood pressure in patients of both groups at all time intervals. ($p > 0.05$).

No complications in the form of nausea, vomiting, hypotension, hypertension, tachycardia were noted in any of the patients.

In our study we found that intrathecal dexmedetomidine in a dose of 10µg when given as an adjuvant to bupivacaine , decreases the mean onset of sensory and motor blockade significantly as compared to intrathecal nalbuphine 0.4 mg. The duration of sensory and motor blockade was significantly prolonged in the dexmedetomidine group in comparison with nalbuphine group. The duration of analgesia was significantly prolonged with intrathecal dexmedetomidine. No complications were noted in any patient of either group.

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