"A COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE AND CLONIDINE AS PRE EMPTIVE ANALGESIA TO INTRATHECAL BUPIVACAINE IN SUBARACHNOID BLOCK - A RANDOMIZED DOUBLE BLIND STUDY"

By

Dr. VIDYA SHREE C

DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, KOLAR, KARNATAKA

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

Under the Guidance of

Dr. RAVI .M DA,DNB,MNAMS

Professor & HOD

DEPARTMENT OF ANAESTHESIOLOGY,

SRI DEVARAJ URS MEDICAL COLLEGE,

TAMAKA, KOLAR-563101

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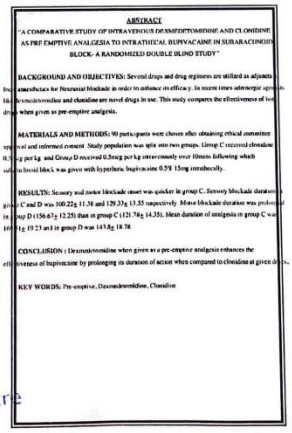

ABSTRACT

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KEY WORDS: Pre-emptive, Dexmedetomidine, Clonidine

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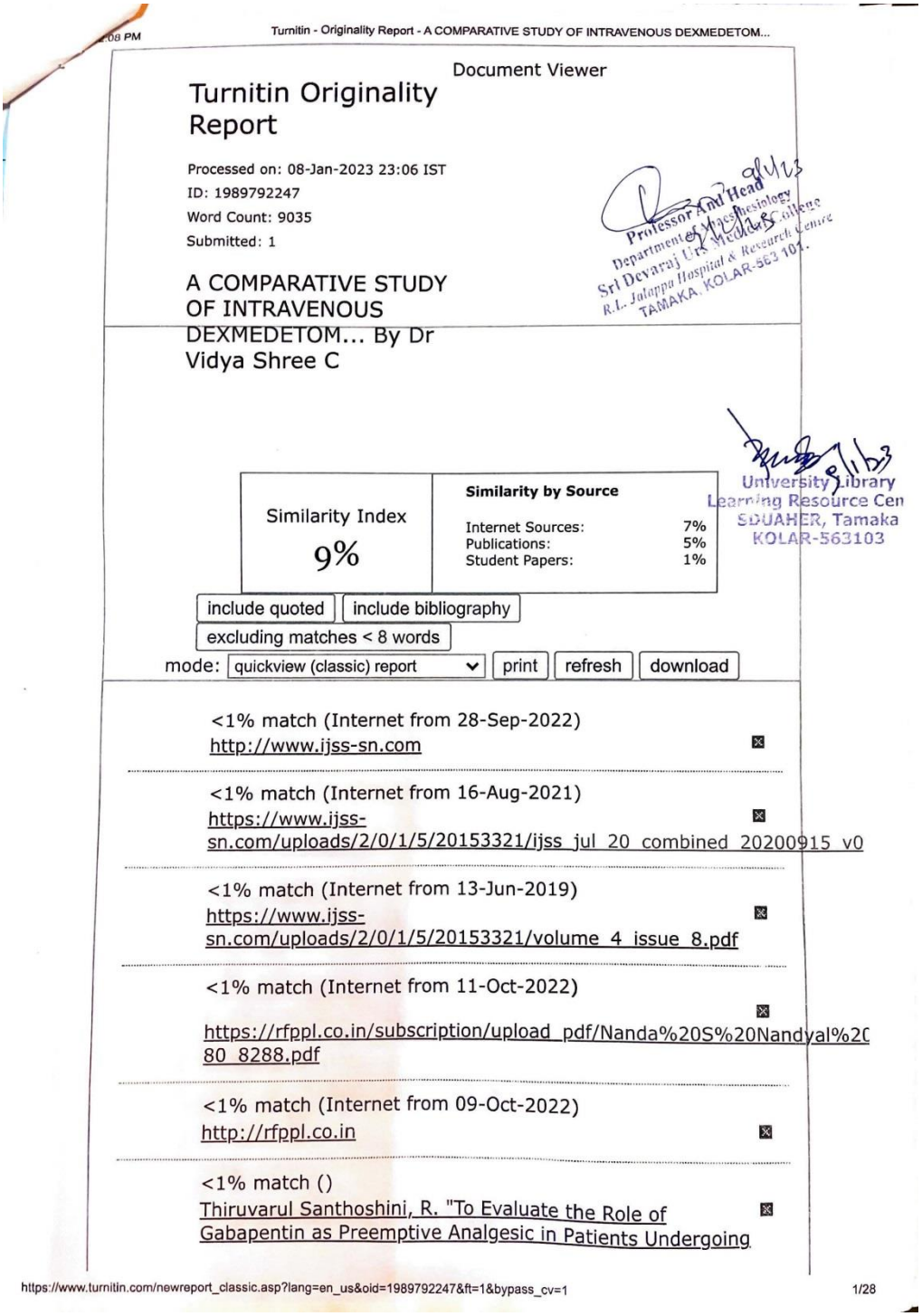

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Date : **Dr VIDYA SHREE C**

Place **:**

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BACKGROUND AND OBJECTIVES: Several drugs and drug regimens are utilized as adjuncts to local anaesthetics for neuraxial blockade in order to enhance its efficacy. In recent times adrenergic agonists like dexmedetomidine and clonidine are novel drugs in use. This study compares the effectiveness of both drugs when given as pre-emptive analgesia.

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CONCLUSION: Dexmedetomidine when given as a pre-emptive analgesia enhances the effectiveness of bupivacaine by prolonging its duration of action when compared to clonidine at given doses.

KEY WORDS: Pre-emptive, Dexmedetomidine, Clonidine, Bupivacaine.

ABBREVATIONS

HR	Heart Rate
Bpm	Beats Per Minute
BP	Blood Pressure
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
MAP	Mean Arterial Pressure
SPO_2	Peripheral capillary oxygen saturation
SAB	Subarachnoid Block
VAS	Visual Analogue Scale
No.	Number
hrs	Hours
LA	Local anaesthetic
α	Alpha
δ	Delta
CNS	Central Nervous System
IV	Intravenous
IM	Intramuscular
ASA	American Society of Anaesthesiologists
NS	Nociceptive Specific
WDR	Wide Dynamic Range
CSF	Cerebrospinal Fluid
PKa	Acid Dissociation Constant

µg	Microgram
Kg	Kilogram
mcg	Microgram
G	Gram
Ml	Millilitres
Da	Daltons
T1/2	Half-life
mins	Minutes
ACTH	Adrenocorticotropic hormone
IL	Interleukin
SD	Standard Deviation

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INTRODUCTION

Regional anesthesia or Neuraxial blockade are considerably applied for lower extremities and abdominal surgeries. Due to its early onset, better blockade, low rate of infection, lower error rates, and cost effectiveness, spinal blockade remains first choice. However brief duration of anaesthetic blockade are its disadvantages.[1] Bupivacaine is the frequently administered LA drug for spinal block, which has relatively shorter duration of action.[2]

To enhance the effectiveness of duration of anaesthesia and analgesia during surgeries and extend its action in the postoperative period various drugs and drug regimens are used as adjuvants like opioids, are used but it has acute side effects which includes nausea, vomiting, itching, respiratory distress, and urinary statis.[11] α -adrenergic agonists such as dexmedetomidine and clonidine are novel, used through intrathecal, epidural or intravenous route to enhance the effectiveness of subarachnoid block in terms of both sensory and motor blockade. [3,12]

These drugs act on pre and postsynaptic action sites of spinal cord. Stimulation of substance 'P' is blocked by α –receptors pre-synaptically and post synaptically comprehensive pain signal propagation is prevented.[4]

Clonidine, a partial α2 -adrenoreceptor agonist when administered intrathecally, is highly efficacious and safer drug. An α2 -adrenoreceptor agonist, i.e., dexmedetomidine has eight to ten times α2/α1 selectivity ratio greater than clonidine.[5] As per data clonidine is relatively 1.5 to 2 times more potent than dexmedetomidine in terms of similar dose.[6-10]

Till date very few researches have studied the equivalent dose of previously mentioned drugs. Henceforth, the research was dealt to analyze the effectiveness of both the drugs when given as pre-emptive analgesia to prolong the action of bupivacaine spinal anaesthesia.

AIMS & OBJECTIVES

Primary Objectives:

To compare and analyze the effectiveness of intravenous dexmedetomidine as well as clonidine for prolongation of bupivacaine spinal anaesthesia.

1. Sensory blockade- onset time and period of blockade.
2. Motor blockade- onset time and period of blockade.
3. Period of analgesia.
4. Hemodynamic stability.
5. Rescue analgesic requisite in the post-op period.

REVIEW OF LITERATURE

PRE-EMPTIVE ANALGESIA

Crile (1913) conceived pain prevention concept, and it was subsequently refined "by Wall and Woolf."[13]

"Pre-emptive analgesia is an analgesic intervention, which is given before painful stimuli to attenuate the sensitization of central and peripheral pain pathways, which intensifies post-operative pain".[14]

Principles:

a) Pre-emptive analgesia inhibits pain-related pathological CNS modulation. It reduces acute pain following injury to tissue, prevents the emergence of chronic pain and the persistence of post-operative pain.[15]
b) Numerous pharmacologic agents are used for effective pre-emptive analgesia.
c) They decrease activation of nociceptors by restricting or reducing activation of receptor and prevents the stimulation of pain chemical messenger.

Concept:

Pain generated from injured tissues causes changes in the somatosensory system, increasing the sensitivity of both central and peripheral neurons. As a result, there is an increased reaction to successive stimuli, which amplifies the pain.[16]

Nociceptors are first order neurons that detect tissue damage. They act as transducers, converting all injuries into electrical signals that are conveyed to second-order nerve cells. They are classified into several category. Myelinated Aδnociceptors cause the first pain, which is rapid, sharp, and localized. Unmyelinated 'C' nociceptors causes second pain, which is dull, slow-onset, and ill-defined.[17]

Dorsal horn contains two groups of neurons.

-**Nociceptive specific (NS)** neurons are the only neurons that respond to painful stimuli.

-**Wide dynamic range (WDR)** neurons respond to both noxious and non-noxious stimuli.

Nociceptors transmit harmful impulses to NS & WDR, altering their sensitivity. Impulse from the Aδ and C fibres are augmented, whereas stimuli from the A fibers are misinterpreted. This is referred to as central sensitization.

Pre-emptive analgesia aids in the prevention of the neurological and biochemical effects of painful stimuli to the CNS.

METHODS OF POSTOPERATIVE PAIN ASSESSMENT

It is essential to evaluate the patient's pain levels during postoperative period. After surgery, assessment of pain is thought to be a crucial vital sign, which should be performed on a regular basis.[18]

Postoperative pain assessment entails educating the patient prior to surgery about post-op pain. This sensitization assists the patient in acquiring knowledge that eases anxiety about surgery and fear of surgery related pain. It also assists to build up a positive attitude toward pain, eventually patient satisfaction is improved.

Assessment of postoperative pain allows analyzing the extent of pain, analgesic to be used, and evaluate the treatment response. Several methods for assessing pain are available. These methods must be simple and easy for patients to understand.

“Commonly used pain scales are:

1) Visual analogue scale.
2) Numerical rating scale.
3) Verbal rating scale.
4) Wong baker faces rating scale."

LOCAL ANAESTHETICS

BARICITY

As CSF dilutes the LA, its original concentration decreases sharply after injecting into the subarachnoid space. The initial sharp drop is caused by combining with CSF and ability to dissolve into nerve roots and spinal cord. Its elimination is primarily due to vascular absorption. The drug is either metabolized in plasma or liver. Adding vasoconstrictor reduces drug absorption and hence increases the duration of anaesthesia.

Densities of both local anaesthetic & CSF are compared at a given temperature to calculate baricity. This is about 1.0003±0.0003 g/mL at 37°C. Isobaric solutions have similar density like CSF. Hyperbaric solutions are denser than CSF, whereas hypobaric solutions are denser than CSF.

Baricity is the most crucial determinant for the local anaesthetics spread and block height. The local anaesthetic solution is combined with 5% to 8% dextrose to make hyperbaric solutions.[18]After administering a hyperbaric drug in lateral position and turning the patient, the drug flows to head and legs accumulates in the thorax and sacrum. This is because of the normal spine curvature causing the subsequent movementof the drug injected.

Gravity has no effect on isobaric solutions. Thus choice of anesthetic solution and proper patient positioning can have a considerable influence on the block height.

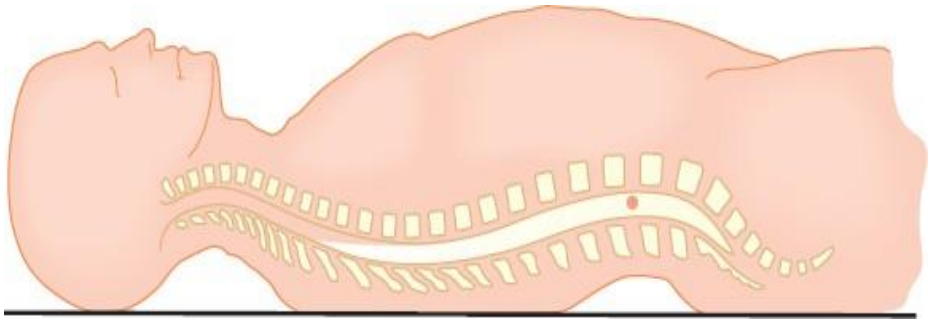


Figure 1: Hyperbaric drug distribution at the lumbarlordosis (circle)

DETERMINANTS OF SPREAD OF LA'S [20]

1) Local anaesthetic drug
    a) Baricity
    b) Volume
    c) Dose
    d) concentration
2) Patient
    a) Age, sex, weight, height
    b) Pregnant or non-pregnant
    c) Position
    d) Procedure
3) Site of injection

a) Barbotage

b) Needle bevel direction

c) Additives

d) Speed of injection

SUBARACHNOID BLOCK

SYSTEMIC EFFECTS[19]

Cardiovascular effects

Sympathetic fibres that emerge through T5 -L1, as well as innervate arterial and venous smooth muscle to control vasomotor tone. As a result, sympathetic block causes a reduction in BP, which is associated with reduction in pulse rate. Higher level of block, also blocks sympathetic cardiac accelerator fibres originating at T1-T4, resulting in reduced cardiac contractility.

Respiratory effects

The tidal volume is constant even at higher level block. The paralysis of abdominal muscles causes a minimal decrease in vital capacity. With higher levels of block, coughing and secretion clearance may be impaired.

Digestive tract function

Up to 20% of cases experience nausea and vomiting. It is caused by unopposed parasympathetic activity that causes hyperperistalsis of gastrointestinal system. Vagal tone dominance causes active peristalsis, which creates suitable conditions. Reduced mean arterial pressure leads to a reduction in hepatic blood flow.

POSITIONING:

1) Sitting Position
2) Lateral Decubitus
3) Buie's (Jack knife) Position

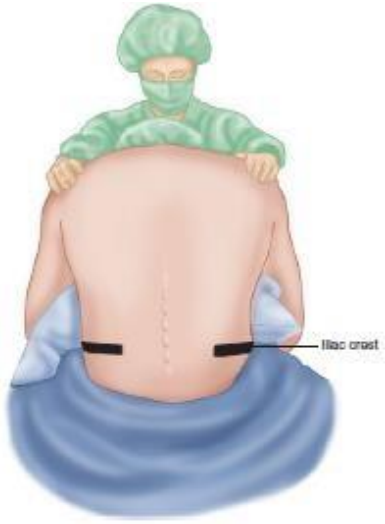


Figure 2: Sitting posture

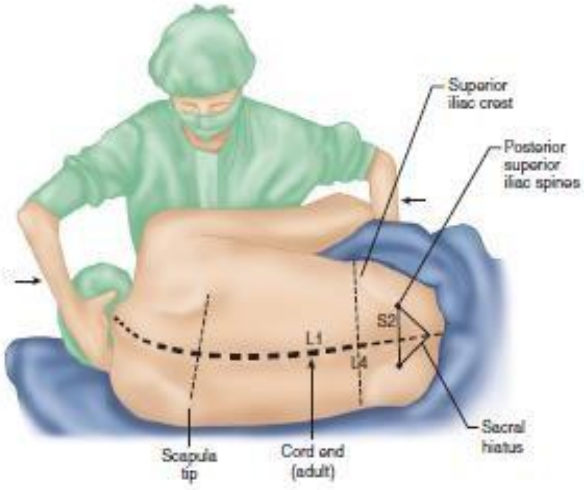


Figure 3: Lateral decubitus position

Figure 4: Jack knife position

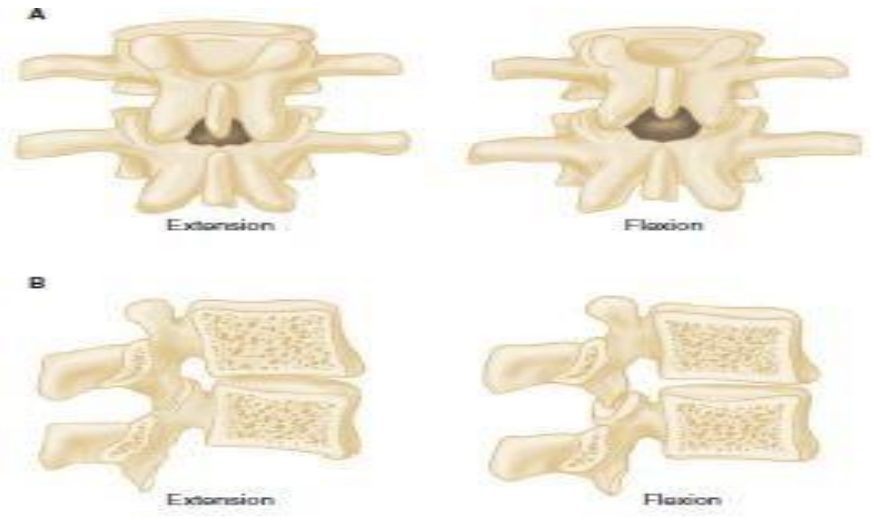


Figure 5: Flexion effect on adjacent vertebrae.

A: Posterior view B: Lateral view

APPROACH

1) Midline

2) Paramedian

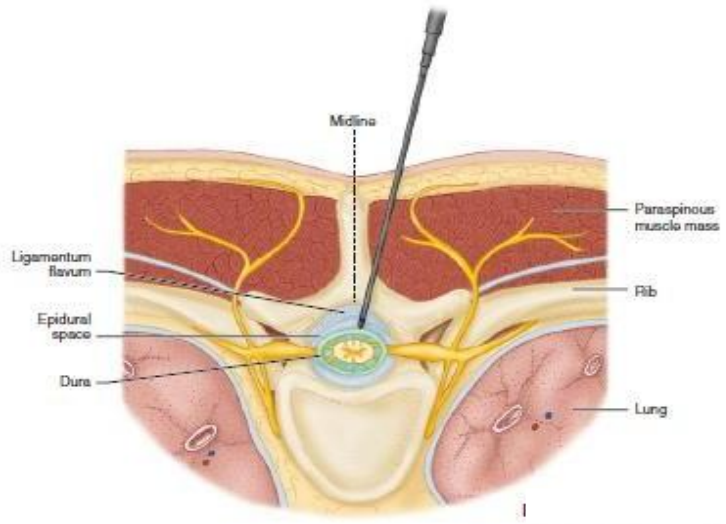


Figure 6: Paramedian approach

NERVE MODALITY BLOCK ORDER:

1) Vasomotor block.
2) Blocks cold temperature fibres.
3) Temperature discrimination.
4) Slow pain.
5) Fast pain.
6) Tactile senses.
7) Motor paralysis.
8) Pressure senses.
9) Proprioception and joint senses.

	INDICATIONS	**CONTRAINDICATIONS (Absolute)**	**(Relative)**
1.	Surgeries like, lower abdominal	Injection site infections	Sepsis
2.	Urogenital	Non cooperative	Neurological disorders
3.	Anorectal	Coagulopathy	Demyelinating lesions
4.	Caesarean sections	Severe hypovolemia	Severe spinal deformity
5.	Lower limb surgeries	Raised intracranial pressure	Heart valve stenosis

Table 1: Indications and contraindications of SAB

COMPLICATIONS:

1) **Adverse or exaggerated physiological responses**

   a) Hypotension , bradycardia

   b) Urinary stasis

   c) High neural block

   d) Complete spinal anesthesia

   e) Cardiac arrest

2) **Related to needle or catheter insertion**

   a) Misplacement-inadequate anesthesia or analgesia

      -intravascular injection

   b) Post-dural puncture headache

   c) Back pain

   d) Neural injury

   e) spinal hematoma

   f) infection- Arachnoiditis

      -Meningitis

3) **Drug toxicity**

   a) Local Anesthetic Systemic Toxicity

   b) Transient neurological symptoms

PHARMACOLOGY OF BUPIVACAINE [19]

Chemical structure:

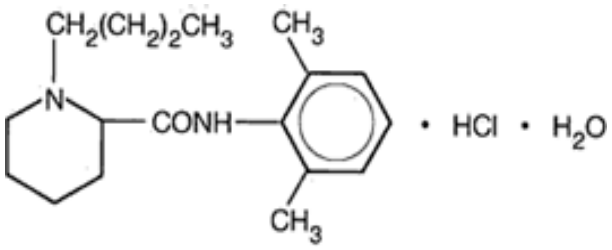


Figure 6: Chemical structure of Bupivacaine[19]

Bupivacaine pharmacology:

"Bupivacaine hydrochloride is an amide type of local anaesthetic drug that is chemically 1-butyl-2', 6' pipecoloxylidide hydrochloride. It was synthesized by Ekenstam AF in 1957 and used clinically in 1963."[19]

Bupivacaine is produced by adding a butyl group to piperidine nitrogen in mepivacaine. It's extremely lipid soluble. Its potency and duration of action are more than mepivacaine. A pipecoloxylidide local anaesthetic is bupivacaine.

Physicochemical properties:

a) Molecular weight- 288 (base) 325 (chloride salt)

b) pKa- 8.1

c) Plasma protein binding- 95%

d) Solubility-The base is only barely soluble in water, but the hydrochloride is highly soluble.

e) Stability and sterilization: extremely stable.

f) Melting temperature: 258^0 C.

g) Potency: 3-4 times potent than lidocaine.

Distribution and Absorption:

Variables affecting drug absorption from administrating site into circulation includes injection site , drug dosage, the addition of vasoconstrictive agent, the properties of drug, tissue distribution rate, and drug clearance rate.

The solubility of lipids is essential in allocation, and LA's attaching with protein influences their dispersion and excretion. Bupivacaine is highly protein bound.

CNS toxicity:

Initially, symptoms include perioral tingling and numbness, agitation, dizziness, ringing in the ears, and impaired concentration.

Slurring of speech and skeletal muscle spasms result from higher concentration. Tonic-clonic seizures are frequently preceded by skeletal muscle twitching in the face and extremities. Seizures are precipitated by drowsiness and occurs following CNS depression.

Seizures are closely linked with plasma concentrations of 4.5 to 5.5 µg/ml.

Cardiac toxicity:

Following an adventitious intravascular injection of bupivacaine, a considerable quantity of unbound drug is diffused in the heart's conducting tissue. This can cause severe hypotension, dysrhythmias, and AV heart block. Bupivacaine has a cardio-toxic plasma concentration of 8 to 10 g/ml.

PHARMACOLOGY OF DEXMEDETOMIDINE[21]

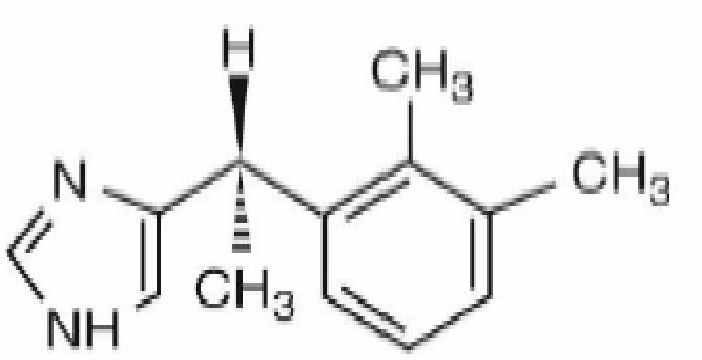


FIGURE 7: CHEMICAL STRUCTURE OF DEXMEDETOMIDINE[21]

"Medetomidine (4-[1-(2,3-dimethylphenyl) ethyl]-1H-imidazole) is a sedative/analgesic compound that has efficacy and selective activity at α-2 adrenoreceptors."[21]

Dexmedetomidine is the dextro isomer (s- enantiomer) of medetomidine, an imidazole compound. $C_{13}H_{16}N_2HCL$ is its empirical formula and 236.7 Da is its molecular weight.

Considerably high ratio of α2/α1-activity is seen in Dexmedetomidine (1620:1 versus 220:1 for clonidine) and regarded as α2 - receptor full agonist. As a result of α1 receptor activation it results in more effective sedation without undesirable cardiovascular effects.[21]

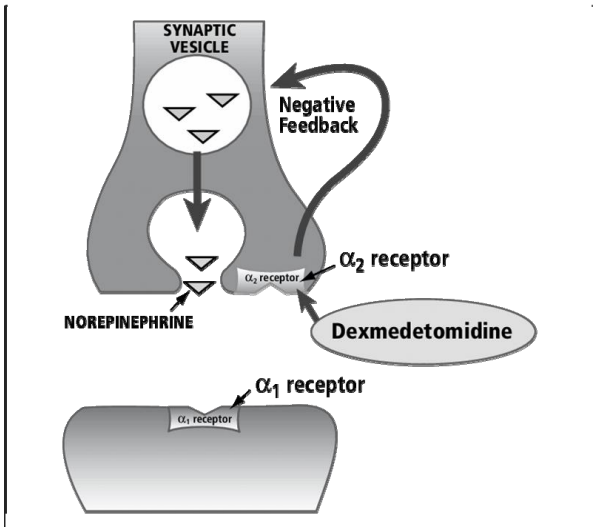


FIGURE 8: MECHANISM OF ACTION OF DEXMEDETOMIDINE[21]

Pre-synaptic α2 receptors are clinically important as they regulate norepinephrine and adenosine triphosphate release via a negative feedback. Pre-synaptic activation of α2 adrenoceptor prevents norepinephrine release, thus stopping the transmission of pain signals. Activates α2 Post-synaptic receptor activation and prevents sympathetic action, which lowers BP as well as pulse rate. When these effects combine, they can cause analgesia, sedation, and anxiolysis. [22]

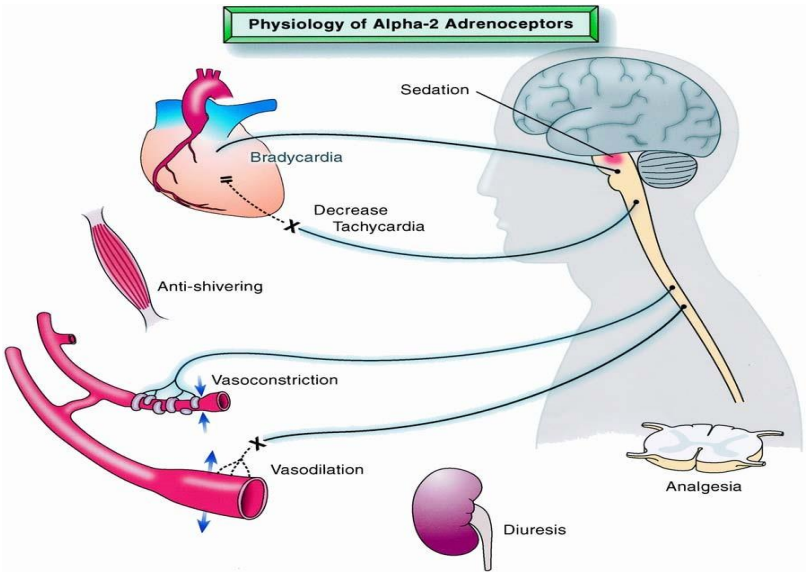


Figure 9: SITE OF ACTION[22]

These agents have hypnotic and sedative effects mediated by supraspinal pathways involving the locus coeruleus (LC). Whereas the antinociceptive response to α2 agonists administered intrathecally is controlled primarily in the spinal cord. [23,24]

Cardiac effect is decrease in heart rate through vagomimetic action and also through cardio accelerator nerve block. Peripheral vascular effects are vasoconstriction via smooth muscle receptors and vasodilation via sympatholysis. Diuresis occurs as a result of a reduction in the release of vasopressin and rennin.[25] It stimulates both pre-synaptic and post-synaptic α-2 receptors causing inhibition of firing of nociceptive neurons.[26]

The action on G1-protein-gated potassium channels causes hyperpolarization of membranes. This mechanism is said to be significant for a receptor inhibitory activity.[27]

PHARMACOKINETICS:

It is administered by oral, intramuscular and transdermal routes. It follows zero order kinetics and not first order kinetics.

Following IV administration, it has a T1/2 of about 6 mins; context sensitive half-life after infusion of 10 mins is from 4-250 mins after an 8 hour infusion; T1/2 elimination is 2 hours. Estimated clearance resulted in a mean body weight of 72kg.[28] Dexmedetomidine has linear pharmacokinetics from 0.2-0.7mcg/kg/hour when administered intravenously for up to 24 hours. [29,30]

Distribution:

About 94% of the drug is approximately bound to serum proteins like α1 glycoprotein and albumin. In patients with deranged liver function tests, dose should be reduced as free fraction of drug is elevated due to decreased serum proteins.[31]

The drug dosage also depends upon the age of the patient. In children as the volume of distribution is more, we tend to give more dosage.

Metabolism:

Dexmedetomidine is metabolized in liver by the cytochrome p450 enzyme. It is also conjugated with glucuronide. About 94% of the metabolites are eliminated in the urine, while 4% in faeces. [32]

PHARMACODYNAMICS:

Central Nervous System

Sedation

The other drugs act through the GABA (Gamma Amino Butyric Acid) systems while dexmedetomidine acts upon by promoting endogenous sleep pathways. Patients will be in a state from where they can easily wake up and they follow commands. It is said to have wide safety margin as it provides good sedation with minimal effect on respiration.[33]

Analgesia

The primary site of action for analgesia is Spinal cord. It provides analgesia when it is injected via epidural or intrathecal route. It prevents the secretion of substance P from the spinal cord's dorsal horn, exerting primary analgesic effects.[34]

Cardiovascular System

Dexmedetomidine is said to have biphasic cardiovascular response.[23]

Dexmedetomidine of 1mcg/kg in younger patients causes temporary rise in BP with a reflex decline in heart rate. [35] It is managed by giving the drug slowly over 10mins. Even then, there was 7% increase in the mean arterial pressure and 16-18% reflex decline

in heart rate.[36]

Both BP and heart rate fall below baseline following initial rise. The outcomes are due to suppression of central sympathetic outflow.[37] The drop in HR and BP is thought to be due to presynaptic α2-adrenoceptor stimulation which leads to decrease in norepinephrine release.[38]

Although the baroreceptor reflex is maintained with dexmedetomidine, bradycardia and hypotension may occur, which can be managed with atropine or ephedrine. [27]

Respiratory System

Oxygenation and compliance are improved with dexmedetomidine. It also reduces the dead space ventilation.[28] When administered intravenously, dexmedetomidine causes bronchodilation.[37] Though it is seen to reduce the pulmonary blood pressure in patients with pulmonary vasoconstriction, there are no studies done on it extensively.[38]

Endocrine System

Serum cortical and ACTH levels are not altered in patients on dexmedetomidine infusion.[21] Dexmedetomidine does not inhibit cytochrome P450 enzyme, including steroidogenesis.[31] Dexmedetomidine acts on α-2 receptors in pancreas and decreases insulin production thereby causing hyperglycemia.[39] It also stimulates growth hormone and decreases inflammatory response and the levels of IL-6.[3]

Renal System

The norepinephrine release is decreased because of its α2B receptor action on locus coeruleus. This leads to vasodilatation and increase in renal blood flow.[39]

INDICATIONS OF DEXMEDETOMIDINE

Dexmedetomidine is available in 0.5, 1 and 2ml ampoules. 1ml contains 100mcg of dexmedetomidine.[40]

Premedication[41] – because of its anxiolytic, sedative, analgesic, anti-sialagogue and sympatholytic properties. It is given at 1mcg/kg over 10mins.

ICU sedation[41] - loading dose is given at 1mcg/kg IV over 10mins, maintenance dose of 0.2-1.4 mcg/kg/hr IV.

To attenuate intubation response[41] -Loading dose- 0.25-1mcg/kg I.V over 10 mins.

To attenuate extubation response[35] - Loading dose-0.5-1.0mcg/kg I.Vover 10 mins.

For subarachnoid block[42] - 3-5mcg is added to local anaesthetic.

For caudal anesthesia[3] - 1-2mcg/kg is added to local anaesthetic.

Intravenous regional anesthesia[35] - 0.5mcg/kg is added to local anaesthetic solution.

CONTRAINDICATIONS OF DEXMEDETOMIDINE[44]

1. Infusion over 24 hours.
2. In obstetrics, as the safety is not studied.
3. In patients with pre-existent bradycardia, heart blocks and related brady-arrhythmia.
4. In hypovolemic or hypotensive patients.
5. Allergy or known hypersensitivity to dexmedetomidine

ADVERSE EFFECTS

It includes decreased heart rate, low BP, nausea, atrial fibrillation, hypoxia, and first or second-degree heart block. Many of these occur during administering loading dose of drug. Adverse effects can be minimized by lowering the loading dose or eliminating the drug itself.[9]

PHARMACOLOGY OF CLONIDINE[45]

"Clonidine is a centrally acting, partial α2-adrenergic agonist that works as an antihypertensive by decreasing sympathetic nervous system outcome from the CNS."[45]

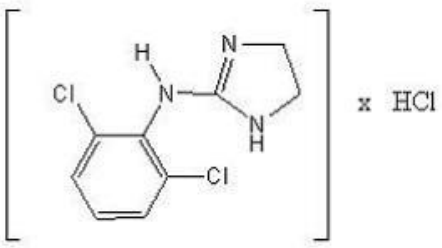


Figure 9: chemical structure of Clonidine[45]

PHARMACOKINETICS[45]

Clonidine is quickly and entirely absorbed from the digestive tract with 100% bioavailability. Maximum plasma level is attained within 60-90 minutes of oral administration. Clonidine has half-life of 9-12 hours, nearly half undergoes hepatic metabolism and converts into P-hydroxy clonidine and the remaining is removed in urine without change. The transdermal route generates plasma concentrations within 48 hours. Clonidine can be given as oral, IV, IM, transdermal, epidural, or intrathecal route.

PHARMACODYNAMICS

Cardiovascular system:

It has a complicated effect on blood pressure after systemic infusion due to antagonizing actions on different sites. Receptors of noradrenergic imidazoline are stimulated in the lateral reticular nucleus, resulting in fall in BP and an anti-arrhythmic effect. Excitation of presynaptic α2-adrenoceptors at the periphery of nerve terminals in sympathetic system will decrease norepinephrine secretion, which may result in

relaxation of vessels and decreased chronotropic drive. Direct peripheral vasoconstriction nullifies the excitation effects of brainstem and α2 adrenoceptors with the action of clonidine. U-shaped dose response of clonidine is seen when systemically administered.[46]

Heart rate is decreased by clonidine through presynaptically mediated suppression of norepinephrine and it inhibits the transmission of atrioventricular nodes.[19]

Respiratory effects:

Clonidine causes depression of respiration and does not intensify the opioid's depressant effect. [45] Drugs that relieve pain, anxiety, and cause sedation by acting on CNS, also decrease alveolar ventilation.

CNS:

Clonidine causes sedation. Stage I and II sleep are enhanced while reducing rapid eye movement is produced by clonidine. Anaesthetic properties of α2-adrenergic agonists are achieved through inhibitory actions via G-protein coupled mechanism. Dose-dependent sedation is produced with clonidine irrespective of route of administration.[47]

USES OF CLONIDINE:

1. In resistant hypertension or renin-dependent disease.
2. Can be used as pre-anesthetic drug.[12]
3. Dose-dependent analgesia can be observed by administration of clonidine into epidural or subarachnoid space.[9]
4. Postoperative analgesia is intensified by adding 1 g/kg clonidine to lidocaine.[51]
5. Perioperative myocardial ischemia is prevented by clonidine.
6. Withdrawal symptoms of opioid and alcohol are managed with clonidine.
7. Shivering can be decreased by clonidine.

Chavi Sethi et al. [50] found that sensory block onset among groups A, B was (1.81±1.75), (2.56±1.62) respectively. Group A (T5–T7) sensory level was higher than group B (T6-T8). In group A (121.45±25.74) 2- segment regression time was higher than group B (87.38±15.94). In group A (234.34±47.82) cumulative sensory block duration was more than group B (141.66±30.20). Motor block onset in group A (3.54±3.07) was faster than group B (4.64±2.91). The motor block duration was higher in group A (265.45±41.50) than group B (223.12±26.43).

In **Kiran Kumar S et al.** study, [51] the onset of analgesia in control, clonidine, and Dexmedetomidine groups was (5.02+1.03), (4.02 ± 1.06) and (2.58 ± 1.18) respectively, and this difference was significant. Sensory block time was (137.4 ± 10.9), (124.32 ± 15.01), and (102.8+14.8) in Dexmedetomidine, clonidine and control groups respectively. Motor block onset time was decreased in dexmedetomidine group (3.54 ± 0.45) mins, than in the clonidine and control groups (4.26 ± 1.39) and (4.59+1.26) min.

In **Reddy VS et al.** study, [11] sensory block onset was (2.91 ± 1.16) min, and (3.58 ± 1.06) min in dexmedetomidine and clonidine group. Motor block onset time in dexmedetomidine, clonidine, and placebo was (3.64 ± 0.75) min, (4.21 ± 1.49) min and (4.57 ± 0.83) min respectively. Sensory regression time was (148.54 ± 20.66) min, (126.38 ± 16.04) min and (95.38 ± 17.41) min in the dexmedetomidine, clonidine and placebo groups. Postoperative analgesia time was (243.35 ± 56.82) min, (190.93 ± 42.38) min and (140.75 ± 28.52) min in Dexmedetomidine, clonidine and placebo.

In Kumar SK et al.[52] study the analgesic onset time in IT group, IV group was (4.20± 1.02) min and (4.53 ± 3.06) min respectively. Sensory analgesic period was (226.1 ± 6.8) min and (196.1 ± 5.9) min in IT and IV group. In IT group 4% and 2% of cases had hypotension, bradycardia respectively.

Raushan R, and Prakash A study[53] reported that mean age in group 1 and group 2 are 46.5 and 44.2 years. Majority of cases were males in both the study groups. Mean BMI of 24.3, 22.8 respectively in group 1 and group 2. Mean sensory onset duration was (1.1± 0.4), (1.5± 0.5) in group 2 and group 1 respectively. Time to first rescue analgesia was (391.2 ± 63.9)minutes, (356.5 ± 55.7) minutes in group 2 and group 1 respectively. Mean VAS in both group 1 and 2 was (4.9 ± 1.1) and (4.1 ± 0.8) respectively.

Bamel S et al. study [54] in group NS mean time to sensory level to regress two dermatome levels was (112.60+ 20.86) minutes. P-value was statistically highly significant on comparison of group D with group NS and Clonidine (138.9 ± 17.4) as compared to control (90.1 ± 9.4) Sensory block duration was highly significant in group D versus group C and Clonidine (138.9 ± 17.4) as compared to control (90.1 ± 9.4). Sensory block duration was highly significant in a group C.

In Patil KN et al. study, [55] the sensory regression duration to S1 dermatome in dexmedetomidine, clonidine, and placebo was (231.20+24.84) min, (200+23.67) min, and (171+12.25) min respectively. The motor block in (135.20+12.87) min, (180.40 + 24.70) min and (205.20+25.56) min in placebo, clonidine and with dexmedetomidine. Dexmedetomidine, clonidine, and placebo has (255+23.14) min,(221.40+24.30) min, and (202.60+14.08) min The MAP was significantly higher in placebo than both dexmedetomidine and clonidine.

In Ganesh M, and Krishnamurthy D study, [12] onset of sensory block in 3 groups B, C, D was (2.8 ± 0.7)min, (1.4 ± 0.5)min, and (1.2 ± 0.4)min respectively. Motor blockade onset in groups B,C, and D was (4 ± 0.7)min, (1.6 ± 0.5)min, and (1.1 ± 0.4)min

respectively. Sensory regression duration in groups B,C and D was (78.5 ± 9.9)min, (136.7 ± 10.7)min, and (136.4 ± 11.7)min. Motor blockade duration in groups B,C, and D was (167.9 ± 20.6) min, (279.2 ± 24.1)min, and (302.6 ± 36.6)min. Rescue analgesic time in groups B,C,D was (167.9 ± 20.6)min,(344.4 ± 28.9)min, and (366.6 ± 37.5)min respectively. VAS scores in groups B,C and D was (5.9 ± 0.8), (4.9 ± 0.8), and (4.7 ± 0.7).

MATERIALS AND METHODS

Source of data:

Study was done on **90 participants** satisfying inclusion criteria and undergoing elective lower extremities and lower abdominal surgeries under spinal blockade and at R. L. Jalappa Hospital and Research Centre, A unit of SDUAHER, Tamaka, Kolar, from **January 2021-May 2022**.

Study design: Prospective, double-blind comparative study.

Method of sampling: computerized random sample.

Method of collection of data:

Inclusion criteria:

- Age group among 18 – 60 years.
- ASA-physical status I/II.
- Either gender.

Exclusion criteria:

-Patient with Ischemic heart disease, hepatic and renal disease.

-Uncontrolled diabetes and hypertension.

-Parturients.

-Structural abnormalities of spine

-Coagulopathies, contaminated prick site, previous neurological deficiency.

-Allergy to the study drugs.

-Patients refusal.

Sampling procedure:

- The ethical clearance was taken prior to start of the study. 1 day prior to the surgery a thorough preanaesthetic check-up was carried out, history was taken and systemic examination was done.
- Relevant investigations were checked.
- Anaesthetic procedure explained and informed permission was taken.
- Standard fasting guidelines were followed.
- Patients were divided into GROUP-D and GROUP-C
- GROUP- D received Dexmedetomidine 0.5mcg per kg IV.
- GROUP- C received Clonidine 0.5mcg per kg IV.
- The drug was premixed to 10ml and given IV over 10min duration as a bolus dose.
- Five minutes after administrating the drug in both the groups, SAB was done and Bupivacaine (H) 0.5% 15mg was administered in intra-thecal space. Both patients and treating anaesthesiologist involved in the study were double blinded and recordings were taken by an anaesthesiologist who was unaware of groups.
- Post operatively VAS score was recorded. If the score was 3 or more inj. Diclofenac 75mg intramuscularly was given and number of doses given were recorded.

Parameters to be observed:

1. Sensory blockade- onset time and period of block.
2. Motor blockade- onset time and period of block.
3. Time of 1st rescue analgesia and number of doses required in 24 hours post- operative period based on VAS score.
4. Hemodynamic parameters- HR, SBP,DBP, MAP, SPO2.
5. Any dangerous events like hypotension, bradycardia, pruritis were noted.

Statistical analysis

Sample size is calculated based on a study by Kanazi et al.[3] with mean difference of 30% in time for sensory regression by 2 dermatomes with 99% confidence interval and 1% absolute precision is 90.

$$\text{Sample size (n)} = \frac{Z^2_{1-\alpha/2}\,\sigma^2}{d^2}$$

Where,

σ: Standard Deviation

d: Precision

$\alpha/2$: desired confidence level

Statistical methods

Collected data were entered into Microsoft Excel (Windows 10) and analysis was done using the Statistical Package for Social Sciences (SPSS version 25.0; Chicago). Continuous variables were shown as mean, S.D, categorical variables were shown as percentage. For statistical analysis, Independent t test, and Chi square test was applied. P-value <0.05 was taken as statistically significant.

RESULTS AND OBSERVATIONS

Table 2: MEAN AGE DISTRIBUTION.

Group	Mean age	S.D	P-value
Group C	45.62	10.75	0.1 (Non Significant)
Group D	41.60	12.16	

The mean age of subjects was 45.62 ± 10.75, and 41.60 ± 12.16 in both group C and D respectively. This mean age difference was statistically non-significant

Figure 11: AGE DISTRIBUTION OF SUBJECTS DEPICTED BY BAR DIAGRAM.

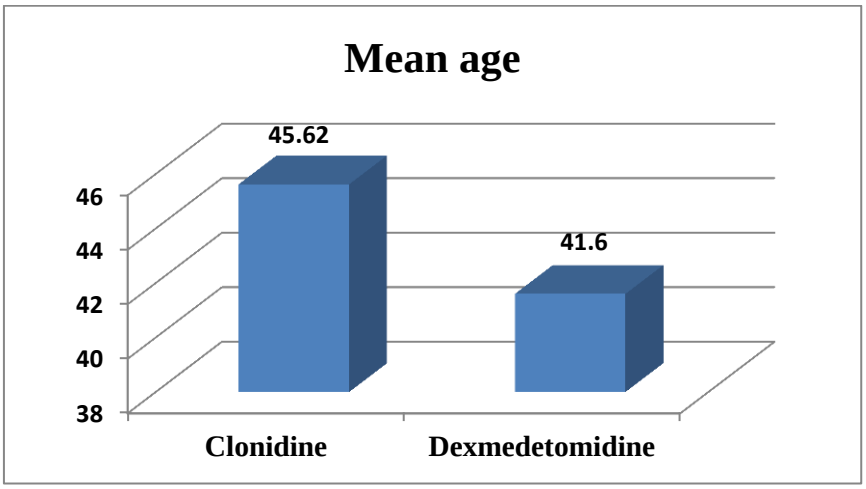


Table 3 : MEAN WEIGHT DISTRIBUTION

Group	Mean weight	S.D	P value
Group C	63.00	6.58	0.25 (Non Significant)
Group D	61.53	5.49	

Mean weight of subjects in Group C was (63.00 ± 6.58)kgs, and Group D was (61.53 ± 5.49)kgs. The results are statistically insignificant.

FIGURE NO 12: WEIGHT DISTRIBUTION DEPICTED BY BAR DIAGRAM

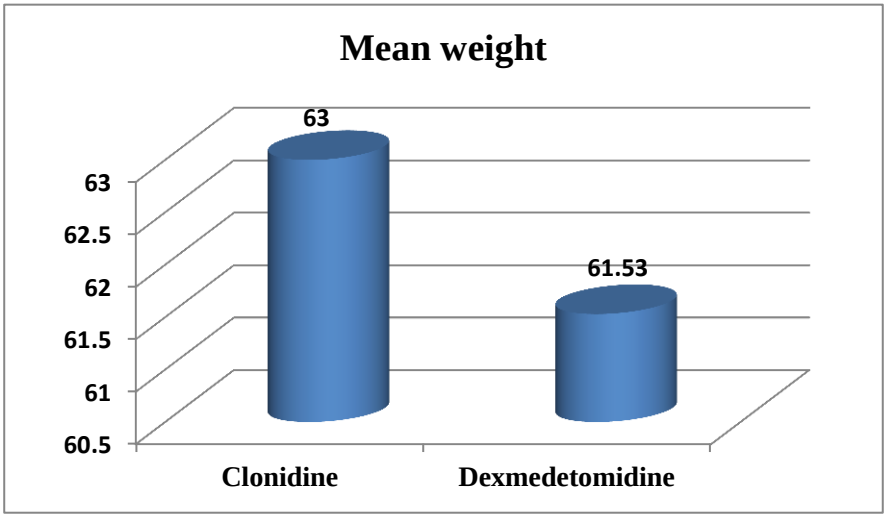


Table 4: TREND OF HEART RATE

PR	Group C		Group D		P value
	Mean	Standard deviation	Mean	Standard deviation	
At Pre op	85.84	7.79	85.82	9.67	0.99
At intra op	83.04	8.76	80.16	10.35	0.157
At 3 minutes	81.33	9.03	76.11	9.59	0.009*
At 5 minutes	82.93	9.11	72.07	10.09	0.0001*
At 10 minutes	79.04	7.41	71.96	8.67	0.0001*
At 20 minutes	77.31	7.57	71.82	6.34	0.0001*
At 30 minutes	74.27	6.87	70.69	5.01	0.006*
At 60 minutes	74.64	5.44	70.80	4.54	0.0001*
At 90 minutes	76.73	5.59	72.09	6.34	0.0001*
At 120 minutes	77.58	8.09	73.91	6.95	0.024*

***** Significant

The trend of mean HR observation shows that heart rate in group D is lower than group C and is statistically significant. At 5th minute after spinal anaesthesia, there was decrease in HR of about 80.73±8.57 bpm in Group C and 72.07±10.09 bpm. At any given point heart rate is always >60bpm which indicates hemodynamic stability.

FIGURE 13: LINE DIAGRAM DEPICTING HEART RATE TREND.

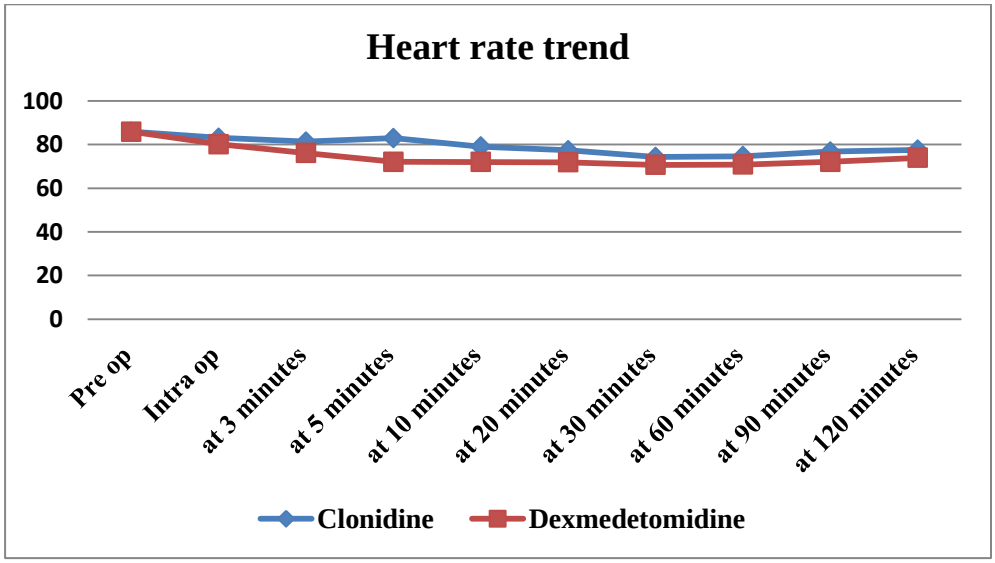


Table 5: TREND OF SBP

SBP	Group C		Group D		P value
	Mean	Standard deviation	Mean	Standard deviation	
At Pre op	126.91	7.81	126.13	8.71	0.657
At intra op	122.38	8.67	118.60	7.84	0.033
At 3 minutes	119.07	8.43	114.82	7.51	0.013*
At 5 minutes	120.69	9.21	117.76	7.41	0.099
At 10 minutes	113.44	10.29	113.56	6.66	0.952
At 20 minutes	109.38	7.18	108.78	7.04	0.69
At 30 minutes	107.93	6.52	107.87	7.742	0.965
At 60 minutes	107.18	4.27	110.22	6.77	0.013*
At 90 minutes	116.22	6.61	114.76	5.67	0.262
At 120 minutes	123.89	5.89	123.04	3.58	0.414

*significant

SBP (in mm Hg) in both Group C and Group D, fluctuations were observed in both group. The difference was statistically insignificant.

FIGURE 14: LINE DIAGRAM DEPICTING SBP TREND.

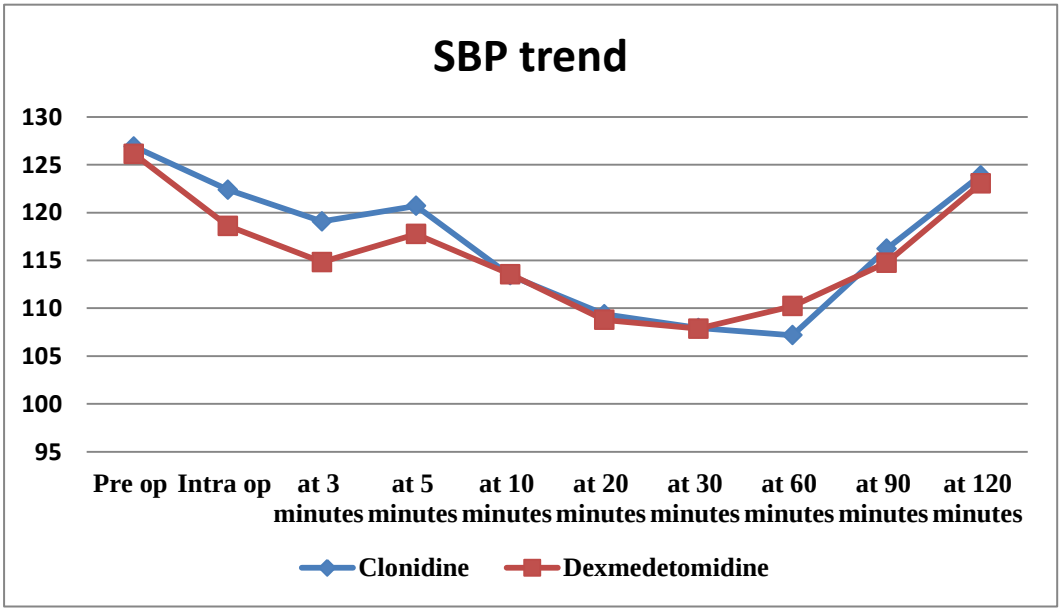


Table 6: TREND OF DBP

DBP	Group C		Group D		P-value
	Mean	Standard deviation	Mean	Standard deviation	
At Pre op	83.51	6.53	80.27	9.32	0.059
At intra op	79.87	6.76	75.67	9.31	0.016*
At 3 minutes	76.04	7.51	73.60	7.37	0.123
At 5 minutes	78.31	8.49	76.71	8.07	0.362
At 10 minutes	75.18	9.02	73.31	6.47	0.263
At 20 minutes	71.69	6.97	70.93	7.16	0.613
At 30 minutes	69.42	7.16	69.84	8.96	0.806
At 60 minutes	68.20	4.68	71.89	9.51	0.022*
At 90 minutes	73.60	6.18	70.44	8.35	0.045*
At 120 minutes	78.58	7.35	78.87	5.15	0.830

*significant

DBP (in mm Hg) in Group C and Group D, fluctuations were observed in both group. The difference was statistically insignificant.

FIGURE 15: LINE DIAGRAM DEPICTING DBP TREND.

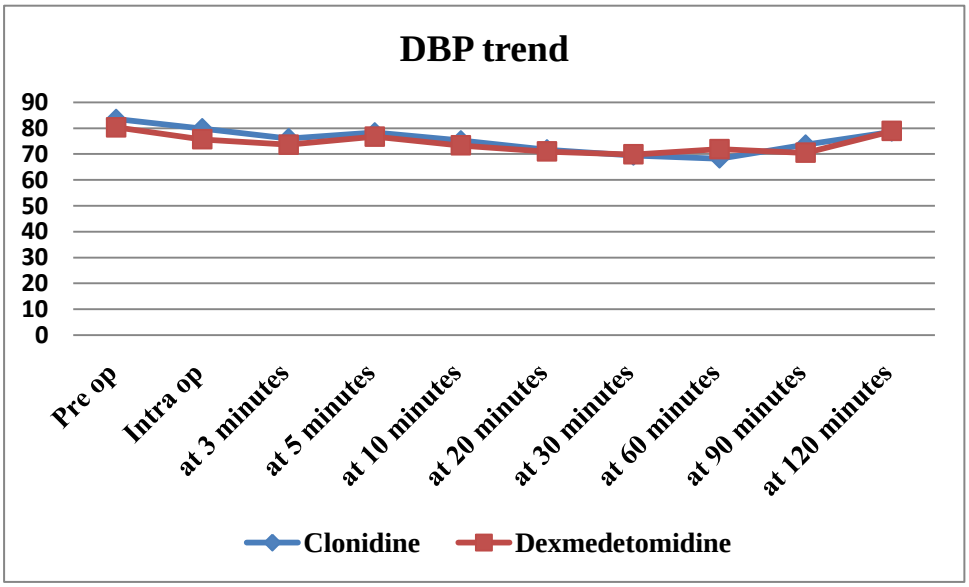


Table 7: TREND OF MAP

MAP	Group C		Group D		P value
	Mean	Standard deviation	Mean	Standard deviation	
At Pre op	97.84	7.63	96.13	8.45	0.316
At intra op	93.47	6.96	89.22	8.73	0.013
At 3 minutes	90.02	7.63	87.69	6.86	0.131
At 5 minutes	92.20	9.47	89.22	7.48	0.102
At 10 minutes	87.76	8.21	86.73	5.54	0.491
At 20 minutes	82.73	6.83	80.91	8.76	0.274
At 30 minutes	82.07	5.74	80.67	9.58	0.403
At 60 minutes	81.16	4.04	84.16	8.85	0.042*
At 90 minutes	88.02	5.31	85.80	7.67	0.114
At 120 minutes	93.51	5.45	93.56	3.69	0.964

*significant

The mean MAP in study illustrates non-significant difference in both groups excluding at 60 mins after spinal block where MAP was significantly lower (P=0.042). Peri-operative MAP was above 75mmHg, indicating hemodynamic stability.

FIGURE 16: LINE DIAGRAM DEPICTING MAP TREND

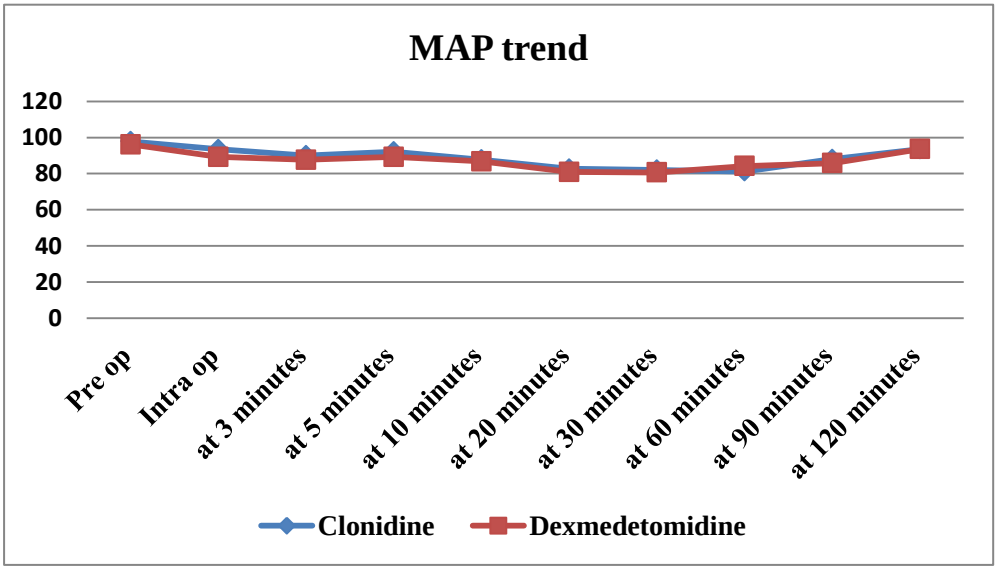


Table 8: TREND OF SPO2%

SPO2	Group C		Group D		P value
	Mean	Standard deviation	Mean	Standard deviation	
At Pre op	99.47	0.66	99.58	0.65	0.426
At intra op	99.40	0.61	99.47	0.62	0.612
At 3 minutes	99.44	0.62	99.20	0.69	0.082
At 5 minutes	99.44	0.62	99.20	0.69	0.082
At 10 minutes	99.44	0.62	99.20	0.69	0.082
At 20 minutes	99.42	0.65	98.80	0.58	0.0001*
At 30 minutes	99.42	0.65	98.80	0.58	0.0001*
At 60 minutes	99.42	0.65	98.80	0.58	0.0001*
At 90 minutes	99.44	0.62	98.91	0.55	0.0001*
At 120 minutes	99.40	0.61	99.47	0.62	0.612

*significant

The trend of SPO2 illustrates insignificant difference among groups except from 20mins to 90 mins after spinal anesthesia where SPO2 was significantly lower in dexmedetomidine group. Intra-operative SPO2 was above 96%, indicating hemodynamic stability.

FIGURE 17: LINE DIAGRAM DEPICTING SPO_2% TREND.

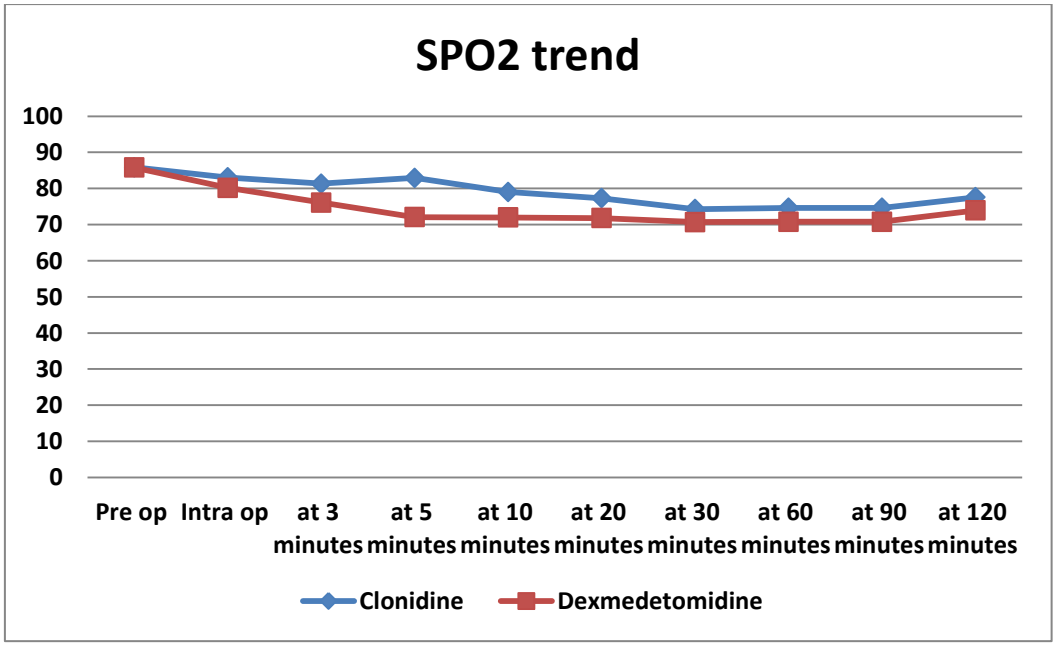


TABLE 9: MEAN SENSORY BLOCKADE ONSET TIME.

Group	Mean sensory block onset	S.D	P value
Group C	3.80	0.84	0.0001 (Significant)
Group D	2.40	0.81	

Pre-emptive intravenous dexmedetomidine in Group D resulted in faster sensory blockade (2.40± 0.81) whereas in Group C (3.80± 0.84) and is statistically significant

FIGURE 18: BAR DIAGRAM DEPICTING MEAN SENSORY BLOCKADE ONSET

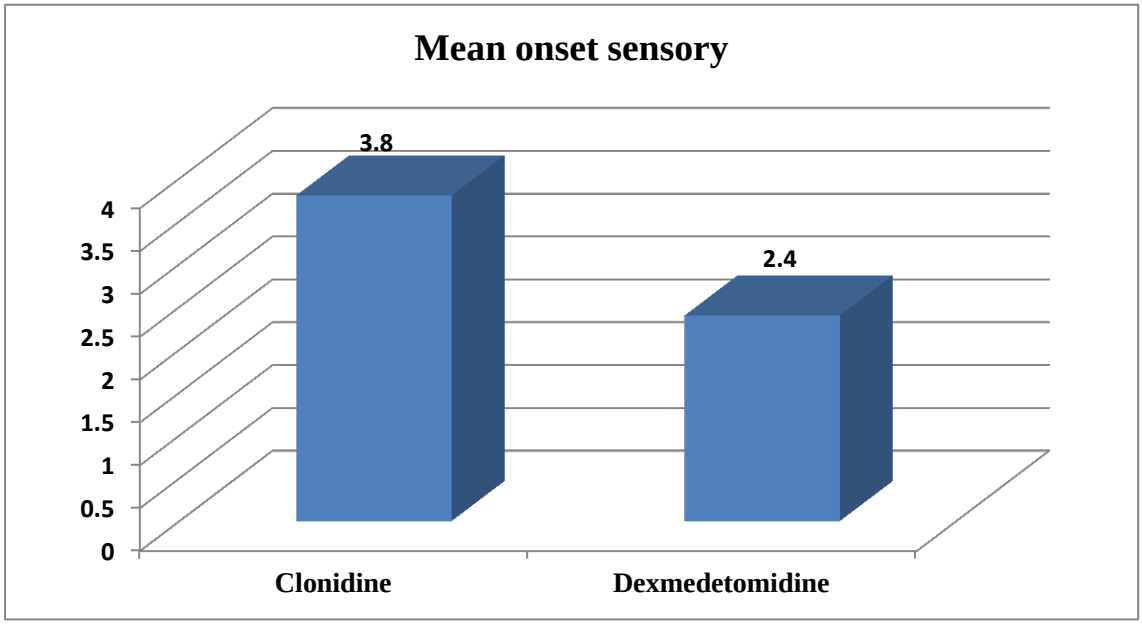


TABLE 10: HIGHEST SENSORY BLOCKADE

Highest sensory blockade	n,%	Group C	Group D	Total
T3	**N**	0	12	12
	%	0.0%	26.7%	13.3%
T4	**N**	1	27	28
	%	2.2%	60.0%	31.1%
T5	**N**	15	6	21
	%	33.3%	13.3%	23.3%
T6	**n**	14	0	14
	%	31.1%	0.0%	15.6%
T7	**n**	14	0	14
	%	31.1%	0.0%	15.6%
T8	**n**	1	0	1
	%	2.2%	0.0%	1.1%
Total	**N**	45	45	90
	%	50.0%	50.0%	100.0%

Highest sensory blockade level in Group D was (T4±1) which is more than Group C (T6±1).

Association between groups and highest sensory block was significant.

FIGURE 13: BAR DIAGRAM DEPICTING HIGHEST SENSORY BLOCK

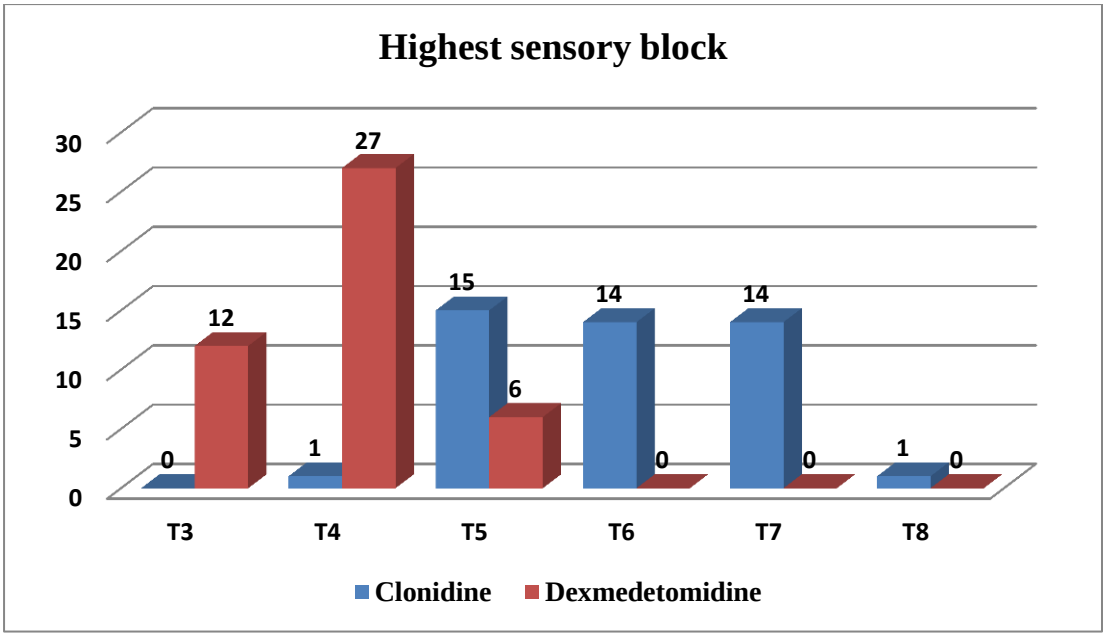


TABLE 11: MEAN MOTOR BLOCKADE ONSET TIME

Group	Mean motor block onset	S.D	P value
Group C	4.47	0.79	0.0001 (Significant)
Group D	2.78	0.88	

Motor blockade onset was reduced in Group D (2.78± 0.88) contrary to Group C (4.47± 0.79) and is statistically significant.

FIGURE 19: QBAR DIAGRAM DEPICTING MEAN MOTOR BLOCKADE ONSET TIME

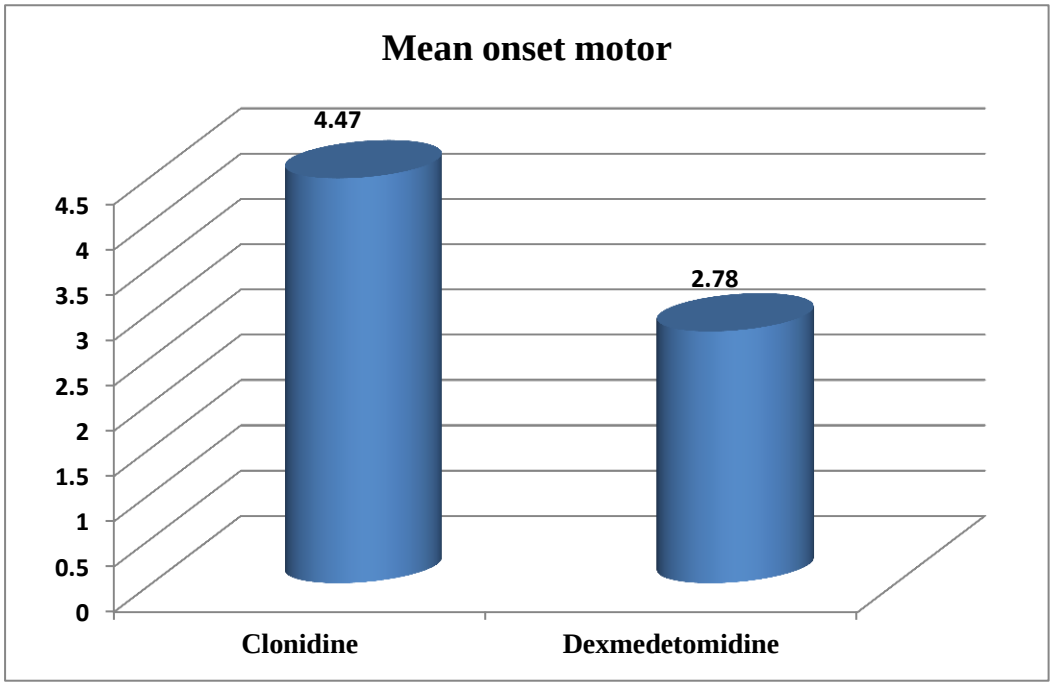


TABLE 12: MEAN SENSORY BLOCKADE PERIOD

Group	Mean sensory block period	S.D	P value
Group C	100.22	11.38	0.0001 (Significant)
Group D	129.33	13.55	

Sensory blockade duration was prolonged in Group D (129± 13.55 mins) than in Group C (100.22± 11.38 mins) and is statistically significant.

FIGURE 20: BAR DIAGRAM DEPICTING MEAN SENSORY BLOCKADE PERIOD

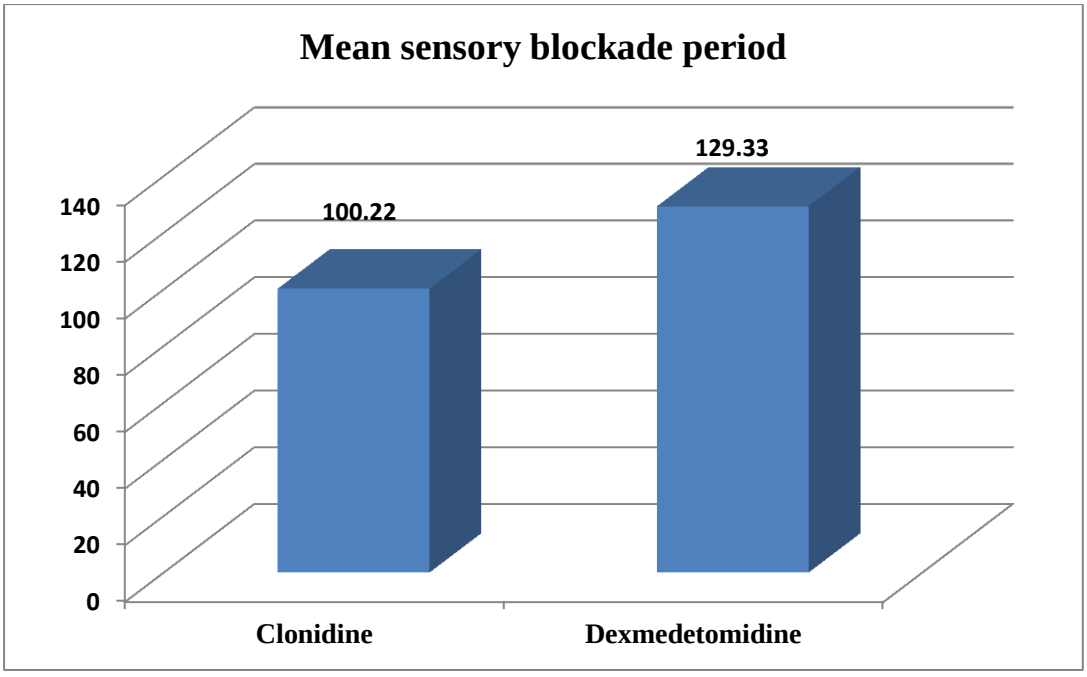


Table 13: MEAN MOTOR BLOCKADE PERIOD

Group	Mean motor blockade duration	S.D	P value
Group C	121.78	14.35	0.0001 (Significant)
Group D	156.67	12.25	

Mean motor blockade duration among Group C and D was 121.78 ± 14.35, and 156.67 ± 12.25, respectively and is statistically significant.

FIGURE 21: BAR DIAGRAM DEPICTING MOTOR BLOCKADE PERIOD

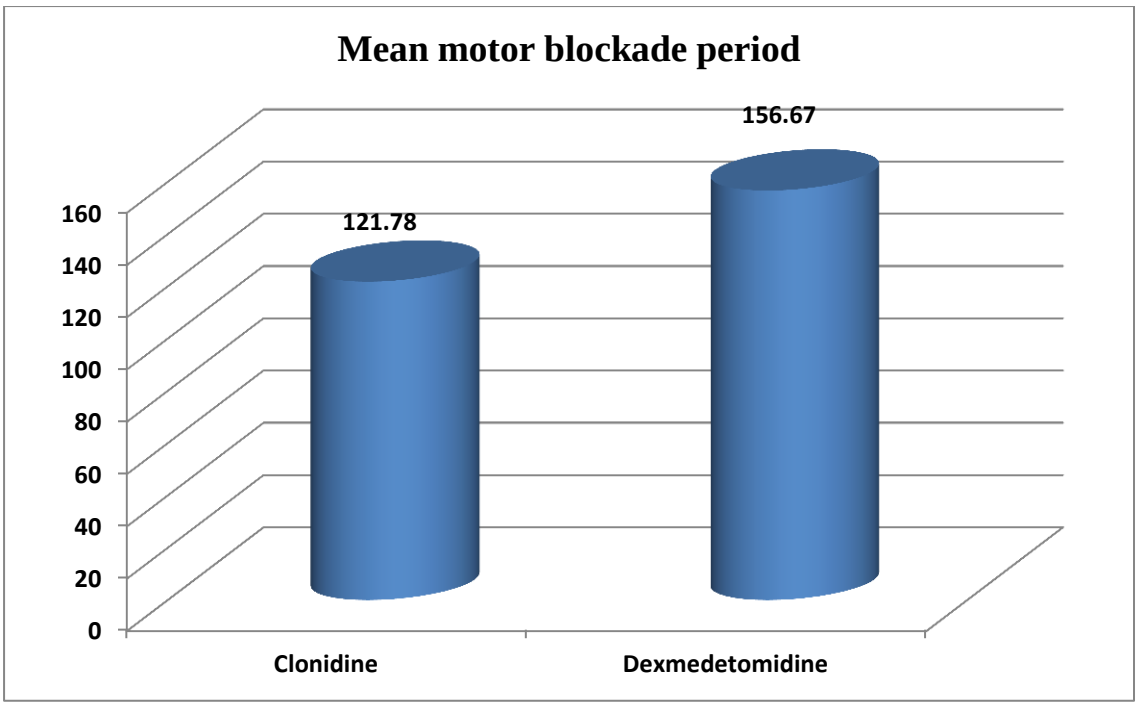


TABLE 14: MEAN SURGERY DURATION

Group	Mean surgery duration	S.D	P value
Group C	105.56	18.78	0.933 (Non significant)
Group D	105.22	18.56	

The mean duration of surgery in Group C (105.56±18.78mins) and Group D (105.22±18.56mins) and was not significant.

FIGURE 22: BAR DIAGRAM DEPICTING MEAN SURGERY DURATION

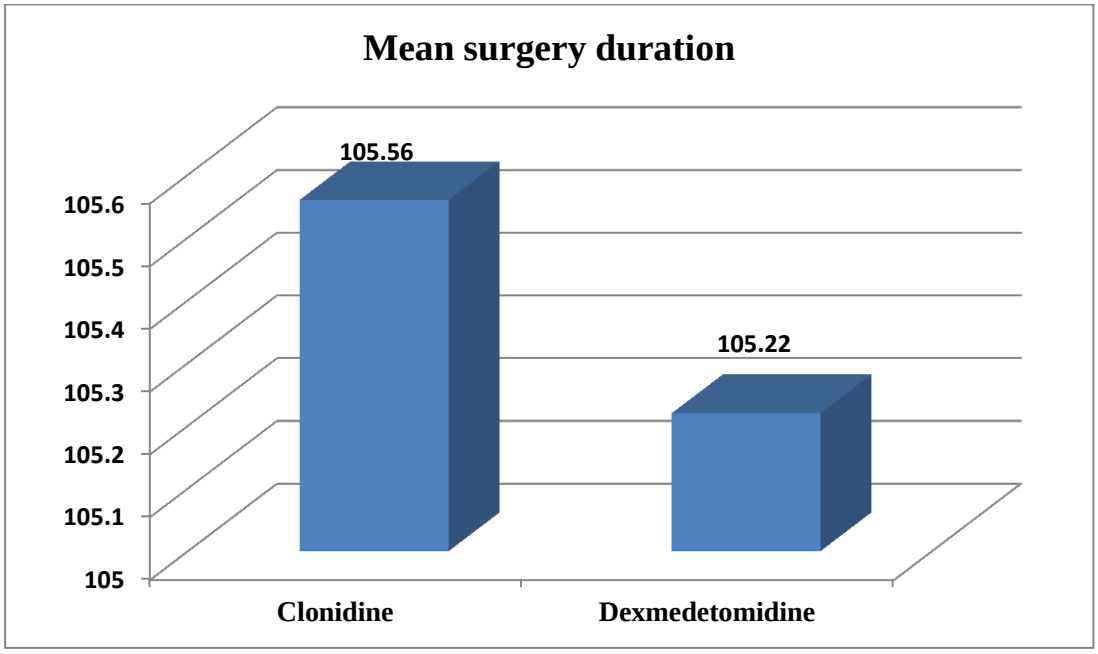


TABLE 15: MEAN PERIOD OF ANALGESIA

Group	Period of analgesia	S.D	P value
Group C	143.80	21.22	0.0001 (Significant)
Group D	169.51	19.23	

The duration of analgesia was prolonged in Group D(169± 19.23mins) and in Group C (143± 21.22mins) and this difference is statistically significant.

FIGURE 23: BAR DIAGRAM DEPICTING MEAN PERIOD OF ANALGESIA

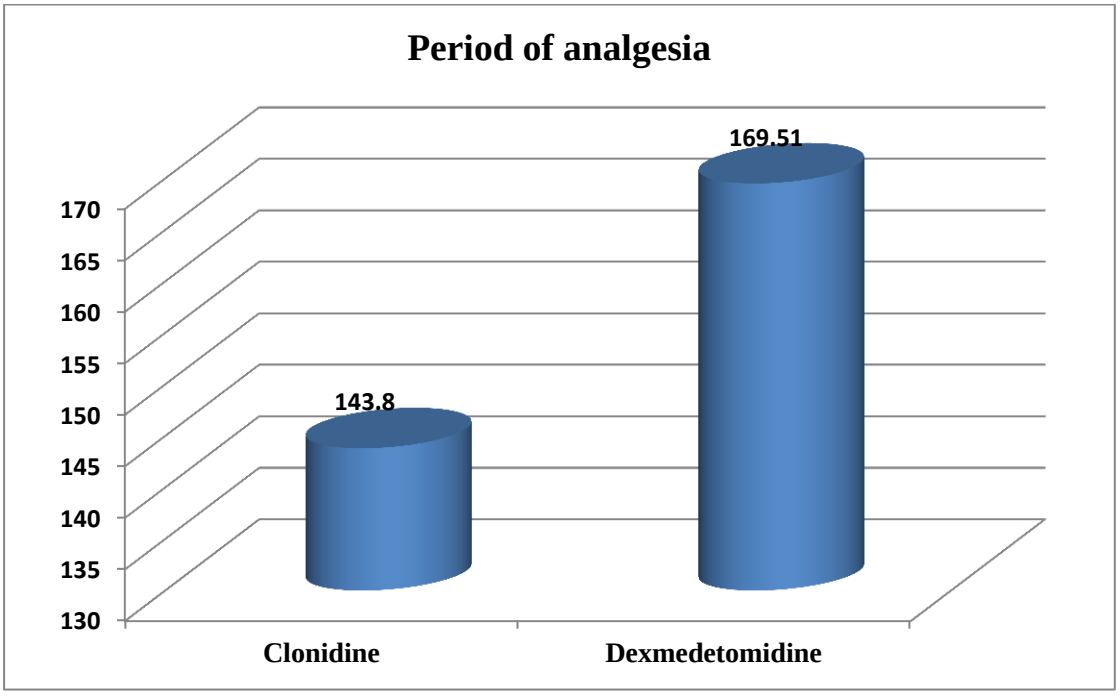


TABLE 16: MEAN VAS SCORE

VAS score	Group C		Group D		P value
	Mean	Standard deviation	Mean	Standard deviation	
At 1 hour	1.40	0.81	1.13	0.84	0.129
At 4 hour	3.04	0.79	2.20	0.66	0.0001*
At 8 hour	4.62	1.15	2.89	1.31	0.0001*
At 12 hour	6.73	1.26	5.51	1.54	0.0001*
At 24 hour	8.09	0.90	7.04	1.04	0.0001*

***significant**

Mean VAS score showed increasing trend in both Group C and D, but it was more in Group C than Group D. Except at 1st hr, at the remaining time periods mean difference was significant in between the groups.

FIGURE 24: LINE DIAGRAM DEPICTING VAS SCORES

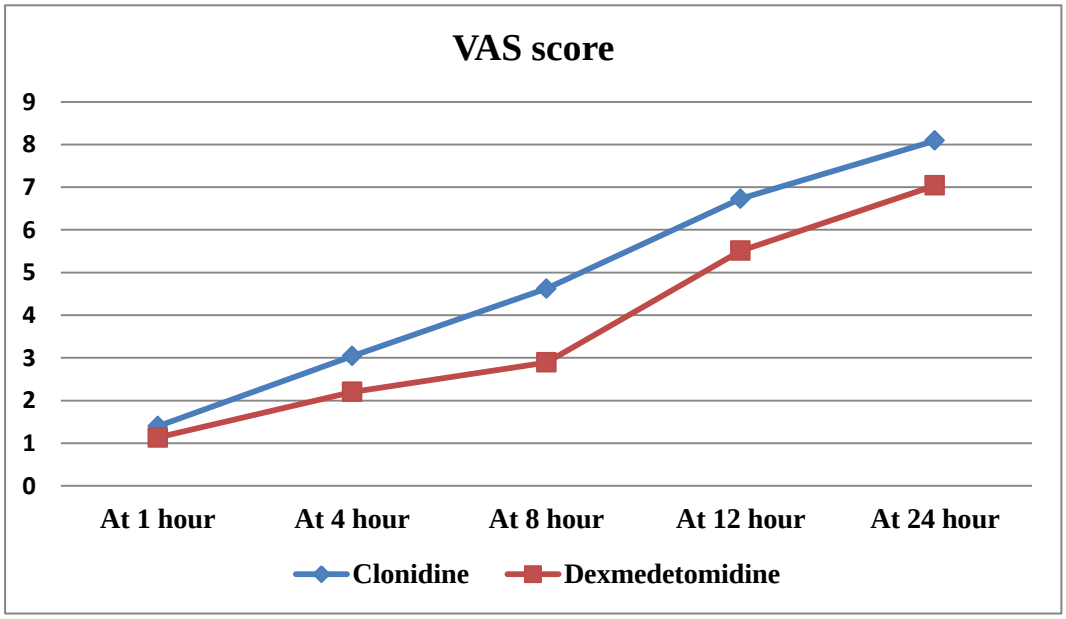
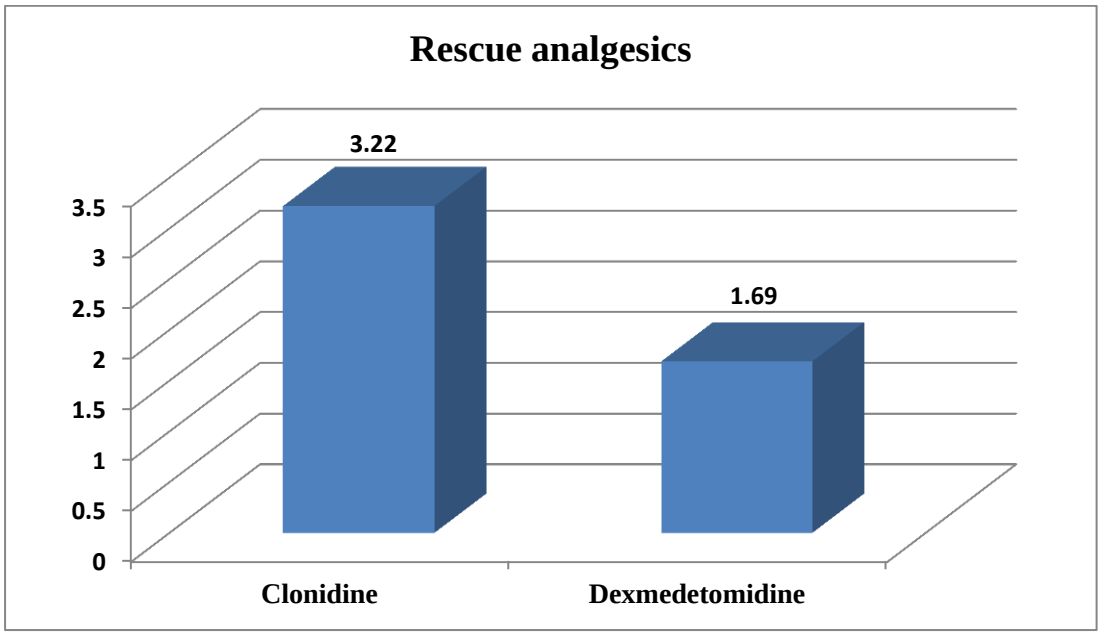


TABLE 17: NO. OF RESCUE ANALGESIC DOSES IN FIRST 24hrs

Group	Rescue analgesia	S.D	P value
Group C	3.22	0.67	0.0001 (Significant)
Group D	1.69	0.71	

No. of rescue analgesics in first24hrs between the two groups is Group C (3.22± 0.67) in contrary to Group D (1.69±0.71) and is statistically significant.

FIGURE 25: BAR DIAGRAM DEPICTING RESCUE ANALGESICS



DISCUSSION

This study was prospective, double-blind comparative study, done on 90 participants undergoing elective lower extremity and lower abdominal surgeries requiring spinal anesthesia and satisfying the inclusion criteria at R. L. Jalappa Hospital and Research Centre, A unit of SDUAHER, Tamaka, Kolar, from January 2021-May 2022.

Study included 2 groups, of them first group (Group C) was given Clonidine 0.5 mcg per kg IV bolus dose over a period of 10 min, and the second group (Group D) was given Dexmedetomidine 0.5mcg per kg IV bolus dose over a period of 10 min, prior to spinal anaesthesia with hyperbaric 0.5% Bupivacaine 15mg intrathecally.

Mean age

In this study, mean age of Group C was 45.62 ± 10.75 years, which was similar to Raushan R, and Prakash A study[53] (46.5 ± 3.2), lesser than Reddy VS et al.[11] (47.23±6.84), but higher than Chavi Sethi et al.[50] (40.56±10.8), Bhashyam S et al.[58] (40.02±9.92), Patil KN et al. study[55] (38.72+13.81).

In this study, mean age of Group D was 41.60 ± 12.16, which was similar to study by Patil KN et al. study[55] (42.20+13.14), and higher than Bhashyam S et al.[58] (38.81±10.16), but lesser than Reddy VS et al.[11] (47.7±6.93), Raushan R, and Prakash A study[53] (44.2 ± 5.4).

In this study, mean age difference of Group C and Group D was non-significant, which was similar to Chavi Sethi et al.,[50] and Bhashyam S et al.,[58] Reddy VS et al.[11]

Mean weight

In this study, mean weight of Group C was 63.00 ±6.58, which was similar to Patil KN et al.[55] study (62.80+8.53) (59.72+5.962), higher than Chavi Sethi et al.[50] (61.64±8.49),

Bhashyam S et al.[58] (56.20±5.49), Reddy VS et al.[11] (56.2±5.49).

In this study, mean weight of Group D was 61.53 ± 5.49, which was similar to Patil KN et al.[55] study (59.72+5.962), and lesser than Chavi Sethi et al.[50] (64.25±5.72), but higher than Bhashyam S et al.[58] (55.43±5.8), and Reddy VS et al.[11] (56.71±6.23).

In this study, mean weight difference of Group C and Group D was non-significant, which was similar to Chavi Sethi et al.,[50] and Bhashyam S et al.[58]

Pulse rate trend

In the present study, baseline pulse rate in Group C, and Group D was 85.84 ± 7.79, 85.82 ± 9.67 respectively, which was higher than Patil KN et al.[55] study (77.28+9.03 78.72+9.09) respectively, and the mean difference was non-significant in this study, which was similar to Patil KN et al. study.[55]

In Patil KN et al.[55] study, mean PR difference was significant at 45 minutes except pre op, at intra op.

In this study, decrease in pulse rate was seen in immediately in both the groups, while it was seen 10 minutes after in the study by Chavi Sethi et al.[50]

Ganesh M, and Krishnamurthy D study[12], a remarkable dissimilarity in HR was observed at 5, 10, and 15 min between Group C and D.

Mean heart rate trend was more in Group D, than Group C, while it was different in the study by Kiran Kumar S et al.[51]

MAP trend

In the present study, baseline MAP in Group C, and Group D was 97.84 ± 7.63, 96.13 ± 8.45 respectively, which was higher than Patil KN et al.[55] study (96.28 + 4.73, 93.8+ 4.56)

respectively, and the mean difference was non-significant in this study, which was similar to Patil KN et al.[55] study.

Regarding MAP, in Group C declining trend was seen up to 60 minutes, thereafter MAP was increased and in Group D also declining trend was seen up to 30 minutes, thereafter MAP was increased.

In the study by Chavi Sethi et al.,[50] decrease in MAP was seen after 10 minutes in both the groups, MAP was maintained above 80 mm Hg, that showed hemodynamic stability with both the drugs, which was similar in the study by Chavi Sethi et al.[50]

In this study, MAP difference between the groups was non-significant, except at 60 minutes, while MAP was non-significant in the study by Kiran Kumar S et al.,[51] and it was significant at 30, and 45 minutes in Patil KN et al.[55]

Trend of SPO2

Regarding SPO2, in Group C more or less same levels were maintained, and in Group D also slight fluctuations were seen throughout the time period.

Mean onset sensory

Mean onset sensory in Group C, and was 3.80 ± 0.84, which was similar to Reddy VS et al.[11] (3.58±1.06), but lesser than Kiran Kumar S et al.[51] (4.02+1.06), Bhashyam S et al.[58] (4.51±1.32), but higher than Chavi Sethi et al.[50] (2.56±1.62) Raushan R, and Prakash A study[53] (1.5 ± 0.5).

Mean onset sensory in Group D was 2.40 ± 0.81, which was similar to Kiran Kumar S et al.[51] (2.58±1.18), Reddy VS et al.[11] (2.91±1.16), but higher than Chavi Sethi et al.[50] (1.81±1.75), but lesser than Bhashyam S et al.[58] (3.58±1.16), Raushan R, and Prakash A[53] study (1.1 ± 0.4), Ganesh M, and Krishnamurthy D[12] study (1.2 ± 0.4). Mean onset sensory in between

the groups was significant, which was similar to Bhashyam S et al.,[58] Chavi Sethi et al.,[50] Whizar-Lugo et al.,[59] Kaya et al.[60] and Reddy VS et al.,[11]study

Mean onset motor

Mean onset motor in Group C was 4.47 ± 0.79, which was similar to Chavi Sethi et al.[50] (4.64±2.91), Reddy VS et al.[11] (4.21±1.49), but lesser than Bhashyam S et al.[58] (5.46±1.04).

Mean onset motor in Group D was 2.78 ± 0.88, which was lesser than Chavi Sethi et al. [50] (3.54±3.07), Bhashyam S et al. [58] (4.56±1.32), and Ganesh M, and Krishnamurthy D study[12] (1.1 ± 0.4).

In this study sensory and motor blockade onset was extended in both the groups, which was identical to study by Chavi Sethi et al.[50], Kaya FN et al.,[60] and Bhashyam S et al.[58]

Sensory block duration

Sensory block duration in Group C was 100.22 ± 11.38, which was higher than Chavi Sethi et al.[50] (141.66±30.20), Kiran Kumar S et al.[51] (196.1+5.9).

Total duration of sensory block was higher in Group D than Group C, and the difference was distinct which was similar to Chavi Sethi et al.,[50] Kiran Kumar S et al.[51]

Motor block duration

Motor block duration in Group C was 121.78 ± 14.35, which was lesser than Chavi Sethi et al.[50] (223.12±26.43), Bamel S et al.[54] study (210.00 ± 28.04), Patil KN et al.[55] (180.40 + 24.70).

Mean duration of motor blockade in Group D was 156.67 ± 12.25, which was lesser than Chavi Sethi et al.[50] (265.45±41.50), Bamel S et al. [54] study (244.00± 29.43), Patil KN et al. [55] (205.20 + 25.56)and Ganesh M, and Krishnamurthy D study[12] (302.6 ± 36.6)

These differences in the findings were because of the dose they administered. Duration of motor blockade between the groups were distinctive, which was similar to Patil KN et al.[55], Chavi Sethi et al.[50]

Mean duration of surgery

Mean duration of surgery in Group C and D was non-significant, which was similar to Bhashyam S et al.[58], Chavi Sethi et al.[50] and Patil KN et al.[55]

Highest sensory block

In this study, highest sensory level was achieved in T5-T7 in Group C, which was different from Chavi Sethi et al.[50] study. (T6-T8). Highest sensory level was achieved in T3- T4 in Group D, which was similar to Reddy VS et al.[11] (T3-T5), WhizarLugo et al.,[59] (T3-T4), Kaya et al.,[60] (T3-T4), but different from Chavi Sethi et al.[50] study (T5-T7).

Mean Duration of analgesia

Mean duration of analgesia in Group C was 143.8 ± 21.22, which was lesser than Kiran Kumar S et al.[51] (382.54 ± 6.53), Bamel S et al.[54] study (247.33 ± 38.23)

Mean duration of analgesia in Group D was 169.51 ± 19.23, which was lesser than Kiran Kumar S et al. [51] (432.45 ± 8.31), Bamel S et al. [54] study (275.33± 29.33). These differences in the findings were because of the dose they administered.

Mean VAS score

Mean VAS score between Group C, and Group D except at 1 hour, at remaining time periods was significant, which was similar to study by Raushan R, and Prakash A[53], Ganesh M, and Krishnamurthy D. Highest VAS scores were seen in Group C than Group D, which was

similar to Ganesh M, and Krishnamurthy D[12].

Mean rescue analgesic

Mean difference of rescue analgesia in both Group C, and D was statistically distinctive, which was similar to Raushan R, and Prakash A study[53].

LIMITATIONS

It includes a smaller group of participants from a single centre. ASA-physical status 3 or more is not involved also parturients are not a part of the study since the safety of drug is not established in these population. Sedation scores were not included during the data collection. Better pain detecting scales can be used to address postoperative pain. To conclude a larger sample from multicentric study can be carried out and also sedative character of the study also to be studied further.

CONCLUSION

We hereby infer from the study that, pre-emptive administration of dexmedetomidine at 0.5µg/kg over 10mins prior to spinal anaesthesia has better hemodynamic stability, quicker sensory and motor blockade onset, extended sensory block and motor block period. Dexmedetomidine also provides better analgesia in comparison to clonidine as duration of analgesia was higher and VAS score were lower and requiring lesser rescue analgesia in Dexmedetomidine group.

SUMMARY

A prospective randomized double blinded comparative study was carried out at R L Jalappa Hospital and Research Centre, Tamaka, Kolar from January 2020-May 2021. 90 patients satisfying inclusion criteria were chosen.

Participants were allotted into 2 groups after informed consent has been taken based on computer generated table. Group D received Dexmedetomidine at 0.5mcg per kg IV over 10mins and Group C received Clonidine at 0.5mcg per kg IV over 10mins. Five minutes after administrating the study drug in both the groups lumbar puncture was performed and Bupivacaine hyperbaric 0.5% 15mg was administered.

Vitals were noted starting from the time of spinal anaestheisa till 120mins. Also the sensory and motor blockade onset, sensory and motor blockade duration were noted, period of analgesia, VAS scores assessed and no. of recue analgesics required in the first 24hrs in each group were also noted.

There was significant decrease in HR in dexmedetomidine group after spinal anaesthesia. Other hemodynamic variables insignificant.

Dexmedetomidine group had significantly quicker sensory and motor blockade onset, extended sensory and motor blockade duration. Post-operative analgesia was better in dexmedetomidine group than clonidine group.

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ANNEXURE I

PROFORMA

A COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE AND CLONIDINE AS PRE EMPTIVE ANALGESIA TO INTRATHECAL BUPIVACAINE IN SUBARACHNOID BLOCK

INVESTIGATORS: Dr. Vidya shree C & Dr. Ravi M, Professor & HOD

DIAGNOSIS:

PROCEDURE:

UHID No: Age:

Sex: Weight:

ASA Grade :

PRE-ANAEASTHETIC EVALUATION:

General examination:

HR : BP:

Pallor/Icterus/Clubbing/Cyanosis/Lymphadenopathy/Edema:

Systemic examination:

Respiratory system –

Cardiovascular system -

Central nervous system -

Per abdomen -

Investigations:

Hemoglobin -

Total leukocyte count -

Platelet count -

Blood grouping -

Blood urea -

Serum creatinine -

Serum sodium -

Serum potassium -

Bleeding time -

Clotting time -

Groups:

Group D will receive dexmedetomidine 0.5mcg per kg IV bolus dose over a period of 10 min before giving spinal anaesthesia with hyperbaric 0.5% Bupivacine 15mg intrathecally.

Group C will receive clonidine 0.5 mcg per kg IV bolus dose over a period of 10 min before giving spinal anaesthesia with hyperbaric 0.5% Bupivacine 15mg intrathecally.

Baselines:

Heart rate -

Systolic blood pressure -

Diastolic blood pressure -

Mean arterial pressure -

Oxygen saturation-

Regional anaesthesia:

Procedure -

Posture -

Space -

Drug -

Level of blockade –

INTRAOPERATIVE VITALS

	0 MIN	3	5	10	20	30	60	90	120
HR									
SBP									
DBP									
MAP									
SPO_2									

Total duration of surgery:

Time of Onset of sensory blockade:

Time of Onset of motor blockade:

Duration of sensory regression by two segments:

Recovery from motor block:

Time of first analgesia request:

Total analgesic use in 24hours:

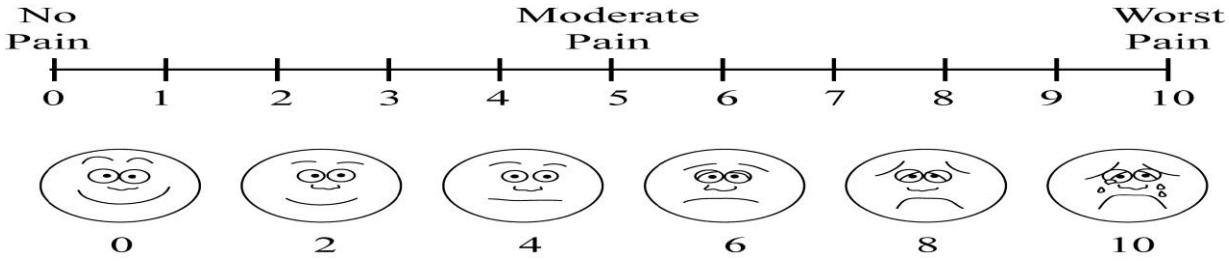
VAS - VISUAL ANALOGUE SCALE (for pain)

0 - No pain

1-3 - mild pain

4-6 - moderate pain

7-10 – severe pain



ANNEXURE II

PATIENT INFORMATION SHEET

Title of the study: **"A COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE AND CLONIDINE AS PRE EMPTIVE ANALGESIA TO INTRATHECAL BUPIVACAINE IN SUBARACHNOID BLOCK"**

Investigators: Dr Vidya shree C/ Dr Ravi M

Study location: R L Jalappa Hospital and Research centre attached to Sri Devaraj Urs Medical College , Tamaka, Kolar.

Details: All patients posted for lower abdominal and lower limb surgeries under spinal anesthesia will be included in this study. Patients with co morbid conditions will be excluded from the study.

This study aims to prolong the duration of spinal anaesthesia and prolong the post-operative analgesia without any significant side effects. Patient and the attenders will be explained about the procedure being done i.e. use of dexmedetomidine and clonidine.

The study drugs will be avoided in patients with ischemic heart disease, uncontrolled hypertension/diabetes, uncompensated hepatic/renal disease, spinal deformities or any contraindication to spinal anaesthesia(coagulation defects, infection at puncture site, pre-existing neurological defects in the body), allergy to amide local anesthetics, psychiatric disorders, alcohol/substance abuse.

Procedures and protocol:

This a randomized double blind prospective study. 90 patients undergoing lower abdominal and lower limb surgeries at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar, during the period from January 2021 to May 2022will be included in the study.

After obtaining informed consent, 90 patients will be randomly divided into 2 groups of 45 each. Randomization will be done by computer generated table.

Group D will receive dexmedetomidine 0.5mcg per kg IV bolus dose + hyperbaric 0.5% Bupivacine 15mg intrathecally.

Group C will receive clonidine 0.5mcg per kg IV bolus dose + hyperbaric 0.5% Bupivacine 15mg intrathecally.

Reimbursements: You will not be given money or gifts to take part in this research.

Confidentiality: We will not be sharing the identity of the participant. The information we collect from you will be kept confidential and only researchers involved in this project will have access to it.

Right to Refuse or Withdrawal: You do not have to take part in this research if you do not wish to do so and you can refuse to participate.

Whom to Contact: If you have any questions you may ask us now or later, even after the study has started, you may contact the following person:

For more information contact:

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ANNEXURE III

INFORMED CONSENT FORM

Name of the institution: Sri Devaraj Urs academy of higher education and research.

Title of the project: "A COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE AND CLONIDINE AS PRE EMPTIVE ANALGESIA TO INTRATHECAL BUPIVACAINE IN SUBARACHNOID BLOCK"

Name of the principal investigator: Dr. Vidya shree C

Name of the guide: Dr. Ravi M

Name of the subject/participant:

I, _____ aged _____, after being explained in my own vernacular language about the purpose of the study and the risks and complications of the procedure, hereby give my valid written informed consent without any force or prejudice for taking intravenous dexmedetomidine and clonidine as adjuvant to bupivacaine in spinal anaesthesia for the purpose of prolonging anaesthetic and analgesic effect, it also acts as a sedative and also prolongs the post-operative analgesic period hence decreasing the number of analgesic dose requirement in post-operative period which is beneficial to patients. The side effects associated with the drugs that is hypotension will be treated with Ringer's lactate solution and incremental doses of inj.Mephenteramine 3.0mg IV, bradycardia will be treated with atropine 0.6mg.The nature and risks involved have been explained to me to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research. I here by give consent to provide my history, undergo physical examination, undergo the procedure, undergo

investigations and provide its results and documents to the doctor / institute etc. All the data may be published or used for any academic purpose. I will not hold the doctors / institute responsible for any untoward consequences during the procedure / study. A copy of this Informed Consent Form and Patient Information Sheet has been provided to the participant.

_____ _____

(Signature & Name of Pt. Attendant) (Signature & Name of Pt)

(Relation with patient)

DATE: Investigator signature

KEY TO MASTER CHART

Group D	Dexmedetomidine group
Group C	Clonidine group
KGS	Kilograms
YRS	Years
HR	Heart Rate
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
MAP	Mean Arterial Pressure
mmHG	Millimetre of Mercury
SPO_2	Peripheral Capillary Oxygen Saturation
VAS	Visual Analogue Scale
MINS	Minutes
B/L	Bilateral
IMIL	Intramedullary Interlocking
PFN	Proximal Femoral Nailing
AUB	Abnormal uterine bleeding
UV	Utero-vaginal
TENS	Titanium Elastic Nailing
TAH+BSO	Total Abdominal Hysterectomy + Bilateral Salphingo-ophorectomy
ORIF	Open Reduction and Internal Fixation
VH	Vaginal Hysterectomy
TURP	Trans-urethral Resection Of Prostate
URSL	Ureteroscopy and Laser Stone Fragmentation
DJ	Double J
BPH	Benign Prostatic Hypertrophy

S.No.	Group	Age	Sex	Wt.	UHID.NO	DIAGNOSIS	SURGERY	Pre-operative					Onset	Onset	Duration	Duration	Duration	highest	Intra-operative																																														Duration		VAS score				rescue
								PR	SBP	DBP	MAP	SPO2	sensory	Motor	Of Sens.	Of Motor	of surgery	sensory	0min					3min					5min					10min					20min					30min					60min					90min					120min					of analgesia	1hr	4hrs	8hrs	12hrs	24hrs	analgesia
													(min)	(min)	regression	regression	(min)	block	PR	SBP	DBP	MAP	SPO2	PR	SBP	DBP	MAP	SPO2	PR	SBP	DBP	MAP	SPO2	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SPO2							
1	D	20	female	55	948787	post op case of ORIF	Wound debridement	76	137	89	105	100	2	2	140	150	95	T4	68	130	80	94	100	67	127	79	95	99	74	125	90	97	99	74	115	74	88	99	75	109	72	84	99	78	106	67	80	99	75	124	80	95	99	72	117	74	88	99	83	121	78	92	100	210	0	2	4	6	6	1
2	D	56	male	60	952530	inguinal hernia	herinoplasty	86	127	70	88	99	3	2	150	150	120	T4	65	120	70	84	99	65	121	81	92	99	68	122	68	81	99	70	121	60	84	99	74	104	70	77	99	77	115	98	105	99	75	115	98	105	99	77	117	51	66	99	80	123	85	100	99	194	1	2	3	5	7	2
3	C	49	Male	65	951746	femur fracture	ORIF+IMIL Nailing	86	122	80	94	99	3	4	90	110	140	T5	74	116	78	91	99	70	115	79	96	99	68	114	77	89	99	66	109	77	88	99	70	107	74	85	99	68	109	77	88	99	70	102	72	78	99	78	120	69	86	99	80	125	65	85	99	160	2	4	5	7	9	4
4	C	50	female	60	952573	Necortizing fascitis of left leg	Wound debridement	92	136	100	115	98	4	5	90	130	80	T6	96	134	86	102	99	94	130	80	94	100	95	126	95	103	100	88	123	88	97	100	86	124	83	79	100	84	118	73	82	100	76	105	66	78	100	82	118	73	82	100	86	120	84	94	99	168	2	3	5	7	9	3
5	D	27	Male	65	950130	Appendicitis	open appendicectomy	66	134	93	107	100	3	3	130	140	90	T4	70	130	55	80	99	72	126	74	91	99	78	124	85	98	99	76	114	76	89	99	72	115	76	89	99	69	118	76	90	99	70	110	75	87	99	66	115	75	97	99	72	123	74	90	99	188	0	2	2	6	8	2
6	C	55	Male	62	935123	inguinal hernia	herinoplasty	94	128	89	99	99	4	4	100	100	130	T7	93	126	89	98	99	90	122	82	95	99	94	118	80	90	99	78	108	94	99	99	65	103	58	66	99	64	98	73	81	99	70	104	72	78	99	80	115	75	88	99	90	121	80	94	99	160	2	4	6	6	8	4
7	C	51	Male	68	944681	healing ulcer over foot	split skin grafting	78	135	82	100	100	2	3	90	100	100	T5	74	134	84	101	99	76	128	70	89	99	72	132	78	99	99	68	113	70	84	99	64	103	70	81	98	70	104	72	78	98	76	107	69	82	98	78	108	68	80	99	80	116	78	91	99	160	2	4	4	6	7	3
8	D	35	male	63	40588	Appendicitis	open appendicectomy	96	136	95	109	100	2	2	120	140	110	T3	66	130	90	103	100	64	127	86	99	98	60	124	88	100	98	68	108	75	86	98	68	98	63	75	98	69	108	75	86	98	68	110	78	90	98	75	118	70	86	98	80	123	74	90	100	178	1	2	2	4	6	2
9	D	28	male	70	51451	Appendicitis	open appendicectomy	82	116	78	91	100	4	4	130	160	120	T4	70	107	63	74	99	72	109	77	88	99	72	113	79	90	99	66	109	76	87	99	69	108	75	86	99	68	106	72	83	99	74	116	78	69	99	80	118	71	87	99	82	122	78	93	99	184	0	2	2	3	5	1
10	C	50	female	56	51452	Non healing ulcer of L foot	Wound debridement	84	140	96	111	99	4	5	100	120	90	T5	82	136	91	107	99	78	131	84	100	99	80	133	89	104	99	76	118	86	97	99	80	116	84	95	99	70	110	81	91	99	75	108	64	81	99	78	113	76	88	99	85	120	80	93	99	144	3	4	5	8	9	4
11	C	45	female	57	43702	UV prolapse	vaginal hysterectomy	75	127	79	95	100	3	4	90	130	120	T6	73	117	63	86	100	72	121	81	92	100	74	121	70	87	100	72	118	70	82	100	70	107	63	75	100	68	105	66	77	100	76	105	64	81	100	80	113	84	90	100	82	116	78	91	100	150	0	3	3	6	6	3
12	D	36	Male	64	51621	paraumbilical hernia	herinoplasty	90	134	92	112	100	2	3	140	160	100	T4	80	126	81	102	99	82	115	79	91	99	80	118	71	87	99	78	116	78	91	99	72	116	77	90	98	76	121	71	90	98	74	126	75	92	98	77	118	71	74	98	82	122	80	94	99	174	0	2	3	6	9	2
13	C	32	Male	76	57166	perianal abcess	incision & drainage	88	120	80	94	100	4	5	110	120	80	T7	83	121	70	88	99	80	110	85	94	100	76	102	64	77	100	70	89	60	70	100	75	101	69	80	100	76	100	65	77	100	70	101	69	80	100	84	116	81	93	100	86	123	80	94	99	154	2	3	5	7	7	3
14	D	35	female	64	51546	Appendicitis	open appendicectomy	96	120	70	84	100	3	3	130	150	90	T5	80	116	73	87	100	84	110	79	89	100	80	111	71	85	100	75	113	68	81	100	68	104	72	78	100	69	108	78	86	100	70	111	59	74	100	74	117	68	83	100	78	125	65	85	100	178	1	2	3	6	8	2
15	C	57	Male	70	59584	fracture of ankle	ORIF+Plating	84	136	93	108	99	5	5	110	100	130	T5	94	130	82	98	99	90	132	78	96	99	80	134	90	105	99	86	124	88	100	99	84	108	75	86	99	78	104	72	78	99	82	106	72	83	99	78	116	78	91	99	80	134	90	105	99	144	2	3	5	7	9	4
16	D	51	female	58	57409	UV prolapse	vaginal hysterectomy	80	129	73	89	99	2	3	150	160	120	T3	68	120	78	88	99	68	108	68	79	98	52	120	69	84	98	70	116	71	85	98	68	98	61	73	98	68	109	59	66	98	74	113	55	70	98	70	116	61	83	98	74	120	80	93	99	160	3	4	5	5	7	2
17	C	42	Male	65	143013	haemorrhoids	open haemorrhoidectom	78	130	80	94	100	4	5	100	100	80	T5	77	124	81	95	100	74	116	74	88	100	62	106	65	83	100	74	110	76	84	100	70	106	64	76	100	72	109	76	87	100	70	113	79	90	100	76	116	78	91	100	76	134	70	91	100	138	1	4	5	6	9	3
18	D	49	female	60	143015	non healing ulcer of right foot	Wound debridement	80	136	91	107	100	3	4	130	140	90	T4	75	133	80	98	100	72	127	86	99	99	78	126	95	103	99	76	123	88	97	99	75	124	83	97	99	76	118	73	82	99	70	105	69	75	99	76	107	64	78	99	80	130	80	97	100	158	1	2	3	5	6	1
19	C	58	male	66	139812	healing ulcer over foot	split skin grafting	86	134	86	102	99	5	6	110	130	110	T6	83	130	82	98	99	85	121	70	88	99	90	122	81	95	99	86	110	73	85	99	87	110	71	84	99	85	108	69	82	99	84	110	73	85	99	86	118	71	87	99	81	125	65	85	99	120	2	4	5	7	7	3
20	D	35	Male	70	1418611	left femur fracture	orif + PFN nailing	85	130	55	80	100	2	2	120	150	140	T4	73	126	81	102	100	70	119	81	96	100	75	120	66	81	100	78	121	65	83	100	74	108	61	73	99	80	80	60	66	99	78	104	50	67	99	74	107	44	63	99	75	118	80	93	100	175	0	1	2	5	7	1
21	D	40	male	74	129408	umblical herina	meshplasty	75	117	63	86	100	3	2	120	160	110	T4	72	110	78	89	100	70	106	64	78	99	70	114	70	86	99	76	107	71	85	99	72	102	64	76	99	75	105	61	77	99	75	110	73	86	99	70	111	71	87	99	74	123	80	94	100	170	1	2	2	5	8	2
22	C	47	female	65	140339	AUB-leiomyoma	vaginal hysterectomy	86	122	82	95	99	4	4	100	120	120	T6	85	117	74	88	99	82	113	73	90	99	80	119	76	90	99	78	112	75	87	99	80	103	73	83	99	78	100	71	81	99	76	110	74	86	99	78	117	76	89	99	80	129	80	96	99	150	2	4	5	6	8	3
23	D	38	male	59	141543	fibula fracture	ORIF+Plating	71	120	77	89	100	2	2	130	170	130	T4	68	118	71	87	100	70	110	75	87	100	66	115	74	84	100	56	118	69	86	100	65	120	70	84	99	71	121	71	90	99	75	124	75	89	99	75	120	80	93	99	75	126	73	90	100	190	2	2	2	2	5	1
24	C	41	Male	63	141552	patellar tendon rupture	patellar tendon repair	88	129	84	114	100	4	4	100	130	110	T7	86	119	81	96	100	85	117	78	89	100	97	121	77	99	100	90	120	78	88	100	89	111	74	91	100	86	102	70	84	100	78	110	70	83	100	73	120	61	80	100	78	131	71	91	100	145	0	2	4	6	8	4
25	D	58	female	60	139567	UV prolapse	vaginal hysterectomy	84	115	79	96	98	4	4	120	150	110	T4	80	106	65	83	99	80	107	71	85	99	76	109	77	88	99	74	106	80	89	99	75	104	80	88	99	68	113	71	81	99	68	107	74	85	99	66	125	70	88	99	74	131	71	91	99	170	1	2	2	4	7	2
26	C	45	male	63	142654	inguinal hernia	herinoplasty	68	121	81	92	99	5	5	90	110	90	T8	78	109	77	88	99	80	108	73	83	99	86	105	75	90	99	80	108	68	79	99	78	105	70	82	99	72	115	78	90	99	71	114	74	87	99	75	119	81	94	99	78	126	86	99	99	150	2	3	5	5	9	4
27	D	42	female	65	142435	umblical herina	Mayos repair	94	140	80	100	99	3	4	110	140	100	T4	86	129	88	102	99	82	123	79	93	99	70	131	92	105	99	78	117	80	92	99	74	90	50	63	99	72	92	52	65	99	70	100	63	75	99	70	115	82	93	100	80	119	87	98	99	175	0	1	2	5	7	1
28	C	36	female	56	142452	fissure in ano	ateral anal sphincetrotom	88	126	89	98	100	4	5	90	130	90	T6	85	118	80	90	100	81	116	84	95	100	78	123	83	103	100	76	122	79	92	100	80	109	83	81	100	78	106	61	77	100	76	105	65	78	100	74	116	81	93	100	72	119	82	94	100	140	2	3	6	8	8	3
29	D	36	male	65	141661	non healing ulcer over foot	Wound debridement	90	116	81	97	100	4	4	110	160	90	T4	84	108	61	73	100	85	105	61	77	100	76	107	61	72	100	75	103	68	80	100	72	102	56	70	99	70	107	61	72	99	68	116	81	97	99	74	120	80	93	99	76	125	77	93	100	165	2	2	2	5	6	2
30	C	58	female	64	142093	UV prolapse	vaginal hysterectomy	96	116	73	87	99	5	5	90	120	100	T7	90	112	75	87	99	74	109	75	90	99	78	107	63	74	99	85	103	65	78	99	74	102	69	80	99	63	103	61	75	99	70	108	63	78	99	75	117	72	87	99	70	135	95	108	99	150	1	3	5	7	8	3
31	D	36	Male	62	850375	Closed diaplaced fracture of right tibia	ORIF + plating	85	134	86	102	100	2	2	120	150	80	T3	80	126	86	99	100	78	114	74	87	98	76	130	80	96	98	78	120	80	93	98	72	120	80	93	98	71	109	69	82	98	68	107	71	83	98	70	118	70	87	99	69	120	90	100	100	180	2	2	2	4	7	2
32	C	54	male	68	850345	open type II fracture of metatrasals	Wound debridement	90	130	82	98	100	3	4	100	110	90	T6	85	127	86	99	99	83	121	70	87	99	80	116	74	88	99	76	88	52	64	99	70	101	61	74	99	68	107	72	84	99	66	104	66	79	99	68	102	67	79	99	60	112	76	88	99	145	0	3	3	7	8	3
33	D	20	male	56	768116	9 month old nail	Implant removal	105	127	90	99	100	2	2	110	150	90	T4	96	124	83	97	100	95	117	74	88	100	90	125	90	97	100	80	118	91	96	100	74	109	72	84	100	75	101	63	78	100	72	110	73	85	100	78	113	76	88	100	68	120	80	93	100	170	1	2	2	4	6	1
34	D	35	Male	60	850792	Closed displaced fracture of L tibia	ORIF + Plate fixing	98	130	91	106	100	2	3	110	170	130	T3	94	120	77	91	100	80	113	72	85	99	72	127	86	99	99	55	117	78	92	99	78	108	73	83	98	74	97	63	73	98	70	110	80	90	98	78	112	79	94	98	75	123	85	100	100	165	1	3	3	5	7	2
35	C	37	Male	58	851464	6 yr old Femur IMIL nail	Implant removal	76	130	90	105	100	3	4	120	150	100	T7	75	128	84	98	99	81	121	65	83	99	88	133	80	98	99	75	91	63	72	99	68	99	70	80	99	70	126	86	99	99	78	112	66	81	99	78	134	82	99	99	68	130	80	97	99	154	3	4	4	6	9	4
36	D	25	Male	55	850373	Fracture of Femur	ORIF + TENS nailing	100	113	76	92	100	3	3	100	140	130	T4	96	109	72	84	100	90	104	70	77	100	85	110	72	84	100	80	108	84	94	100	76	105	74	81	99	74	100	58	73	99	66	99	65	76	99	82	108	72	82	99	86	120	84	94	100	165	2	2	2	5	8	2
37	C	20	female	58	851540	Closed R shaft of femur fracture	ORIF + IML nailing	90	120	80	93	100	4	4	110	130	140	T6	87	113	84	90	100	85	107	63	74	100	88	118	84	94	100	84	108	73	83	100	80	104	66	80	100	76	105	74	81	100	78	103	71	83	100	84	115	75	97	100	90	115	75	87	100	154	1	3	3	7	9	3
38	D	30	male	64	851725	Closed fracture of both bone right	ORIF +IML nailing of R tibia	102	108	77	87	99	2	2	130	170	120	T5	100	100	58	73	99	96	98	61	73	99	90	105	65	78	99	84	101	68	79	99	80	100	66	77	99	65	98	67	77	99	67	98	69	79	99	64	100	66	77	99	60	121	80	94	99	170	1	3	3	6	7	2
39	C	34	Male	65	851757	open type III fracture of metatrasals	Wound debridement	84	117	78	89	100	2	3	100	120	90	T7	86	117	80	92	100	78	110	71	84	100	72	114	77	79	100	76	114	77	91	100	71	103	71	83	100	73	99	72	85	100	72	90	69	76	100	65	108	68	80	100	74	114	77	91	100	130	2	4	4	7	9	4
40	C	59	female	63	838664	Closed fracture of both bone right	ORIF + IML nailing	78	118	80	78	98	4	4	90	100	110	T6	80	112	75	87	98	77	114	77	79	98	75	113	73	90	98	72	109	75	90	98	73	113	80	97	98	69	108	80	92	98	70	110	78	95	98	69	111	81	96	98	75	123	74	90	98	130	2	3	5	7	8	3
41	D	56	female	58	856184	left serous adenoma	TAH+BSO	75	130	90	102	99	1	2	140	170	120	T3	73	127	83	98	99	71	117	76	89	99	70	124	81	95	99	66	122	80	94	99	62	123	79	94	98	64	104	64	77	98	64	106	64	78	98	68	111	78	89	98	62	122	78	93	99	145	0	2	2	3	5	1
42	C	38	Female	64	856108	DUB	TAH+BSO	88	110	85	94	100	3	3	120	150	110	T5	60	109	72	84	100	56	102	64	76	100	94	107	63	74	100	85	108	62	85	100	86	105	66	77	100	80	104	60	76	100	84	108	64	81	100	78	113	76	88	100	82	120	80	93	100	140	1	3	5	8	8	3
43	D	50	Female	57	857223	Fibroid	TAH+BSO	88	118	78	96	100	1	3	130	160	130	T4	85	113	70	84	100	72	108	62	85	100	65	116	71	87	100	53	118	70	82	100	72	107	63	75	99	75	105	66	77	99	71	105	64	71	99	90	113	84	90	99	71	116	78	91	100	180	1	2	2	4	7	2
44	C	26	Female	55	859018	DUB	TAH+BSO	96	121	70	88	100	4	5	110	130	120	T7	93	115	74	84	100	91	107	61	72	100	90	118	71	87	100	89	116	78	91	100	85	116	77	90	100	84	110	54	73	100	88	108	64	81	100	90	108	63	95	100	92	119	87	98	100	120	3	5	7	9	9	4
45	D	38	Female	50	862913	Leiomyoma	TAH+BSO	100	127	86	99	100	2	2	110	150	100	T4	97	111	78	89	100	95	110	73	85	100	95	113	84	90	100	72	109	74	77	100	85	105	63	73	99	67	108	74	84	99	67	108	74	84	99	62	116	81	93	99	66	123	80	94	100	170	1	2	2	5	7	2
46	C	60	female	60	855685	Adenomyoma	TAH+BSO	74	119	81	96	98	5	6	90	100	110	T5	75	108	83	91	98	72	119	76	90	98	76	117	74	88	98	75	114	77	79	98	72	112	65	81	98	74	107	65	79	98	70	109	61	77	98	64	120	69	86	98	70	125	65	85	98	110	1	3	6	8	9	4
47	C	43	Female	65	862946	AUB	TAH+BSO	98	131	88	102	100	3	5	80	120	120	T7	95	129	82	94	100	92	128	84	98	100	93	129	88	102	100	90	122	81	95	100	87	121	79	93	100	85	117	74	88	100	82	113	70	84	100	78	110	73	85	100	80	122	81	95	100	130	1	3	6	9	9	3
48	D	52	Female	60	863448	Grade II UV prolapse	VH	90	120	80	93	100	2	2	130	160	90	T3	88	114	77	89	100	75	107	63	74	99	60	116	78	91	99	52	117	75	89	99	65	113	72	66	99	78	107	72	64	99	80	116	61	93	99	69	120	61	81	99	67	119	82	94	100	170	2	2	2	5	7	2
49	D	60	female	63	850754	AUB	TAH+BSO	92	126	81	102	99	2	2	120	170	100	T4	90	118	72	82	99	86	122	68	81	99	80	124	81	101	99	80	118	75	96	99	82	104	71	84	99	68	103	64	73	99	75	105	55	75	99	66	112	63	78	99	66	120	80	93	99	150	1	3	5	8	6	1
50	C	45	female	62	865281	AUB	TAH+BSO	100	135	88	100	100	4	4	90	120	120	T5	97	123	79	94	100	96	126	95	103	100	98	129	82	94	100	93	123	77	92	100	90	111	73	86	100	82	104	64	77	100	80	107	64	78	100	85	107	64	78	100	80	123	77	92	100	180	0	2	3	4	7	3
51	D	49	female	64	866255	Right ovarian cyst	TAH+BSO	95	134	86	102	99	4	5	130	180	130	T5	92	110	54	73	99	87	116	76	87	99	82	122	81	95	99	76	110	73	85	99	67	110	71	84	99	65	108	69	82	99	64	110	73	85	99	72	118	71	87	99	71	122	80	94	99	160	2	2	3	5	6	1
52	C	45	female	59	866161	Grade III Uv prolapse`	VH	100	127	83	98	99	5	5	120	130	120	T7	98	129	82	94	99	97	120	69	86	99	97	121	82	95	99	90	114	70	86	99	90	107	64	78	99	86	104	66	77	99	84	112	63	78	99	82	116	81	93	99	85	123	80	94	99	150	1	2	3	5	7	3
53	D	60	Female	54	866234	Grade I UV prolpase	VH	80	117	63	86	98	2	2	150	170	110	T3	70	107	61	72	98	64	101	61	74	98	53	114	70	86	98	90	107	71	85	98	88	102	64	76	98	65	105	61	77	98	65	110	73	86	98	60	111	71	87	99	65	116	78	91	98	180	1	2	5	9	9	2
54	C	28	Female	58	867389	Appendicitis	open appendicectomy	84	122	82	95	100	3	3	130	150	90	T5	82	120	75	84	100	78	118	72	82	100	74	119	76	90	100	76	112	75	87	100	80	103	73	83	100	78	100	71	81	100	76	110	74	86	100	78	117	76	89	100	80	125	77	93	100	125	1	4	6	8	8	4
55	D	50	female	50	847414	AUB	TAH +Bso	95	123	72	83	100	3	3	140	170	120	T4	94	118	80	90	100	90	116	71	87	100	86	118	72	82	100	83	116	76	87	100	78	105	64	78	99	70	105	69	79	99	72	105	64	78	99	69	109	70	83	99	64	126	73	90	100	160	1	2	2	8	8	2
56	C	60	female	63	835424	Fib.Ut.	TAH+BSO	78	122	80	93	99	4	4	110	140	130	T5	76	117	78	89	99	77	121	70	87	99	74	122	79	93	99	72	123	79	93	99	70	120	77	91	99	72	113	72	85	99	71	110	70	83	99	73	120	61	80	99	78	131	71	91	99	130	1	3	5	7	8	3
57	D	60	male	60	844861	Renal calculi	URSl + DJS	75	132	78	96	98	2	3	120	150	80	T4	73	120	69	84	98	70	118	71	87	98	70	123	72	83	98	68	118	72	82	98	60	116	76	87	98	68	113	71	65	98	69	107	74	85	98	66	125	70	88	98	60	129	80	96	98	155	2	2	2	6	7	1
58	C	26	male	64	845503	Stricture urthera	B/L DJS	90	136	90	105	100	3	5	100	130	100	T6	89	134	84	101	100	88	124	81	95	100	88	126	87	100	100	75	118	83	95	100	78	116	79	91	100	72	115	78	90	100	71	114	74	87	100	75	119	81	94	100	78	126	86	99	100	120	1	2	5	7	7	2
59	D	60	female	68	845064	L upper utretric calculi	L URSL + DJS	84	110	79	89	98	2	2	130	160	80	T3	80	112	65	81	98	76	110	72	84	98	73	108	83	91	98	69	109	75	90	98	66	112	82	92	98	68	106	62	77	98	67	100	63	75	98	70	115	82	93	98	75	119	87	98	98	175	2	2	2	4	6	1
60	C	44	male	63	843900	Stricture urthera	VIU	80	131	84	101	100	4	4	100	110	70	T5	77	130	80	96	100	76	121	82	95	100	78	128	84	98	100	76	106	65	83	100	80	105	64	78	100	78	106	61	77	100	76	105	65	78	100	74	116	81	93	100	72	120	80	93	100	120	1	2	3	6	8	3
61	D	57	male	70	847969	BPA	TURP	86	122	81	100	99	2	2	150	180	80	T3	82	116	78	91	99	78	113	73	90	99	72	120	75	84	99	70	109	72	84	99	71	107	71	83	98	68	103	69	80	98	70	100	66	77	98	74	129	68	88	98	76	123	74	90	99	170	1	2	2	5	8	2

S.No.	Group	Age	Sex	Wt.	UHID.NO	DIAGNOSIS	SURGERY	Pre-operative					Onset	Onset	Duration	Duration	Duration	highest
								PR	SBP	DBP	MAP	SPO2	sensory	Motor	Of Sens.	Of Motor	of surgery	sensory
													(min)	(min)	regression	regression	(min)	block
62	C	59	male	64	847812	Stricture urthera	urtheroplasty	94	116	73	87	99	3	4	130	140	110	T7
63	D	50	female	62	851156	R uretheral calculi	R URSL + DJS	98	134	86	102	100	1	2	130	150	90	T3
64	C	26	female	60	851926	L VUT calculi	L URSl + DJS	82	140	82	101	100	2	3	100	130	80	T7
65	D	34	Male	57	848454	Desmoid tumor	Exploration	96	137	89	105	100	2	2	140	160	80	T4
66	D	22	male	60	857257	Phimosis	circumcison	86	127	70	88	100	3	4	130	170	70	T4
67	C	56	male	65	856329	Stricture urthera	EJU	86	122	80	94	99	5	6	90	110	90	T6
68	C	60	MALE	55	866911	Penile odema	Wound debridement	100	136	100	115	98	3	5	90	100	100	T7
69	D	60	Male	65	865430	L epidymorthitis	Wound debridement	85	134	93	107	100	2	3	140	150	90	T4
70	C	38	male	38	860346	B/l hydrocele	B/L Jaoulay	78	128	89	99	100	4	5	100	130	110	T5
71	D	42	male	57	142083	haemorrhoids	open haemorrhoidectom	80	134	86	102	100	2	3	110	140	90	T4
72	D	44	female	62	142177	inguinal hernia	herinoplasty	76	127	83	98	100	2	2	110	150	120	T5
73	D	35	female	60	140454	inguinal hernia	herinoplasty	84	117	63	86	99	3	4	150	170	130	T4
74	C	45	male	65	140398	fissure in ano	ateral anal sphincetrotom	90	122	82	95	100	4	5	100	110	110	T5
75	D	42	female	58	139795	patellar tendon rupture	patellar tendon repair	82	123	72	83	99	3	3	130	150	100	T5
76	D	47	male	65	139904	achilles tendon rupture	tendon repair	76	122	80	93	99	4	5	120	130	120	T3
77	C	40	female	70	140806	AUB	TAH+BSO	88	132	78	96	100	5	5	90	120	130	T4
78	D	45	female	74	139574	metacarpal fracture	K-wire fixation	90	136	90	105	100	2	2	150	170	90	T3
79	C	45	male	76	142627	medial malleolous fracture	CRIF+Ccscrew fixation	85	110	79	89	99	4	4	100	140	120	T5
80	C	55	male	68	142317	acetabular fracture	ORIF+Plating	72	131	84	101	99	3	5	90	120	130	T7
81	C	39	female	58	115108	fissure in ano	ateral anal sphincetrotom	77	122	81	100	100	4	4	100	110	80	T6
82	D	28	female	60	113201	paraumbilical hernia	meshplasty	82	116	73	87	100	2	3	130	150	110	T5
83	C	57	male	65	114404	healing ulcer over foot	split skin grafting	90	134	86	102	99	5	5	90	130	100	T6
84	D	48	male	70	114987	tibia fracture	IMIL nailing	64	140	82	101	100	3	3	140	150	140	T4
85	C	50	female	56	104802	AUB	vaginal hysterectomy	80	137	89	105	100	4	5	90	120	110	T5
86	C	39	male	65	110130	medial malleolous fracture	ORIF+CC screw fixation	95	127	70	88	100	4	5	100	110	130	T6
87	C	59	male	74	109365	BPH	TURP	84	140	82	101	99	3	4	100	130	70	T6
88	D	31	female	56	105936	umblical herina	meshplasty	72	136	91	107	100	1	2	150	180	110	T4
89	C	50	male	75	104198	Appendicitis	open appendicectomy	85	123	88	97	100	4	4	110	140	90	T7
90	D	20	male	60	732241	3 month old tibial implant	Implant removal	90	115	74	88	100	2	3	140	150	90	T4

S.No.	Intra-operative														
	0min					3min					5min				
	PR	SBP	DBP	MAP	SPO2	PR	SBP	DBP	MAP	SPO2	PR	SBP	DBP	MAP	SPO2
62	85	112	65	81	99	86	110	71	84	99	88	107	63	74	99
63	96	127	86	99	100	80	129	88	102	99	68	134	86	102	99
64	80	136	90	105	100	83	132	78	99	100	82	134	84	101	100
65	90	126	87	100	100	82	124	81	101	100	74	125	90	97	100
66	83	118	83	95	100	75	116	79	91	100	68	122	68	81	100
67	80	119	76	90	99	77	116	71	87	99	68	114	77	89	99
68	97	135	88	100	98	98	132	78	96	98	95	126	95	103	98
69	83	131	84	101	100	80	121	82	95	100	78	124	85	98	100
70	76	115	76	89	100	78	117	74	88	100	80	118	80	90	100
71	77	125	90	97	99	75	122	79	93	99	70	117	75	89	99
72	73	118	84	94	100	70	116	74	88	100	66	109	75	90	100
73	80	115	74	84	99	67	108	62	85	99	56	110	72	84	99
74	88	122	80	94	100	87	117	74	88	100	89	120	75	84	100
75	87	114	77	89	99	83	115	76	89	99	80	110	71	84	99
76	68	117	78	92	99	57	118	80	90	98	55	107	71	85	98
77	77	124	81	95	100	74	116	74	88	100	75	124	81	101	100
78	86	120	69	84	100	80	118	71	87	100	74	123	72	83	100
79	60	109	72	84	99	56	102	64	76	99	94	107	63	74	99
80	97	123	79	94	99	96	126	95	103	99	98	129	82	94	99
81	85	112	65	81	100	86	110	71	84	100	88	107	63	74	100
82	75	115	74	84	99	72	108	62	85	99	70	110	72	84	99
83	77	130	80	96	99	76	121	82	95	99	78	128	84	98	99
84	60	125	90	97	100	54	122	79	93	100	50	117	75	89	100
85	80	136	90	105	100	83	132	78	99	100	82	134	84	101	100
86	85	118	80	90	100	81	116	84	95	100	78	123	83	103	100
87	82	136	91	107	99	78	131	84	100	99	80	133	89	104	99
88	66	117	78	92	100	64	118	80	90	100	62	107	71	85	100
89	80	126	90	105	100	83	132	78	99	100	82	134	84	101	100
90	88	115	74	84	99	80	108	62	85	99	78	110	72	84	99

S.No.	10min					20min					30min				
	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02
62	85	103	65	78	99	74	102	69	80	99	63	103	61	75	99
63	59	137	83	101	99	75	120	80	93	98	70	109	69	82	98
64	71	134	79	97	100	70	123	73	89	100	68	119	64	83	100
65	74	115	74	88	100	75	109	72	84	98	78	106	67	80	98
66	70	121	60	84	100	66	104	70	77	99	77	115	98	105	99
67	66	109	77	88	99	70	107	74	85	99	68	109	77	88	99
68	88	123	88	97	98	86	124	83	79	98	84	118	73	82	98
69	76	114	76	89	100	72	115	76	89	99	69	118	76	90	99
70	78	108	94	99	100	65	103	58	66	100	64	98	73	81	100
71	65	114	70	86	99	63	110	73	85	99	64	105	64	78	99
72	64	105	65	78	100	61	101	61	74	100	63	102	64	76	100
73	67	106	67	80	99	65	107	72	64	99	65	110	73	86	99
74	85	117	78	89	100	82	112	75	87	100	77	114	70	86	100
75	74	112	65	81	99	71	113	84	90	99	69	116	79	91	99
76	86	109	75	90	98	80	114	70	86	98	79	118	83	95	98
77	74	110	76	84	100	70	106	64	76	100	72	109	76	87	100
78	68	118	72	82	100	65	116	76	87	99	66	113	71	65	99
79	85	108	62	85	99	86	105	66	77	99	80	104	60	76	99
80	93	123	77	92	99	90	111	73	86	99	82	104	64	77	99
81	85	103	65	78	100	74	102	69	80	100	63	103	61	75	100
82	66	106	67	80	99	68	107	72	64	99	64	110	73	86	99
83	76	106	65	83	99	80	105	64	78	99	78	106	61	77	99
84	85	114	70	86	100	82	110	73	85	99	80	105	64	78	99
85	71	134	79	97	100	70	123	73	89	100	68	119	64	83	100
86	76	122	79	92	100	80	109	83	81	100	78	106	61	77	100
87	76	118	86	97	99	80	116	84	95	99	70	110	81	91	99
88	62	109	75	90	100	65	114	70	86	100	63	118	83	95	100
89	71	134	79	97	100	70	123	73	89	100	68	119	64	83	100
90	76	106	67	80	99	75	107	72	64	99	73	110	73	86	99

S.No.																Duration		VAS score				rescue
	60min					90min					120min					of analgesia	1hr	4hrs	8hrs	12hrs	24hrs	analgesia
	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SP02	PR	SBP	DBP	MAP	SPO2							
62	70	108	63	78	99	75	117	72	87	99	70	135	95	108	99	130	1	3	5	6	9	4
63	77	107	71	83	98	84	102	67	77	99	75	123	77	92	100	160	1	3	5	7	7	1
64	67	105	68	81	100	68	132	68	89	100	60	126	73	91	100	110	2	2	3	8	9	3
65	75	124	80	95	98	72	117	74	88	98	83	121	78	92	100	210	1	2	4	6	8	1
66	75	115	98	105	99	77	117	51	66	99	78	123	85	100	100	194	0	2	3	5	7	2
67	70	102	72	78	99	78	120	69	86	99	80	125	65	85	99	160	1	3	5	7	8	3
68	76	105	66	78	98	82	118	73	82	98	86	120	84	94	98	168	1	2	5	7	9	4
69	70	110	75	87	99	66	115	75	97	99	72	123	74	90	100	188	0	2	2	6	8	2
70	70	104	72	78	100	80	115	75	88	100	90	121	80	94	100	160	2	4	6	6	7	3
71	66	111	73	86	99	70	110	74	86	99	75	126	87	100	99	130	3	5	7	9	9	4
72	67	100	63	75	100	68	116	61	93	100	72	125	70	88	100	160	1	2	2	5	7	2
73	68	115	82	93	99	72	111	71	87	99	84	123	73	89	99	110	1	2	6	8	9	4
74	75	112	63	78	100	78	108	69	82	100	80	123	79	93	100	210	1	4	6	9	9	3
75	70	117	74	88	99	76	116	61	93	99	77	122	81	95	99	194	0	2	2	5	7	2
76	83	113	68	81	98	85	116	78	91	99	85	130	80	96	99	160	2	3	5	8	6	1
77	70	113	79	90	100	76	116	78	91	100	76	134	70	91	100	168	1	2	3	4	7	3
78	65	107	74	85	99	62	125	70	88	99	63	129	80	96	100	188	1	2	3	5	6	1
79	84	108	64	81	99	78	113	76	88	99	82	120	80	93	99	160	1	2	3	5	7	3
80	80	107	64	78	99	85	107	64	78	99	80	123	77	92	99	180	2	3	5	9	9	2
81	70	108	63	78	100	75	117	72	87	100	70	135	95	108	100	130	2	3	6	8	8	4
82	65	115	82	93	99	66	111	71	87	99	67	123	73	89	99	160	1	2	2	8	8	2
83	76	105	65	78	99	74	116	81	93	99	72	120	80	93	99	120	0	2	5	7	8	3
84	76	111	73	86	99	75	110	74	86	99	75	126	87	100	100	140	1	2	2	6	7	1
85	67	105	68	81	100	68	132	68	89	100	60	126	73	91	100	110	2	3	5	7	7	2
86	76	105	65	78	100	74	116	81	93	100	72	119	82	94	100	140	1	2	2	4	6	1
87	75	108	64	81	99	78	113	76	88	99	85	120	80	93	99	144	0	2	3	6	8	3
88	64	113	68	81	100	65	116	78	91	100	70	130	80	96	100	140	2	2	2	5	8	2
89	67	105	68	81	100	68	132	68	89	100	60	126	73	91	100	110	2	3	5	6	9	4
90	74	115	82	93	99	72	111	71	87	99	84	123	73	89	99	160	3	3	5	7	7	1