EFFECT OF INTRAVENOUS DEXMEDETOMIDINE ON PROLONGING SPINAL ANESTHESIA, A RANDOMISED CONTROLLED STUDY

Submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

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BRANCH – X

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K.K.NAGAR ,CHENNAI

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY
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APRIL 2015

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This is to certify that the dissertation named **"EFFECT OF INTRAVENOUS DEXMEDETOMIDINE ON PROLONGING SPINAL ANESTHESIA, A RANDOMISED CONTROLLED STUDY"** is a bonafide work performed by Dr.T.S.Nandhini, post graduate student, Department of Anaesthesiology, ESIC Medical College & PGIMSR, Chennai-78, under my guidance and supervision in fulfillment of regulations of The Tamilnadu Dr. M.G.R Medical University for the award of M.D. Degree during the academic year 2012-2015.

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This is to certify that this dissertation titled **"EFFECT OF INTRAVENOUS DEXMEDETOMIDINE ON PROLONGING SPINAL ANESTHESIA, A RANDOMISED CONTROLLED STUDY"** submitted by **Dr.T.S.Nandhini,** appearing for M.D Degree Branch – X ANAESTHSIOLOGY examination in April 2015 is a bonafide record of work done by her under my direct guidance and supervision in partial fulfillment of the regulations of Tamilnadu Dr.M.G.R Medical University, Chennai. I forward this to the Tamilnadu Dr. M.G.R Medical University, Chennai Tamilnadu, India.

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DECLARATION

I solemnly declare that this dissertation entitled **"EFFECT OF INTRAVENOUS DEXMEDETOMIDINE ON PROLONGING SPINAL ANESTHESIA, A RANDOMISED CONTROLLED STUDY"** has been conducted by me at ESIC Medical College & PGIMSR, Chennai, under the guidance and supervision of **Prof.Dr.KAMALINI SRIDHARAN, M.D.**, and **Dr.K.RADHIKA, M.D.,** Department of Anesthesiology, ESIC Medical College & PGIMSR, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch X (Anesthesiology)**.

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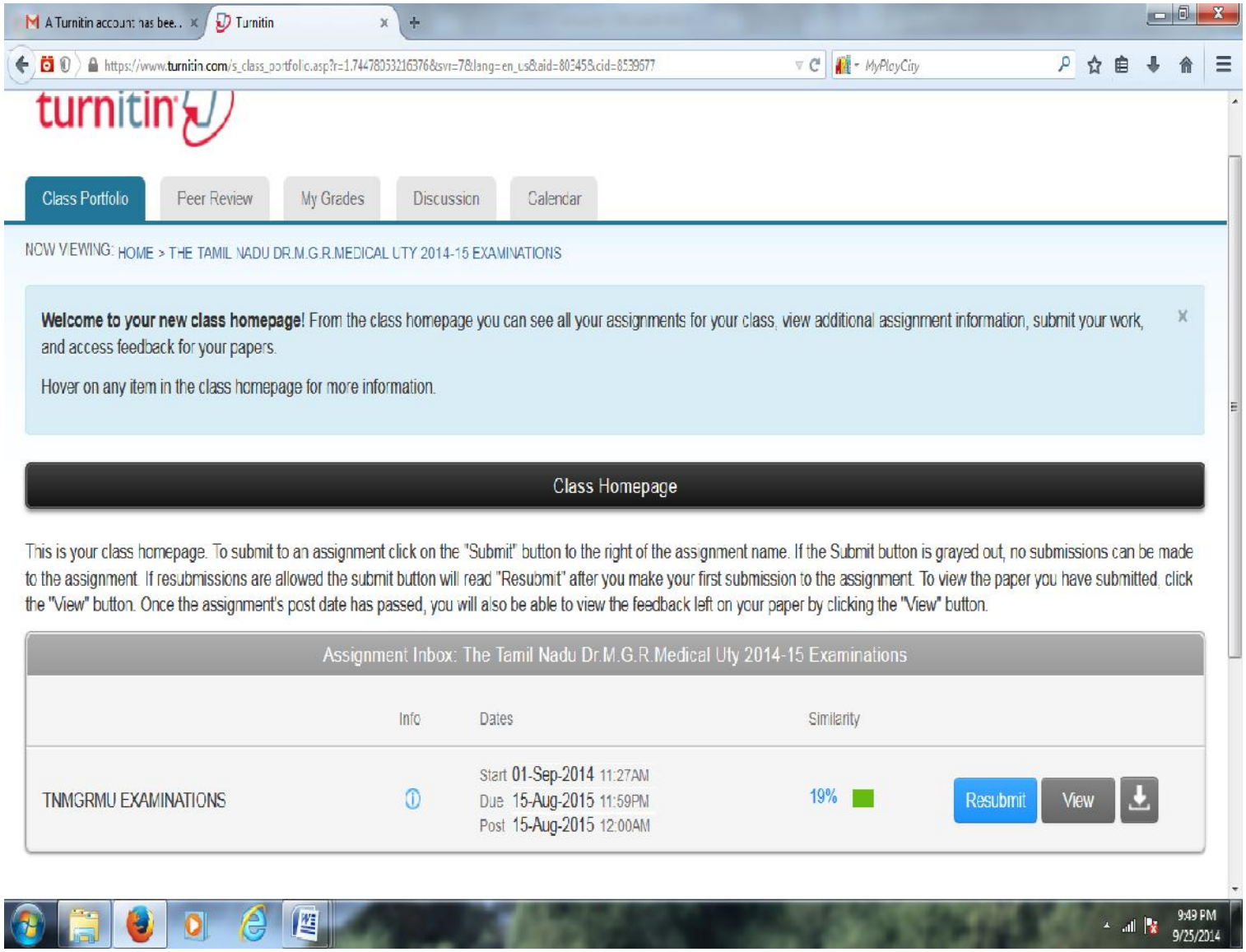
Dr. T.S.Nandhini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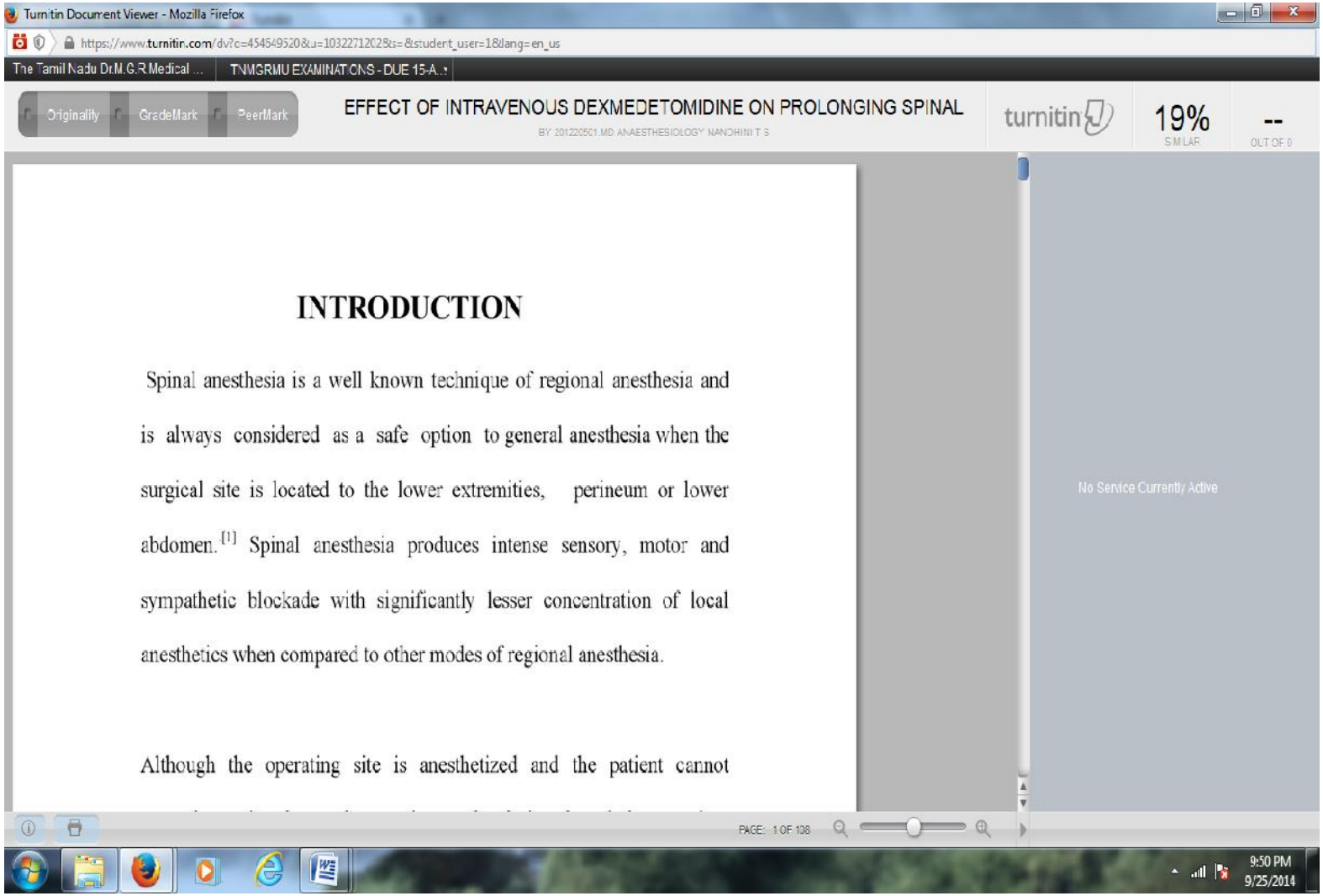
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INTRODUCTION
Spinal anesthesia is a well known technique of regional anesthesia and is always considered as a safe option to general anesthesia when the surgical site is located to the lower extremities, perineum or lower abdomen.[1] Spinal anesthesia produces intense sensory, motor and sympathetic blockade with significantly lesser concentration of local anesthetics when compared to other modes of regional anesthesia.
Although the operating site is anesthetized and the patient cannot
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CONTENTS

ABSTRACT

BACKGROUND AND OBJECTIVES

The aim of this study was to evaluate the effect of intravenous dexmedetomidine on prolongation of spinal anesthesia.

METHODS

Study population comprised of 100 patients scheduled for abdominal/vaginal hysterectomy under spinal anesthesia. 100 adult patients classified as ASA 1 or 2 were studied. Patients were randomly assigned to one of the two groups

In Group-D patients received hyperbaric intrathecal bupivacaine anesthesia 3.5ml 0.5% (17.5 mg) and intravenous Dexmedetomidine 0.5micro grams/Kg in10 ml normal saline over 10 minutes after initiation of spinal block.

In Group C patients received hyperbaric bupivacaine anaesthesia 3.5 ml 0.5% (17.5mg) and intravenous normal saline 10 ml over 10 minutes.

RESULTS

The time for the motor block to become B0 was 243±17.0 minutes in the study group and in the control group it was 211.2±16.7 minutes The total time for sensory level to reach S1 was 255±8.6in the study group while it was 210.8±33,1 in the control group. The time for two dermatome regression from the

maximal level was 125.2±17.5minutes in the study group and 94.6±18.9 in the control group. This proved the significant prolongation of motor block, sensory block, sensory block to regress from the maximal level in the study group with a p value of 0.001***.

CONCLUSION

Dexmedetomidine in the dose of 0.5 microgram/kg given as single intravenous dose to patients who underwent abdominal/vaginal hysterectomy under spinal anesthesia significantly prolonged the duration of sensory and motor blockade and also caused arousable sedation.

INTRODUCTION

Spinal anesthesia is a well known technique of regional anesthesia and is always considered as a safe option to general anesthesia when the surgical site is located to the lower extremities, perineum or lower abdomen[1]. Spinal anesthesia produces intense sensory, motor and sympathetic blockade with significantly lesser concentration of local anesthetics when compared to other modes of regional anesthesia. Although the operating site is anesthetized and the patient cannot appreciate pain, he or she remains awake during the whole procedure which contributes to mental stress ranging from mild to severe depending on the patient's mentality.

Spinal anesthesia has many advantages like low cost, reduced risk of aspiration even in patients who are considered to be full stomach and reduced blood loss. There is relaxation of abdominal muscles and this facilitates surgical approach. The main limitation of spinal anesthesia is that it is limited in duration. The patient's anxiety adds to the technical difficulties.

Usually spinal anesthesia with hyperbaric bupivacaine lasts for 2 to 2.5 hours.[2]. To extend the duration of spinal anesthesia adjuvants like opiods, epinephrine and neostigmine are added to local anesthetics and instilled into the

subarachnoid space. These added substances have their own advantages and disadvantages.

Sedation in adequate dose during neuraxial block alleviates the anxiety of the patient[3]. When the patient is relaxed ,the surgeon finds it easy to operate[4]. Under sedation ,patients should be able to respond to command and maintain a patent airway with minimal oxygen supplementation.

Two commonly used drugs for sedation are propofol and midazolam. Intravenous propofol in the dose of 0.2to 0.3 mg/kg is used for sedation. This produces a rapid decline in the level of consciousness. With a continuous infusion of propofol both the cardiovascular and respiratory function are depressed to a considerable extent. The newer water soluble benzodiazepine, midazolam given in the dose of 0.03mg/kg has a quick onset of action. But, recovery is slow.

In day to day practice although we use midazolam and propofol for sedating patients, they are vulnerable to cause significant reduction in blood pressure and respiratory function. This effect can sometimes be deleterious to the patient. Hence there has been always a search for the ideal sedative which can be used to relieve anxiety.

The newer drug Dexmedetomidine is a more specific alpha 2 adrenoreceptor agonist. It causes analgesia, sedation and sympatholysis. Food and Drug Administration (FDA) approved the use of dexmedetomidine in 1999 for short-term sedation and analgesia (<24 hours) in the intensive care unit. It is becoming very popular because it maintains hemodynamic stability and does not cause significant respiratory depression.

α 2-adrenergic receptor (α 2-AR) agonists have been used in varied clinical situations because of their actions which include sedation, analgesia, anxiolysis, perioperative sympatholysis, cardiovascular stabilizing effects, reduced anesthetic requirements, and preservation of respiratory function.

Many studies are available in the literature which prove the efficacy of clonidine ,a first generation alpha2 agonist to prolong spinal anesthesia whether administered by intravenous or intrathecal route.[2][5] Clonidine is also known to decrease the anesthetic requirements in general anesthesia[6] .

Dexmedetomidine being a second generation alpha2 agonist is more specific for alpha2 receptors. Dexmedetomidine acts on the locusceruleus area of brain

stem which is concerned with modulation of sleep and respiratory control. This results in sedation without respiratory depression.

Dexmedetomidine has all the properties of an ideal sedative. There is a hypothesis that by its actions in the substantia gelatinosa in the spinal cord (spinal action)and locus ceruleus in the brain (supra spinal action) dexmedetomidine can prolong spinal anesthesia. This is the basis of its antinociceptive action.[7]Studies have been conducted to prove that dexmedetomidine when given intravenously or intrathecally prolongs the duration of spinal anesthesia. [8][9][10]

In this study we investigated the effect of a single intravenous dose of dexmedetomidine on hyperbaric bupivacaine spinal anesthesia. In addition to prolonging the duration of spinal anesthesia, dexmedetomidine causes a decrease in stress response, heart rate and blood pressure by lowering secretion of catecholamines. This can be of great value in the perioperative period during which most of the vulnerable hemodynamic variations occur due to stress.

AIM OF THE STUDY

AIM OF THE STUDY

The main aim of this study was to investigate the effect of a single dose of 0.5micrograms/kg of dexmedetomidine administered intravenously over 10 minutes after initiation of neuraxial block, on prolonging duration of sensory and motor block in hyperbaric bupivacaine spinal anesthesia. Proper approval from the Institutional ethical board was obtained and the study was conducted over a period of six months.

OBJECTIVES

PRIMARY OUTCOME

Total duration of both sensory and motor blockade after hyperbaric bupivacaine anesthesia was studied.

SECONDARY OUTCOME

Grade of sedation

REVIEW OF LITERATURE

Aantaa , Kanto J, Kallio A et al[11] had done a study in patients undergoing minor gynecologic surgery . Nineteen women who had been posted for dilatation and curettage of the uterus were given dexmedetomidine in the dose of 0.5 micrograms/kg fifteen minutes before induction and another set of 20 patients received saline in the same frame. Anesthetic induction was given with thiopental. The maintenance of anesthesia was with N2O/O2 (70/30%) and with incremental doses of thiopentone sodium . In their study they had observed that "The total amount of thiopental required to maintain patient in a good plane of anesthesia for performing the procedure was reduced by approximately 30%, in the group that had received dexmedetomidine". They had observed that the recovery from anesthesia was much better with dexmedetomidine as measured by the visual analogue scale. They measured the concentration of norepinephrine and found a 56%reduction in concentration of nor epinephrine because of the sympatholysis caused by dexmedetomidine. They had observed moderate decrease in systolic and diastolic blood pressure after dexmedetomidine administration. The authors concluded that "Premedication with dexmedetomidine decreased thiopental anesthetic requirements and also improved the recovery from anesthesia with no serious hemodynamic compromise".

Khaled Taha[12] had done a study in 60 patients evaluating analgesic ,sedative and hemodynamic effects of Dexmedetomidine following major abdominal surgeries. It was a randomized ,double blinded comparative study with morphine. All surgeries were under general anesthesia. Twenty minutes before surgery random allocation of groups was done. One group received dexmedetomidine as intravenous infusion 4 microgram/kg/hr for 15 minutes and a maintenance dose for 3 hours at the rate of 0.4 microgram/kg/hour. Another group received a single dose of morphine 0.07mg/kg. All patient received patient controlled analgesia with morphine. They concluded that "There was significant decrease in the total PCA morphine in the dexmedetomidine group". The author had emphasized that cardiovascular effects of dexmedetomidine could be beneficial in patients with ischemic or non ischemic heart disease. The authors had concluded that "The cardiovascular protective profile and the lack of respiratory depression makes dexmedetomidine a suitable drug for post operative analgesia after major abdominal surgeries".

Kanazi GE, Aouad MT, Jabbour-Khoury SI et al, [8] did a prospective, double-blinded study on 60 patients posted for transurethral resection of prostate or bladder tumor under spinal anesthesia. Patients were allocated to three groups randomly. Patients in Group 1 were given hyperbaric bupivacaine 12 mg.

Patients in group 2 were given 12 mg of bupivacaine supplemented with dexmedetomidine 3 microgram . Patients in group 3 were given 12 mg of bupivacaine supplemented with clonidine 30 microgram. .The onset time for peak sensory and motor levels, and the sensory and motor block regression time were recorded.. The authors concluded that "Dexmedetomidine (3 microgram) or clonidine (30 microgram), when added to intrathecal bupivacaine, produces a similar prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation".

Murat Teikin, kati I,Yakup et al[13] had done a double-blind, prospective study in 60 patients classified as American Society of Anesthesiologists grade I to II who were posted for lower abdominal, anorectal, lower extremity surgery under spinal anesthesia. Patients were assigned to 1 of 2 groups. All patients received prilocaine 2% for spinal anesthesia. After 10 minutes patients in group 1 received a loading dose of dexmedetomidine 1 μg/kg IV, followed by a maintenance dose of 0.4 μg/kg / h for 50 minutes; group 2 (control) received the same amount of physiologic saline in the same time schedule. Hemodynamic parameters were also assessed. They concluded that "Intravenous dexmedetomidine significantly prolonged the duration of spinal anesthesia and provided a significantly higher level of sedation compared to placebo and was well tolerated by all patients."

Menon DV, Wang Z, Fadel PJ, Arbique D, [14] et al, had done a study to determine whether cocaine's sympathomimetic actions could be reversed by dexmedetomidine which is a alpha2 agonist. They had conducted a study in 22 healthy cocaine-naïve humans. Intranasal cocaine [2 mg/k g] was given to all the subjects ,and then they were divided into two groups. One group received intravenous dexmedetomidine and the other group received intravenous saline. The parameters studied were sympathetic neuronal activity (SNA)measured by microneurography, skin vascular resistance as measured by laser doppler velocitometry ,heart rate and mean arterial pressure. They had observed that in the group that received dexmedetomidine there was no increase in sympathetic neuronal activity ,skin vascular resistance heart rate blood pressure. Dexmedetomidine abolished these increases, whereas intravenous saline was without effect. The authors had concluded that "Dexmedetomidine was effective in blocking sympathomimetic actions of cocaine".

Al-Mustafa MM, Badran IZ, Abu-Ali HM, et al,[10] did a study in 48 patients who underwent transurethral resection of prostate, trans urethral resection of bladder tumor under spinal anesthesia. In that study they had randomly allocated patients into 2 equal groups after spinal isobaric bupivacaine 12.5mg. One group received intravenously a loading dose of dexmedetomidine 1 microgram/kg over 10 minutes and a maintenance of 0.5 micrograms /kg/hour. Another group received normal saline in the same frame. The regression time to reach S1 sensory

level, Bromage scale 0, hemodynamic changes during surgery and level of sedation were studied. In their study they had concluded that “Dexmedetomidine given by intravenous administration prolonged the sensory and motor blocks of bupivacaine spinal anesthesia with good sedation effect and hemodynamic stability”. They had assessed motor level using Bromage scale, sedation using Ramsay sedation scale and time for regression to S1 dermatome.

Kaya FN, Yavascaoglu B, Turker G et al [9]had done a study to compare intravenous dexmedetomidine with midazolam and placebo on spinal block duration, analgesia, and sedation in patients undergoing transurethral resection of the prostate. In this double-blind randomized placebo-controlled trial, 75 American Society of Anesthesiologists' I and II patients were divided into 3 groups .One group received dexmedetomidine 0.5 microgram / kg, Second group received midazolam 0.05 mg / kg and the third group received saline intravenously before spinal anesthesia. All patients received bupivacaine 0.5% 15 mg intrathecally. In their study they had observed that the duration of motor block was similar in all groups. Dexmedetomidine also increased the time to first request for postoperative analgesia ($P < 0.01$) and decreased analgesic requirements. The maximum Ramsay sedation score was greater in the dexmedetomidine and midazolam groups than in the saline group ($P < 0.001$). They had concluded that “Intravenous dexmedetomidine, but not midazolam, prolonged spinal bupivacaine anesthesia”.

Ok HG, Baek SH, Baik SW, Kim HK et al, [15] had done a study to determine the optimal dose of dexmedetomidine that can be given for sedation during spinal anesthesia. In their study they had emphasized on the need of sedation in patients under spinal anesthesia. They had selected one hundred and twenty eight patients, aged 20-70 years who underwent surgery under spinal anesthesia. After spinal anesthesia was initiated with hyperbaric bupivacaine (13 mg), dexmedetomidine (1 µg/kg)as loading dose intravenously was administered over 10 min for all the patients .After that patients were divided into 3 groups and followed by the maintenance infusion which differed in each group. Group A comprising of 33 patients received normal saline, Group B comprising of 35 patients received dexmedetomidine in the dose of 0.2 µg/kg/hr, and Group C with 39 patients received dexmedetomidine in the dose of 0.4 µg/kg/hr. Heart rate, blood pressure, and the bispectral index score (BIS) were monitored and noted during the operation. In the recovery room, modified aldrete score (MAS) was measured. They had concluded that "The loading dose (1 µg/kg/10 min) of dexmedetomidine was sufficient for sedation for surgery of less than 60 min done under spinal anesthesia. This should be followed by a maintenance dose of dexmedetomidine (0.2 µg/kg/hr) for surgeries which last for 90 min".

Annamalai A, Singh S, Singh A, Mahrous DE et al, [16] had done a study in ninety ASA1 or 2 patients posted for surgeries below umbilicus under spinal anesthesia. Patients had been double blind randomized in to three groups. One

group received normal saline 10 ml over 10 minutes before spinal anesthesia. Second group received dexmedetomidine 1 microgram/kg through intravenous route 10 minutes before spinal anesthesia. Third group received dexmedetomidine 1 microgram/kg via intravenous route 10 minutes after spinal anesthesia. All the patients had been advised to take tablet alprozolam 0.25mg and tab ranitidine 150 mg on the previous night and on the day of surgery. They concluded that dexmedetomidine through intravenous route prolonged spinal "sensory blockade in both the groups irrespective of the timing whether it was given before or after spinal anesthesia. The onset of post operative pain was delayed in the group which received dexmedetomidine". The authors further concluded that "The patients in the dexmedetomidine group needed lesser doses of post operative analgesic than the other group".

Jia Song, Woong-Mo Kim et al,[17] had done a study in 45 ASA1 or 2 patients who underwent surgery under spinal anesthesia. In that study they had given dexmedetomidine in three different doses to evaluate the hemodynamic changes and their main aim was to get the optimal dose of dexmedetomidine. All patients were given a loading dose of dexmedetomidine 1 microgram/kg. Then the patients were divided randomly into one of the 3 groups for maintenance dose. One group received dexmedetomidine in the dose of 0.25 microgram/kg/hr, second group received dexmedetomidine in the dose of 0.5 microgram/kg /hr and the third group received dexmedetomidine in the dose of 0.75microgram/kg/hr .They had

clearly stated that patients were able to remain calm after sedation with dexmedetomidine. They had stressed on the need of adequate sedation if the advantages of spinal anesthesia are to be fully appreciated. In their conclusion Jia song et al had stated about the incidence of hypotension as the dose increased. They had emphasized on the fact that "To minimize the risk of hemodynamic instability a maintenance dose of 0.25micrograms/Kg/h r may be most appropriate".

SS Harsoor, D Devika Rani, Bhavana et al[18] did a study to determine the effects of intravenous dexmedetomidine on sensory, motor, haemodynamic parameters and sedation after spinal anesthesia. 50 patients posted for infra umblical and lower limb surgeries under neuraxial blockade were selected and divided into 2 groups. Group D received dexmedetomidine in the dose of 0.5 mcg/kg intravenously bolus over 10 min prior to spinal , followed by an infusion of dexmedetomidine 0.5 mcg/kg/h for the duration of the surgery. Group C received similar volume of normal saline infusion. They concluded that "Administration of intravenous dexmedetomidine during spinal anesthesia hastened the onset of sensory block and prolonged the duration of sensory and motor block with satisfactory arousable sedation".

Abdallah FW1, Abrishami A, Brull et al, [19] had evaluated whether intravenous dexmedetomidine can prolong the duration of sensory block

associated with spinal anesthesia. The parameters assessed by the authors were duration of sensory and motor block, onset time for sensory and motor block, postoperative pain scores, time to first analgesic request, total analgesic requirement and side effects. A total of 364 patients were analyzed from 7 randomized controlled trials. The authors had concluded that "When intravenous dexmedetomidine accompanied spinal anesthesia, sensory block duration was prolonged by about 34% , motor block duration was prolonged by about 17%, and time to first analgesic request was increased by 53% with a significant p value". They had stated that there was increased incidence of bradycardia in dexmedetomidine group. They had concluded that "Intravenous dexmedetomidine prolonged the duration of sensory block, motor block, and time to first analgesic request associated with spinal anesthesia."

Seung Hwan Jung et al[20] had done a study in sixty adult patients who were scheduled for lower extremity surgery under spinal anesthesia. Patients were randomly allocated to one of three groups and administered hyperbaric intrathecal bupivacaine 12 mg. After 5 minutes of spinal anesthesia, patients in groups 1 were administered normal saline 10 ml intravenously, patients in group 2 were given intravenous dexmedetomidine 0.25 microgram/kg, and the third group received dexmedetomidine i.v 0.5 microgram/kg over 10-minutesThey concluded that "The single-dose intravenous dexmedetomidine 0.25–0.5 μg/kg, administered 5 min after intrathecal hyperbaric bupivacaine, improved the

duration of spinal anesthesia without significant side effects". They stated that this effect on spinal anesthesia could be seen even when dexmedetomidine is administered several minutes after spinal anesthesia.

Reddy VS, Nawaz Ahmed Shaik and Venkatsiva Janga[21] had compared the efficacy of intravenous dexmedetomidine with clonidine and placebo on spinal blockade duration, analgesic effect post operatively and sedation in patients undergoing surgery under bupivacaine neuraxial block. 75 patients of the ASA I or II, scheduled for orthopedic lower limb surgery under spinal anesthesia, were randomly divided into three groups each group consisting of 25 patients. Group 1 received dexmedetomidine 0.5 microgram/kg/hr, group 2 received clonidine 1.0 microgram/kg/hr and placebo group 3 received 10 ml of normal saline intravenously before subarachnoid anesthesia with 15 mg of 0.5% hyperbaric bupivacaine They concluded that "Premedication with intravenous dexmedetomidine was better than clonidine for intraoperative sedation and postoperative analgesia during spinal anesthesia with hyperbaric bupivacaine".

Dinesh CN, Sai Tej NA, Yatish B et al, [22] had done a study to evaluate the effects caused by intravenous dexmedetomidine on spinal anesthesia with 0.5% of hyperbaric bupivacaine. One hundred patient posted for elective surgeries under spinal anesthesia were randomized into two groups of 50 each. After subarachnoid block with 0.5% hyperbaric bupivacaine 3 ml, patients in

dexmedetomidine group were given a loading dose of dexmedetomidine 1 microgram/kg of intravenously over 10 min followed by a drip in the dose of 0.5 microgram/kg/hour as maintenance till the end of surgery, whereas patients in control group received an equivalent quantity of normal saline. In their study they concluded that “Intravenous dexmedetomidine prolonged the duration of sensory and motor block of hyperbaric bupivacaine spinal anesthesia”. The authors had observed that the occurrence of bradycardia was higher when intravenous dexmedetomidine was used in bupivacaine spinal anesthesia.

Park SH, Shin YD, Yu HJ, Bae JH, et al[23] had compared the effects caused by two different doses of intravenous dexmedetomidine in elderly patients during spinal anesthesia. They had selected 45 elderly patients (≥ 60 years) classified as ASA1 or II who were posted for transurethral resection of the prostate or transurethral resection of the bladder tumor and the patients were divided randomly into three treatment groups. The group 1 received dexmedetomidine in the dose of 0.5 µg/kg while the second group received dexmedetomidine 1 µg/kg intravenous injection over 10 min before anesthetic induction. The Control group received normal saline. Comparison was done regarding the maximum sensory block level, extension of anesthesia, degree of motor block, sedation level and complications. They had concluded that “There was not much of difference in the groups on achieving the maximum level of sensory block and motor block. But the total time of sensory block was significantly longer in group which received

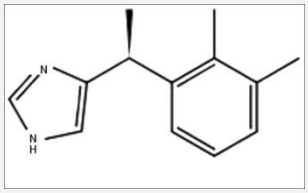
dexmedetomidine 1microgram/kg than in the control group". There was significant increase in bradycardia in the patients who received dexmedetomidine. No complications such as hypotension, nausea, tremor, and hypoxia was reported by them .

DEXMEDETOMIDINE –PHARMACOLOGY

Dexmedetomidine is the dextrorotatory S-enantiomer of medetomidine, which is widely used in veterinary practice[24].

Chemically, Dexmedetomidine is (S)-4-[1-(2,3-dimethylphenyl) ethyl]-3H-imidazole

CHEMICAL FORMULA is $C_{13}H_{16}N_2$[11][12]



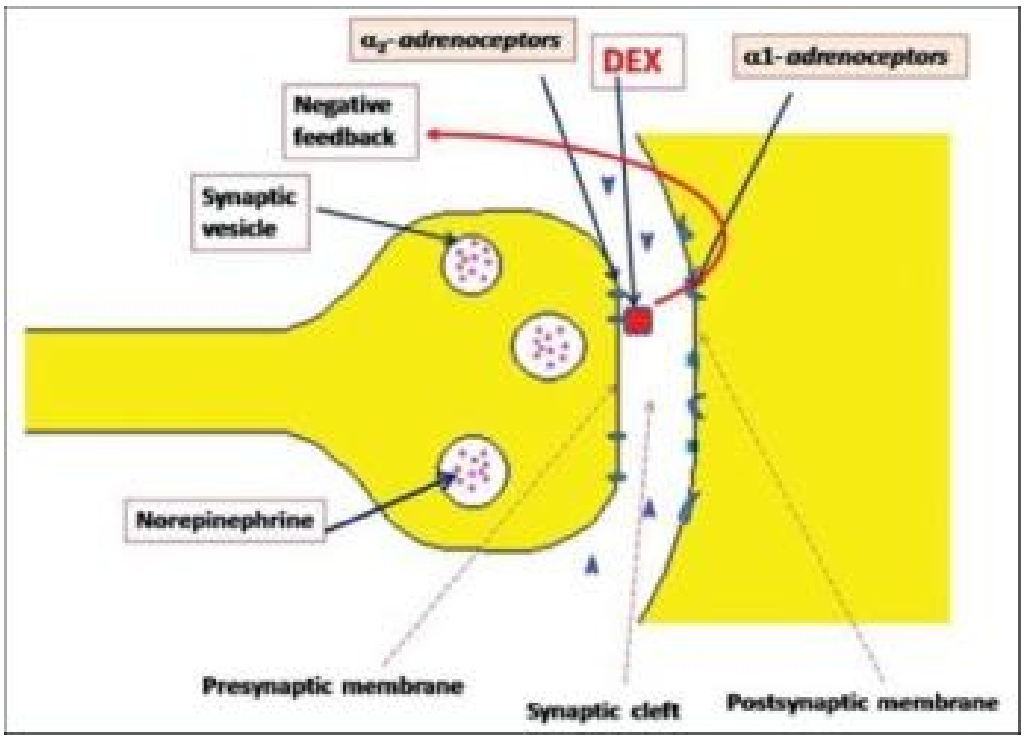
Structure of dexmedetomidine

Clonidine, the first generation alpha 2 agonist has been in use for many years. It is used as an antihypertensive by oral route. When given intrathecally, it prolongs the duration of spinal anesthesia[2]. Intravenously it decreases anesthetic requirements. Dexmedetomidine is a newer drug in the same group and has many advantages when compared to clonidine.

Differences between clonidine and dexmedetomidine[25][26]

CLONIDINE	DEXMEDETOMIDINE
It was first synthesized in 1960s	Dexmedetomidine was first produced in 1980s
Started to use clinically as antihypertensive in 1966.	Approved for clinical use as analgesic and sedative in 1999.
Alpha2;Alpha1 receptor binding ratio is 220:1.	Alpha2;Alpha1 receptor binding ratio is 1620:1
Acts as a partial agonist at alpha receptor.	Acts as a full agonist at alpha receptor.
Octanol /buffer partial coefficient is 0.8.	Octanol /buffer partial coefficient is 2.8.It is 3.5 fold more lipophilic than clonidine.
Plasma half life is 9-11.5 hours.	Plasma half life is 2-2.25 hours.
It is 50% bound to proteins.	It is 94%bound to proteins.
Elimination half life is 8 hours.	Elimination half life is 2 hours.
Distribution half life >10 minutes.	Distribution half life is 5 minutes.
It has been proved that there is 50% reduction in MAC of inhalational agents when clonidine is used.	It has been proved that there is 90% reduction in MAC of inhalational agents when dexmedetomidine is used.

ALPHA 2 ADRENORECEPTOR



Schematic representation of alpha2 Adrenoreceptor

The prime sympathetic neurotransmitter nor adrenaline and the most important adrenal medullary hormone adrenaline mediate their central and peripheral actions through a special type of receptors called adrenergic receptors.

Adrenergic receptors are abundantly present in nearly all peripheral tissues and in the neurons of the central nervous system.[27] There are three types of adrenergic receptors. They are alpha1,alpha2,and beta receptors. These adrenergic receptors are one among cell surface receptors that arbitrate their actions through guanine nucleotide binding proteins [G-Proteins][26].

Alpha2 receptors are again subdivided into 3 subtypes alpha2A,alpha2B,alpha2C[28].They have individual patterns of tissue distribution in the two types of nervous system.

ALPHA 2A are found in	Locus ceruleus of brain, nor adrenergic cell body regions, spleen, pancreas, kidney, blood vessels, urethra, thrombocytes.
ALPHA2B are found in	Kidney, placenta, liver smooth muscle of blood vessel ,thalamus
ALPHA2C are found in	Central nervous system

There are two mechanisms of action of alpha2 receptor agonists. When the alpha2 receptor is activated, calcium entry into the nerve terminal is decreased and this action is responsible for the inhibitory effect on catecholamine secretion[24][29]. N-type voltage-gated calcium channels are directly involved in this particular action. G0 proteins mediate this action.

Alpha2 receptor stimulation also inhibits the enzyme adenylate cyclase. Adenylate cyclase is the key enzyme which is responsible for the production of 3,5-cyclic adenosine monophosphate . The net result is decreased availability of 3 5 cyclic AMP, which is a second messenger.

Specific cyclic AMP-dependent kinases alter the phosphorylation status of target proteins. Due to decreased levels of 3,5,cyclic AMP , major alterations occur in the ion channel activity[26]. This results in hyperpolarization of the cell membrane. Thus neuronal firing is suppressed to a great extent. Activation of G1-protein gated potassium channels on the cell surface causes hyperpolarization of membrane which in turn decrease the firing rate of excitable cells in the central nervous system.

Activation of the $\alpha_2$adrenoceptor present in the presynaptic regions leads to the reduction in the release of neurotransmitter nor epinephrine. Because of the decreased concentration of the prime neurotransmitter, cell signals are not propagated. This leads to decreased sympathetic activity and reduction in blood pressure and heart rate.

Dexmedetomidine, a single drug can produce all these effects and thus avoiding much complicated multiple drug therapy. In multiple drug therapy many

drugs belonging to different classes are usually given to produce all these beneficial effects.

Till date ,there is no clear mention of the mechanism by which alpha 2 agonist cause analgesia. Most likely postulated mechanisms include supraspinal action in the locus ceruleus and spinal action in the substantia gelatinosa that modulate the transmission of nociceptive signals in the central nervous system[29]. Drugs may perform action at any of these sites resulting in analgesia.

By the result of all these actions neither the nerve can fire nor it can propagate signal to the neighboring cells. Ultimately, this results in analgesia by central, spinal and peripheral mechanisms. The net result is a considerable reduction in the stimulation and propagation of nervous signals.

Action in the brain stem

Alpha2 receptors are present in highest densities in the locus ceruleus[12] the chief noradrenergic nucleus in the brain . The locus ceruleus is one of the important centers which control vigilance. The hypnotic and sedative effects of alpha2 adrenergic receptor is due to the action on the locus ceruleus [26] [29].

The locus ceruleus is also the place of origin for the descending medullospinal noradrenergic pathway , which is mainly involved in nociceptive

transmission. This may be the reason for the anti nociceptive action of dexmedetomidine.

The ratios of α_2:α_1 activity is 1620:1 for dexmedetomidine and 220:1 for clonidine. Therefore dexmedetomidine is a more suitable sedative and analgesic agent than clonidine.

Spinal action of dexmedetomidine

Besides actions in the locus ceruleus of the brain stem, dexmedetomidine causes direct stimulation of alpha2 receptors in the spinal cord. The alpha2 receptors are found in abundance in the substantia gelatinosa of the dorsal horn of the spinal cord .On stimulation , these receptors inhibit the firing of neurons accountable for nociception perceived by Aδ type and C type fibers [10][24][25][29]. Release of substance P is also inhibited. This spinal mechanism is responsible for dexmedetomidine action when used epidurally and when administered as an intravenous drug .

Dexmedetomidine causes sedation which resembles physiological sleep without causing respiratory depression.

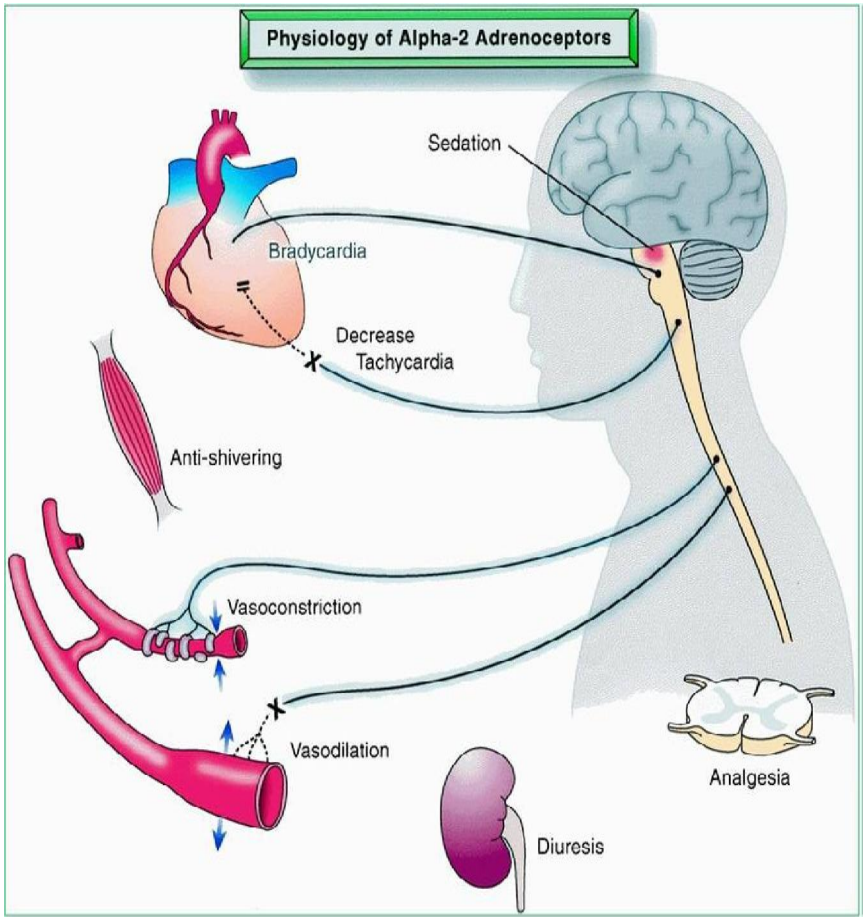


Diagram Showing Physiological Response To Alpha2 Receptor Stimulation

Type of receptor	**Physiological functions and responses of alpha receptors**
Alpha $_{2A}$	Presynaptic inhibition of neurotransmitter release Sedation and anaesthesia Analgesia Bradycardia and hypotension Regulation of blood glucose and insulin homeostatasis Hypothermia

	Inhibition of epileptic seizures Decrease in intraocular pressure. Inhibition of gastrointestinal motility
Alpha$_{2B}$	Vascular smooth muscle contraction Hypertension Placental angiogenesis
Alpha$_{2C}$	Presynaptic inhibition of catecholamine release. Modulation of motor behavior, vascular smooth muscle contraction, Controlled balance of dopamine and serotonin release in the brain.

Pharmacokinetics of Dexmedetomidine

Absorption

Dexmedetomidine is not orally active. The conventional route of administration of dexmedetomidine is intravenous route. Dexmedetomidine shows good bioavailability when administered via other routes such as intranasal, intramuscular, buccal, sublingual, intragastric, neuraxial, regional, intraarticular[24].

Distribution

In elimination phase the half life is 2-3 hours. The steady state volume of distribution is 118 liters.

Protein binding

Dexmedetomidine is 94%protein bound. Hepatic impairment slightly decreases the fraction bound to plasma proteins. In vitro studies conclude that dexmedetomidine does not displace phenytoin, warfarin, propanolol, theophyline, digoxin from plasma proteins. Pharmacokinetics of dexmedetomidine does not change with age, sex or in patients with renal failure[26].

Metabolism

DEX undergoes (> 95%) biotransformation in liver into inactive metabolites. Direct N-glucuronidation is the main pathway of metabolism and glucuronides are the important circulatory and urinary metabolites of dexmedetomidine[24]. Hydroxylation and oxidation are the minor pathways. It is a must to decrease the dose of dexmedetomidine in patients with hepatic failure, because the half life is prolonged in hepatic failure . The half life of dexmedetomidine is 7.5 hours in hepatic failure whereas the elimination half-life in healthy patients is approximately 2 hours.

In clinical doses ,dexomedetomidine acts as a decongestant and as an antisialagogue. It also has antishivering and antiemetic effects. Added benefits of

dexmedetomidine include less respiratory depression when compared to other drugs with additional benefits of cardioprotection, neuroprotection and renoprotection.

Adverse Effects

The commonly seen side effects of dexmedetomidine are bradycardia, hypotension and dry mouth. Both bradycardia and hypotension respond promptly to anticholinergics and vasopressors respectively.

Transient hypertension is seen when given in large doses(due to peripheral alpha2 B receptor stimulation). Other reported side effects include nausea, vomiting, atrial fibrillation, pyrexia, chills, pleural effusion, pulmonary edema, atelectasis, hyperglycemia, hypocalcaemia, acidosis. After administration for more than 24 hours as an infusion , sensitization and up regulation of receptors occur. After abrupt discontinuation, a withdrawal syndrome of nervousness, agitation, severe headaches, and emergency hypertensive crisis can occur[26].

Dexmedetomidine is contraindicated in patients with advanced heart block and ventricular dysfunction. FDA has classified it as a category C risk in pregnancy. Hence the drug should be used with caution in pregnancy.

PHARMACODYNAMICS **Effects on the respiratory & cardiovascular system**;

Activation of alpha $_2$ receptors leads to dose dependent reduction in catecholamine level (up to 89%)[26].Due to inhibition of sympathetic medullary vasomotor center, bradycardia and hypotension occur.

In the respiratory centre alpha2 receptors do not have any active role and so, dexmedetomidine (up to 8 nanogram/ml), has minimal effects on the respiratory system[24]. Hence, dexmedetomidine does not cause respiratory depression.

Dexmedetomidine does not have any direct action on the myocardium[26]. After administering it rapidly in a larger dose (>1 microgram/kg), a biphasic response on BP is seen. There is an initial short hypertensive phase mediated by peripheral alpha2B adrenergic receptor stimulation. Subsequent hypotension is mediated by presynaptic α 2A adrenergic receptors. The direct action on the peripheral vascular smooth muscle causing usually lasts for 10 minutes.

Dexmedetomidine causes dose dependent decrease in the vasoconstriction and shivering thresholds.

The postulated neuro protective action of dexmedetomidine

Dexmedetomidine reduces cerebral blood flow and cerebral metabolic requirement of oxygen . There are many studies which suggest that neuroprotective action is achieved by reducing the levels of circulating and brain catecholamines[26]. Thus it causes balancing of the ratio between cerebral oxygen supplies and demand . It reduces excitation levels, and improves the perfusion in the ischemic penumbra[26]. It reduces glutamate levels responsible for brain cell injury. This suggests the application of dexmedetomidine in head injury patients to enhance cerebral perfusion.

The postulated renoprotective action of dexmedetomidine

Its renoprotective effects include inhibition of renin release, increased glomerular filtration, and increased secretion of sodium and water in the kidney. These actions are probably mediated through peripheral alpha2 receptors.

Antagonism of actions by Atipamezole

After continous infusion is stopped, dexmedetomidine has a rapid and predictable offset of action. Though not orally active, Atipamezole[30](antisedan) is considered to be an effective antagonist for reversing psychomotor disturbance and vigilance caused by dexmedetomidine. Both dexmedetomidine and Atipamezole show linear pharmacokinetics . The elimination half-lives of the two drugs is approximately 2 hours. This is a clear benefit while considering the

promising clinical applications for long term use of dexmedetomidine in intensive care unit.Any adverse effect can be countered by Atipamezole.

Clinical actions of dexmedetomidine

Centrally mediated actions of dexmedetomidine

- Bradycardia and hypotension
- Sedation, anxiolysis ,hypnosis
- Analgesia

Peripherally mediated actions of dexmedetomidine

- Decrease of GI secretions, salivary secretion and decreased gastro intestinal peristaltic movement.
- Contraction of smooth muscle including blood vessels .
- Renin release is reduced by the inhibition of rennin angiotensin system. Glomerular filtration rate (GFR) is increased. Sodium excretion and water excretion is enhanced. All these effects contribute to the diuretic effect of dexmedetomidine.
- Significant reduction in intra-ocular pressure
- Decreased release of insulin from the pancreas .
- Reduced platelet aggregation
- Shivering threshold is decreased approximately by 2ºC.

Clinical Applications of dexmedetomidine

Peri-operative uses of dexmedetomidine

1.Attenuation of intubation response

Dexmedetomidine decreases stress response to tracheal intubation/extubation when given in the dose of 1 microgram /kg with lesser doses not being effective. It has analgesic sparing effect which lasts up to 24 hour[31].

2.As an adjuvant to GA

Dexmedetomidine boosts the anesthetic effects of all anesthetic agents despite the method of administration (intravenous, volatile or regional block). It has minimum alveolar concentration (MAC) reducing and opioid sparing properties, which results in decreased use of inhalation anesthetics and opioids[32][33].

The reduction in myocardial oxygen demand and rate pressure product reduce myocardial ischemia and infarction which is very beneficial for cardiac patients. When used in obstructive sleep apnoea and in morbidly obese patients, it does not cause any cardio-respiratory depression and helps in faster, neuromuscular recovery[34]. In literature search, case reports are available stating

the use of dexmedetomidine as an anesthetic adjuvant intraoperatively in reducing episodes of abrupt hypertension that occurs during manipulation of the tumor in surgery for pheochromocytoma .

3.As an agent for producing Controlled hypotension

In the literature there are many studies which say that dexmedetomidine is equally potent as remifentanil and esmolol in controlled hypotension application. The parameters studied were intraoperative bleeding, preoperative hemodynamics, lactate levels[24].

4.As an adjuvant to regional anesthesia

Researchers are doing intense search to find an ideal adjuvant to regional anesthesia . The alpha 2 adrenergic agonists, in particular dexmedetomidine has both analgesic and sedative actions. 3 μg DEX and 30 μg clonidine are equipotent intrathecally. The addition of 5 μg of intrathecal dexmedetomidine prolonged the post-operative analgesic effect of ropivacaine by 8 hours[25].

5.As an adjuvant in peripheral nerve block

Dexmedetomidine (in the dose of 0.5 microgram/kg)when added to bupivacaine in nerve blocks prolongs the duration of sensory block, and decreases tourniquet pain.

6. The role of dexmedetomidine in Cardiac anesthesia-

In American Heart Association (AHA) guideline 2002 α2-adrenoceptor agonist has been mentioned as a grade IIb agent . They are particularly of use in situations when β –blockers are contraindicated. In the human physiology hemodynamic, sympathetic activity and renal function are closely interrelated. Dexmedetomidine induced sympatholysis might attenuate harmful hemodynamic events responsible for deterioration of renal function in patients undergoing elective CABG with extracorporeal circulation[24].

7. The role of dexmedetomidine in Neuroanesthesia-

Anesthesia for awake craniotomy which needs cooperation of patients presents a challenge to the anesthesiologist. Common side effects associated with conventionally used neuroleptanalgesia are drowsiness, respiratory depression, agitation and intra operative seizure. Using dexmedetomidine we can achieve a level of sedation and analgesia to complete the neuropsychiatric testing for electrocorticography ,for the mapping of the cortical language area, for bone flap removal, and to perform an awake tumor resection [35].

8. The role of dexmedetomidine in monitored anesthesia care

Dexmedetomidine is an ideal agent for many procedures like fiberoptic bronchoscopy, ophthalmic procedures ,head and neck procedures, ,vascular surgeries and dental procedures. Dexmedetomidine provides better patient satisfaction, less respiratory depression and less opiod requirements. Intraocular pressure is decreased by dexmedetomidine which is an added advantage in ophthalmic procedures. Intravenous dexmedetomidine in the dose of 0.6microgram/kg prevented the rise of intraocular pressure after suxamethonium.

9.As Post operative analgesic

Its wide safety margins and respiratory function preservation allows continued use of dexmedetomidine in extubated patients. It decreases the incidence of nausea and vomiting postoperatively. Dexmedetomidine when added to morphine in patient controlled analgesia has been proved to increase post operative analgesia .

10. The role of dexmedetomidine in Intensive care unit

Sedation plays an important role in intensive care. The sleep induced by dexmedetomidine mimics normal sleep and this is an advantage during weaning from mechanical ventilation.

Reduced stay in intensive care unit, decreased duration of ventilation, haemodynamic stability and reduced agitation are the proven advantages of

dexmedetomidine. Dexmedetomidine need not be stopped and the sedation can be maintained following tracheal extubation[36, 37]. Dexmedetomidine is an alternative in patients developing tolerance to opiods.

COMPARISON OF SEDATIVES COMMONLY USED IN ICU

EFFECTS	DEXMEDETOMIDINE	MIDAZOLAM	PROPOFOL	OPIODS	HALOPERIDOL
sedation	YES	YES	YES	YES	YES
analgesia	YES			YES	
anxiolysis	YES	YES			
organ protection	YES		YES		
control of stress response	YES				
mimics normal sleep	YES				
anti shivering agent	YES				
cooperative sedation	YES				
facilitation of ventilation during weaning	YES				
respiratory depression	NO				NO
control of delirium	YES				YES

11.The role of dexmedetomidine in pediatrics

We can avoid unnecessary needle pricks and reduce the dose of opiods by using dexmedetomidine through noninvasive routes (intranasal, buccal). The pharmacokinetics of dexmedetomidine in infants and children is more or less similar to that in adults. In pediatrics the main upcoming role of dexmedetomidine is to prevent emergence delirium [36][37]. In children, it is used in various applications including procedural-sedation, sedation for mechanical ventilation, for preventing emergence delirium. Dexmedetomidine via intravenous route or intramuscular route has been used to sedate children for procedures without stimulation like MRI and CT scan. In children the dose required for bolus is 2to3 microgram/kg and for infusion is 2 µg/kg/hour. The combination of dexmedetomidine and ketamine makes pharmacologic sense as the two

medications have the potential to balance the hemodynamic and adverse effects which make both a very effective combination. Khaled Al Zaben *et al* had reported the use of dexmedetomidine (5-10 μg /kg/h) as the main anesthetic , supplemented by incremental propofol dose (100 μg/kg/min)for three children with tracheomalacia[24].

12.The role of dexmedetomidine in Obstetric anesthesia

In view of its high lipophilic nature ,dexmedetomidine is retained in the placental tissue and this results in less foetal transfer and a reduced incidence of fetal bradycardia. Continuous intravenous dexmedetomidine infusion is being used as an adjuvant to opioids in labour analgesia[24]. Dexmedetomidine has an antinociceptive effect to visceral pain. Dexmedetomidine also provides hemodynamic stability, anxiolysis. Dexmedtomidine causes stimulation of uterine contraction which is a beneficial effect in parturient mothers.

Caution about loading dose

Most of the adverse events associated with use of dexmedetomidine occur during or briefly after loading of the drug. Multiple studies have demonstrated that by omitting or reducing the loading dose, adverse effects can be

reduced. Although, avoiding the loading dose may prevent erratic hemodynamic effects ,it may cause delay in onset of action and time to reach steady state.

BUPIVACAINE IN SPINAL ANESTHESIA

Basic pharmacology of bupivacaine;

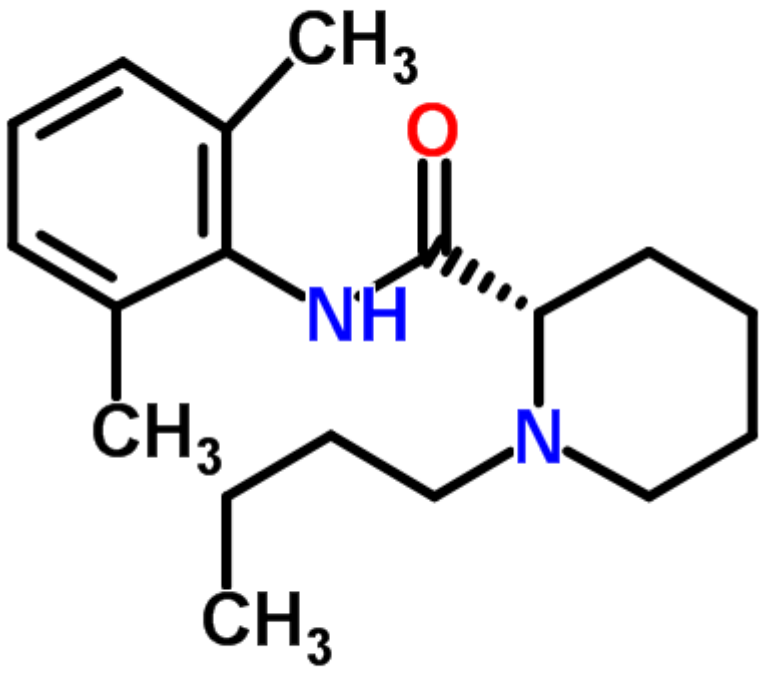
Molecular Formula: C18H28N2O

Average mass: 288.427704 Da

Chemical name;

(2S)-1-Butyl-N-(2,6-dimethylphenyl)-piperidinecarboxamide

Chemical structure;



Bupivacaine is a long acting spinal anesthetic .Other long acting local anesthetics are tetracaine and levo bupivacaine.

Amide type-Bupivacaine and Levo bupivacaine.

Onset time-5to 10 minutes.

Total duration of spinal block-90-120 minutes.

MECHANISM OF ACTION OF BUPIVACAINE

All local anesthetics block sodium channels and block entry of sodium into the cells thereby preventing depolarization. So the nerve cannot get depolarized and the signal is not propagated. In spinal anesthesia we commonly use hyperbaric bupivacaine.

BARICITY OF THE SOLUTION; Baricity determines the spread of local anesthetic in the spinal space and is equal to the density of the local anesthetic divided by the density of the CSF at 37^0 c.

The density of cerebrospinal fluid is less than 1.0069. In spinal anesthetics baricity is mentioned in comparison to that of cerebrospinal fluid.

HYPOBARIC SOLUTION

When the solution of the drug has a density lesser than cerebrospinal fluid ,it is called hypobaric bupivacaine. Hypobaric bupivacaine is produced when we boil bupivacaine to 37^0c. These solutions tend to spread upwards against gravity. It is of use particularly in fracture hip when the patient has to lie in a lateral position with the operating site positioned above.

ISOBARIC SOLUTION

Isobaric solution of tetracaine is produced by adding nymphanoid crystals to cerebrospinal fluid. Isobaric bupivacaine is also available. The height of the block is dependent on the total milligram of the drug instilled in to the subarachnoid space. Isobaric bupivacaine is available in the concentration of 0.5% and 0.75%.

HYPERBARIC SOLUTION

Hyperbaric bupivacaine is available in the concentration of 0.5% and 0.75% in dextrose 8.25%. It is widely used. The height of block is more dependant on the position of the patient after the block.

SADDLE BLOCK

Make the patient sit. The local anesthetic gets concentrated in the sacral area.

HEAD DOWN POSITION

More concentrated in the thoraco lumbar region.

LATERAL POSITION

Dense block on the dependant side.

FACTORS DETERMINING THE CHARACTER OF BLOCK

- Potency of the spinal anesthetic is related to the lipid solubility.
- The total duration of action of the anesthetic is more related to the protein binding.
- The onset of action is related to the availability of the drug in the base form.

Lipid solubility determines the potency of the anesthetics. Low lipid soluble medications need to be given in higher concentrations of local anesthesia to obtain the expected nerve blockade. High lipid solubility can elicit anesthesia at low concentrations. Protein binding determines the duration of action of the anesthetic. Higher proportions of protein binding results in longer duration of action.

pKa of a solution

The pKa of a local anesthetic is defined as the pH at which ionized and nonionized forms are present in equal concentrations in solution. pKa of

bupivacaine is 8.1.This is important because the nonionized easily diffuses across the lipophilic nerve sheath and acts on the sodium channels in the nerve membrane. The onset of action is more dependant on the amount of the medication available in the base form. All local anesthetics obey the rule that "If the pKa is lower , the onset of action is faster".

The fate of local anesthetics in the Subarachnoid Space

Pharmacokinetics of local anesthetic consist of uptake and elimination of the drug. Four factors play a role in the uptake of local anesthetics from the cerebrospinal fluid into neuronal tissue.

The factors are

(1) concentration of the dug in cerebrospinal fluid,

(2) surface area of neurons present in CSF,

(3) lipid content of neurons,

(4) vascularity of the nervous tissue.

The uptake of local anesthetic is most dense at the site of highest concentration in the CSF and is decreased proportionately upwards and downwards from this point.

Local anesthetics in the subarachnoid space are taken up both by the nerve roots and the spinal cord. If the surface area of the nerve root is high , the the uptake of local anesthetic is greater.

There are two postulated mechanisms for the uptake of local anesthetics in the spinal cord.

The first method is by simple diffusion from the CSF to the pia mater and thence into the spinal cord, which is comparatively a slow process. Only the superficial layer of the spinal cord is affected by diffusion of local anesthetics.

The second method of uptake of the drug is by extension into the Virchow–Robin spaces , which are the layers of pia mater that surround the vasculature that penetrate the central nervous system. The spaces of Virchow–Robin are inter connected with the neuronal clefts which surround nerve cell bodies in the spinal cord and penetrate through to the deeper areas of the spinal cord.

The intensity of anesthetic effect depends on the

1.Diameter of the nerve fibers

2.Myelination of the nerve fibers.

3.conduction velocity

Order of affection of fibres in spinal anesthesia

1.Sympathetic neurons

2.Pain

3.Temperature

4.Touch

5.Proprioception

6.Tone of skeletal muscles

Spread of local anesthetic in the subarachnoid space depends upon

1. **Attributed to the properties of the drug**

- Baricity of the drug
- Dose given
- Volume of the entire solution
- Specific gravity of the solution

2.Patient characteristics

- Position of the patient during and after injection
- Height of the patient which alters anatomy of the spinal column.
- Decrease in CSF volume which plays a major part when there is increased intra abdominal pressure due to increased weight, pregnancy, etc.

3.Technique

- Injection site and the direction of the bevel of the needle.

FUNCTIONAL ANATOMY OF SPINAL BLOCKADE

Five ligaments hold the spinal column together.

They are;

1.supraspinous ligaments connect the apices of spinous processes

2.Inter spinous ligaments connect the spinous processes.

3.Ligamentum flavum connect the lamina above and below.

4.Anterior longitudinal ligament connect the vertebral bodies.

5.Posterior longitudinal ligament connect the vertebral bodies.

Important dermatomal levels

The tenth thoracic (T10) dermatome -Umbilicus.

The sixth thoracic (T6) dermatome -Xiphoid.

The fourth thoracic (T4) dermatome- Nipples

Dermatomal levels needed for various surgeries

Procedure	Dermatomal Level
For Upper abdominal surgery	T4
Intestinal, gynecologic, urologic surgery	T6
Transurethral resection of the prostate	T1O
Vaginal delivery of a fetus, and hip surgery	T10
Lower leg surgery	L1
Foot and ankle surgery	L2
Perineal and anal surgery	S2 to S5 (saddle block)

Absolute contraindications to spinal anesthesia*:*

- When there is Patient refusal
- Presence of Sepsis at the site
- Severe Hypovolemia
- Coagulopathy
- Indeterminate neurologic disease

- Increased intracranial pressure

Relative contraindications

- Infection distant from the site of injection
- Duration of surgery is not known.

PHYSIOLOGY OF SPINAL ANESTHESIA

Cardiovascular changes after spinal anesthesia

Spinal anesthesia causes sympathectomy. So major hemodynamic changes occur during spinal anesthesia. Sympathetic flow is thoraco lumbar flow. The height of the block determines the extent of blockade of sympathetic system. So hypotension and bradycardia, the important effects of sympathetic blockade are common after spinal anesthesia.

Hypotension is caused due to both arteriolar dilatation and veno dilatation. Veno dilatation is more than arteriolar dilatation. Pre load to the heart mainly depends on the position of the patient after spinal anesthesia. Veins above the heart cause increase in venous return whereas veins below the heart cause pooling of blood.

Bradycardia occurs due to sympathetic blockade of cardio accelerator fibers. Bradycardia is exaggerated in young people and in patients and in patients who are on betablockers for a long time.

Risk factors for causing exaggerated hypotensive response after spinal anesthesia

1.Volme contracted state(Hypovolemia)

2.History of Hypertension

3.High Level of sensory block

4. Age more than 40 years

5.Obesity,elevated BMI

6.Combination of general and spinal anesthesia

7.Addition of adjuvants like phenylephrine to the local anesthetic

8.History of Chronic alcohol consumption

Decreased venous return can be treated by

- Crystalloid infusion
- Trendelenburg position
- Combined alpha and beta adrenergic agonist like ephedrine.

Excessive crystalloid infusion can result in cardiac failure and pulmonary edema. It may necessitate catheterization of bladder also.

Head down position should be restricted to 20^0 down. Inclination more than this can decrease cerebral perfusion due to increased pressure in the internal jugular vein.

The Bezold Jarisch reflex

This is a cardio inhibitory reflex. It may occur after central neuraxial blockade.

Classical triad consists of

- Bradycardia
- Hypotension
- Cardio vascular collapse.

Bezold Jarisch reflex is not a vaso vagal reflex.

Changes in respiratory system after spinal anesthesia

Pulmonary function is not altered much after spinal anesthesia. Lung volumes, dead space, arterial blood gas, minute ventilation and shunt fraction do not change to a great extent after spinal anesthesia. The main effect seen is paralysis of intercostal and abdominal muscles which result in decrease in peak expiratory flow.

Patients with obstructive pulmonary disease who depend on accessory muscles for effective ventilation can show a reduction in respiratory function after spinal anesthesia.

Patients with normal respiratory function may experience dysnoea sometimes. If they are able to vocalize properly ,there will not be any respiratory compromise.

Minimal oxygen supplementation is a must in spinal anesthesia.

Changes in gastrointestinal system after spinal anesthesia

Gastro intestinal system receives sympathetic fibres from T6 toL2.

Due to unopposed vagal activity ,the following changes occur

- Relaxation of sphincters
- 2.Increase in secretions.
- 3.contraction of bowel

These changes usually lead to nausea. So, atropine is more beneficial in combating nausea after spinal anesthesia.

Changes in hepatobiliary system after spinal anesthesia

Hepatic blood flow is predominantly related to arterial blood flow. Spinal anesthesia decreases venous return. Pre load is decreased. Hence arterial pressure and cardiac output get reduced. As arterial blood supply is decreased, total blood flow to the liver decreases after spinal anesthesia. Hepatic blood flow predominantly depends on the mean arterial pressure. If mean arterial pressure (MAP) is maintained , hepatic blood flow is maintained.

Patients with liver diseases should be carefully monitored and mean arterial pressure should be maintained with in normal limits. In patients with liver disease either regional or general anesthesia can be given, as long as the MAP is kept close to baseline.

AUTOREGULATION OF RENAL BLOOD FLOW

Autoregulation of blood flow to the kidney is well maintained above a mean arterial pressure of 50 mm Hg.Renal blood flow is decreased when the mean arterial pressure becomes lower than 50 mm Hg.

EQUIPMENTS FOR SPINAL ANETHESIA;

1.Spinal tray

a.sponge holding forceps

b.sterile gauzes

c.bowl

d.sterile drapes

2.Spinal Needle

Spinal needle consists of a needle and a close fitting removable stylet.

Different types available are;

a. Quinke's needle

b. Sprotte's needle } Pencil point needles

c. Whitaker's needle }

Needles are available in gauges of 29,27,25,23.

POSITION OF THE PATIENT

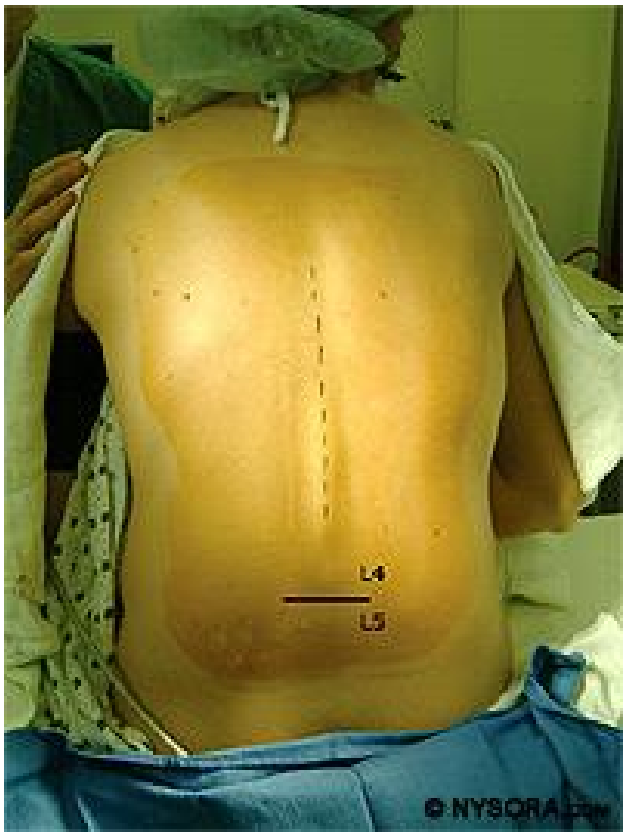
Proper positioning is essential for technical ease and a resultant successful block. A trained technician should be present to keep the patient in optimal position.

The different positions are

1.Lateral decubitus position.

2.Sitting position.

3.Prone position in rectal, perineal and lumbar surgeries if the patient needs to be in that position during surgery.



Patient In Sitting Posture

Technique of lumbar puncture

Appropriate monitors must be connected.

Airway and resuscitation equipments are kept available.

Oxygen supplementation for all patients.

Skin is cleaned with sterile cleaning solution

The area is draped with a sterile central hole towel.

A small wheal of local anesthetic,2% lignocaine is injected at the site of insertion.

The various approaches are;

1. Midline approach.
2. Paramedian approach
3. Taylor's approach.

MIDLINE APPROACH

1. Iliac crests are palpated .The line between the two iliac crests intersects L4 vertebra or L4-L5 space.

2. Palpate the interspace and the spinal needle is inserted.

3. The spinal needle passes through the following structures;

   a.Skin

   b.Subcutaneous tissue

   c.Supraspinous ligament

   d.Inter spinous ligament.

   e.Ligamentum flavum.

   f.Epidural space.

   g.Duramater

   h.Arachnoid mater

2.Paramedian or lateral approach

Two methods are available

First method is

- ❖ The needle is inserted 1 cm lateral to the spinous process.
- ❖ First structure to be felt is usually ligamentum flavum.
- ❖ Then the needle is directed towards the midline.

Second method is

- The needle is inserted 1 cm lateral and inferior to the interspace.
- Lamina is encountered.
- Walk through the lamina and enter the sub arachnoid space

PARAMEDIAN APPROACH OF LUMBAR PUNCTURE

3.TAYLOR APPROACH

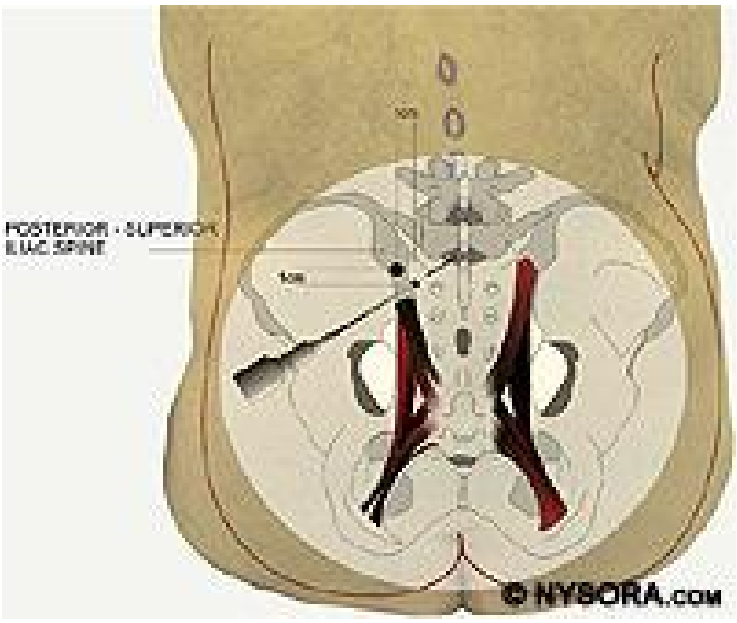
A paramedian approach in which the needle is directed toward the L5-S1 interspace.

L5-S1 interspace is the largest space and can be tried if other methods fail.

It can be done in any position namely lateral decubitus, sitting or prone.

The needle is inserted at a point 1 cm medial and inferior to the posterior superior iliac spine, then angled cephalad 45–55 degrees.

The needle is directed medially to reach the midline at the L5 spinous process. The first significant resistance is the ligamentum flavum, and then the dura mater is punctured.

. 

Complications of spinal anesthesia

A.Local anesthetic induced neurotoxicity and neurological injury.

B.Cardio vascular instability.

C.High blockade.

D.Post dural puncture headache.

E.Transient neurological symptoms more common with lidocaine.

F.Permanent neurological injury.

1. Cauda equina syndrome.
2. Arachnoiditis.
3. Meningitis
4. Spinal hematoma formation.

Factors to be followed to reduce neurological complications

- Absolute sterility.

- Assurance of normal coagulation parmeters.
- Lowest efficient dose of the drug.
- Complete neurological examination before spinal anesthesia.
- Use of preservative free solution.

MATERIALS AND METHODS

AIM OF THE STUDY

The purpose of this study was to investigate the effect of small single dose intravenous dexmedetomidine administration on prolonging duration of hyperbaric bupivacaine spinal anesthesia. Institutional ethical board committee approval was obtained before the commencement of the study.

Sample size calculation

This study was a prospective randomized controlled study. Study population comprised of 100 adult patients classified as ASA 1 or 2 who were scheduled for total abdominal hysterectomy or vaginal hysterectomy under spinal anaesthesia.

INCLUSION CRITERIA

1) ASA grade I-II

2) Age < 60 years

3)Patients who were posted for Total abdominal Hysterectomy and vaginal hysterectomy under spinal anesthesia.

EXCLUSION CRITERIA

1) Patients on sedatives/opioids/antidepressants in the week prior to surgery.

2) Patients with morbid obesity.

3) Patients with diabetes and renal disease.

4) Pre-operative baseline heart rate equal to or less than 60/min

5) Pre-operative baseline systolic blood pressure equal to or less than 90 mm Hg.

All patients were examined on the day prior to surgery and pre anesthetic evaluation chart was checked. Special consideration was given to elicit hypertension, breathlessness, pain, cough, wheezing ,previous anesthesia and drug sensitivity. The patient's weight, height was measured. The nutritional status, airway assessment, spine examination were also done on the previous day.

A detailed examination of all systems was done. Pre operative routine investigations such as hematocrit ,renal function tests, complete blood count, blood grouping, platelet count, chest radiography, electrocardiography were checked properly.

All patients were informed about the procedure and written consent was taken. All patients were kept nil per oral for 10 hours and were given premedication with tablet alprazolam 0.5 milligram, tablet. ranitidine 150 milligrams and tablet metaclopramide 10 milligram on the night before surgery.

After putting the patient on operating table electrocardiography, peripheral saturation of oxygen (SpO2) and non-invasive blood pressure monitor and all the basal parameters were recorded. An IV access with 18 gauge cannula and all patients were preloaded with Ringer lactate solution 10 ml/kg body weight. Patients were randomly allocated to one of the two groups by slips in box technique.

Patient was put in lateral decubitus position.Lumbar puncture was performed at L3-L4 level with Quincke type 25 gauge spinal needle and injection hyperbaric bupivacaine 17.5 mg was given intrathecally over 30 seconds. If there was technical difficulty at L3- L4 level ,one more try was given at L2-L3 level with Quinckes needle25 gauge. If found un successful those patients were excluded from the study.

In group D patients received hyperbaric intrathecal bupivacaine anesthesia 3.5ml 0.5% (17.5 mg) and intravenous Dexmedetomidine 0.5mcg/Kg in10 ml normal saline over 10 minutes.

In group C patients received Hyperbaric bupivacaine anaesthesia 3.5 ml 0.5% (17.5mg) and intravenous normal saline 10 ml over 10 minutes.

Vitals were recorded [Heart rate, Non invasive blood pressure monitoring, pulseoximetry, Respiratory rate] every 5 min till the end of surgery and then every 5 min in post anaesthesia care unit.

MONITORING OF PATIENTS

Hypotension was defined as systolic BP of less than 90 mm Hg or 25% lesser than the baseline value and was treated with 6 mg of Inj. Mephenteramine intravenously.

Bradycardia was defined as heart rate <50/min and was treated Inj. Atropine 0.6 mg.

ASSESSEMENT OF SENSORY BLOCKADE

Sensory blockade was checked with an alcohol swab in mid axillary line . Sensory blockade was assessed after 5 minutes and there after maximum level of blockade was noted . After this point surgery was started. Vitals monitored through out the procedure. At the end of surgery, sensory level was noted. Two dermatome regression time from the maximal level and regression to level S1was noted every 20 min post operatively. Time of spinal injection was taken as 0.

ASSESSMENT OF MOTOR LEVEL

Motor level was assessed using Modified Bromage scale[38] at 5th minute and every 20 min after the end of surgery.

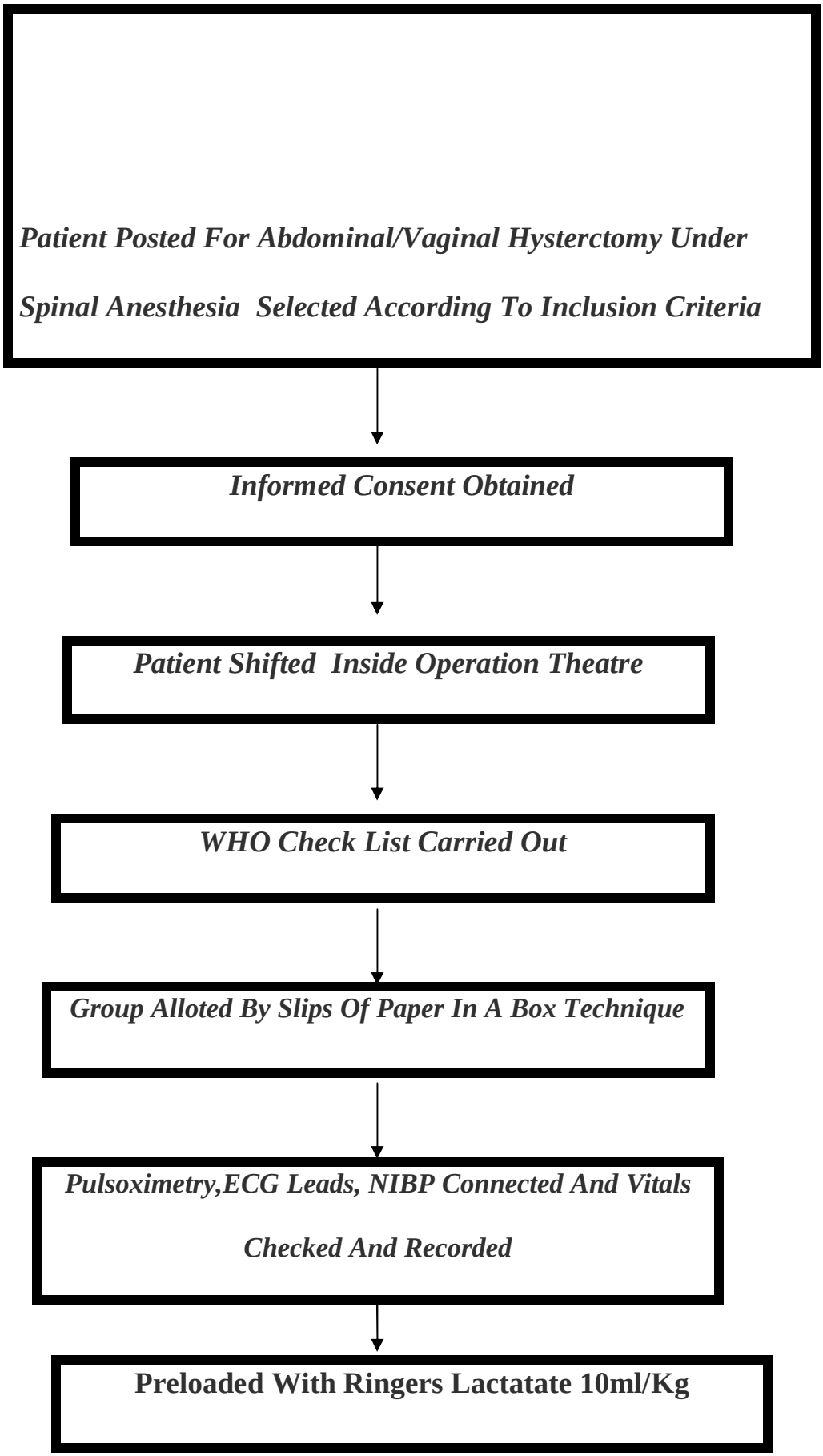
1. BROMAGE0-Able to move hip, knee, ankle.
2. BROMAGE1-Unable to move hip ,but is able to move knee and ankle.
3. BROMAGE2-Unable to move hip and knee but is able to move the ankle.
4. BROMAGE3-Unable to move hip, Knee and ankle.

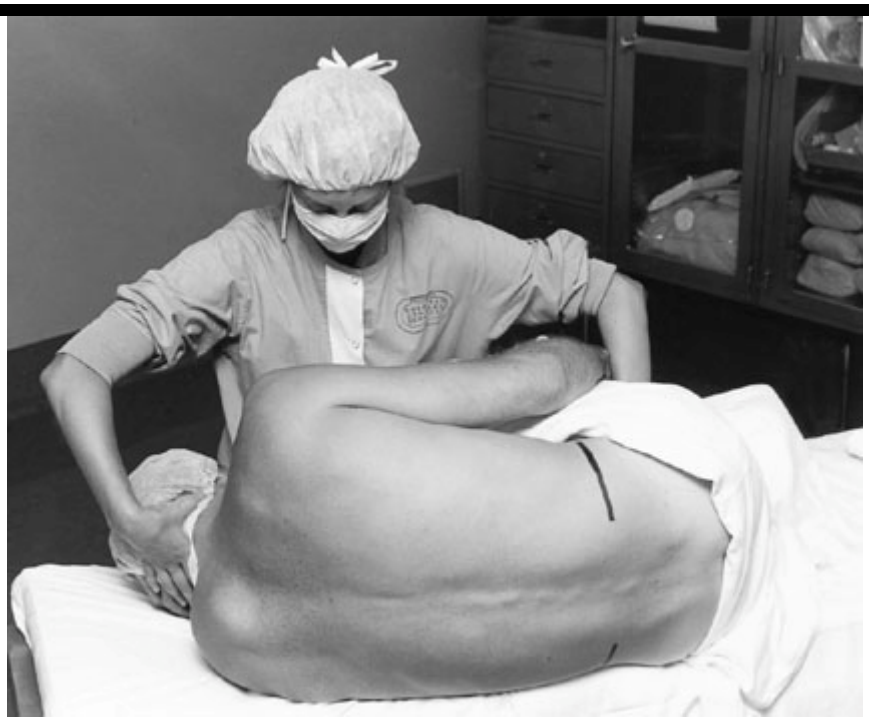
ASSESSMENT OF SEDATION

Sedation was assessed by Ramsay sedation scale[39] at the 5th minute. Again sedation was assessed at the end of the surgery. Level of sedation was evaluated every 20 minutes post operatively for 4 hours.

Ramsay Level of sedation scale.

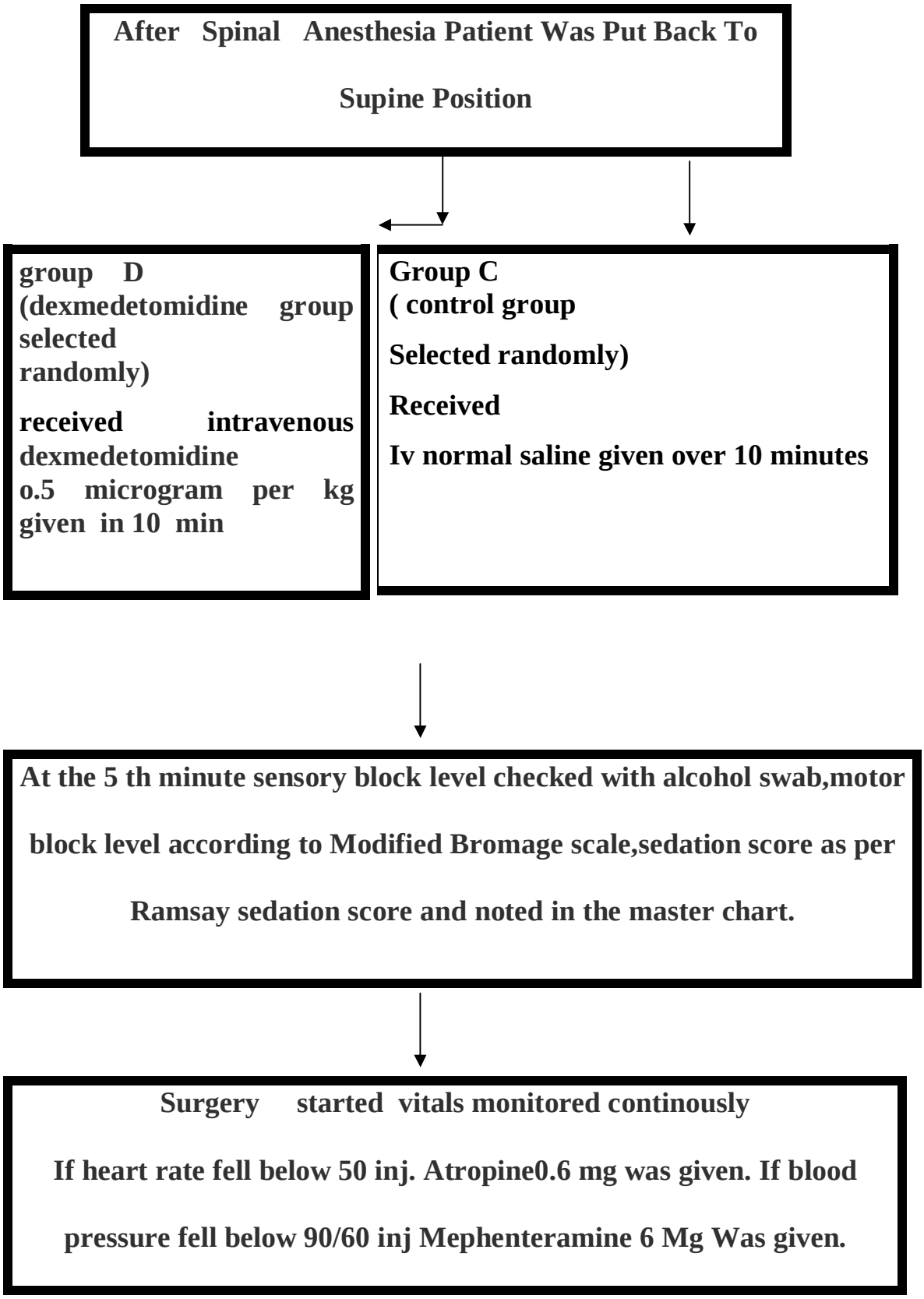
1. Awake and anxious, agitated, or restless
2. Awake, cooperative, accepting ventilation, oriented, tranquil
3. Awake; responds only to commands
4. Asleep; brisk response to light glabellar tap or loud noise
5. Asleep; sluggish response to light glabellar tap or loud noise stimulus but does not respond to painful stimulus
6. Asleep; no response to light glabellar tap or loud noise


Patient Posted For Abdominal/Vaginal Hysterctomy Under
Spinal Anesthesia Selected According To Inclusion Criteria
Informed Consent Obtained
Patient Shifted Inside Operation Theatre
WHO Check List Carried Out
Group Alloted By Slips Of Paper In A Box Technique
Pulsoximetry,ECG Leads, NIBP Connected And Vitals
Checked And Recorded
Preloaded With Ringers Lactatate 10ml/Kg



Spinal Block Performed In The Lateral Decubitus Position

Patient was placed in lateral decubitus position, Quinkes 25 gauge needle was inserted . Sub arachnoid block performed by giving 0.5% hyperbaric bupivacaine 3.5 ml(17.5 mg) given over 30 seconds.


After Spinal Anesthesia Patient Was Put Back To
Supine Position
group D
(dexmedetomidine group selected randomly)
received intravenous dexmedetomidine o.5 microgram per kg given in 10 min
Group C
(control group
Selected randomly)
Received
Iv normal saline given over 10 minutes
At the 5 th minute sensory block level checked with alcohol swab,motor block level according to Modified Bromage scale,sedation score as per Ramsay sedation score and noted in the master chart.
Surgery started vitals monitored continously
If heart rate fell below 50 inj. Atropine0.6 mg was given. If blood pressure fell below 90/60 inj Mephenteramine 6 Mg Was given.

At The End Of Surgery Sensory Level, Grade Of Motor Block , Sedation Score Noted

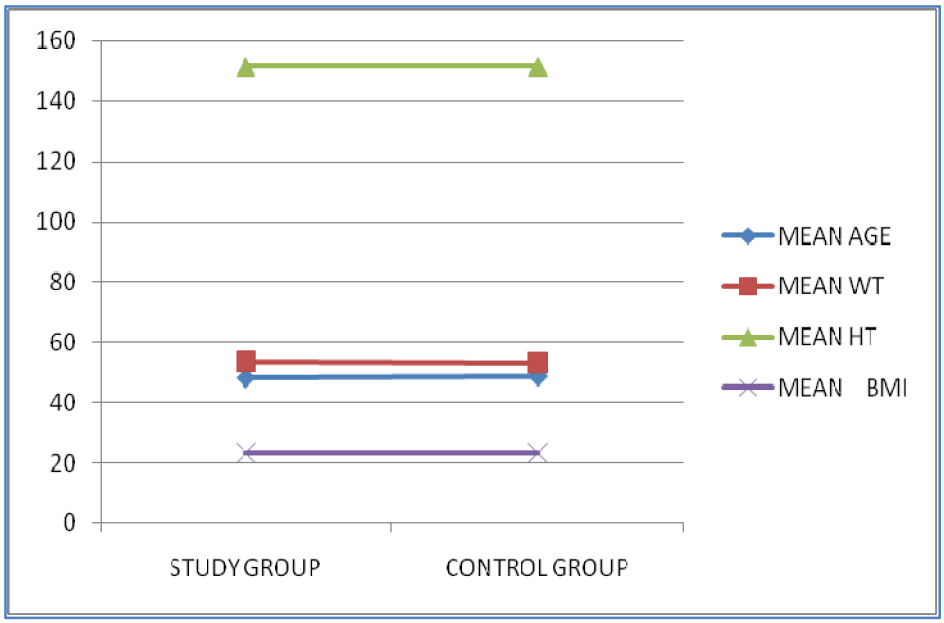
After this sensory level, grade of motor block , sedation score checked every 20 minutes for 260 minutes. Continous monitoring of vitals carried on till 260th minute.

RESULTS AND ANALYSIS

100 patients were enrolled in the study ,50 patients were randomly allocated into the study group and 50 patients to the Control group. All 100 patients successfully completed the protocol and they were included in the analysis of data. The demographic data of the patients in the two groups were studied and the analysis revealed no significant difference in both the groups. In the demographic data the continuous variables studied were age, body mass index.

DEMOGRAPHIC DATA

character	Group Statistics				
	groupcode	Number	Mean	Std. Deviation	Std. Error Mean
Age	study group	50	48.24	4.792	0.678
	control group	50	48.78	4.82	0.682
wt	study group	50	53.64	2.905	0.411
	control group	50	53.2	2.399	0.339
Height	study group	50	151.54	3.215	0.455
	control group	50	151.38	3.09	0.437
BMI	study group	50	23.39	1.67	0.24
	control group	50	23.24	1.41	0.20



GRAPHIC REPRESENTATION OF DEMOGRAPHIC VARIABLES IN BOTH THE GROUPS

From this graph as the line joining the means of both groups is a straight line it is clearly evident that both the groups were similar in all the characteristics like age, height, weight, BMI. As the study was conducted in abdominal hysterectomy and vaginal hysterectomy only, the type of surgery and the sex of the patients were not taken for comparison.

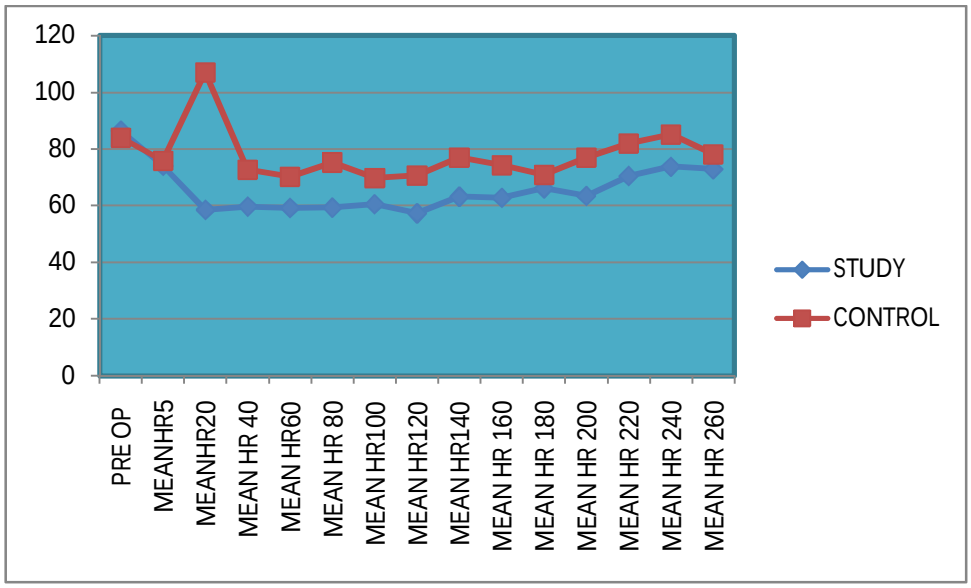
DESCRIPTIVE ANALYSIS OF DEMOGRAPHIC VARIABLES

character	Independent Samples Test									
	Levene's Test for Equality of Variances					t-test for Equality of Means				
								95% Confidence Interval of the Difference		
		F	P value	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Age	Equal variances assumed	0.001	0.977 (NS)	-0.562	98	0.576(NS)	-0.54	0.961	-2.448	1.368
wt	Equal variances assumed	0.809	0.371	0.826	98	0.411(NS)	0.44	0.533	-0.617	1.497
Height	Equal variances assumed	0.258	0.612	0.254	98	0.8(NS)	0.16	0.631	-1.091	1.411
BMI	Equal variances assumed	0.294	0.589	0.482	98	0.631(NS)	0.1487867	0.308793	-0.4640029	0.7615764

Demographic variables like age, weight, height and BMI were compared using Levene's test for equality of variances and independent sample T test The p value was found not to be significant.

COMPARISON OF HEART RATE IN THE TWO GROUPS THROUGHOUT THE STUDY PERIOD

Heart Rate	STUDY	CONTROL
PRE OP	86.44	84
MEAN HR at 5 min	74.14	75.9
MEAN HR at 20 mi	58.64	107
MEAN HR 40min	59.78	72.7
MEAN HR60 min	59.32	70.3
MEAN HR 80min	59.4	75.3
MEAN HR100min	60.6	69.8
MEAN HR120min	57.42	70.68
MEAN HR140min	63.22	77.06
MEAN HR 160min	62.86	74.36
MEAN HR 180min	66.2	70.87
MEAN HR 200min	63.54	77.01
MEAN HR 220min	70.56	82.01
MEAN HR 240min	73.8	85.19
MEAN HR 260min	72.9	78.2

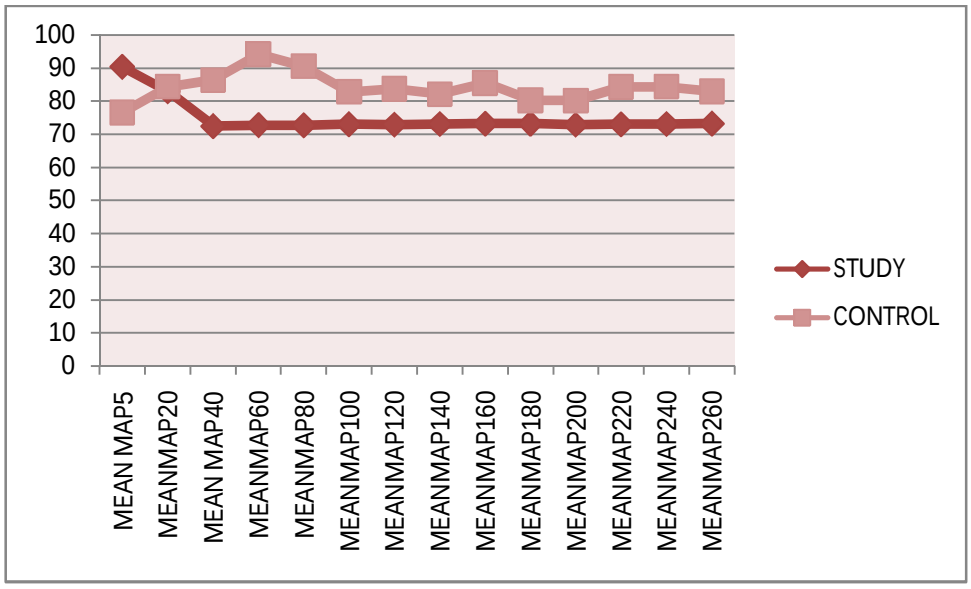


GRAPHIC REPRESENTATION OF MEAN HEART RATE THROUGH OUT THE STUDY PERIOD

It is clearly evident that the mean heart rate pre operatively and 5 minutes after spinal anesthesia was almost similar inboth the groups. But after this both intra operatively and post operatively patients in the study group had significantly lower heart rate than in the control group.

COMPARISON OF MEAN ARTERIAL PRESSURE IN BOTH THE GROUPS THROUGH OUT THE STUDY PERIOD

Mean arterial pressure	Study group	Control group
MEAN MAPat 5 min	90.29	76.6
MEANMAP at 20 min	82.92	84.4
MEAN MAPat 40 min	72.46	86.4
MEANMAPat 60 min	72.74	94.2
MEANMAP at 80 min	72.7	90.6
MEANMAPat 100 min	73.03	82.87
MEANMAPat 120 min	72.9	83.82
MEANMAPat 140 min	73.07	82.14
MEANMAPat 160 min	73.14	85.45
MEANMAPat 180 min	73.24	80.26
MEANMAPat 200 min	72.86	80.19
MEANMAPat 220 min	72.95	84.31
MEANMAP at 240 min	73.07	84.4
MEANMAPat 260 min	73.24	83.03



GRAPHIC REPRESENTATION OF MEAN ARTERIAL PRESSURE THROUGH OUT THE STUDY PERIOD

This graph clearly depicts that the mean arterial pressure was comparatively low in the study group which received dexmedetomidine than in the control group.

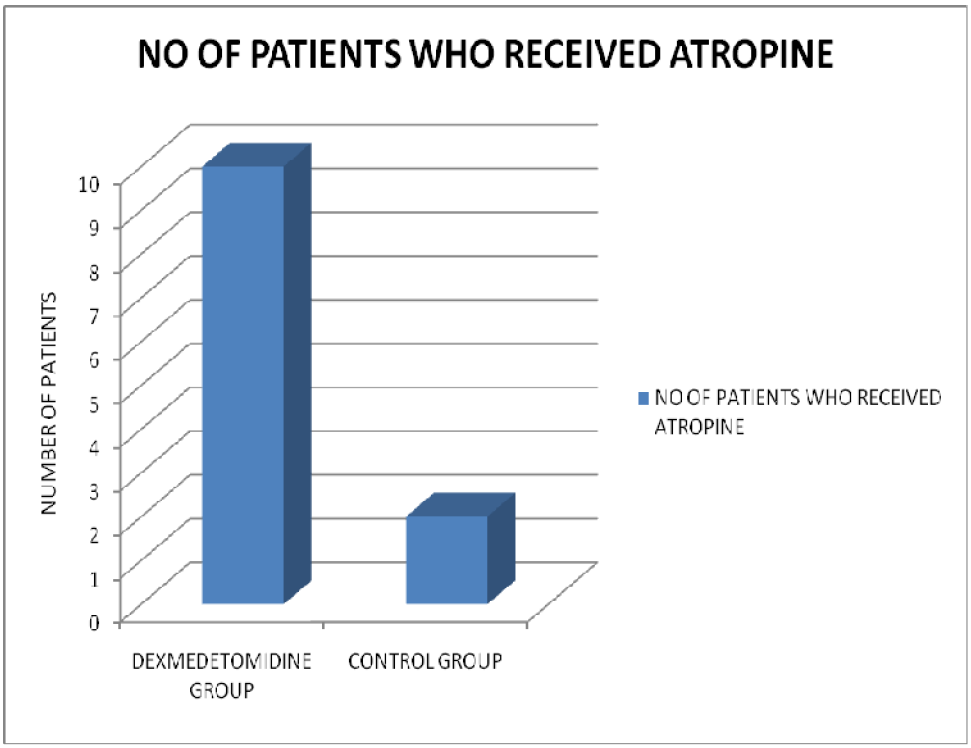
COMPARITIVE STATISTICAL ANALYSIS OF MEAN ARTERIAL PRESSURE AND MEAN HEART RATE IN THE TWO GROUPS

		Levene's Test for Equality of Variances					t-test for Equality of Means
		F	P value	t	df	Sig. (2-tailed)	Mean Difference
MEANMAP	Equal variances assumed	3.01	0.086	-32.98	98	0.0001***	-17.9047619
MEANHR	Equal variances not assumed	11.41	0.001	-15.79	98	0.0001***	-13.3528571
		Levene's Test for Equality of Variances					t-test for Equality of Means
		F	P value	t	df	Sig. (2-tailed)	Mean Difference
MEANMAP	Equal variances assumed	19.8	-0.084	1.387	98	0.0001***	-8.8009523
MEANHR	Equal variances not assumed	28.2	-0.169	18.57	98	0.0001***	-4.2490475

Both groups were compared in terms of mean arterial pressure and mean heart rate by independent sample test and Levene's test for equality of variances and the p value was found to be highly significant.

COMPARISON OF PATIENTS WHO RECEIVED ATROPINE IN BOTH THE GROUPS

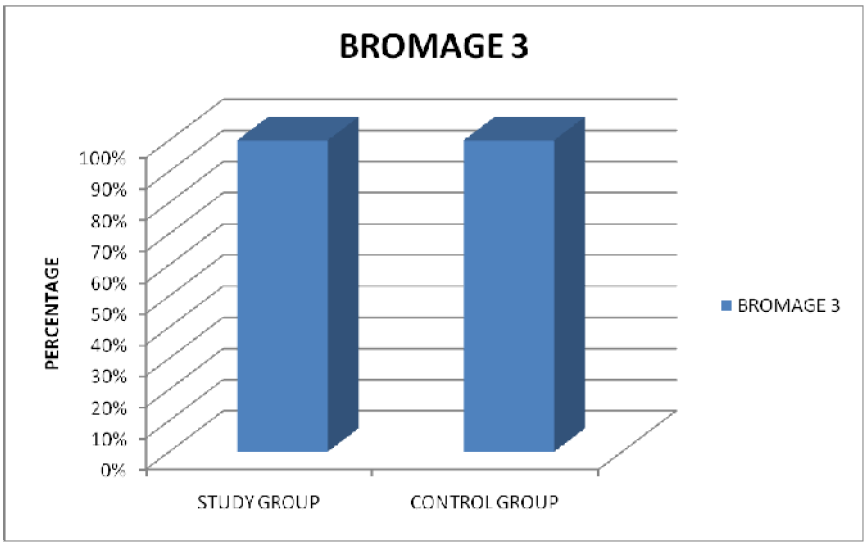
PARAMETER	DEXMEDETOMIDINE GROUP	CONTROL GROUP
NO OF PATIENTS WHO RECEIVED ATROPINE	10	2



In the dexmedetomidine a total of 10 patients recived atropine while only 2 patients in the control group received atropine.

ASSESSMENT OF MOTOR LEVEL AT 5 MINUTES

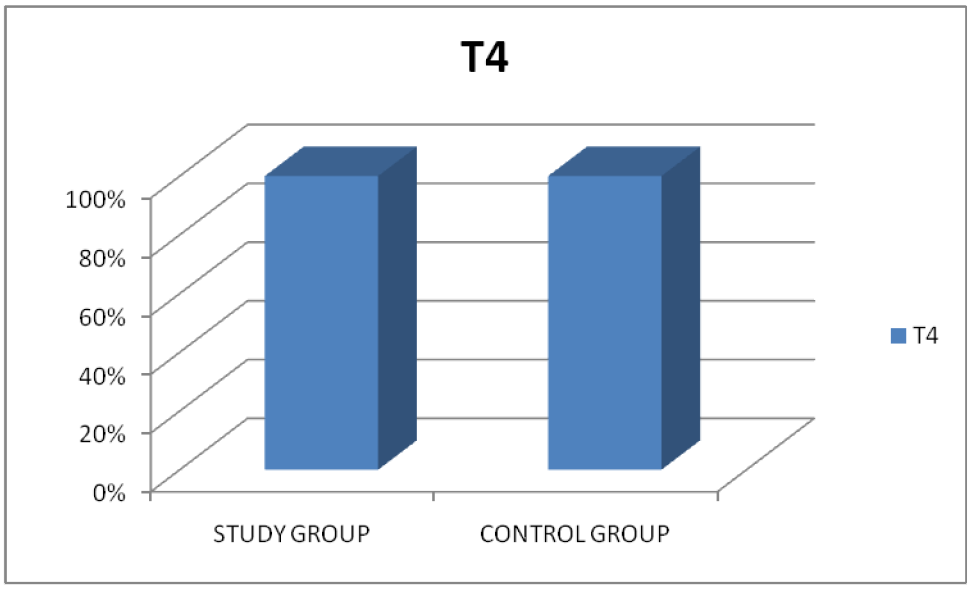
Percentage	Study group		Control group	
	Number of patients	Percentage	Number of patients	
Bromage 3	50	100%	50	100%



At the 5th minute ,before the onset of surgery motor level was checked. All the patients in both the groups were not able to move the hip and showed Bromage grade 3. It is clear from this graph that there was no change in achieving the maximal level in both the groups. Although the onset of motor block was not compared in our study ,we could not make out any significant difference in both the groups in the onset of sensory and motor blockade.

ASSESSMENT OF SENSORY LEVEL AT 5 MINUTES

SENSORY LEVEL AT 5MIN	STUDY GROUP		CONTROL GROUP	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
T4	50	100%	50	100%



It is evident from the graph that both in the study and control groups the maximal level of block was the same.

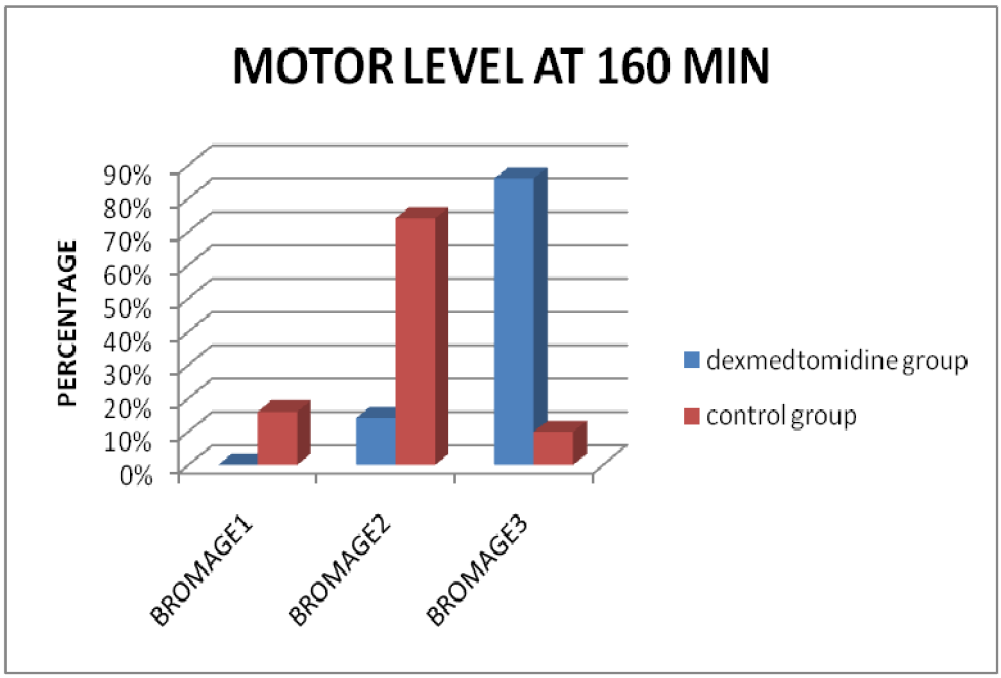
MOTOR BLOCK AT 160 MIN

Motor block	Dexmedetomidine group		Control group	
At 160 minutes	Number of patients	Percentage	Number of patients	Percentage
B1	0	0%	8	16%
B2	7	14%	37	74%
B3	43	86%	5	10%

After 160 minutes of spinal anesthesia ,in the study group 43 out of 50 patients were not able to move the hip, knee and ankle .But in the control group,37 out of 50 patients were able to move only the ankle while 8 out of 50 were able to move knee and ankle. Only 5 patients (10%) had Bromage 3 while 43 patients (86%) in the study group had Bromage 3.

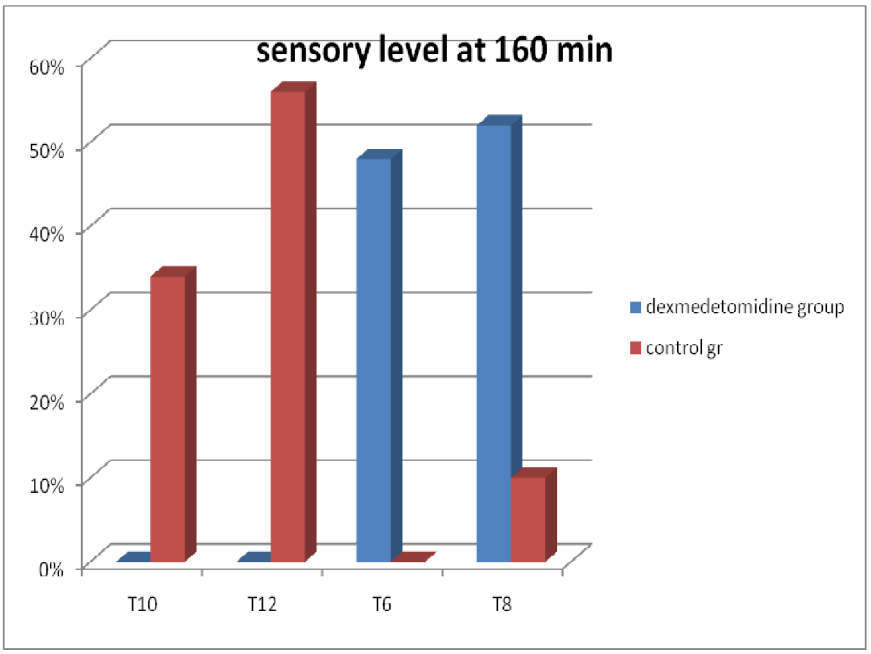
ASSESSMENT OF MOTOR BLOCK AFTER 160 MINUTES

Motor block was assessed using modified Bromage scale . This bar diagram clearly depicts the significant difference in the motor block in both the groups.



ASSESSMENT OF SENSORY BLOCKADE AT 160 MIN

sensory level at 160 min	STUDY GROUP		CONTROL GROUP	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
T10	0	0%	17	34%
T12	0	0%	28	56%
T6	24	48%	0	0%
T8	26	52%	5	10%



SENSORY BLOCK AT 160 MINUTE

Sensory block assessed at 160 minutes showed a level of T6 in 48% andT8 in 52% of the patients in the study group . In the control group it was T10 IN 34% and T12 in 56% of the patient .Only 10% of thr patients in the control group showed a level of T8.

COMPARISON OF DURATION OF MOTOR BLOCK IN TWO GROUPS

PARAMETER	Group Statistics				
	groups	NUMBER	Mean	Std. Deviation	Std. Error Mean
TIME FOR MOTOR BLOCK TO BECOME BROMAGE O	DEXMEDETOMIDINE GROUP	50	243.6	17.0	2.4
	CONTROL GROUP	50	211.2	16.7	2.4

The time for the motor block to become B0 was 243±17.0 minutes in the study group and in the control group it was 211.2±16.7 minutes. This showed a significant prolongation of motor block in the dexmedetomidine group with a p value of 0.001***.

			Independent Samples Test					
Levene's Test for Equality of Variances			t-test for Equality of Means					
							95% CI of the	
Equal variances assumed	F test value	p value	t test value	p value	Mean Difference	Std. Error Difference	Lower	Upper
TIME FOR MOTOR BLOCK TO BECOME BROMAGE O	0.223	0.638	9.605	0.001***	32.4	3.373	25.706	39.094

COMPARISON OF DURATION OF SENSORY BLOCK IN TWO GROUPS

PARAMETER		Group Statistics			
	groups	NUMBER	Mean	Std. Deviation	Std. Error Mean
TIME FOR SENSORY LEVEL TO BECOME S1	DEXMEDETOMIDINE GROUP	50	255.2	8.6	1.2
	CONTROL GROUP	50	210.8	33.1	4.7

The total time for sensory level to reach S1 was 255±8.6in the study group while it was 210.8±33,1 in the control group. This also proved significant prolongation in the study group with a p value of 0.001***.

			Independent Samples Test					
Levene's Test for Equality of Variances			t-test for Equality of Means					
							95% CI of the	
Equal variances assumed	F test value	p value	t test value	p value	Mean Difference	Std. Error Difference	Lower	Upper
TIME FOR SENSORY LEVEL TO REACH S1	7.281	0.008	9.172	0.001***	44.4	4.841	34.793	54.007

COMPARISON OF TIME OF TWO DERMATOME REGRESSION IN TWO GROUPS

PARAMETER	Group Statistics				
	groups	NUMBER	Mean	Std. Deviation	Std. Error Mean
TIME FOR REGRESSION FROM MAXIMAL LEVEL	DEXMEDETOMIDINE GROUP	50	125.2	17.5	2.5
	CONTROL GROUP	50	94.6	18.9	2.7

The time for two dermatome regression from the maximal level was 125.2±17.5minutes in the study group and 94.6±18.9 in the control group. This proved the significant prolongation of sensory block to regress from the maximal level in the study group with a p value of 0.001 ***.

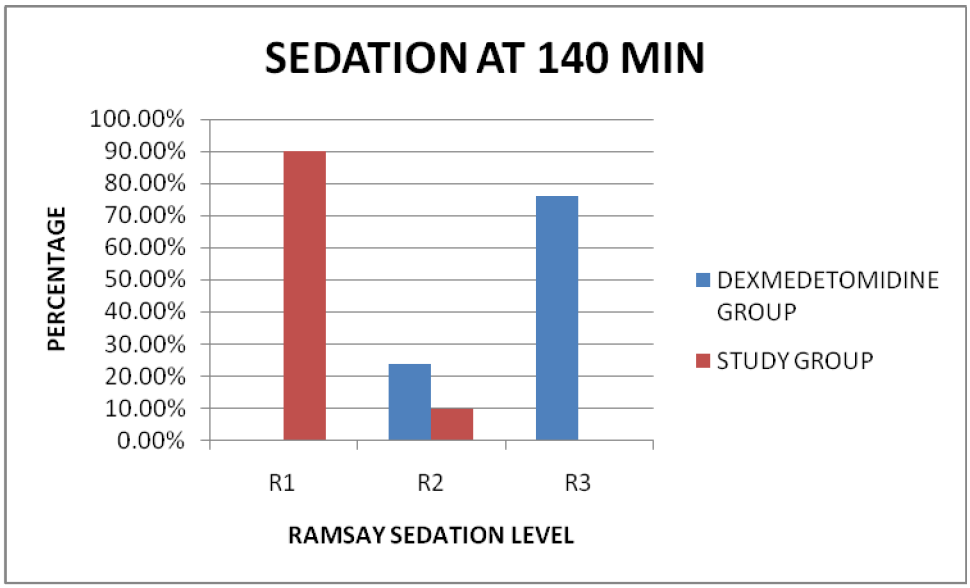
	Independent Samples Test							
	Levene's Test for Equality of Variances			t-test for Equality of Means				
							95% CI of the	
Equal variances assun	F test value	p value	t test value	p value	Mean Difference	Std. Error Difference	Lower	Upper
TIME FOR THE REGRESSION OF SENSORY LEVEL FROM MAXIMUM	1.062	0.305	8.403	0.001***	30.6	3.642	23.373	37.827

SEDATION LEVEL AT 140 MINUTES

At 140 minutes the patients who received dexmedetomidine remained calm and sedated with Ramsay sedation grade of 3 or 2.

	STUDY GROUP		C ONTROL GROUP	
Sedation 140 min	**Numberof patients**	**Percentage**	**Number of patients**	**Percentage**
R1	0	0.00%	45	90.00%
R2	12	24.00%	5	10.00%
R3	38	76.00%	0	0.00%

SEDATION SCALE AT 140 MINUTES



DISCUSSION

There has always been immense research to improve the effects of spinal anesthesia by changing drug regimens and technical methods. Usually adjuvants are added to hyperbaric bupivacaine and instilled intrathecally to prolong the anesthetic effects. These adjuvants act perineurally or at different sites in the spinal cord and exert their antinociceptive action. They prolong anesthesia and decrease pain in the post operative period.

In the past clonidine, alpha 2 agonist has been used in oral, intrathecal, intravenous routes to prolong spinal anesthesia. The previous studies have proved that clonidine 30 micrograms is equivalent to dexmedetomidine 3 micrograms intrathecally. The proven advantages of dexmedetomidine are minimal depression of respiration cardioprotection, renoprotection and neuroprotection.

This prospective randomized controlled study conducted in 100 patients who underwent abdominal/vaginal hysterectomy under spinal anesthesia demonstrated that dexmedetomidine given in the dose of 0.5 microgram/kg prolonged the sensory and motor block significantly.

Both the groups were comparable in demographic parameters like age, weight, height and BMI. The mean age of all the patients in the dexmedetomidine group was 48.24±4.7.The mean age of the patients in the control group was 48.78±4.82. The mean body mass index for all the patients in dexmedetomidine

group was 23.39±1.67.The mean body mass index for all the patients in the control group was 23.24±1.41. They were compared using independent sample test and Levene's test for equality of variances and the p value was found not significant.

At the 80th minute the average mean arterial pressure in the dexmedetomidine group was around 72 whereas in the control group it was around 90 . The mean heart rate of all the patients after 40 minutes of spinal anesthesia was 72 in the control group whereas in the dexmedetomidine group it was 58.Statistical analysis was done for mean arterial pressure and mean heart rate and the p value was found to be highly significant. This has proved the fact that dexmedetomidine has got a definite role in hypotensive anesthesia.

In our study the number of patients who received atropine was more than in the control group because of bradycardia caused by dexmedetomidine induced sympatholysis. In the dexmedetomidine group 10 out of 50 patients needed atropine whereas in the control group only 2 patients needed atropine. This bradycardia promptly responded to Inj. Atropine 0.6mg intravenously. During our study there was no other adverse effect of dexmedetomidine observed in the study group. This may be due to the fact that we had used only moderate dose of dexmedetomidine as a single intravenous injection given slowly over 10 minutes.

At the fifth minute of spinal anesthesia ,grade of motor level and sensory level was checked. All the patients in both the groups were not able to move the

hip and showed Bromage 3. All the patients in both the groups had a sensory level of T4.This showed that there was no difference in achieving the maximum motor and sensory level in both the groups.

At the 160th minute of spinal anesthesia grade of motor level was Bromage 3 in 43 patients in the dexmedetomidine group(86%). But in the control group only 5 patients(10%) had Bromage grade 3.This demonstrated that there was a prolongation of motor block in the dexmedetomidine group.

At the 160th minute of spinal anesthesia,24 patients(48%) had a sensory level of T6 in the dexmedetomidine group. But in the control group no patient had a sensory level of T6.In the control group,17 patients (34%) had a sensory level of T10. This was the maximum level seen at 160th minute in the control group.

The time for the motor block to become Bromage grade 0 was 243±17.0 minutes in the dexmedetomidine group and in the control group it was 211.2±16.7 minutes. This on statistical analysis by independent sample test and t test for equality of means showed a significant prolongation of motor block in the dexmedetomidine group with a p value of 0.001***.

Al Mustafa et al. in their study in 48 patients had demonstrated similar prolongation 199 ± 42.8 min vs. 138.4 ± 31.3 min ($P < 0.05$). They had given isobaric bupivacaine 12.5 mg for spinal block In our study the total duration of motor block was more in both the control and study groups when compared to Al

mustafa et al . This may be due to the fact that we had given hyperbaric bupivacaine 17.5 mg.

Dinesh et al had done a similar study in 100 patients with 15 mg of hyperbaric bupivacaine and they had given dexmedetomidine 1 microgram/kg as a loading dose and 0.5 microgram/kg/hour as maintenance dose. They demonstrated the regression time to reach the modified Bromage scale 0 was significantly prolonged in the dexmedetomidine group (220.7 ± 16.5 min) compared to the control group (131.6 ± 10.5 min).

In our study, the total time for sensory level to reach S1 was 255±17.5in the study group while it was 210.8±33.1 in the control group. Dinesh et al had demonstrated that the total duration of sensory blockade was significantly prolonged in the dexmedetomidine group (269.8 ± 20.7 min) whereas it was 169 minutes in the control group (169.2 ± 12.1) . We had got the almost similar to the results seen in other studies. Al Mustafa et al., whose study formed the basis of our dissertation had 261.5 ± 34.8 min in the study group vs. 165.2 ± 31.5 min in the control group ($P < 0.05$. Dexmedetomidine group had higher level of sensory block compared to the control group in our study, similar to the study results of Kaya et al.

In our study the time for two dermatome regression from the maximal level was 125.2±17.5minutes in the study group and 94.6±18.9 in the control group.

This proved the significant prolongation of sensory block to regress from the maximal level in the dexmedetomidine group with a p value of 0.001***. This showed the prolongation of sensory block by intravenous dexmedetomidine.

Dinesh et al had given 15 mg of hyperbaric bupivacaine . They had given dexmedetomidine 1 microgram/kg as a loading dose and 0.5 microgram/kg/hour as maintenance dose. They demonstrated that the mean time for two-dermatomal regression of sensory block was significantly prolonged in the group that received dexmedetomidine (137.4 ± 10.9 min) compared to the other group (102.8 ± 14.8).

Sudhesh,K.Harsoor in the article dexmedetomidine a wonder drug has clearly mentioned about the transient hypertensive response when dexmedetomidine is given in the dose of 1-4 microgram/kg. Jia Song et al in the article titled dexmedetomidine for sedation in patients undergoing surgery under regional anesthesia has clearly mentioned that as the dose increased the incidence of hypotension also increased. In their study they had given a loading dose of 1 microgram/kg and they had advised that maintenance dose 0.25 microgram/kg/hour may be most appropriate if severe bradycardia and hypotension have to be avoided. Dexmedetomidine is given intravenously in doses ranging from 0.1 to 1 μg/kg/h but higher doses is usually associated with a significant incidence of bradycardia and hypotension. Aantaa et al., had concluded that “The optimal dose of dexmedetomidine for single dose intravenous premedication in minor surgery has wide safety margins in the range of 0.33 to

0.67 μg/kg". Hence we selected a dose of 0.5 μg/kg in our study. While deciding on the dose of single intravenous dose of dexmedetomidine these articles were given utmost importance.

We decided on the dose 0.5microgram/kg to be given slowly over 10 minutes so as to avoid side effects and to get the desirable therapeutic effect. When given intravenously the half life of dexmedetomidine is 2-3 hours. All the patients were closely monitored for 5 hours. This is a great advantage of dexmedetomidine over clonidine whose half life is 6-10 hours.

In our study no patient had transient hypertension . The transient hypertensive response due to peripheral alpha2 receptor stimulation occurs when dexmedetomidine is given in the dose more than 1 microgram/kg.

Post operatively when the sensory level touched T12-L1 most of our patients complained of pain with some discomfort. Rescue analgesic Inj. Paracetamol 1gram intravenously was administered to those patients who complained.

It is a common practice to sedate patients with midazolam who are under spinal anesthesia. Kaya etal in their article had compared midazolam and dexmedetomidine and had clearly explained about the superiority of dexmedetomidine over midazolam.

Intraoperatively the patients in the study group showed significantly high sedation scores than in the control group. In their study' Kaya et al had reported about the paradoxical reactions of midazolam when given in high doses. Dexmedetomidine is unique in causing arousable sedation. All patients who received dexmedetomidine had good sedation score through out the intra operative period (Ramsay sedation score R3-R2)compared to the control group . At 140 th minute 76% of the patients in dexmedetomidine group remained sedated with the grading of Ramsay 3.

We had assessed sedation level at the 5th minute and then at the end of surgery. The average duration of the surgery was around 130 minutes. The peak action of dexmedetomidine is around 10-20 minutes. We could see the patients sleeping well when the surgery was going on. Some patients snored but there was no incidence of desaturation.

All patients in the study and control group were given oxygen at the rate of 2 liters/minute through ventimask. This clearly demonstrated the nature of dexmedetomidine in causing arousable sedation without respiratory depression.

As dexmedetomidine do not affect synthesis ,storage or metabolism of catecholamines its actions can be easily reversed by vasopressors or anticholinergics. The availability of antagonist Atipamezole with similar distribution and elimination characteristics is a great advantage for

dexmedetomidine over other anesthetic agents. Atipamezole is of particular use in reversing the sedative effects of dexmedetomidine. In our study bradycardia caused by dexmedetomidine promptly responded to anticholinergics.

CONCLUSION

Dexmedetomidine in the dose of 0.5 microgram/kg given as single intravenous dose to patients who underwent abdominal/vaginal hysterectomy under spinal anesthesia significantly prolonged the duration of sensory and motor blockade. There was also significant prolongation of the time for the two segment dermatome regression in the dexmedetomidine group compared to the control group. All these effects were achieved without causing deep level of sedation and with minimal hemodynamic side effects.

SL.No.	NAME						IP NO		PRE OP	DRUG										20 MIN							40 MIN						60MIN	
		AGE	WEIGH	HEIGHT	BMI	ASA		BP	HR	AFTER 5 M	DIA	SYS	HR	DRUG	MOTO	SENSOF	SEDAT	SYS	DIA	BP	HR	DRUG	MO	SENSOR	SEDAT	BP	HR	DRUG	MOTOF	SENSOR	SEDAT	BP	HR
68	BANUMAT	43	57	154	24.0344	1	22163896	145/90	102	NS	82	124	73		B3	T4	R1	100	70	100/70	89					123/84	73					112/76	71
69	NEELA	44	56	154	23.6128	1	12410869	134/86	99	NS	70	119	68		B3	T4	R1	109	78	126/76	80					120/76	78					112/56	67
70	SUGANTHI	55	55	150	24.4444	1	14411811	144/74	98	DEX 0.5 m	78	132	67		B3	T4	R4	98	68	100/67	60					98/72	60	M6				111/77	50
71	MUNIYAM	43	50	149	22.5215	1	2288096	110/80	87	DEX 0.5 m	80	140	92		B3	T4	R4	99	67	128/88	68					100/78	56					90/56	58
72	PAPPATHY	56	54	154	22.7694	1	16972056	144/74	86	NS	65	98	78	M6	B3	T4	R1	90	78	90/78	70	M6				100/68	67					100/76	70
73	JAYAMALA	46	50	150	22.2222	1	43808024	158/84	69	NS	76	109	87		B3	T4	R1	92	68	98/78	67					110/67	76					98/87	78
74	SASIKALA	47	56	143	27.3852	2	20743083	150/100	78	DEX 0.5 m	57	108	60	M6	B3	T4	R3	100	89	100/89	56	A0.6				100/80	50	A0.6				100/78	56
75	RAMANI	40	50	154	21.0828	1	15619413	136/84	87	NS	78	110	78		B3	T4	R1	109	78	109/78	69					98/68	76	M6				100/70	78
76	JAYALAKSH	42	55	152	23.8054	1	21413547	146/80	87	DEX 0.5 m	67	129	70		B3	T4	R4	100	78	100/78	50	A0.6				98/78	54	A0.6				90/50	62
77	GOMATHI	44	50	148	22.8269	1	15931401	130/92	78	DEX 0.5 m	65	109	58		B3	T4	R4	122	90	98/78	58					90/78	67	M6				98/78	58
78	ARPUDAM	47	53	149	23.8728	2	16541215	160/80	79	NS	67	110	65		B3	T4	R1	123	89	100/87	78					110/89	77					112/78	66
79	CHINNAPO	46	54	149	24.3232	1		124/88	76	NS	78	98	65	M6	B3	T4	R1	124	87	100/70	56					100/78	62					110/78	61
80	LILLY	45	55	150	24.4444	1		136/78	77	NS	90	140	87		B3	T4	R3	100	60	116/76	60					106/68	66					99/86	78
81	KAVITHA	46	56	151	24.5603	1	17746051	132/68	79	DEX 0.5 m	80	140	92		B3	T4	R4	99	67	128/88	68					100/78	56					90/56	58
82	KUMARI	46	49	148	22.3703	2	21716914	134/69	78	NS	65	98	78	M6	B3	T4	R1	90	78	90/78	70	M6				100/68	67					100/76	70
83	KASTHURI	50	56	150	24.8889	1	21155291	120/80	76	NS	76	109	87		B3	T4	R1	92	68	98/78	67					110/67	76					98/87	78
84	CHANDRA	51	52	152	22.5069	1	11818766	134/67	75	DEX 0.5 m	57	108	60	M6	B3	T4	R3	100	89	100/89	56	A0.6				100/80	50	A0.6				100/78	56
85	RAJALAKSI	52	53	154	22.3478	1	13871711	122/78	74	NS	78	110	78		B3	T4	R1	109	78	109/78	69					98/68	76	M6				100/70	78
86	AMUL	54	53	155	22.0604	1	16830219	120/78	65	DEX 0.5 m	67	129	70		B3	T4	R4	100	78	100/78	50	A0.6				98/78	54	A0.6				90/50	62
87	VIJAYAKSH	55	54	156	22.1893	1	20030759	144/89	66	DEX 0.5 m	65	109	58		B3	T4	R4	122	90	98/78	58					90/78	67	M6				98/78	58
88	SHANTHI	56	57	153	24.3496	1	21488650	140/80	68	NS	67	110	65		B3	T4	R1	123	89	100/87	78					110/89	77					112/78	66
89	JOTHI	54	56	154	23.6128	1	20513236	136/84	90	NS	78	98	65	M6	B3	T4	R1	124	87	100/70	56					100/78	62					110/78	61
90	GIRIJA	51	55	150	24.4444	1	20816437	136/84	89	NS	90	140	87		B3	T4	R3	100	60	116/76	60					106/68	66					99/86	78
91	CHANDRA	46	56	151	24.5603	1	21925194	146/80	88	NS	78	98	65	M6	B3	T4	R1	123	89	100/70	89					100/78	76					110/78	61
92	MAYA	46	49	148	22.3703	2	14004768	130/92	102	NS	78	122	87		B3	T4	R1	124	87	119/89	98					119/87	77					100/67	76
93	SIVASANK	50	56	150	24.8889	1	15067666	134/86	99	NS	82	124	73		B3	T4	R1	100	70	100/70	89					123/84	73					112/76	71
94	MALA	51	52	152	22.5069	1	22500301	144/74	98	NS	70	119	68		B3	T4	R1	109	78	126/76	80					120/76	78					112/56	67
95	MINI	52	53	154	22.3478	1	22180993	122/68	87	DEX 0.5 m	78	132	67		B3	T4	R4	98	68	100/67	60					98/72	60	M6				111/77	50
96	KALAVATH	54	53	155	22.0604	1	20859793	122/78	74	DEX 0.5 m	80	140	92		B3	T4	R4	99	67	128/88	68					100/78	56					90/56	58
97	SHAHEEN	55	54	156	22.1893	1	10331987	120/78	65	NS	65	98	78	M6	B3	T4	R1	90	78	90/78	70	M6				100/68	67					100/76	70
98	GEETHA	56	57	153	24.3496	1	14292770	144/89	66	NS	76	109	87		B3	T4	R1	92	68	98/78	67					110/67	76					98/87	78
99	CHIMRA	54	56	154	23.6128	1	13335215	140/80	68	DEX 0.5 m	57	108	60	M6	B3	T4	R3	100	89	100/89	56	A0.6				100/80	50	A0.6				100/78	56
100	SAGAYAM	51	52	152	22.5069	1	16754259	136/84	90	NS	78	110	78		B3	T4	R1	109	78	109/78	69					98/68	76	M6				100/70	78

				80 MIN						100 MIN						120 MIN						140 MIN						160 MIN					
DRUG	MOTO	SENSO	SEDATI	BP	HR	DRUG	MOTOR	SENSOR	SEDATI	BP	HR	DRUG	MOTOF	SENSORY	SEDATIO	BP	HR	DRUG	MOTOF	SENSOF	SEDATI	BP	HR	DRUG	MOTOR	SENSORY	SEDAT	BP	HR	DRUG	MOTOF	SENSO	SEDATIO
				110/87	87					122/78	70					132/86	79		B3	T8	R1	110/70	88		B2	T10	R1	112/6	78		B2	T10	R1
M6				110/78	88					112/89	68					110/65	65		B2	T8	R1	128/87	87		B2	T10	R1	112/8	87		B2	T12	R1
A0.6				100/68	60					100/68	60		B3	T4	R3	122/78	50	A0.6	B3	T4	R3	130/80	60		B3	T6	R3	110/7	60		B3	T6	R2
M6				89/56	52	M6				110/78	62		B3	T4	R3	112/67	58		B3	T6	R3	100/78	62		B3	T6	R3	122/8	66		B2	T8	R2
				111/87	67					12O/80	70		B3	T6	R1	113/59	67		B3	T8	R1	110/88	77		B3	T10	R1	138/7	78		B2	T12	R1
				100/789	78					108/78	68		B3	T4	R1	100/76	77		B3	T8	R1	132/86	77		B3	T10	R1	123/6	79		B2	T12	R1
A0.6				112/67	56					128/86	60		B3	T4	R4	98/78	65		B3	T4	R3	110/65	62		B3	T6	R3	147/9	67		B3	T6	R3
				113/78	65					106/68	68		B3	T4	R1	102/70	78		B3	T8	R1	122/78	75		B2	T10	R1	120/8	76		B2	T12	R1
M6				114/69	60					100/76	65		B3	T6	R4	100/70	56		B3	T6	R4	112/67	57		B3	T6	R3	12O/7	50	A0.6	B3	T6	R3
				112/56	59					98/67	59		B3	T6	R4	102/76	58		B3	T4	R3	113/59	58		B3	T6	R3	112/8	58		B3	T8	R3
				122/78	87					110/87	77		B3	T6	R1	104/67	77		B3	T8	R1	100/76	69		B2	T10	R1	110/7	67		B2	T12	R1
				100/76	67					110/80	56		B3	T6	R1	122/78	54		B2	T8	R1	109/78	57		B2	T8	R1	132/8	60		B2	T10	R1
				93/58	69	M6				100/68	68					99/70	50	A0.6	B3	T6	R3	100/68	77		B3	T8	R2	110/7	62		B3	T8	R1
M6				89/56	52	M6				110/78	62		B3	T4	R3	112/67	58		B3	T6	R3	100/78	62		B3	T6	R3	122/8	66		B2	T8	R2
				111/87	67					12O/80	70		B3	T6	R1	113/59	67		B3	T8	R1	110/88	77		B3	T10	R1	138/7	78		B2	T12	R1
				100/789	78					108/78	68		B3	T4	R1	100/76	77		B3	T8	R1	132/86	77		B3	T10	R1	123/6	79		B2	T12	R1
A0.6				112/67	56					128/86	60		B3	T4	R4	98/78	65		B3	T4	R3	110/65	62		B3	T6	R3	147/9	67		B3	T6	R3
				113/78	65					106/68	68		B3	T4	R1	102/70	78		B3	T8	R1	122/78	75		B2	T10	R1	120/8	76		B2	T12	R1
M6				114/69	60					100/76	65		B3	T6	R4	100/70	56		B3	T6	R4	112/67	57		B3	T6	R3	12O/7	50	A0.6	B3	T6	R3
				112/56	59					98/67	59		B3	T6	R4	102/76	58		B3	T4	R3	113/59	58		B3	T6	R3	112/8	58		B3	T8	R3
				122/78	87					110/87	77		B3	T6	R1	104/67	77		B3	T8	R1	100/76	69		B2	T10	R1	110/7	67		B2	T12	R1
				100/76	67					110/80	56		B3	T6	R1	122/78	54		B2	T8	R1	109/78	57		B2	T8	R1	132/8	60		B2	T10	R1
				93/58	69	M6				100/68	68					99/70	50	A0.6	B3	T6	R3	100/68	77		B3	T8	R2	110/7	62		B3	T8	R1
				100/76	67					110/80	76		B3	T6	R1	122/78	78		B2	T8	R1	109/78	81		B2	T10	R1	132/8	71		B2	T10	R1
				98/67	78					122/90	78					124/78	80		B2	T8	R1	112/87	80		B2	T10	R1	120/8	77		B1	T10	R1
				110/87	87					122/78	70					132/86	79		B3	T8	R1	110/70	88		B2	T10	R1	112/6	78		B2	T10	R1
M6				110/78	88					112/89	68					110/65	65		B2	T8	R1	128/87	87		B2	T10	R1	112/8	87		B2	T12	R1
A0.6				100/68	60					100/68	60		B3	T4	R3	122/78	50	A0.6	B3	T4	R3	130/80	60		B3	T6	R3	110/7	60		B3	T6	R2
M6				89/56	52	M6				110/78	62		B3	T4	R3	112/67	58		B3	T6	R3	100/78	62		B3	T6	R3	122/8	66		B2	T8	R2
				111/87	67					12O/80	70		B3	T6	R1	113/59	67		B3	T8	R1	110/88	77		B3	T10	R1	138/7	78		B2	T12	R1
				100/789	78					108/78	68		B3	T4	R1	100/76	77		B3	T8	R1	132/86	77		B3	T10	R1	123/6	79		B2	T12	R1
A0.6				112/67	56					128/86	60		B3	T4	R4	98/78	65		B3	T4	R3	110/65	62		B3	T6	R3	147/9	67		B3	T6	R3
				113/78	65					106/68	68		B3	T4	R1	102/70	78		B3	T8	R1	122/78	75		B2	T10	R1	120/8	76		B2	T12	R1

180 MIN						200 M						220 MIN						240 MIN						260 MIN								
BP	HR	DRUG	MOTOR		SEDATI	BP	HR	DRUG	MOTOR	SENSO	SEDAT	BP	HR	DRUG	MOTOR	SENSORY	SEDATI	BP	HR	DRUG	MOTOR	SENSORY	SEDATI	BP	HR	DRUG	MOTOR	SENSOR	SEDATI	BP	HR	SPO2
110/78	77		B2	L2	R1	136/84	71		B1	S2	R1	122/78	89		B0	S2	R1	135/87	80		B0	S2	R1	138/89	87		B0	S2	R1			
100/67	78		B1	L2	R1	146/80	75		B0	S2	R1	124/78	87		B0	S2	R1	143/87	85		B0	S2	R1	122/78	89		B0	S2	R1			
98/76	77	A0.6	B3	T8	R2	130/92	56		B2	T10	R2	136/84	98		B1	L3	R1	136/86	71		B0	S2	R1	124/78	78		B0	S2	R1			
132/84	61	A0.6	B2	T10	R2	130/76	60		B1	T10	R1	134/72	77		B0	L3	R1	145/78	92		B0	S2	R1	136/84	78		B0	S2	R1			
132/80	53		B1	L2	R1	128/67	77		B0	S2	R1	132/80	78		B0	L3	R1	128/89	80		B0	S2	R1	132/76	80		B0	S2	R1			
109/78	56		B1	L2	R1`	147/98	89		B0	S2	R1	132/80	70		B0	S1	R1	130/80	82		B0	S2	R1	132/76	89		B0	S2	R1			
112/87	65		B3	T8	R3	120/80	66		B2	T10	R2	109/78	67		B2	T12	R2	140/88	69		B1	T12	R2	138/89	69		B0	S2	R1			
110/70	76		B1	L2	R1	12O/78	76		B0	L4	R1	112/87	80		B0	S2	R1	145/95	98		B0	S2	R1	122/78	78		B0	S2	R1			
128/87	63		B2	T8	R3	112/80	67		B2	T10	R3	110/70	62		B2	T12	R3	132/76	65		B1	T12	R2	124/78	77		B0	S2	R1			
130/80	51	A0.6	B2	T8	R3	100/60	62		B2	T10	R2	128/87	62		B2	T12	R2	138/89	70		B1	L2	R2	136/84	71		B0	S2	R1			
100/78	76		B1	L2	R1	98/67	89		B0	L4	R1	130/80	89		B0	S1	R1	122/78	89		B0	S2	R1	146/80	53		B0	S2	R1			
12O/78	65		B2	T12	R1	122/78	66		B1	L2	R1	132/76	68		B1	S1	R1	134/87	69		BO	S2	R1	145/95	56		B0	S2	R1			
124/78	67		B2	T8	R1	112/76	67		B1	T10	R1	123/89	77		B0	L1	R1	132/76	76		B0	L3	R1	144/86	56		B0	S2	R1			
132/84	61	A0.6	B2	T10	R2	130/76	60		B1	T10	R1	134/72	77		B0	L3	R1	145/78	92		B0	S2	R1	136/84	78		B0	S2	R1			
132/80	53		B1	L2	R1	128/67	77		B0	S2	R1	132/80	78		B0	L3	R1	128/89	80		B0	S2	R1	132/76	80		B0	S2	R1			
109/78	56		B1	L2	R1`	147/98	89		B0	S2	R1	132/80	70		B0	S1	R1	130/80	82		B0	S2	R1	132/76	89		B0	S2	R1			
112/87	65		B3	T8	R3	120/80	66		B2	T10	R2	109/78	67		B2	T12	R2	140/88	69		B1	T12	R2	138/89	69		B0	S2	R1			
110/70	76		B1	L2	R1	12O/78	76		B0	L4	R1	112/87	80		B0	S2	R1	145/95	98		B0	S2	R1	122/78	78		B0	S2	R1			
128/87	63		B2	T8	R3	112/80	67		B2	T10	R3	110/70	62		B2	T12	R3	132/76	65		B1	T12	R2	124/78	77		B0	S2	R1			
130/80	51	A0.6	B2	T8	R3	100/60	62		B2	T10	R2	128/87	62		B2	T12	R2	138/89	70		B1	L2	R2	136/84	71		B0	S2	R1			
100/78	76		B1	L2	R1	98/67	89		B0	L4	R1	130/80	89		B0	S1	R1	122/78	89		B0	S2	R1	146/80	53		B0	S2	R1			
12O/78	65		B2	T12	R1	122/78	66		B1	L2	R1	132/76	68		B1	S1	R1	134/87	69		BO	S2	R1	145/95	56		B0	S2	R1			
124/78	67		B2	T8	R1	112/76	67		B1	T10	R1	123/89	77		B0	L1	R1	132/76	76		B0	L3	R1	144/86	56		B0	S2	R1			
12O/78	76		B2	L2	R1	122/78	78		B1	S1	R1	132/76	98		B1	S2	R1	134/87	88		BO	S2	R1	145/95	90		B0	S2	R1			
112/80	78		B1	L2	R1	124/78	77		B0	S2	R1	138/89	87		B0	S2	R1	134/78	98		B0	S2	R1	132/76	98		B0	S2	R1			
110/78	77		B2	L2	R1	136/84	71		B1	S2	R1	122/78	89		B0	S2	R1	135/87	80		B0	S2	R1	138/89	87		B0	S2	R1			
100/67	78		B1	L2	R1	146/80	75		B0	S2	R1	124/78	87		B0	S2	R1	143/87	85		B0	S2	R1	122/78	89		B0	S2	R1			
98/76	77	A0.6	B3	T8	R2	130/92	56		B2	T10	R2	136/84	98		B1	L3	R1	136/86	71		B0	S2	R1	124/78	78		B0	S2	R1			
132/84	61	A0.6	B2	T10	R2	130/76	60		B1	T10	R1	134/72	77		B0	L3	R1	145/78	92		B0	S2	R1	136/84	78		B0	S2	R1			
132/80	53		B1	L2	R1	128/67	77		B0	S2	R1	132/80	78		B0	L3	R1	128/89	80		B0	S2	R1	132/76	80		B0	S2	R1			
109/78	56		B1	L2	R1`	147/98	89		B0	S2	R1	132/80	70		B0	S1	R1	130/80	82		B0	S2	R1	132/76	89		B0	S2	R1			
112/87	65		B3	T8	R3	120/80	66		B2	T10	R2	109/78	67		B2	T12	R2	140/88	69		B1	T12	R2	138/89	69		B0	S2	R1			
110/70	76		B1	L2	R1	12O/78	76		B0	L4	R1	112/87	80		B0	S2	R1	145/95	98		B0	S2	R1	122/78	78		B0	S2	R1			

280 MIN							300 MIN																
DRUG	MOTOR	SENSORY	SEDATION	BP	HR	SPO2	DRUG	MOTOR	SENSORY	SEDATION	BP	HR	SPO2	DRUG	MOTOR	SENSORY	SEDATION	BP	HR	SPO2	DRUG	MOTOR	SENSORY

SEDATION	

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PATIENT CONSENT FORM

Study title

Effect of intravenous dexmedetomidine on prolonging spinal anesthesia, a randomized controlled study

Study centre : ESI – PGIMSR, K.K.NAGAR, CHENNAI -78

Participant name : Age: Sex:

I confirm that I have understood the purpose of procedure for the above study . I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique. I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study . I understand that my identity will not be revealed in any information released to third parties or published , unless as required under the law . I agree not to restrict the use of any data or results that arise from the study.

I understand that that I will receive drugs intravenously to prolong spinal anesthesia. I will receive Inj. Dexmedetomidine ,intravenously . I have been explained that the anesthetic technique is a standard and approved technique. I have been explained that the drug will cause sleep and a reduction in heart rate. This may help in future research in the field of anesthesia. I consent to undergo this procedure

Insurance No:

Date: Signature / thumb impression of

Patient

B ´ ÄUPõÚ J ¨ ¦uÀ £ i Á®

எனது கர்பப்பை அகற்றும் அறுவை சிகிச்சையின் போது முதுகெலும்பு மூலம் செலுத்தப்படும் ஊசி மருந்து நன்றாக வேலை செய்வதற்காக "டெக்ஸ் மெடிடோ மிடின்" (Dexmedeto medine) என்ற மருந்தை இரத்தக் குழாயில் செலுத்துவார்கள் என்ற மருத்துவர் மூலம் அறிந்து கொண்டேன். இந்த மருந்தினால் சிறிது நேரம் அதிக தூக்கம் மற்றும் குறைந்த இரத்த அழுத்தம் ஏற்படும் என்றும் மருத்தவர் மூலம் அறிந்து கொண்டேன். இந்த மருத்துவ ஆராய்ச்சிக் குள்ளாக நான் சம்மதம் தெரிவித்துக் கொள்கிறேன்.

இப்படிக்கு

PROFORMA

Name of the patient:

Age:

Sex **Wt:**

Insurance No: **OT:**

Diagnosis: **Duration of Procedure:**

Surgeon: **Anaesthetist**

PREOPERATIVE DETAILS

ASA Grade **Remarks:**

vitals

BP	Pulse rate	Resp. rate	SpO2	Temp	ECG	Xray

Hb	RBS	RFT	LFT	Others

SIGNATURE OF INVESTIGATOR **SIGNATURE OF THE PARTICIPANT**

WITNESS: