Dissertation on

"COMPARISON OF INTRA MUSCULAR DEXMEDETOMIDINE AND INTRAMUSCULAR MIDAZOLAM PREMEDICATION FOR LAPROSCOPIC ABDOMINAL SURGERIES"

Submitted to the

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

in partial fulfilment of the requirements

for the award of degree of

M.D. (Branch-X)

ANAESTHESIOLOGY

GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY,

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APRIL 2013

DECLARATION

I, **Dr.S.SUBHASHINI**, solemnly declare that the dissertation, titled **"COMPARISON OF INTRAMUSCULAR DEXMEDETOMIDINE AND INTRAMUSCULAR MIDAZOLAM PREMEDICATION FOR LAPROSCOPICABDOMINAL SURGERIES",** is a bonafide work done by me during the period of March 2012 to November 2012 at Government Stanley Medical College and Hospital, Chennai under the expert guidance and supervision of **Dr. P. CHANDRASEKAR, M.D. D.A.,** Professor and Head, Department Of Anaesthesiology, Government Stanley Medical College, Chennai.

This thesis is submitted to The Tamil Nadu Dr.M.G.R. Medical University in partial fulfilment of the rules and regulations for the M.D. degree examinations in Anaesthesiology to be held in April 2013.

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CERTIFICATE

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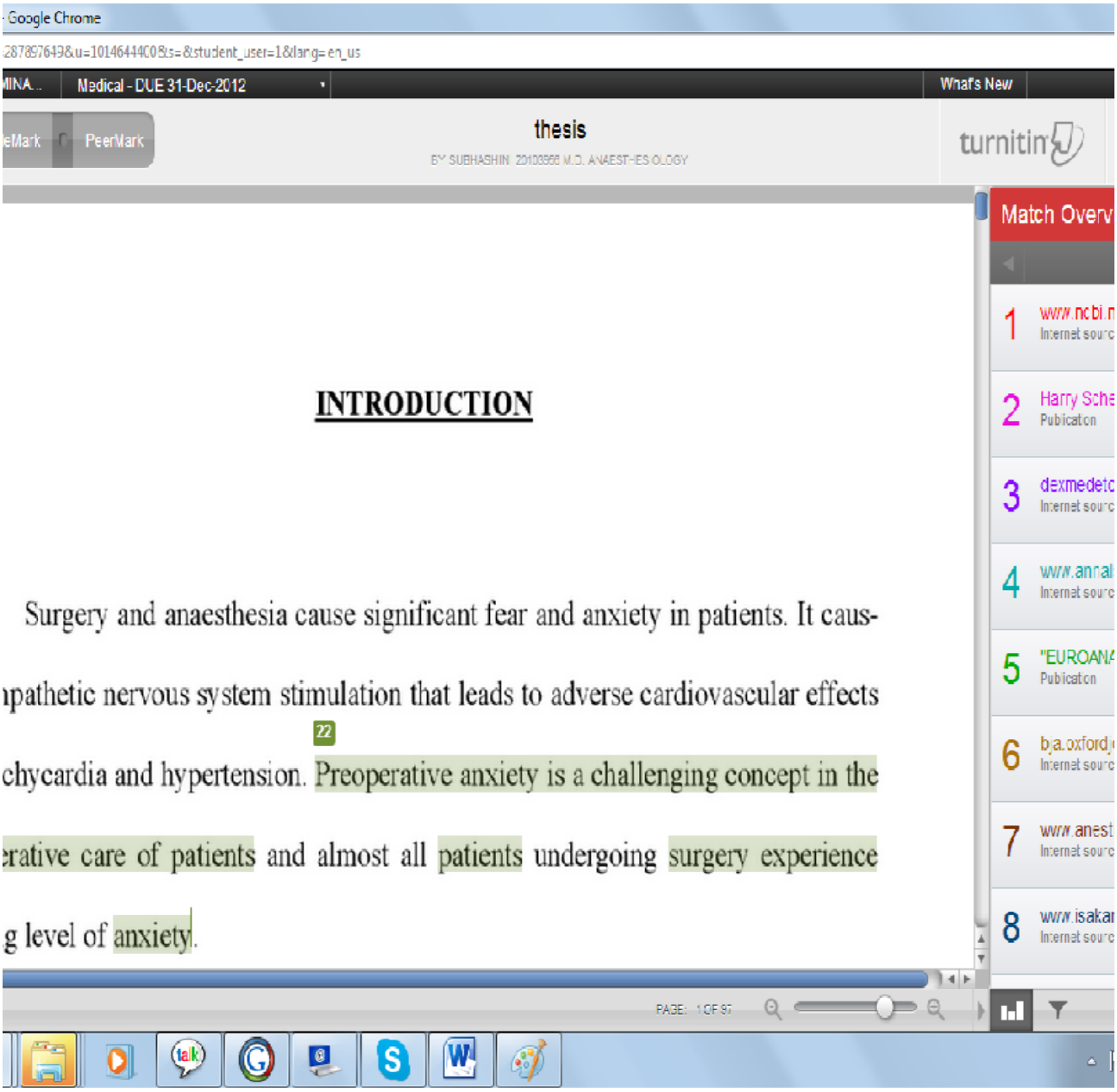
CONTENTS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INTRODUCTION
Surgery and anaesthesia cause significant fear and anxiety in patients. It caus-
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COMPARISON OF INTRAMUSCULAR DEXMEDETOMIDINE AND INTRAMUSCULAR MIDAZOLAM IN LAPAROSCOPIC INTRA ABDOMINAL SURGERIES.

INTRODUCTION

Surgery and anaesthesia cause significant fear and anxiety in patients. It causes sympathetic nervous system stimulation that leads to adverse cardiovascular effects like tachycardia and hypertension.Preoperative anxiety is a challenging concept in the preoperative care of patients and almost all patients undergoing surgery experience varying level of anxiety.

The incidence of preoperative anxiety is 60–80% of surgical patients. Drugs like phenothiazine, barbiturates, opioids and benzodiazepines are used to relieve anxiety preoperatively[29]

Premedication is administration of anaesthetic adjuvant drugs to allay anxiety, decrease post-operative pain, nausea and vomiting and the risk of

pulmonary aspiration.Clinically used routes of administration of premedication are oral, rectal, intramuscular, intravenous and intranasal.

Midazolam, a benzodiazepine is the drug of choice as premedicant to decrease anxiety. Other classes of drugs used for anxiolysis and sedation are barbiturates and α-2-agonists.[1]

After the discovery of alpha agonists, its usefulness in anaesthesia like anaesthetic adjuvant for general anaesthesia and regional anaesthesia, intravenous sedation for short procedures, intravenous sedation in ICU and as an additive to neuraxial and peripheral nerve blocks are investigated.

There are number of reasons for therenewed interest in the use of dexmedektomidine, a newer alpha2 agonist, as sedative premedication. Dexmedetomidine, when compared to clonidine is a more selective alpha2-adrenoceptor agonist, which allows its use in relatively high doses for sedation and analgesia without the unwanted vascular effect from activation of alpha1-receptors. Dexmedetomidine is shorter acting than clonidine. These properties make dexmedetomidine suitable for premedication and as an anaesthetic adjunct for general and regional anaesthesia.

There has been a constant search for an agent that effectively suppresses all hazardous response to obnoxious stimuli with good safety margin. Dexmedetomidine has most of the characteristics of premedication (like sedation, anxiolysis, analgesic sparing effect, sympathetic blockade, dryness of mouth). Hence we decided to study the effectiveness of dexmedetomidine as a pre medication agent.

AIM OF THE STUDY

The aim of our study is to compare sedation and anxiolysis in two groups receiving intramuscular dexmedetomidine 1.0mic/kg and intramuscular midazolam 0.05mg/kg for laparoscopic abdominal surgeries given 60 minutes before surgery.

PREMEDICATION

Premedicationis the administration of medication before anaesthesia. Premedication is used to prepare the patient for anaesthesia and to provide optimal conditions for surgery. “Premedication places the patient in a tranquil frame of mind. That is the principal reason, not on humane grounds only, although the worst part of an operation from the patient’s point of view is often the few hours preceding it, but on physiological grounds, because a patient in a tranquil frame of mind requires less anesthetic than one who is apprehensive, and consequently he makes a better recovery” said De caux about premedication.

History of premedication:

In the past, Opioid analgesics were used as premedication, as it has good sedative and analgesic effects. Opioids enhance the effects of other

anaestheticagents. For this quality, opioids were preferred premedication, when no potent inhalational agents were available.

But there were certain disadvantages with opioid premedication. They caused euphoria when given to patients who did not have any pain and caused delay in gastric emptying and PONV. In addition, augmentation of CNS depressant effect of other anaesthetic agents was undesirable.

Till 1960, the preferred combination was IM opioids like meperidine or morphine given along with atropine 30-45 minutes before surgery. “Twilight sleep” a sedation caused by hyoscine and papaveretum was preferred by some anesthesiologist.[2]

Rectal administration of powerful CNS agents like paraldehyde or thiopentone was used forpre-anaesthetic sedation in the preoperative period especially in uncooperative paediatric patients.

Apart from rectal barbiturates, oral barbiturates were also tried in the past for inducing hypnosis in preoperative period. But all these agents are not preferred after the advent of potent inhalational agents, short acting opioids and short acting muscle relaxants.

Now a day, benzodiazepines are the preferred agents.

PREOPERATIVE ANXIETY:

It is a state of psychological stress which results in low level of hypothalamic-pituitary axis activation and cytokine release. Salivary cortisol levels increases by 50% after the patients come to know about the surgery. Beta endorphin and epinephrine concentration goes up preoperatively. There is no proven additive effect of this preoperative stressor response with the intraoperative stress due to surgery.

Young patients, patients who have not had any previous anesthetics, patients with previous negative experience with anesthesia and female patients usually have higher anxiety scores.

MEASURING LEVELS OF PREOPERATIVE ANXIETY:

Visual analog scale:

This scale was first described by Bond MR and Pilousky in 1966 for measuring pain intensity. It uses 10 cm visual scale, one end of which shows

no pain and the other end showing worst possible pain. The same scale can be used to assess anxiety, where 0 indicates no anxiety and 10 indicates extreme anxiety.

Spiel Berger state anxiety inventory (STAI):

The spiel Berger state anxiety inventory (STAI) has 20 self-reported statements that investigate how a patient feels at a particular time.

STAI is rated on a four-point scale for the patient's agreement with any statement (not at all, somewhat, moderately so, and very much so).The total score for STAI ranges from 20 to a maximum of 80. Low **anxiety** score is 20–37, moderate **anxiety** score is 38–44 and high **anxiety** is 45–80.

Observer's anxiety criteria: The patient's anxiety is assessed by an observer who is not involved in the study. They are graded as follows.

Grade 1: Calm

Grade 2: Mild anxiety

Grade 3: Moderately anxious

Grade 4: Extremely anxious

Other scoring systems to asses anxiety are beck anxiety inventory, Hamilton anxiety rating.

MEASURING LEVELS OF PREOPERATIVE SEDATION:

Subjective sedation scale[21]

1. Fully awake and conscious
2. Awakens on verbal commands
3. Awakens on gentle shaking
4. Awakens on vigorous shaking and painful stimuli
5. Unarousable

Ramsay sedation scores

1. Agitated, restless
2. Cooperative, tranquil
3. Responds to verbal commands while sleeping
4. Brisk response to glabellar tap or loud voice while sleeping
5. Sluggish response to glabellar tap or loud voice
6. No response to glabellar tap or loud voice

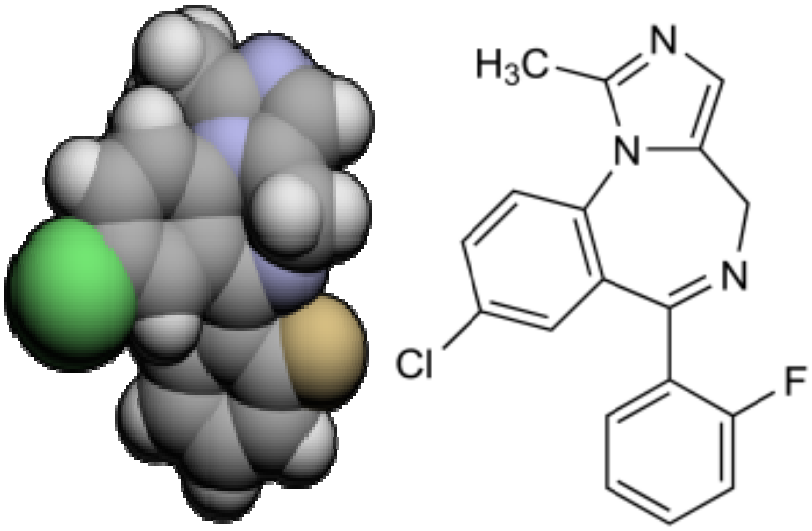
PHARMACOLOGY

MIDAZOLAM

Fryer and Walser's in 1976 first synthesized midazolam, the first clinically used water-soluble benzodiazepine[3]. Midazolam is a water-soluble benzodiazepine that is available in an acidified (pH 3.5) aqueous formulation that produces minimal local irritation after IV or intramuscular (IM) injection. At physiologic pH, an intramolecular rearrangement occurs that changes the physicochemical properties of midazolam such that it becomes more lipids soluble.

All benzodiazepines have anxiolytic, amnestic, sedative, hypnotic, anticonvulsant, and spinally mediated muscle relaxant properties. The dose-dependent pharmacologic activity implies that the CNS effects of various benzodiazepine compounds depend on the affinity for receptor subtypes and their degree of receptor binding. Although benzodiazepines can be used as

hypnotics, they are primarily used as premedicants and adjuvant drugs because of their anxiolytic, sedative, and amnestic properties.

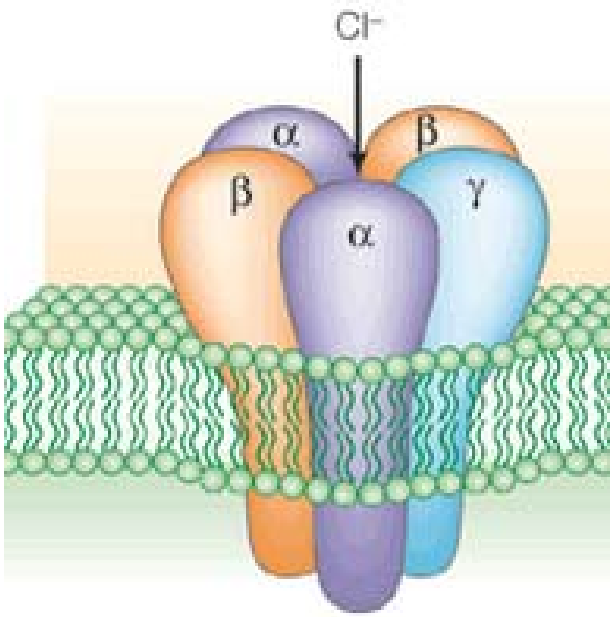


Chemical structure of Midazolam

BENZODIAZEPINE's chemical structure is composed of a benzene ring and a seven-membered diazepine ring. Because all benzodiazepines contain a 5-aryl substituent and a 1, 4-diazepine ring, the term has come to mean the 5-aryl-1, 4 benzodiazepine structure[4].

Mechanism of Action:

GABA is the principal inhibitory neurotransmitter within the CNS. Benzodiazepines facilitate the inhibitory neurotransmission by GABA. After binding to GABA receptors, BZDs induces allosteric modification in GABA receptors and increases the chloride conductance. This leads to hyperpolarization of CNS and CNS becomes resistant to excitation[7].



Schematic diagram of $GABA_A$ Receptor

STRUCTURE OF GABA A RECEPTOR:

GABA A receptor is a pentameric structure containing two alphas, two beta and a gamma glycoprotein subunits. The binding of BZD to receptor site increases the efficiency of coupling between the GABA receptor and the chloride channel.

The degree of allosteric modulation caused by BZD is limited and this explains the "ceiling effect" of CNS depression by BZD.[6]

Alpha 1 receptor binding is responsible for sedation, amnesia and its anticonvulsant properties, whereas alpha 2 receptor binding is responsible for muscle relaxation and anxiolysis.

The concentration dependent receptor occupancy of BZD is responsible for various drug effects. Anxiolysis is produced by 20% receptor occupancy. Amnesia and sedation are produced at 30-50% receptor occupancy. Hypnosis and unconsciousness needs 60% of receptor occupancy[6, 20],

Mechanism of anxiolysis:

The exact mechanism is not known. Midazolam premedication reduces intraoperative epinephrine, norepinephrine and cortisol release. It is observed that midazolam did not suppress cortisol release in response to exogenous

ACTH. This suggests that benzodiazepines act at a higher level of like hypothalamus or pituitary.

Benzodiazepines when given in combination with opioids are more effective in blunting the rise in serum catecholamine, cortisol, arginine vasopressin and ACTH rather than benzodiazepines alone[3].

Commercial Preparation & Dosage

The preservative in injection Midazolam solution is 0.8% sodium chloride, 0.01% disodium edetate, and 1% benzyl alcohol the pH is adjusted to 3 with hydrochloric acid. As midazolam is lipid soluble drug and has pH-dependent solubility, it is water soluble as formulated in a buffered acidic medium.

Stability of midazolam in solution and rapid metabolism is due to the imidazole ring. The rapid CNS effect and large volumes of distribution is due to high lipophilicity[3]. Midazolam 0.04 to 0.08mg/Kg IV/IM is the most common dosage used for premedication.[5,6] oral and midazolam is given at dose of 0.5 mg/kg. Buccal midazolam is available as 5 mg/ml prefilled syringes with 2.5, 5, 7.5 and 10 mg. Preparation for parenteral use is available as 1mg/ml and 5mg/ml solutions.

Metabolism:

Benzodiazepines undergo hepatic metabolism via oxidation and glucuronide conjugation. Oxidation reactions are susceptible to hepatic dysfunction and co administration of other anesthetic drugs.Midazolam undergoes oxidation by hepatic enzymes to form hydroxylated metabolite, which is water soluble and excreted in the urine.

The primary metabolite, 1-hydroxymethylmidazolam, is a mild CNS-depressant. The hepatic clearance rate of midazolam is five times greater than lorazepam and 10 times greater than diazepam. Reduction in hepatic blood flow and age can affect the midazolam's clearance.

CARDIOVASCULAR EFFECTS:

Midazolam produces decrease in systemic vascular resistance and blood pressure when large doses are administered for induction of anaesthesia. However, the cardiovascular depressant effects of benzodiazepines are frequently "masked" by laryngoscopy and intubation. The cardiovascular depressant effects are directly related to the plasma concentration. However, a

plateau plasma concentration appears to exist, above which the changes in blood pressure are less[5].

RESPIRATORY EFFECTS:

The ventilatory response to hypoxia is depressed particularly in hypercarbic patients. Supplemental oxygen may be needed to prevent hypoxia, with continuous observation of airway patency and respiration.

Minor respiratory depression is more profound in the presence of limited respiratory reserve and old age. Profound respiratory depression and apnea are seen with synergistic interaction with other opioids[7].

AIRWAY REFLEXES:

Benzodiazepines depress the swallowing reflex and decrease the upper airway reflex activity by reducing the tonic and phasic contraction of airway muscles[7].

DEXMEDETOMIDINE

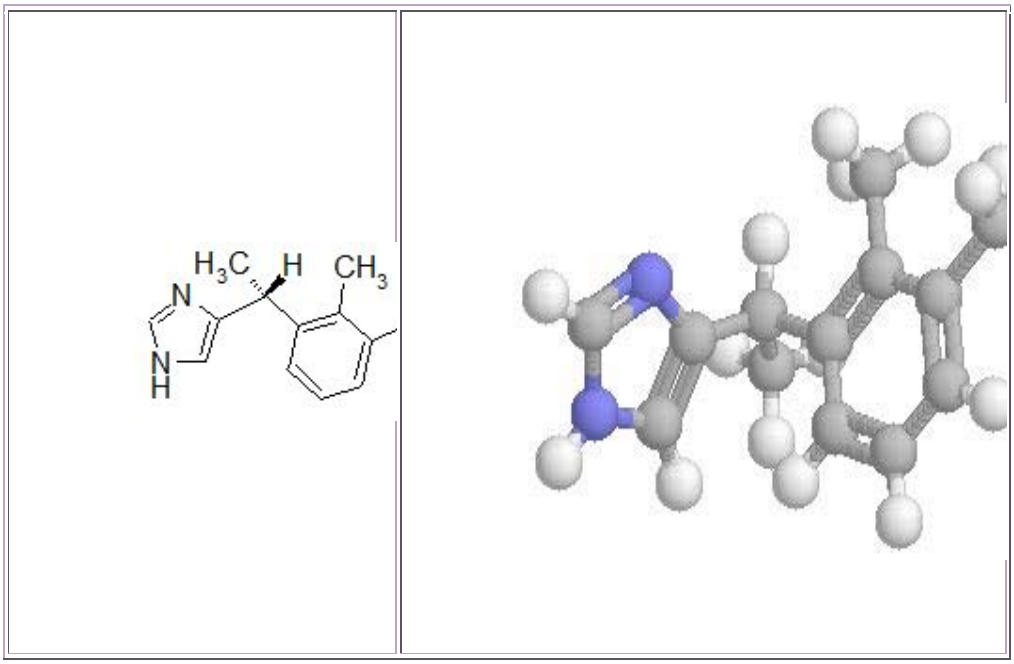
Dexmedetomidine is a selective α_2-agonist, with 1600-fold greater selectivity for the α_2-receptor**.** Adrenergic receptors were first differentiated into α and β by Ahlquist based on their responses to various amines. α_2-

Adrenergicagonists provide sedation, anxiolysis, and hypnosis, as well as analgesia and sympatholysis.

Initially anaesthesiologists were reluctant to use α2-agonists in anaesthesia due to adverse events observed in patients who were receiving clonidine therapy. The MAC reducing property of clonidine increased the use of this alpha agonist in clinical practice. Recently dexmedetomidine has been approved for brief sedation (<24 hours) for mechanically ventilated patients in ICU.

Physicochemical Characteristics

Medetomidine is a selective α_2-adrenergic agonist. Dexmedetomidine is its specific dextro enantiomer and is available as a parenteral formulation. It is freely water soluble. It belongs to imidazole subclass of alpha 2 receptor agonists.



Structure of dexmedetomidine

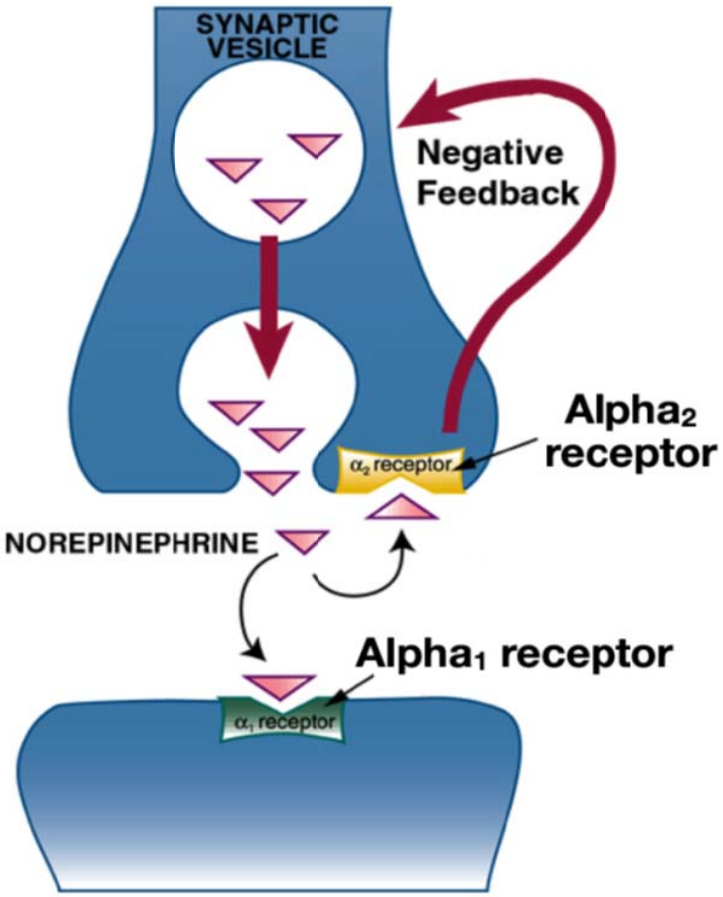
Commercial preparation and dose:

Itis available as 100mic/ml in one or two ml ampoules. The loading dose for intravenous infusion is 0.5 to 1 mic/kg over 10 minutes followed by 0.2to 0.7 mic/kg/hr. The effect starts after 5-10 minutes and lasts for 30 -60 minutes.

Metabolism and pharmacokinetics:

Dexmedetomidine has a rapid distribution and extensive metabolism in the liver. It is excreted both in urine and faeces. It undergoes glucuronide conjugation. Dexmedetomidine is 94% protein bound. The elimination half-life is 2 to 3 hrs.

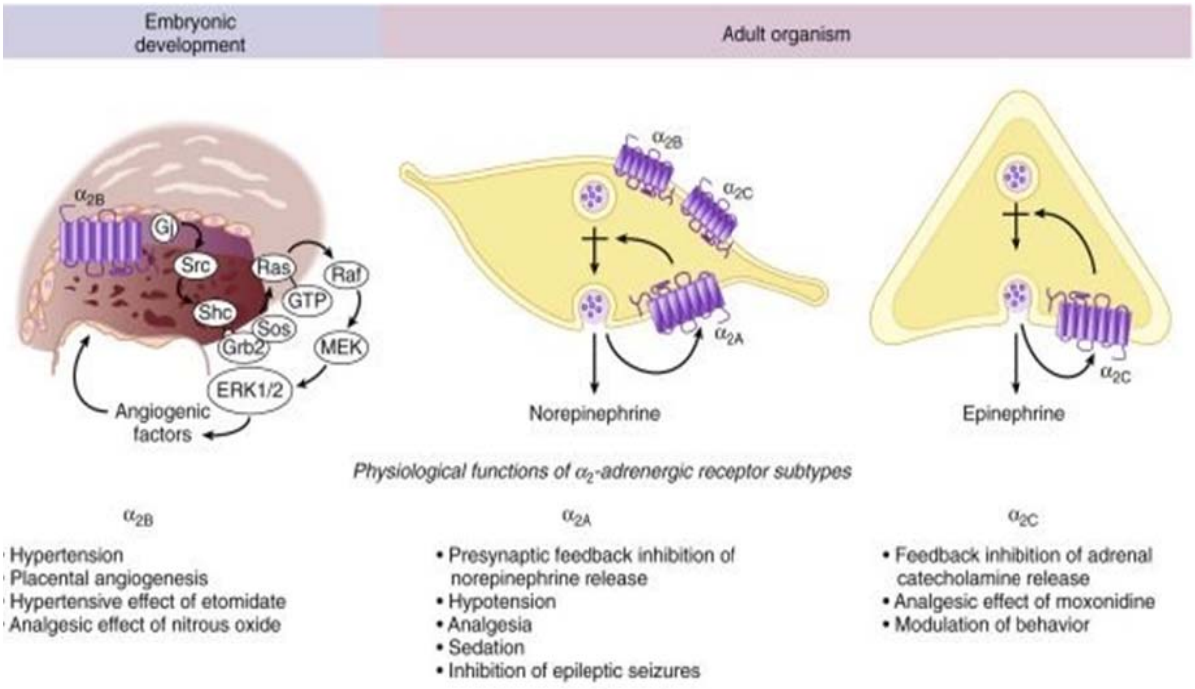
These pharmacokinetic parameters appear to be unaltered by age, weight, or renal failure, but clearance is a function of height. The concentration ratio between whole blood and plasma is 0.66.[3] Time to peak plasma concentration after intramuscular injection is 1.6 to 2.4 hours.[19]



Structure of alpha receptor

Structure of alpha2 receptor:

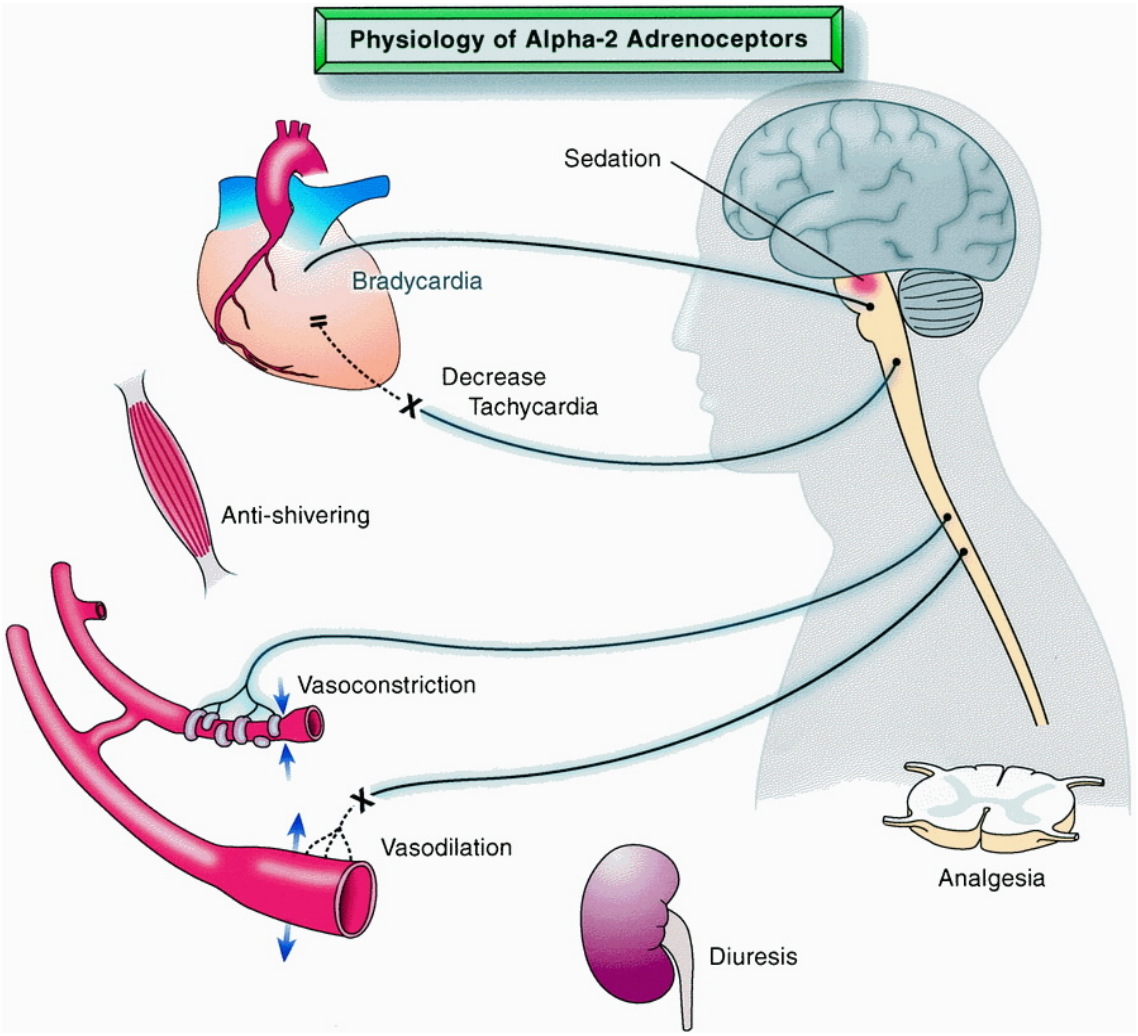
Alpha2 receptors belong to seven transmembrane G protein superfamily. It uses G protein for signal transduction. Presynaptic alpha 2 receptors regulate the release of norepinephrine ATP through a negative feedback mechanism. In response to nerve stimulation, stimulation of alpha receptors inhibits the release of norepinephrine. High density of these receptors is present in the cerebral cortex and medulla, which is responsible for the bradycardia and hypotension caused by alpha2 agonist.



CARDIOVASCULAR EFFECTS:

Dexmedetomidine has profound effect on cardiovascular system and thus may alter its own pharmacokinetics. At high doses it causes marked vasoconstriction, which probably reduces the drug's volumes of distribution. A biphasic response is seen after bolus intravenous dose. That is an initial hypertension followed by hypotension.[3]After an intramuscular injection, the

initial increase in BP is not seen. The heart rate and blood pressure remains within 10% of baseline.



Effects on the Central Nervous System

Sedation:

The α_2 agonists produce their sedative-hypnotic effect by an action on α_2 receptors in the locus caeruleus .The quality of sedation produced by dexmedetomidine seems different compared with that produced by other sedatives acting through the GABA system.

The sedation caused by dexmedetomidine is associated with less respiratory depression. It acts through the endogenous sleep-promoting pathways to exert their sedative effect. It decreases the triggering between locus ceruleus and mediolateralpreoptic nucleus. It increases the histamine release in the cortical and sub cortical projections.

Central Nervous System Protection and Other Central Nervous System Effects:

The CNS protective effects are not well defined. It reduces the cerebral catecholamine outflow during injury and resulted in less neural tissue damage with better neurologic outcome. The neuroprotective properties of dexmedetomidine in humans have not been investigated. Little is known of the effects of dexmedetomidine alone on ICP and CBF. It reduces the muscle rigidity caused by high dose opioids

Analgesia:

The analgesic effect of dexmedetomidine is due to its action on alpha 2 receptors in locus ceruleus and spinal cord. Narcotic sparing effect is seen after systemic use of dexmedetomidine.

Effects on the Respiratory System

Dexmedetomidine sedation reduces minute ventilation, but the slope of the carbon di oxide response curve is preserved. This change is similar to normal sleep. There is no change in pao2 or Ph. Dexmedetomidine induces arousal on hypercarbia. This phenomenon is similar to normal sleep and is a protective mechanism.

Effects on the Cardiovascular System

The basic effects of α_2 agonists on the cardiovascular system are decreased heart rate; decreased systemic vascular resistance; and indirectly decreased myocardial contractility, cardiac output, and systemic blood pressure.

By developing highly selective α agonists, it has been hoped to decrease some of these adverse cardiovascular effects and to maximize the desirable hypnotic-analgesic properties. It has a biphasic response after intravenous bolus injection.

An initial increase in blood pressure due to peripheral alpha2 stimulation and later a fall in BP[22].Such initial increase in BP are not seen after an IM injection. Itremained within 10% of baseline.

Antagonist:

Atipamezole readily reverses the effects of dexmedetomidine. It is not currently approved for human use[3].

ENDOCRINE EFFECTS: Dexmedetomidine decreases the release of catecholamine and reduces the stress response to intubation and surgery.

SIDE EFFECT:

It causes dry mouth, bradycardia, hypotension, hypertension, atrial fibrillation, nausea. These side effects occur mostly during the infusion of loading dose.

Uses

Flacke listed the potential uses of sympatholytic drugs in the future. In addition to the reducing effect of MAC and the absent respiratory depression, the following properties seem particularly valuable to the anaesthesiologist : [3]

1. They are potent analgesics.
2. They are sedatives and anxiolytics.
3. They are antisialogogues.
4. They may promote hemodynamic stability.
5. Homeostatic reflexes remain intact.
6. They attenuate opioid rigidity (in animals).
7. Their circulatory actions can be reversed.

REVIEWOF LITERATURE

1. **H. Ronald Vinik, (Anesthesia & Analgesia 1982)**[32] The authorstudied the effect of premedication with 0.07 mg/kg midazolam , 1.0mg/kg hydroxyzine and placebo midazolam diluent given intramuscularly in 100 ASA PS 1 and 2 patients who underwent general surgery.

In the anxiety evaluation, AVAT and objective anxiety evaluation were done. Midazolam and hydroxyzine produced reduction of anxiety greater than placebo which was significant ($p < 0.05$). Hemodynamic variations were similar in all the groups. No adverse reactions were observed before anesthesia. It was concluded that midazolam is an efficacious and safe premedication in healthy patients. Minimal tissue irritation was observed with midazolam. Onset of action of intramuscular midazolam was found to be prompt.

2. **Riku E. (Anesthesia Analgesia1990)** conducted a study in 20 healthy ASA PS 1 patients by single blind method. The effects on anesthetic requirements, hemodynamics and catecholamine levels in plasma using four different doses (0.167, 0.33, 0.67, and 1 .0 microgram/kg) of dexmedetomidine intravenous infusion when the subjects underwent uterine dilatation and curettage.

Conclusion was tolerance to dexmedetomidine was good and drug-related subjective side effects or adverse events were not serious. Reductions in Blood pressure, heart rate and plasma norepinephrine levels were reduced

after dexmedetomidine administration. The optimal dose for single-dose intravenous premedication in minor surgery seems to be 0.334to 0.67 mic/kg.

3. **MarkkuAnttila (Br J ClinPharmacol. 2003)** studied dexmedetomidine's bioavailability in healthy subjects. 12 healthy males were given 2 µg/kg single dose of dexmedetomidine intravenously, intramuscularly, per orally and buccally. The drug concentration-time data were analyzed by 3 methods. They are linear one-compartment (buccal and per oral data), or two-compartment modeling (intravenous data), or noncompartmental methods (intramuscular data). Mean (95% CI) absolute bioavailability after per oral, buccal and intramuscular administration was 16% (12–20%), 82% (73–92%) and 104% (96–112%), respectively.

4. **M.L. Jaakola et al [4](Acta analgesia DEC 2008)**Dexmedetomidine as a preanaesthetic agent - Phase I-III study Dexmedetomidine effectively induced sedation and anxiolysis in subjective VAS estimates. It was administered as one single i.v bolus before intravenous regional anaesthesia and other as an intramuscular premedication before general anaesthesia. Sedation and anxiolysis produced were same as that produced by i.m. midazolam premedication.

They have acknowledged that in the perioperative setting

dexmedetomidine have many desirable properties. Control of haemodynamic and adrenergic responses to noxious stimuli by dexmedetomidine were good. They concluded that dexmedetomidine alone is not sufficient to produce clinically adequate anaesthesia. But it will remain as a good anaesthetic adjuvant.

5. **C. J. Lawrence et al. (Anaesthesiology 2004)** investigated 50 patients undergoing minor orthopaedic and general surgery. They evaluated the anaesthetic requirement and perioperative hemodynamic stability after administering single dose of dexmedetomidine 2 $\mu g.kg^{-1}$ given before induction as intravenous route. The haemodynamic response to tracheal intubation and extubation was reduced in the dexmedetomidine group. The intra-operative heart rate variability, postoperative analgesic and anti-emetic requirements and perioperative serum catecholamine concentrations were also lower in the dexmedetomidine group. Hypotension and bradycardia after dexmedetomidine at 2 mic/kg infusion was less frequent.

6. **M.Virkkilä (Anaesthesiology 2007)**[43] studied 35 ASA PS patients undergoing cataract surgery. The effects of dexmedetomidine on intra-ocular pressure, haemodynamic parameters, sedation, anxiolysis and dryness of mouth. Dexmedetomidine was used in five doses of 0.25, 0.5, 0.75, 1.0 and1.5 mic/kg.. It was administered intramuscularly 60 min before surgery.

Dexmedetomidine at a dose of 1.0 mic.kg^{-1} produced decrease in intraocular pressure in 32% of patients. This dose also induced moderate sedation, but was not associated with significant haemodynamic changes. Bradycardia and hypotension were observed at1.5 mic/kg. It was concluded that 1.0 μg.kg^{-1} of dexmedetomidine when given intramuscularly as premedication before cataract surgery under regional anaesthesia produces sedation. Dexmedetomidine at this dose reduces the intra-ocular pressure and produced less haemodynamic effects.

7. **Poonam S et al (Journal of anesthesiology clinical pharmacology)** monitored the depth of anesthesia (DOA) using entropy to prevent awareness under anesthesia. ASA I and II patients undergoing laparoscopic surgeries were studied. Dexmedetomidine infusion was started at 1 mcg/kg for 15minutes.it was continued by maintenance infusion of 0.2 mcg/kg/hr. DOA was monitored with entropy. Use of dexmedetomidine resulted in 62.5% reduction in the induction dose of propofol. Dexmedetomidine also decreased end-tidal concentration of isoflurane requirement by 30% for maintenance of anesthesia and concluded that dexmedetomidine is an effective anesthetic adjuvant that can be safely used during laparoscopy without causing awareness.

8. **Dyck JB (Anesthesiology.1993)**[20] observed pharmacokinetics and

hemodynamic changes in 10 volunteers after Dexmedetomidine 2 mic/kg given by IV or IM route. The bioavailability of dexmedetomidine after IM dose was 73 %. After IM administration, the peak concentration was achieved in 12 min (2-60 min). The mean peak concentration was 0.81 ± 0.27 ng/ml. A Biphasic BP response was observed after IV administration of dexmedetomidine. MAP increased by 22% and HR declined by 27% from baseline after 5-min after IV infusion of 2 mic/kg dexmedetomidine. Four hours after the infusion, MAP decreased by 20% from baseline and HR decreased to 5% below baseline values. Four hours after IM administration, MAP decreased by 20% and HR decreased by 10% and concluded that the IM administration of dexmedetomidine avoided the acute hemodynamic changes seen with IV administration.

9. **Jaakola ML(Acta Anesthesiology Scand. 1994)**[36] investigated in 20 ASA I-II patients undergoing elective hysterectomy. Ten patients received dexmedetomidine 2.5 mic/ kg i.m. 60 min before induction and saline placebo i.v 2 min before induction. 10 patients received midazolam 0.08 mg kg-1 i.m. 60 min before induction and fentanyl 1.5 micrograms kg-1 i.v 2 min before induction. Both of the premedication induced comparable sedation, anxiolysis and hemodynamic changes to tracheal intubation. Intraoperatively, systolic and diastolic BP was 15% and 13% lower in Dexmedetomidine-placebo group. The mean heart rate was lower in Dexmedetomidine-placebo group.

Fentanyl requirement was more in Midazolam group. The median HR was 3.5 vs. 2.5 times in Dexmedetomidine vs. placebo group. Postoperative period and analgesic requirements were similar in both groups. The author concluded that dexmedetomidine premedication offers an attractive alternative to current anesthesia practice in elective hysterectomy.

10. **Varshali (Indian Journal Anesthesia 2011)**[12] assessed the efficacy of dexmedetomidine in attenuating pressor response to intubation and analyzed the reduction in intraoperative anesthetic requirement. 60 patients scheduled for elective surgery for more than 3 hours were randomly selected. Dexmedetomidine in a dose of 1 mic/kg was given as 10 min infusion before the induction of anesthesia. It was continued in a dose of 0.2-0.7 mic/kg/Hr until end of procedure. The need for thiopentone and isoflurane was decreased by 30% and 32%, respectively, in the dexmedetomidine group as compared to the control group.

After tracheal intubation, maximal mean increase in SBP was 8% and 11% in DBP in dexmedetomidine group, as compared to 40% and 25%, respectively, in the control group. Similarly, mean increase in HR was 7% and 21% in the dexmedetomidine and control groups, respectively. Fentanyl requirement during was less in dexmedetomidine group intraoperatively. The conclusion was that perioperative infusion of dexmedetomidine is effective in

attenuating pressor response to intubation. It has significant anesthetic and opioid sparing effect.

11. **Gulay Eren[29], (Journal of Anesthesiology Clinical Pharmacology. 2011)** compared the efficacy and effects of dexmedetomidine and midazolam in preoperative sedation. 125 patients in (ASA) I-II were divided into 3.dexmedetomidine and midazolam infusions were compared with control.

There was marked sedation and a decrease in anxiety in both midazolam and dexmedetomidine group. MAP and HR decreased significantly in dexmedetomidine group. There was no associated hypotension (MAP <60 mm Hg) or bradycardia (HR <50 bpm). Respiratory rates and SpO2 values decreased both groups. Differences in respiratory rates were not significant. The author concluded that dexmedetomidine was as effective as higher doses of midazolam in sedation.

The hemodynamic and respiratory effects were minimal. Although dexmedetomidine caused significant decrease in the blood pressure and heart rate, it probably just normalized increased HR and BP that was caused by preoperative anxiety.

12. **Scheinin (Anesthesiology. 1993)**[11] studied the usefulness of dexmedetomidine as preanesthetic agent in 192 ASA PS 1 and 2 patients who

underwent elective abdominal hysterectomy, cholecystectomy, or intraocular surgery under general anesthesia. Dose of 2.5 mic/kg dexmedetomidine IM administered 60 min before and intravenous saline placebo 2 min before induction of anesthesia was compared with a combination of 0.08 mg/kg IM midazolam 60 min and 1.5 micrograms/kg intravenous fentanyl 2 min before induction or a combination of intramuscular dexmedetomidine and intravenous fentanyl.

It was observed that dexmedetomidine and midazolam induced comparable preoperative sedation and anxiolysis. The dexmedetomidine-fentanyl combination decreased intubation response more efficiently when compared with other two groups.

The intraoperative fentanyl requirements were greater in midazolam patients when compared with other two groups by 53% and 36%. Bradycardia was observed more frequently in dexmedetomidine patients (20% in the DEXPLA and 33% in the DEXFENT groups) than in MIDFENT patients (8%) and they concluded that pretreatment with a single intramuscular injection of 2.5 micrograms/kg dexmedetomidine is efficacious, but increased incidence of intraoperative hypotension and bradycardia was observed in ASA PS 1 or 2 patients.

13. **Erkola O, (AnesthAnalg. 1994)**[13]studied 192 female patients undergoing abdominal hysterectomy. They compared the effects of the

i.mdexmedetomidine, and midazolam premedication. The three groups were: 1) i.m. DEX (2.5mic/kg) and intravenous (i.v) placebo 2) i.m. dexmedetomidine and i.v fentanyl (1.5 micrograms/kg) and 3) i.m. midazolam (0.08 mg/kg) and i.v fentanyl.

The author observed that the preoperative sedation and anxiolysis was comparable in both groups. The maximum BP response to intubation was blunted in the patients who received dexmedetomidine-fentanyl combination better than the other groups. However in the two other groups BP increased 30–34 mm Hg after intubation.

During surgery, bradycardia (heart rate < 40 bpm) was observed in 6.2% of dexmedetomidine patients, but none of the midazolam patients developed any bradycardia.

Postoperatively 14.1% patients who received dexmedetomidine and 1.6% of patients who received midazolam had bradycardia. Incidence of shivering was less with dexmedetomidine (10%) than with midazolam (52%). Author concluded that dexmedetomidine has many desirable effects, but side effects such as bradycardia may limit the routine use in ASA PS I-II patients.

14. **Harry Scheinin MD** ***(Clinical Pharmacology and***

***Therapeutics* (1992)**[10]. The author studied the pharmacokinetics and pharmacodynamics of three different doses of intramuscular dexmedetomidine in healthy male volunteers.

Single intramuscular doses of dexmedetomidine (0.5, 1.0, and 1.5 μg/kg) and placebo were administered to six subjects. The drug also caused moderate decreases in blood pressure and heart rate. Plasma norepinephrine was dose-dependently (maximum 89%) decreased.

The intramuscular dose caused linear increase in plasma concentrations of dexmedetomidine. Time to maximum concentration ranges from 1.6 to 1.7 hours. The elimination half-life was 1.6 to 2.4 hours. The total plasma clearance was 0.7 to 0.9 L/hr/kg, and apparent volume of distribution was 2.1 to 2.6 L/kg. The sedation caused by dexmedetomidine lasted for 6-hours. The hemodynamic effects persisted even after 6 hours at higher doses. The author concluded that the profile of intramuscular dexmedetomidine may be suited for preanesthetic use.

15. **R. Aantaa (British Journal of anesthesia 1991)**[17] studied the effect of i.m. dexmedetomidine 1.0 mic/ kg and midazolam 0.08 mg kg^{-1} and placebo given 60 minutes before surgery on vigilance, anaesthetic requirements, haemodynamic state and plasma catecholamine concentrations .

They studied 107 healthy ASA PS I-II female patients undergoing dilatation and curettage. Both premedications were tolerated well without haemodynamic or other adverse events. Moderate reductions in BP (maximally by 20%) and HR (maximally by 15%) in patient receiving Dexmedetomidine .bradycardia occurred in two patients receiving dexmedetomidine. Both drugs decreased the plasma concentrations of nor-adrenaline by 50%, but only dexmedetomidine was effective enough in attenuating the catecholamine response to surgery

16. **M. Aho, (anaesthesia analgesia1992)**[41] the author studied 100 women undergoing gynecologic diagnostic laparoscopy. They studied the hemodynamic and endocrine effects of three different doses of dexmedetomidine 0.6, 1.2, and 2.4 /μg/kg, oxycodone 0.13 mg/kg and saline solution, injected IM 45–60 min before induction.

They observed that HR and MAP increased in all the groups. But the maximal MAP after tracheal intubation was lower with dexmedetomidine 2.4-μg/kg group (104 mm Hg than in the saline solution group 130 mm Hg.

Dexmedetomidine (2.4-and 1.2 μg/kg) attenuated the maximal heart rate after intubation (84 and 101 beats/min respectively) compared with saline

solution (116beats/min). On the other hand, 40% of the patients in the dexmedetomidine 2.4-μg/kg developed bradycardia. (HR ≥40 beats/ min).

Preoperative anxiety and sedation were evaluated by the patients with the aid of a profile of mood-state questionnaire. Dexmedetomidine 2.4 (μg/kg) produced significant anxiolysis and sedation.

17. **Bajwa et al (Indian journal of anesthesia2012)**[21] compared attenuation of pressor response with dexmedetomidine infusion preoperatively and midazolam i.v.o2 desaturation till 94-95% was noted with dexmedetomidine. The mean HR and MAP were significantly lower in DEX group 20 minutes after infusion.

Laryngoscopy was associated with significant increase in HR and MAP in control group. Mean HR and MAP after 1, 3 and 5 min of intubation returned to baseline faster with DEX group. There was no significant hemodynamic difference during intraoperative period.

METHODS

This is a double blinded randomized clinical trial done in general

surgery theatre in Stanley medical hospital after getting approval from ethical committee.The study was conducted from March 2012 to November 2012. 60 patients of ASA PS 1 & 2 were randomly assigned into two equal groups namely Group M & Group D.

Patients undergoing elective laparoscopic abdominal surgeries were enrolled in the study. The randomization was done using sealedenvelope lots containing numbers from 1 to 60. Odd numbers were assigned to Group D and even numbers were assigned to group M. Randomization and blinding were done by an assistant not involved in the study. The assistant diluted the drug into 1 ml solution and administered to patients in the pre-anesthetic room. He maintained a list containing name of patients, serial number and the group to which they belong to.

INCLUSION CRITERIA:

- Age: between 18 years and 60 years

- Sex: both sexes
- ASA physical status: I & II
- Operation: elective laparoscopic abdominal procedures

EXCLUSION CRITERIA:

- Hypertension
- Pre-existing conduction block
- Medications (beta blockers, clonidine, MAO inhibitors)
- Cardiovascular disease[31]
- Epilepsy[21]
- Chronic obstructive pulmonary disease
- Child bearing age
- Intubation attempts lasted more than 25 seconds
- Diabetes[31]
- Difficult airway (modified mallampatti III and IV)

MATERIALS

- **24 G** intramuscular needle and syringe

- **Injection Dexmedetomidine /midazolam**
- Appropriate size intravenous cannula and I.V. fluids
- Drugs for General Anesthesia
- Appropriate size Endotracheal tubes, Other Airway equipments
- Monitors (pulseoximeter, NIBP, ECG, ETCO2)
- All Emergency drugs

A complete pre anaesthetic evaluation was carried out in the premedication room. The patients were explained in detail, about the effects, possible risks and complications of premedication agents.

The concept of Visual Analog Scale (VAS) for anxiety was explained to all the patients under study before surgery. Only those who understood the scale and were capable of expressing their anxiety, in terms of the scale were included in the study.

Informed written consent was obtained from all patients.Total number of patients under study was 60**.**The sixty patients satisfying the inclusion criteria were randomized by drawing enveloped lots.

The patients were given the drugs as follows:

GROUP M (n=30): 0.05mg/kg of midazolam diluted to 1 ml with

distilled water.

GROUP D (n=30): 1 mic/kg dexmedetomidine diluted to 1 ml with distilled water.

In the premedication room intravenous access was secured.The patients were asked about their anxiety scores in visual analog scale and preoperative hemodynamic parameters (HR, SBP, DBP, MAP, and SPO2) were noted.

Visual analog scale for anxiety:

This scale was first described by Bond MR and Pilousky in 1966 for measuring pain intensity. It uses 10 cm visual scale, one end of which shows no pain and the other end showing worst possible pain. The same scale can be used to asses' anxiety, where 0 indicates no anxiety and 10 indicates extreme anxiety.

The study solution was prepared by an assistant, who was not associated with the study and intramuscular injection was also given by the same. Observations were done by the investigator.

Premedication, either i.m midazolam 0.05mg/kg or i.m dexmedetomidine 1 mic/kg was given (according to the group to which they belong) in the gluteal region, 60min before surgery. Patients were monitored for HR, BP, and SPO2 in the premedication room till they were shifted to operating room. Spo2 of the patient was noted at every 10 minutes interval.

A subjective sedation scale[21], derived from the sedation agitation scale, was employed for the purpose of evaluation of sedation effect (1=fully awake and conscious, 2=awakening on verbal command, 3=awakening on gentle shaking, 4=awakening on vigorous shaking and painful stimuli and 5=unarousable) in our study. This sedation scale was used in our study to measure preoperative sedation.

In the theatre, after recording baseline hemodynamic parameters, subjective sedation score and visual analog score for anxiety were noted. Inj.Glycopyrrolate 0.2 mg and Inj.fentanyl 2mic/kg were given intravenously before induction. Pre induction hemodynamics was noted. All patients were preoxygenated with 100% o2 for 3 minutes.

Induction was done with Injthiopentone 5mg/kg and patients were paralyzed with injsuxamethonium 2mg/kg. Laryngoscopy was done with Macintosh 3 sized blade and intubation was done with appropriate sized

cuffed oral endotracheal tube as quick as possible with vigilant monitoring of hemodynamic parameters. All intubations were done by a senior anesthesiologist. Those patients in whom the laryngoscopy lasted more than 25 seconds were excluded from the study. A third person acted as the time keeper using a digital stopwatch to measure the intubation time.

Intubation time was the time taken from removal of facemask from the patient's face, till when ventilation was restarted through the endotracheal tube and carbon dioxide was detected by capnography.

Hemodynamic parameters were measured at 1, 2, 3 minutes after intubation by the investigator.

Maintenance of anesthesia was with N2o 2 liters and 1 liter o2 & 1% sevoflurane. Muscle relaxation for surgery was with atracurium 0.5 mg/kg initially followed by 0.1mg/kg every 20 minutes. All patients received Inj.dexamethsone 0.1mg/kg, 5 minutes after intubation for postoperative nausea vomiting prophylaxis. After intubation hemodynamic parameters were continuously monitored and recorded at 15 minutes interval till the end of surgery.

Mean abdominal pressure was maintained between 10 to 12mm hg & ETCO2 between 35-40 mmHg

Surgical response in form of raise in HR >20% and rise in MAP > 20% from preinduction values when patient was on 1% sevoflurane was given injection. Fentanyl -0.5mic/kg i.v bolus.

Sevoflurane concentration (volumes percent) was titrated at 0.2% decrements or increments according to change in HR and MAP (>/< 20%) from baseline. All patients received Inj.ondensetron 0.1mg/kg 20 minutes before the expected extubation time.

Complications like bradycardia (HR <50/min) was treated with Inj atropine 0.6mg IV bolus. Hypertension (MAP>20 % of pre-induction value) was treated with NTG infusion at a dose of 5 mic/minute. Intraoperative hypotension (MAP< 20% of preinduction value) was treated with 2ml/kg of ringer lactate with decreasing the volatile agents.

At the end of the procedure, after establishment of adequate spontaneous respiration, injection glycopyrrolate 10mic/kg and injection neostigmine 0.05 mg/kg was given intravenously. Patients were extubated, after the standard extubation criteria[3] was met. Patients were shifted to recovery room for further monitoring.

POST OPERATIVE MONITORING

Patients were monitored closely in recovery room for 1hr and later in post-operative ward for 24 hrs. Visual analog scale for anxiety and sedation were observed hourly for two hours.HR, NIBP was recorded every hour for two hours and 2nd hourly for 8 hrs and was observed for 24 hours. Postoperative pain was managed with Inj.tramadol 2mg/kg i.m when visual analog score was more than 4.

Postoperatively all patients were supplemented with oxygen 5L/min via face mask for 4hrs, because it was a laparoscopic surgery. HYPOTENTION (<90mmHg SBP) was treated with 2ml/kg bolus of ringer lactate apart from usual maintenance fluids. Inj. ondansetron 0.1m/kg was repeated if nausea or vomiting occurred.

STATISTICAL ANALYSIS

A sample size of 30 per group was decided during the pilot study.

Sample Selection

Pilot study was done with a sample size of 6 patients in each group, before the start of the study to decide on sample size. The mean and standard deviation of Intubations was calculated from pilot study. The sample size was calculated based on the formula given in NTI Bulletin 2006[46].

From the pilot study, we got the value of mean and standard deviation, the HR change after intubations of Group-D (16.87 ± 2.02) and Group-M (18.23 ± 2.86) from baseline values.

$$n = \frac{[Z1_{-\alpha/2} + Z_{1-\beta}]^2 (2\sigma^2)}{(d)^2} = (8.98 * 12.26)/ 1.85 = \mathbf{59.54}$$

$Z_1 -\alpha/2 = 1.96$ (5%)

$Z_{1-\beta} = 1.037$ (85 % Power)

$$[Z1_{-\alpha/2} + Z_{1-\beta}]^2 = (1.96 + 1.037)^2 = 8.98$$

$S = (s_1 + s_2) / 2$

$S = (2.02+2.86)/2 = 2.44$

$S^2 = (2.44)^2 = 5.95$

$2\sigma^2 = 0.85*2 = 12.26$

d= (Mean1 –Mean2)

= (16.87-18.23) =-1.36

$d^2 = 1.85$

From the above calculation sample size was decided as 60 for 2 samples (30 for each group)

Data was expressed as mean ± SD. Quantitative analysis was compared with Student T- test. Equal variance T-Test section for comparison of discrete variables and Aspin-Welch Unequal variance test for continuous variables.

When using these tests to compare mean among two groups, p-value of less than 0.05 was taken as significant. All analyses were done using SPSS version 11.5 statistical software. All values were rounded off to a maximum of two decimals.

The patients in each group were comparable in distribution in terms of age, weight, and sex distribution.

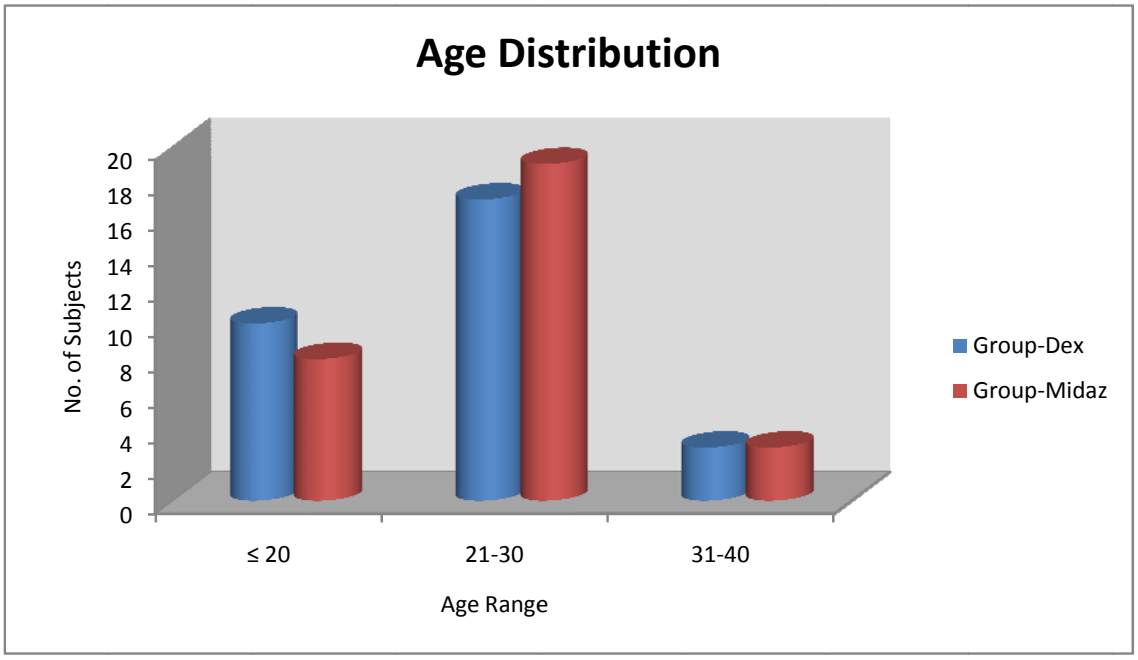
OBSERVATION AND RESULTS

Demographic variables

TABLE 1:

AGE DISTRIBUTION OF THE SAMPLE:

Age	Group - Dexmed		Group - Midaz		Total	
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
≤ 20	6	4	6	2	12	6
21-30	6	11	12	7	18	18
31-40	2	1	1	2	3	3
Mean (SD)	**23.40 (4.58)**		**24.03 (4.59)**		**23.72 (4.56)**	
T-value	**0.54**					
DF	**58**					
P – Value	**0.60 (Not Significant)**					



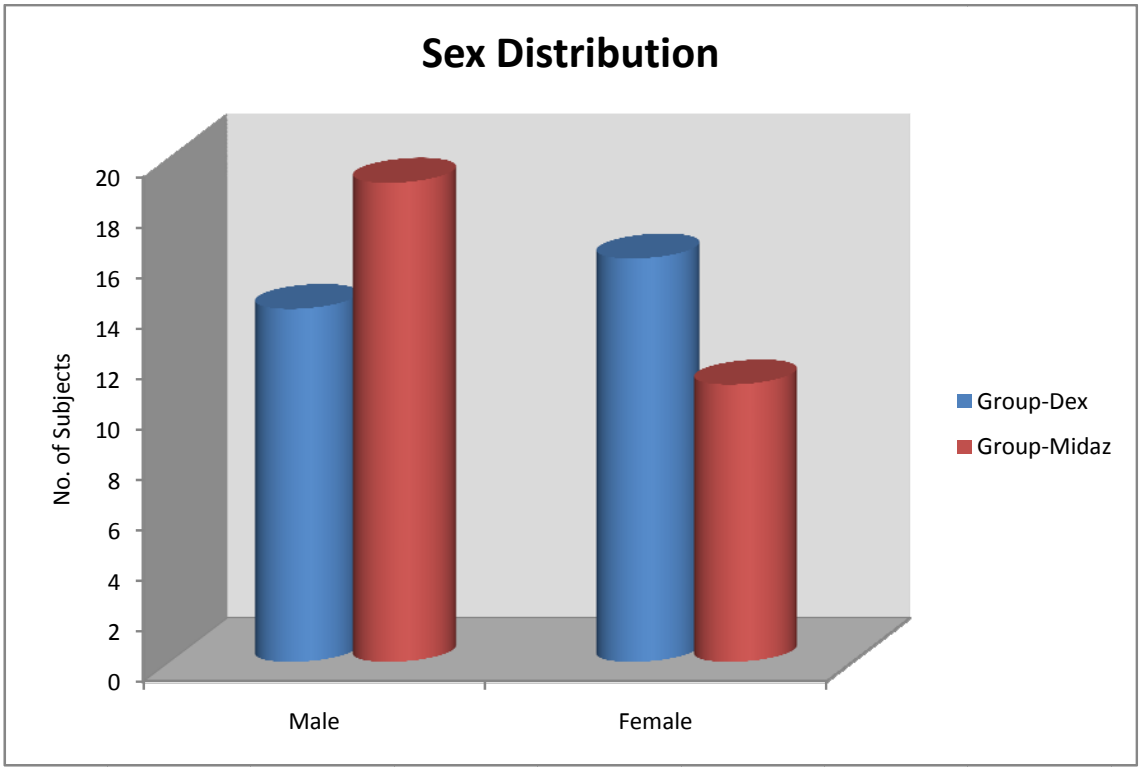
The mean age in both groups was not statistically significant.

TABLE 2:

GENDER DISTRIBUTION OF THE SAMPLE:

Sex	Group - Dexmed N=30	Group – Midaz N=30	Total N=60

	N	%	N	%	N	%
Male	14	46.7	19	63.3	33	55
Female	16	53.3	11	36.7	27	45
Chi-square value	**1.68**					
DF	**1**					
P – Value	**0.19 (Not Significant)**					

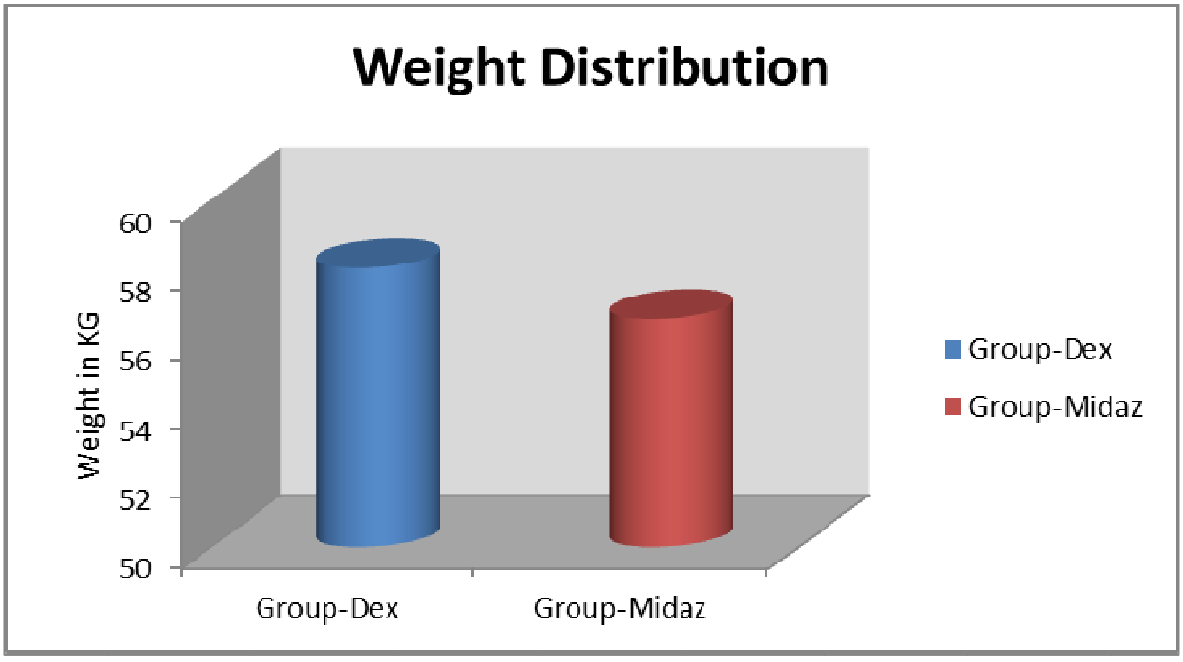


The gender distribution in both groups was similar.

TABLE 3:

MEAN WEIGHT OF THE SAMPLE IN KILOGRAM:

Weight (KG)	Group - Dexmed	Group – Midaz
Mean	58.03	56.57
SD	5.58	5.92
P – Value	**0.16 (Not Significant)**	

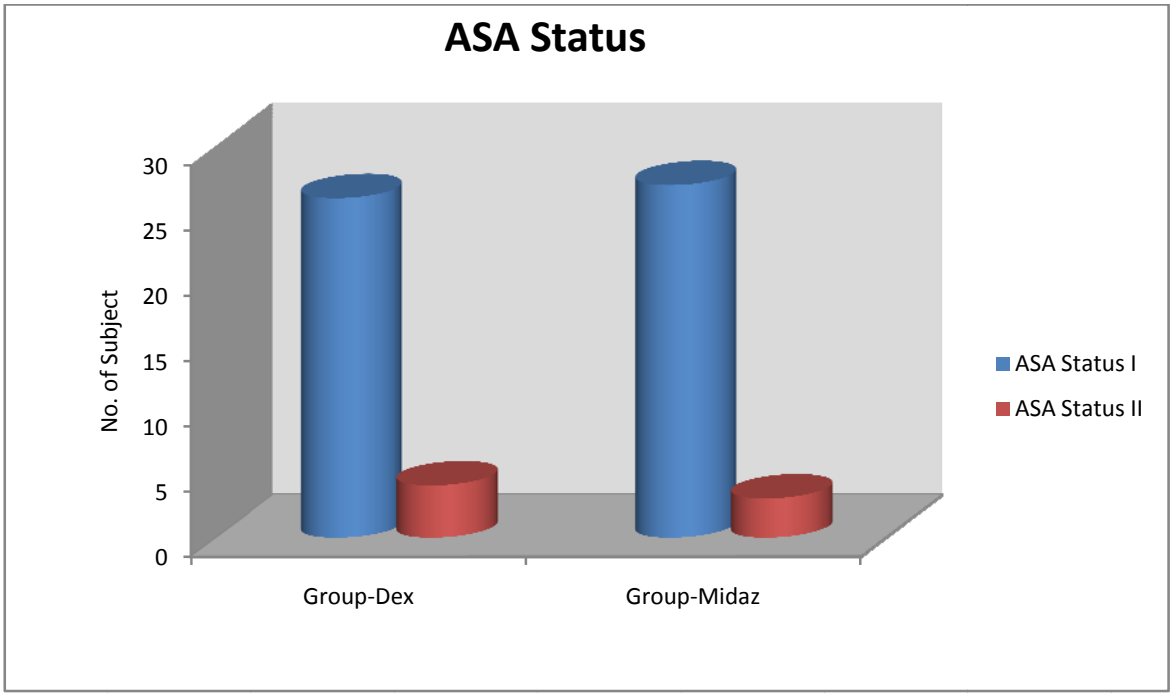


The mean weight in both groups was not statistically significant. The mean weight in kilograms in dexmedetomidine and midazolam were 58.03+/-5.58 and 56.57+/-5.92 respectively.

TABLE 4:

ASA PHYSICAL STATUS:

	Group – Dexmed		Group - Midaz	
	N	%	N	%
I	26	86.70	27	90.00
II	4	13.30	3	10.00
Total	30	100	30	100
Significant	**0.69 (Not Significant)**			

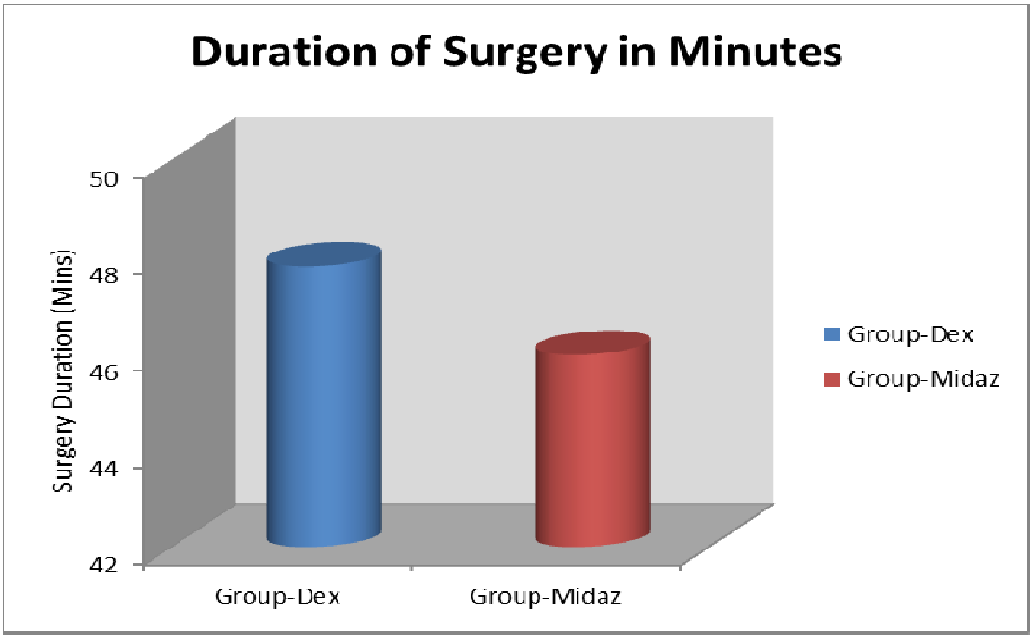


The distribution of ASA physical status I and II in both groups was similar in both groups.

TABLE 5:

DURATION OF SURGERY IN MINUTES:

	Group - Dexmed	Group – Midaz
Mean	47.80	45.97
SD	6.13	4.04
P - Value	**0.18 (Not Significant)**	

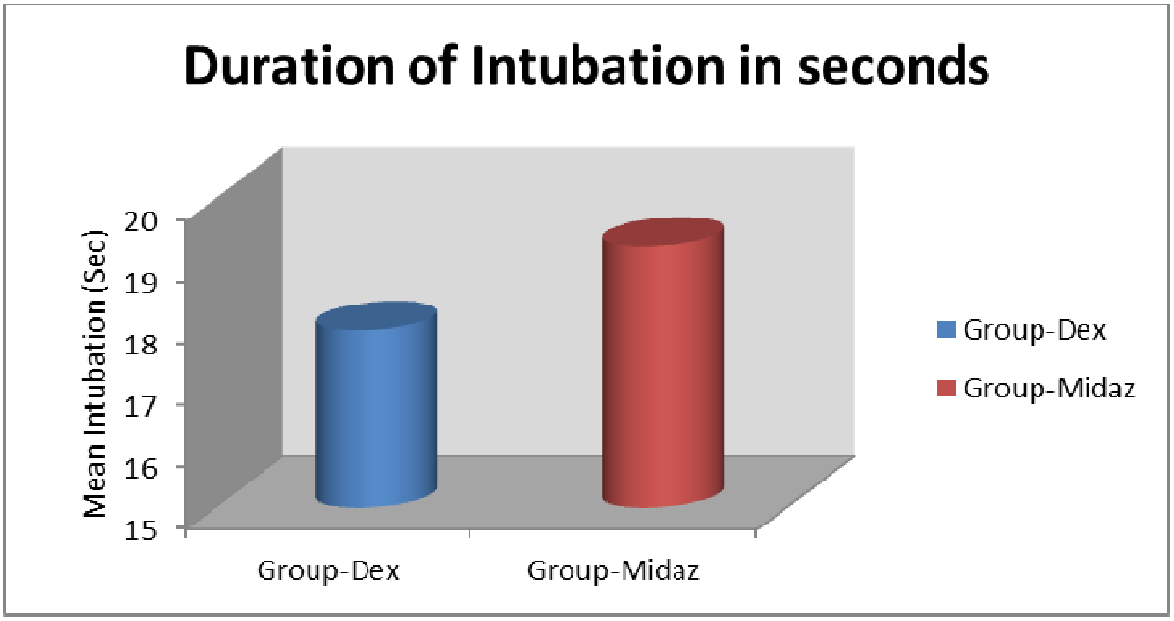


The mean duration of surgery in minutes in both the groups were similar and the difference between then are not statistically significant. The mean duration in dexmedetomidine and midazolam groups were 47.80+/-6.16 and 45.97+/-4.04 minutes respectively.

TABLE 6:

DURATION OF INTUBATION IN SECONDS:

Intubation	Group - Dexmed	Group – Midaz
Mean	17.87	19.23
SD	3.45	4.09
T-Value	-1.42	
DF	58	
P – Value	**0.16 (Not Significant)**	



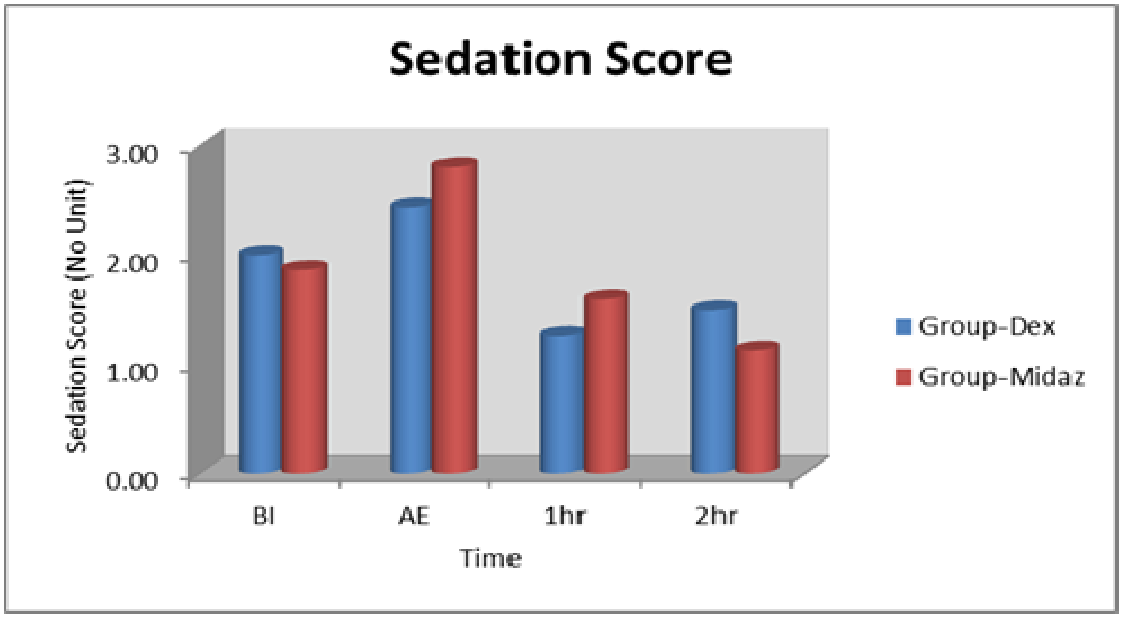
The mean duration of intubation in dexmedetomidine and midazolam groups in seconds was 17.87+/-3.45 and 19.23+/-4.09 respectively. The mean duration in both groups was statistically insignificant.

TABLE 7:

SUBJECTIVE SEDATION SCORE:

Sedation Score	Group – Dexmed	Group – Midaz	T -Value	P – Value DF = 58
BI	2.00	1.87	1.09	0.28
AE	2.43	2.80	2.74	0.008*
1hr	1.27	1.13	1.31	0.20
2hr	1.50	1.60	0.66	0.51

* Significant



Subjective sedation score was measured before induction, after extubation, 1 and 2 hours after extubation. At all these time, the scores were similar and the difference between them being not statistically significant.

TABLE 8:

VISUAL ANALOG SCALE FOR ANXIETY:

VAS	Group –Dexmed	Group –Midaz	T - Value	P – Value DF = 58
Preop	3.87	3.97	0.43	0.67
BI	2.10	1.97	0.64	0.53
AE	1.73	3.43	8.59	0*
1hr	1.57	1.43	0.88	0.38
2hr	1.20	1.30	1.90	0.62

* Significant

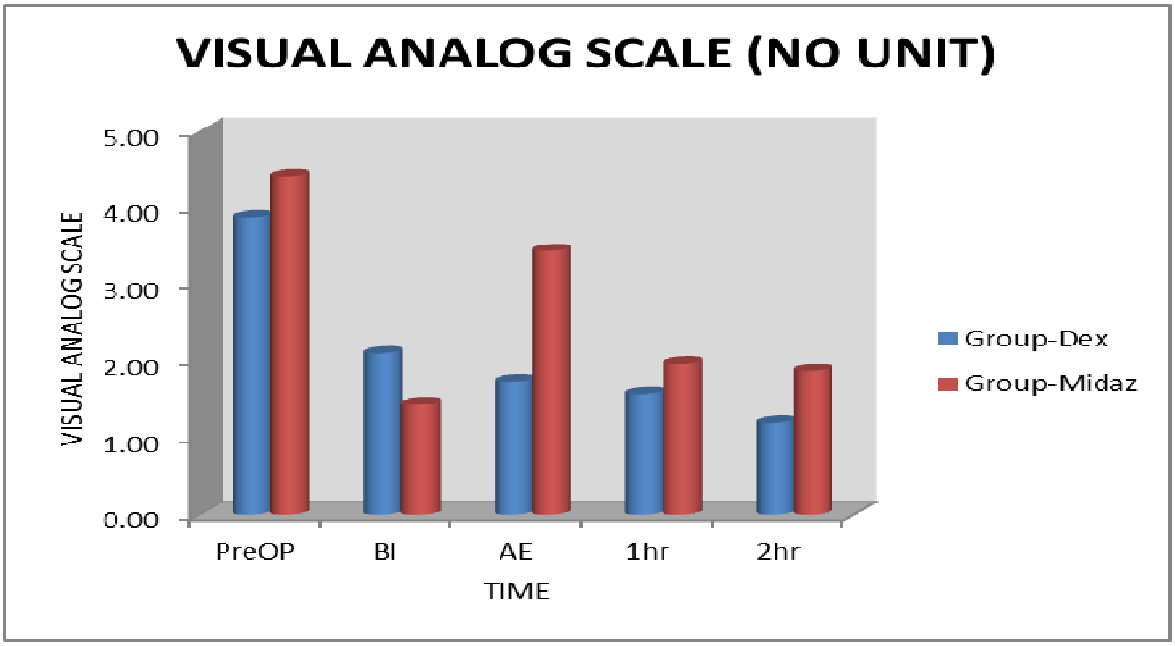
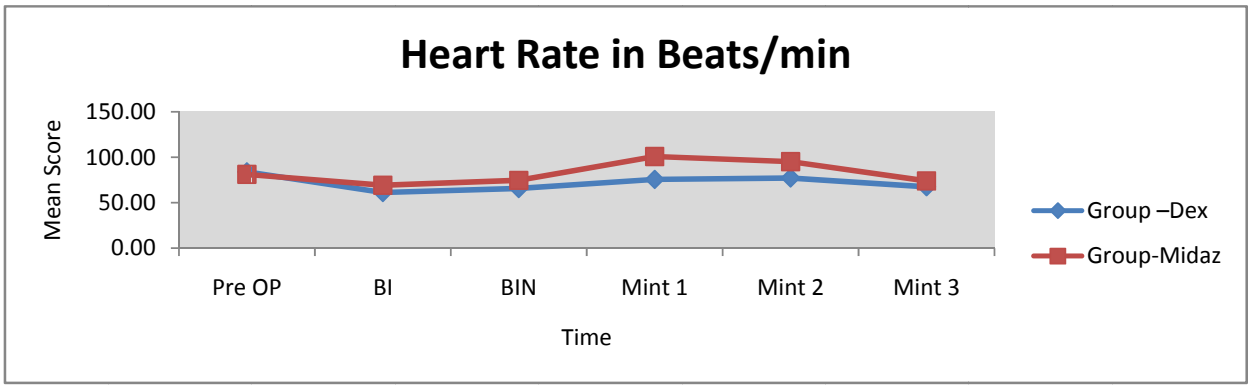
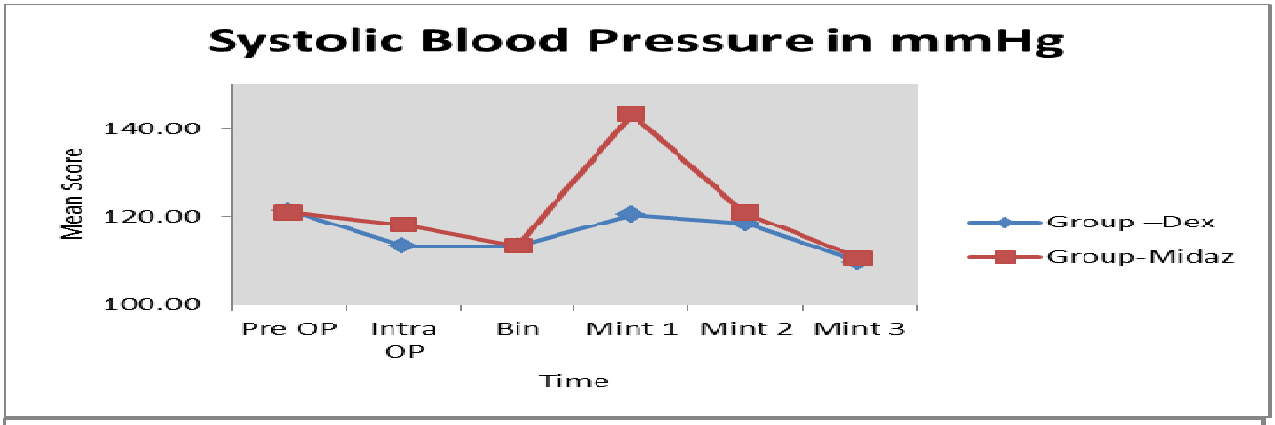


TABLE 9:

HEMODYNAMIC RESPONSE TO INTUBATION:





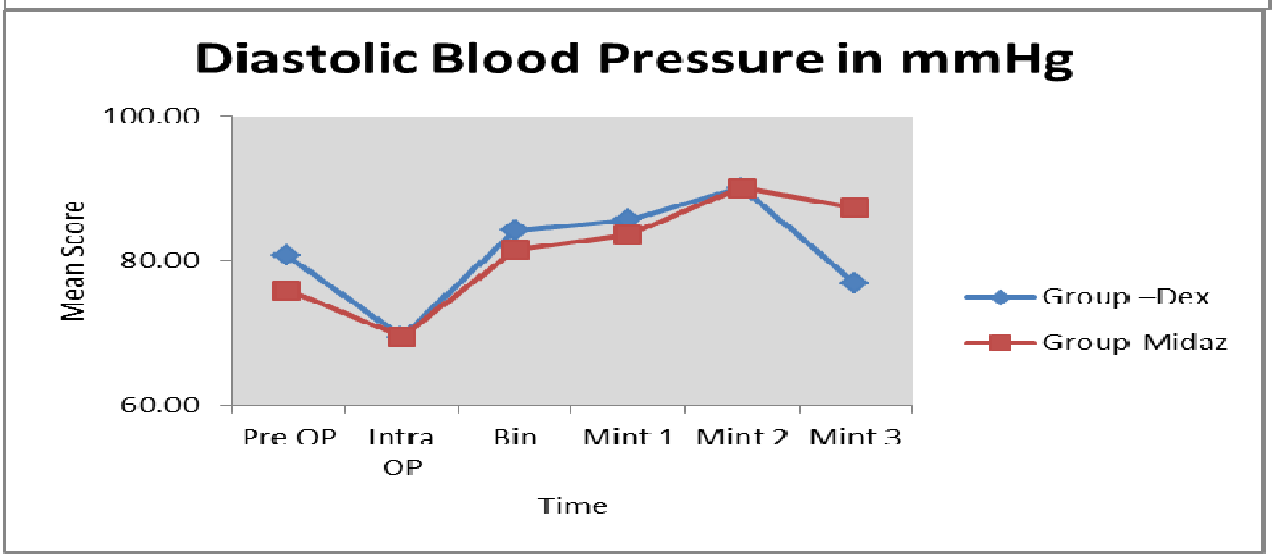


TABLE 10:

CHANGE IN HEART RATE IN BEATS/MINUTE (Mean ± S.D):

Heart Rate	Group -	Group - Midaz	T - Value	P - Value

	Dexmed Mean ± SD	**Mean ± SD**		**DF = 58**
Pre OP	83.93±8.53	81.13±9.42	1.22	0.22
Before Induction	61.13±6.52	69.1±7.42	4.49	**0.000034***
Before Intubation	65.57±6.47	74.53±8.81	4.57	**0.00003***
Mint 1	75.57±7.13	100.8±8.66	12.54	**0.0001***
Mint 2	77.17±12.36	95.13±9.26	6.48	**0.0001***
Mint 3	67.53±6.36	73.93±7.3	3.68	**0.0005***
Mint 5	69.53±8.36	75.07±6.4	3.42	**0.0011***
Mint 10	70.53±9.36	76.9±7.22	3.69	**0.0005***
Mint 15	77.7±13.46	80.2±6.66	0.93	0.3575
Mint 30	66.27±10.62	80.87±9.12	5.81	**0.0001***
Mint 45	60.1±6.84	76.6±5.42	10.53	**0.0001***
Hour 1	78.77±9.47	82.6±8.01	1.72	0.09
Hour 2	73.57±8.34	76.57±6.32	1.596	0.12
Hour 4	76.93±10.35	82.37±11.28	1.98	0.0526
Hour 6	78.77±8.74	81.7±8.45	1.34	0.18
Hour 8	81.03±11.53	83.9±10.4	1.03	0.31
Hour 10	82.27±9.21	85.77±10.65	1.385	0.17

*** Significant**

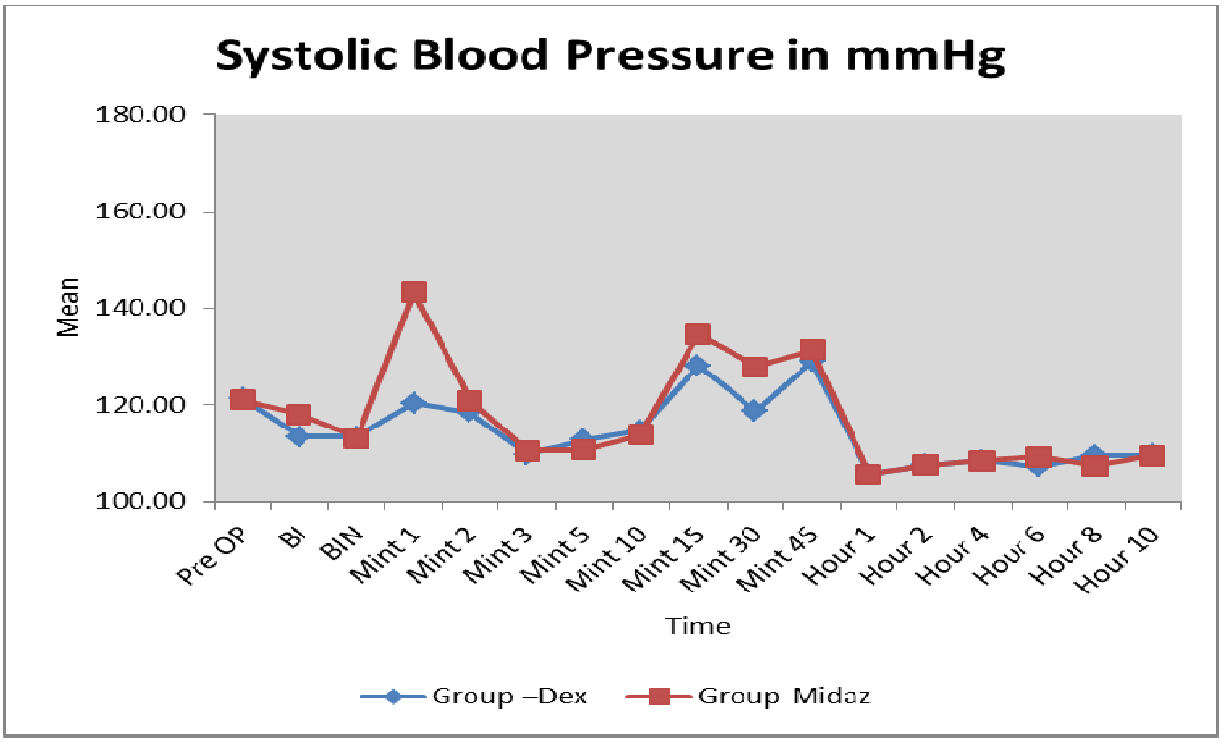
TABLE 11:

CHANGES IN SYSTOLIC BLOOD PRESSURE IN mmHg (Mean ± S.D):

Blood Pressure at	Group – Dexmed Mean ± SD	Group – Midaz Mean ± SD	T – Value	P – Value DF = 58
Pre OP	121.43±10.38	121.00 ± 5.55	0.205	0.84
Before Induction	113.37±8.95	118.13 ± 5.75	2.46	**0.017***
Before Intubation	113.43±5.37	113.43 ± 5.37	0	1
Mint 1	120.43±5.35	143.37 ± 6.18	15.626	**0.001***
Mint 2	118.47±10.86	120.90 ± 13.93	0.767	0.45
Mint 3	109.77±7.1	110.63 ± 6.95	0.48	0.63
Mint 5	112.77±7.1	110.77±7.78	1.06	0.3
Mint 10	114.77±7.1	113.77±7.78	0.53	0.599
Mint 15	128.1±16.75	134.60 ± 9.30	1.86	0.07
Mint 30	118.73±15.94	127.93 ± 15.53	2.397	**0.019***
Mint 45	129.1±18.19	131.40 ± 15.53	0.53	0.6
Hour 1	108.27±6.67	105.4±8.02	1.632	0.108
Hour 2	108.57±6.8	107.57±6.72	0.58	0.56
Hour 4	105.7±7.97	108.47±6.72	1.477	0.145
Hour 6	107.3±6.02	109.3 ± 6.24	1.28	0.2
Hour 8	109.57±4.92	107.53 ± 6.12	1.44	0.15
Hour 10	109.7±3.51	109.57 ± 4.93	0.123	0.9

*** Significant**

CHANGE IN MEAN SYSTOLIC BLOOD PRESSURE IN mm Hg (Mean ±S.D):



The mean systolic blood pressure during intraoperative period is shown in the graph. Statistically significant decrease in systolic BP was seen at 30 minutes in dexmedetomidine group.

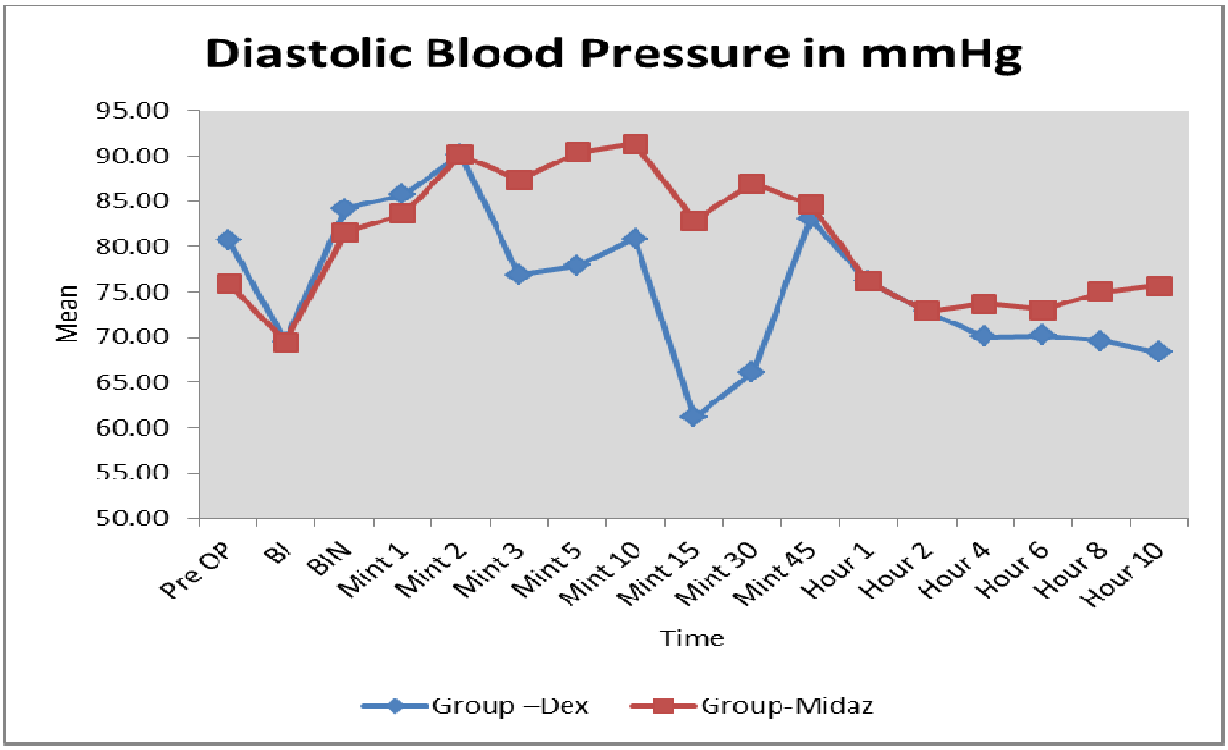
TABLE 12

CHANGE IN MEAN DIASTOLIC BLOOD PRESSURE IN mm Hg (Mean ±S.D):

Blood Pressure at	Group – Dexmed Mean ± SD	Group - Midaz Mean ± SD	T - value	P - Value DF = 58
Pre OP	80.70 ± 4.36	75.97±6.86	3.245	**0.001***
Before Induction	69.2±6.35	69.47±6.48	0.16	0.87
Before Intubation	84.20 ± 7.68	81.5±10.22	1.176	0.24
Mint 1	85.70 ± 7.53	83.57±9.63	0.97	0.33
Mint 2	90.03 ± 7.16	90.1±7.33	0.036	0.97
Mint 3	76.87 ±11.34	87.33 ± 11.67	3.58	**0.001***
Mint 5	77.87±11.34	90.33±11.67	4.27	**0.00007***
Mint 10	80.87±11.34	91.33±11.67	3.58	**0.00069***
Mint 15	61.13 ± 11.71	82.83±8.78	8.26	**0.0001***
Mint 30	66.10 ± 8.87	86.97±7.35	10.08	**0.0001***
Mint 45	83.03 ± 7.65	84.63 ± 6.37	0.895	0.374
Hour 1	76.3 ± 9.92	76.17 ± 9.66	0.05	0.96
Hour 2	72.57 ± 4.41	72.87 ± 4.60	0.26	0.79
Hour 4	70.07 ± 6.28	73.67 ± 3.02	2.88	**0.0056***
Hour 6	70.20 ± 6.29	73.03 ± 4.55	2.03	**0.047***
Hour 8	69.57 ± 7.88	74.93 ± 3.44	3.48	**0.0009***
Hour 10	68.30 ± 6.55	75.67 ± 2.62	5.82	**0.0001***

***Significant**

CHANGE IN MEAN DIASTOLIC BLOOD PRESSURE IN mm HG (MEAN ±S.D):



MEAN ARTERIAL PRESSURE IN mmHG:

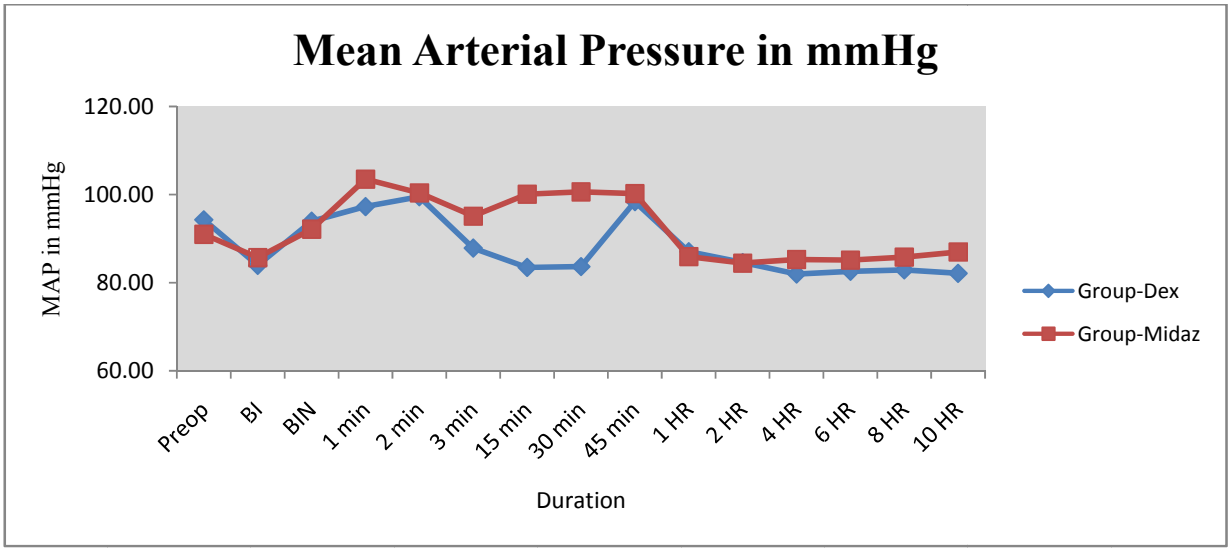


TABLE 13:

MEAN ARTERIAL PRESSURE IN mmHG:

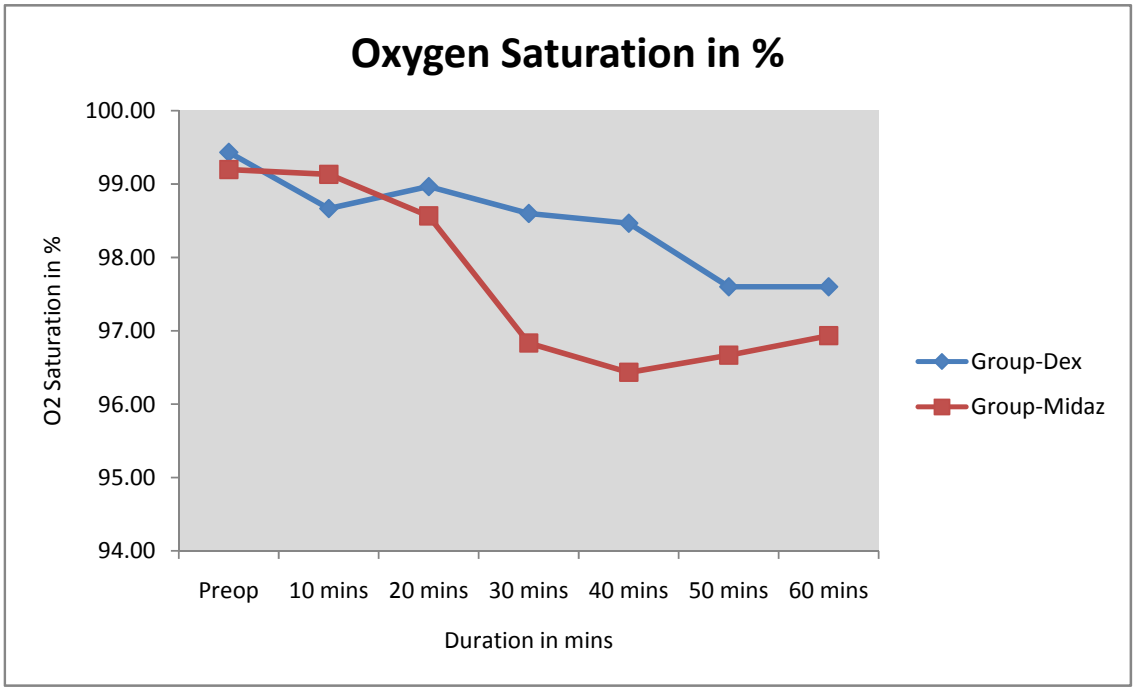
MAP	Group – Dexmed Mean ± SD	Group - Midaz Mean ± SD	T - Value	P – Value DF = 58
Pre OP	94.28±3.24	90.98±4.78	3.29	**0.0018***
Before Induction	83.92±5.48	85.69±5.23	1.32	0.192
Before Intubation	93.94±5.85	92.07±6.62	1.09	0.28
Mint 1	97.28±5.33	103.5±6.93	3.97	**0.0002***
Mint 2	99.51±5.27	100.37±7.02	0.49	.63
Mint 3	87.83±8.25	95.1±8.54	3.4	**0.001***
Mint 5	89.5±8.25	97.14±8.38	3.61	**0.0006***
Mint 10	92.17±8.25	98.81±8.38	3.18	**0.002***
Mint 15	83.36±10.35	99.91±6.96	7.36	**0.0001***
Mint 30	83.64±7.08	100.22±7.24	9.096	**0.0001***
Mint 45	98.39±7.68	100.22±6.28	1.046	0.3
Hour 1	86.59±6.32	85.91±97.9	0.4	0.69
Hour 2	84.57±4.45	84.43±4.62	0.14	0.889
Hour 4	81.94±4.86	85.27±3.44	3.15	**0.003***
Hour 6	82.57±4.98	85.12±4.16	2.27	**0.027***
Hour 8	82.9±5.45	85.8±3.71	2.62	**0.01***
Hour 10	82.1±4.44	86.97±2.44	5.32	**0.000002***

*Significant

TABLE 14:

PREOPERATIVE MEAN OXYGEN SATURATION (in %):

Oxygen Saturation	Group – Dexmed	Group – Midaz
Preop	99.43	99.2
10 mins	98.67	99.13
20 mins	98.97	98.57
30 mins	98.6	96.83
40 mins	98.47	96.43
50 mins	97.6	96.67
60 mins	97.6	96.93

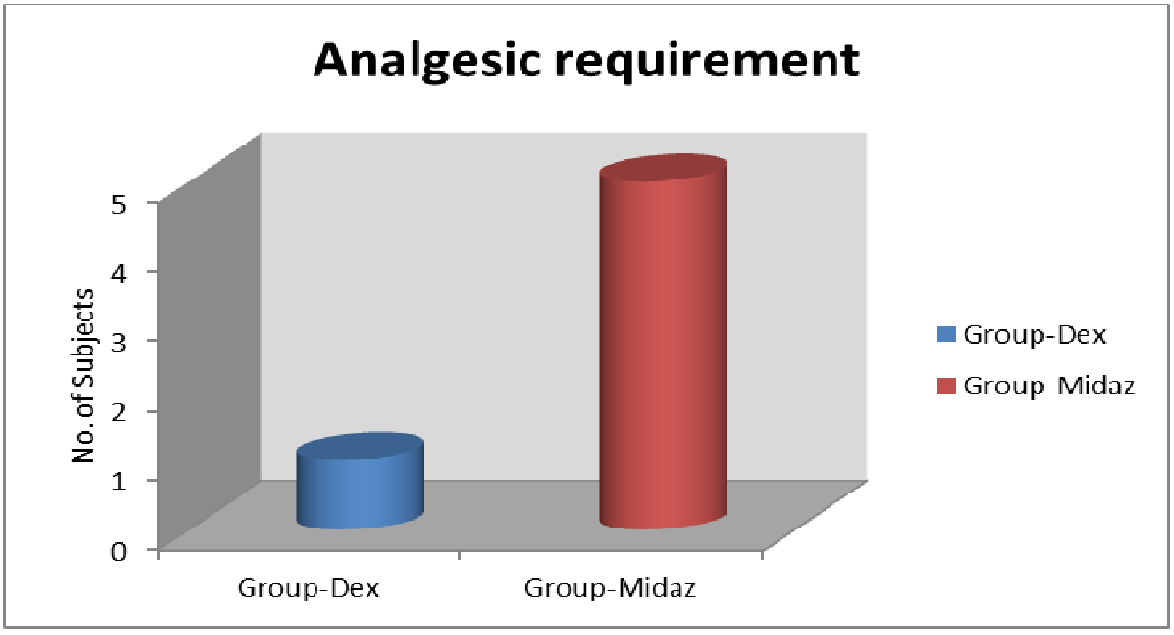


The mean oxygen saturation in dexmedetomidine group was above 98% and 97% with midazolam preoperatively.

TABLE 15:

INTRAOPERATIVE ANALGESIC REQUIREMENTS:

Analgesic Need	Group – Dexmed N=30		Group - Midaz N=30		Total N=60	
	N	%	N	%	N	%
Required	1	3.33	5	16.67	6	20.00
Chi-square value	**3.950617284**					
DF	**1**					
P – Value	**0.046 (Significant)**					

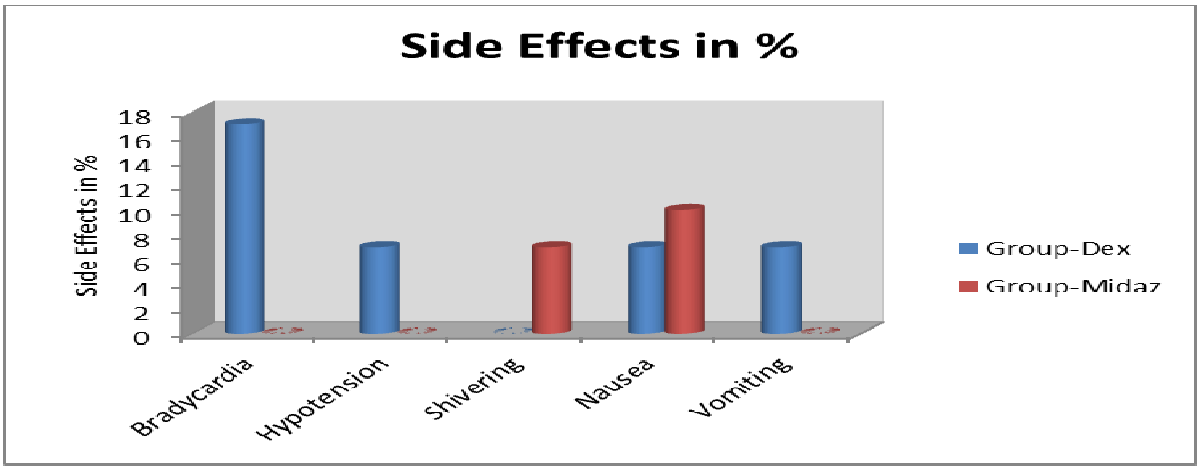


Intraoperative fentanyl requirement was less with dexmedetomidine, when compared to midazolam group. One patient in dexmedetomidine required intraoperative fentanyl top up, whereas 5 patients in midazolam group needed fentanyl.

TABLE 16:

INCIDENCE OF SIDE EFFECTS

Side Effects	Group-D N=30		Group-M N=30		Total N=60	
	N	%	N	%	N	%
Bradycardia	5	17	0	0	5	8
Hypotension	2	7	0	0	2	3
Shivering	0	0	2	7	2	3
Nausea	2	7	3	10	5	8
Vomiting	2	7	0	0	2	3
Chi-square value	**3.84**					
DF	**1**					
P – Value	**0.05 (Not Significant)**					



Side effects observed were bradycardia, hypotension, shivering, nausea and vomiting. Incidence of braycardia, hypotension and vomiting were high in dexmedetomidine group. Incidence of nausea is similar. Incidence of shivering was higher with midazolam group.

DISCUSSION

Ourstudy evaluated the efficiency of midazolam 0.05mg/kg and dexmedetomidine 1 mic/kg given as intramuscular premedication in alleviating anxiety and inducing sedation in patients undergoing laparoscopic abdominal surgeries.

Preoperative anxiety is a challenging concept in the care of patients and almost all patients undergoing surgery experience varying levels of anxiety. The incidence of preoperative anxiety is 60–80% ii surgical patients. It leads to increased catecholamine release. It is associated with adverse hemodynamic responses like hypertension and arrhythmias.

It increases the anesthetic requirement. It decreases patient satisfaction with perioperative care[39]. Sometimes patients may refuse the planned procedure because of anxiety.

Young patients, patients with previous bad anesthetic history, patients who have no previous surgical or anesthetic history and female patients are more prone to have higher anxiety scores.

Decreasing the preoperative anxiety improves surgical outcome and reduces the hospital stay. Relief of anxiety is thus a humane goal and should be provided for all patients.

Benzodiazepines are the drug of choice for preoperative anxiolysis.the mechanism by which it causes anxiolysis is that it binds to alpha 2 subunit of GABA receptor. The concentration dependent receptor occupancy of benzodiazepine is responsible for various drug effects. Anxiolysis is produced by 20% receptor occupancy.

Alpha2 agonist like clonidine were found to have sedative and anxiolytic property and was widely used as a premedication agent. Dexmedetomidine, a selective alpha2 agonist also has sedative anxiolytic property. Dexmedetomidine acts at the level of locus ceruleus in inducing sedation and anxiolysis.

There are various methods of assessing preoperative anxiety. It is a subjective feeling and so it is more appropriate if the patients describe how they feel, preoperatively. In our study, a visual analog scale was used, which is

normally used for pain, also allows the patient select a numerical value from one to ten to narrate about their anxiety.

In the past, various studies have assessed anxiety in different ways. Üstün Y et al used VAS scale for assessing patient satisfaction for sedation anxiolysis in preoperative period. They observed that 65% of their patients were satisfied with the sedation by Dexmedetomidine than Midazolam. The difference between the two groups was statistically significant.

Alhashemi JA also noted in their study, a significant preference for Dexmedetomidine sedation over Midazolam sedation. They used 7-point Likert-like verbal rating scale to measure patient's satisfaction.

Cristopher et al studied the qualitative aspects of anxiety and revealed that three distinct dimensions of preoperative fear exist. They are fear of the unknown, fear of one's life and fear for feeling ill. In patients with high degree of preoperative anxiety, VAS is especially useful to identify specific anesthetic concerns [34].

Miller et al[35]compared three different methods of assessing anxiety, the VAS, STAI AND HAD (hospital anxiety depression scale). They explained the disadvantage of using VAS for the assessment of anxiety. Patients become uncertain about how to respond when using an unfamiliar technique and will avoid extreme scores. They crowd responses in the middle range to express about their subjective sensation. There is central tendency bias in subjective judgment. They concluded that all three scales are equivalent in assessing preoperative anxiety,provided the scores are compared to the normative cut off values to assess the anxiety. Thus in our study we used VAS for measuring preoperative anxiety.

Scheinin H, Jaakola MLin their comparative study observed comparable preoperative sedation and anxiolysis for dexmedetomidine and midazolam.

Olli erkola et al in their study has observed significant increase in sedation scores after premedication with both midazolam and dexmedetomidine. They used subjective visual analog scale and POMS questionnaire for evaluating anxiety and sedation. Both the groups showed equal scores for sedation and anxiolysis which is similar to the finding in our study[13].

A subjective sedation scale[21], derived from the sedation agitation scale, was employed for the purpose of evaluation of sedation effect (1=fully awake and conscious, 2=awakening on verbal command, 3=awakening on gentle shaking, 4=awakening on vigorous shaking and painful stimuli and 5=unarousable) in our study. This scale was previously used in a study by bajwa et al.

Our study evaluated the efficiency of midazolam 0.05mg/kg and dexmedetomidine 1 mic/kg given as intramuscular premedication in alleviating anxiety and inducing sedation in patients undergoing laparoscopic abdominal surgeries.

In our study we also observed the intubation response, preoperative o2 saturation, adverse effects and intraoperative analgesia requirement during the procedure.

Intravenous infusion of dexmedetomidine for anxiolysis, sedation and attenuating stress response was extensively studied. Though dexmedetomidine was very effective, it caused initial hypertension during intravenous infusion due to peripheral vasoconstriction.

Dyck et al studied the pharmacokinetics of dexmedetomidine after intravenous and intramuscular dexmedetomidine in 10 healthy volunteers. They observed initial bradycardia and hypertension at 5 minutes after infusion with 2 mic/kg dexmedetomidine. They observed no such change after intramuscular dose of dexmedetomidine[20].

Duration of action after intravenous infusion is less and titration of infusion is cumbersome in the preoperative period. Additionally the alpha receptor selectivity is dose dependent. Intramuscular route of administering the drug needs no such titration and no such biphasic response was observed. The alpha 2 receptor sensitivity is well preserved after IM injection due to the steady plasma concentration achieved. Hence intramuscular route was chosen for premedication in our study.

Virkila et al conducted a dose finding study to assess the optimum dose of intramuscular dexmedetomidine. They compared five different doses of dexmedetomidine and midazolam premedication for cataract surgery in 35 patients. They observed that at 1 mic/kg, dexmedetomidine produced moderate sedation comparable to midazolam. Dose of 1.5 mic/kg produced significant bradycardia[43].

Scheinin et al's study also showed similar results. They found significant bradycardia and hypotension after 2.5mic/kg intramuscular dexmedetomidine premedication with fentanyl 1.5mic/kg IV given 2minutes before surgery[11]. Hence in our study, dose of 1 mic/kg of dexmedetomidine was chosen to avoid bradycardia.

Inthe study, patients with epilepsy were excluded. Past clinical experience suggests that epileptic patients were resistant to the sedative effects of dexmedetomidine. The pharmacokinetic interaction between the anticonvulsant medications and dexmedetomidine was not well documented. The higher dexmedetomidine dose needed to produce sedation may confound the results of our study. In the same way, the safety of dexmedetomidine in pregnancy was not studied. So child bearing age group was excluded from the study.

Surgical procedure involving laparoscopy was chosen because they are associated with significant stress response. Mean duration of surgery (minutes) were similar in both groups, 47.80$\pm$6.13 minutes in group D and 45.97$\pm$4.04 minutes in group M.

Midazolam's role as a sedative, anxiolytic premedication is well established. But there is scarcity of literature to support its role in attenuating stress response to intubation. H. Ronald Vinik, et al in their study showed that midazolam is an efficacious and safe premedication in healthy patients and caused minimal tissue irritation[32].

Regarding the safety of dexmedetomidine, it was approved by the FDA in 1999. Originally it was approved for use in adults undergoing mechanical ventilation in the ICU for 24 hrs. Dexmedetomidine received FDA approval in 2008 for adult sedation in areas outside the ICU.

Harry Scheinin MD et al studied about the pharmacodynamics and pharmacokinetics of intramuscular dexmedetomidine and stated that the profile of intramuscular dexmedetomidine is suited for preanesthetic clinical use and is safe[11].

Jaakola et al had mentioned that equivalent dose of 2.5 mic/kg of dexmedetomidine is 0.08 mg/kg of midazolam[10].

Harry scheinin et al in their pharmacokinetics and pharmacodynamics study of three different doses of intramuscular dexmedetomidine in healthy volunteers. The time to peak effect was found to be 1.6 to 1.7 hours. Clearance was 0.7 to 0.9 L/hr/kg. The volume of distribution was 2.1 to 2.6 L /kg.

Dyce et al in their study have given totally different results. Time to peak effect after intramuscular injection was 16 minutes[20].

Elimination half-life after intramuscular dexmedetomidine is 1.6 to 2.4 hours[13.] The serum concentration of dexmedetomidine follows linear relationship with intramuscular dose. Intramuscular dexmedetomidine acts longer than intravenous route.

Barsan, William G et al in their study showed that time to peak effect after intramuscular midazolam was 19.6 minutes.[40.]Elimination half life was 2.5 hours. Volume of distribution was 1.5 L/kg. Clearance was 0.39 L/hr/kg.

Olli Erkola et al and M.Aho et al have studied the usefulness of intramuscular route of dexmedetomidine. Bajwaet al[21] found that it is tolerated well without any local reaction at injection site. Similarly in our study also, no patients developed any reaction to dexmedetomidine or midazolam.

The time needed to achieve clinically relevant sedation in adults after intramuscular administration of dexmedetomidine is not documented in any study. Most studies describe intramuscular administration 45–60 minutes before induction of anesthesia.

Intramuscular premedications are administered 45 -60 minutes before the procedure. Olli Erkola et al in his study has administered the premedication 45-90 minutes before the surgery. M.Aho et al administered the drug 45-60 minutes before the surgery. R. Aantaa et al in his study administered at 60 minutes before the surgery. In our study also we have given premedication 60 minutes before the surgery.

Our study showed comparable sedation and anxiolysis preoperatively as assessed by subjective sedation score and visual analog score for anxiety with dexmedetomidine and midazolam intramuscular premedication. The difference between them was statistically not significant ($p=0.28$) for sedation score and ($p=0.53$) for VAS for anxiolysis respectively. This finding of ours is contradictory to that found with M.Aho et al.

M.Aho et al observed that only at doses of 2.4 mic/kg dexmedetomidine IM produce significant anxiolysis and sedation[41]. The sedation and anxiolysis was assessed by mood state questionnaire. 40% patients received atropine for bradycardia at this dose.

Patients who were given midazolam, were more drowsy, but responded with higher VAS for anxiety after extubation giving a statistically significant difference at this time. This shows dexmedetomidine causes more clear headed recovery than midazolam premedication. Both drugs produced equal subjective sedation score and VAS at one and two hours after extubation.

Though comparing dexmedetomidine and midazolam produces comparable sedation and anxiolysis, dexmedetomidine lacks amnestic property[15], which is there for midazolam. This amnestic property of midazolam is preferred one in the perioperative setting.

Hsu et al[30] and yungwei[31]have demonstrated in healthy volunteers that ventilatory effect to hypercapnia is not affected even when patients become unresponsive to vigorous stimuli. Dexmedetomidine exhibit arousal response to

hypercapnia which is similar to the normal sleep and is a safety feature with this drug.

Gulayet al[29] observed more desaturation with midazolam 0.06 mg/kg compared to 1mic/kg dexmedetomidine infusion preoperatively.

Bajwaet al[21] in their study on the contrary, have observed o2 desaturation after dexmedetomidine infusion preoperatively to values as low as 94-95%. This desaturation immediately disappeared after waking the patients up. These findings are contrasting to those in our study.

In our study,the o2 saturation measured preoperatively after administration of IM premedication was analysed. It was observed that the mean o2 saturation in patients who received dexmedetomidine (1 mic/kg IM) was well above 97% at all times before shifting the patient to the operating room.

In patients who received midazolam (0.05 mg/kg IM), the mean o2 saturation dropped till 96%. But the actual spo2 of patients in midazolam group dropped to 93%, whereas in dexmedetomidine group in no patient the spo2 went below 95%.

Reid and Brace were the first to report the hemodynamic responses to laryngeal and tracheal stimulation in an anesthetized patient. Attenuation of

these pressor responses has been one of the most often researched areas in anaesthesia. Suppression of stress response is associated with significant incidence of side-effects.

Stress response after laryngoscopy is due to reflex sympathetic stimulation caused by pharyngeal and laryngopharyngeal stimulation. The increased sympatho-adrenal activity results in increase in heart rate and blood pressure and increases the risk of arrhythmias. This tachycardia and hypertension are only transient and unpredictable. Although these changes are not detrimental in healthy individuals, it may be disastrous in patients with hypertension, ischemic heart disease, valvular heart disease and old age.

This stress response to intubation will be exaggerated when duration of laryngoscopy is prolonged and the force used for laryngoscopy is high. Hypertension starts within five seconds of laryngoscopy, peaks in 1-2 min and returns to baseline within 5 min.

A variety of drugs have been used to control the hemodynamic response, such as vasodilators, beta blockers, calcium channel blockers, $alpha_2$ agonists and opioids. No modality was without any side effect[22].

In the past, alpha2 agonist like clonidine was extensively used for attenuation of sympathoadrenal stimulation caused by tracheal intubation and surgery. Dexmedetomidine is the new alpha-2 agonist having 8 times more affinity for alpha-2 adrenoceptors when compared to clonidine. Dexmedetomidine has shown only partial agonistic activity and is known to decrease the plasma catecholamine. It also suppresses the release of catecholamine after any stress[26, 42, and 28].Dexmedetomidine does not alter the catecholamine synthesis, storage or metabolism, nor does it block any receptors. Thus it provides the possibility of reversing the hemodynamic effects with vasoactive drugs[15].

Similarly in our study, the mean heart rate at 1, 2 and 3 minutes after intubation was less than preoperative heart rate by 10beats/minute in dexmedetomidine group. However in midazolam group, there was an increase in mean heart rate after intubation, when compared to preoperative value by 7beats/minute.

There was statistically significant (p=0.0002) and (p=0.001) difference in mean arterial pressure at first and third minuteafter intubation respectively. Dexmedetomidime blunted the intubation response, although not effectively at

second minute after intubation. The systolic BP was less in dexmedetomidine group in the first minute after intubation, the difference being statistically significant (p=0.001). The diastolic BP was less in dexmedetomidine at third minute when compared to midazolam group.

Bajwa et al showed an increase in systolic BP after intubation. It was 8% in DEX,but in MID group it is 40%. Rise in diastolic BP were 11% in DEX compared to 25% in MID group after intubation. Thus dexmedetomidine did not completely obtund the pressor response to intubation[21]. This finding frombajwa et al's study is in line with that of ours, with respect to MAP response at 2 minutes after intubation.

The study by Bajwaet al[21] shows that the mean HR was significantly lower in patients who received dexmedetomidine infusion after 20 minutes. After laryngoscopy, the HR raised significantly in both the groups. The rate of return of mean HR to baseline values and hemodynamic stabilisation was significantly early in dexmedetomidine group.

Varshaliet al[10] showed that preoperative dexmedetomidine infusion resulted in decrease in HR of 7% compared to 21% in midazolam group.

HR response to intravenous infusion is studied in all the above mentioned studies. However studyby Scheinin H, Jaakola ML showed that dexmedetomidine IM and fentanyl IV combination blunted intubation response more efficiently than dexmedetomidine-placebo and midazolam-fentanyl groups, in which approximately 15 beats/min greater increases were observed.

Aanta et al studied in 107 patients undergoing cervical dilatation and curettage. They observed hemodynamic changes after intramuscular dexmedetomidine 1 mic/kg and midazolam 0.08 mg/kg 60 minutes before the procedure. Heart rate response to intubation was decreased by 15%. Bradycardia (<45beats/min) occurred in two patients who received dexmedetomidine.

Regarding intraoperative hemodynamics, the heart rate was significantly less in dexmedetomidine group when compared to midazolam group. Mean arterial pressure was less intraoperatively in dexmedetomidine group when compared to midazolam. There was a rise in MAP after extubation in both the groups, which means that extubation response was not effectively blunted by both the premedication agent at the given dose.

The analgesic effect of dexmedetomidine is due to its action on alpha 2 receptors in locus ceruleus and spinal cord. Narcotic sparing effect is seen after systemic use of dexmedetomidine.

Varshaliet al[10] analgesic requirement was 33% more with midazolam group when compared to dexmedetomidine. .

Scheinin H, Jaakola ML[11]showed that the intraoperative fentanyl requirements were greater in patients who received midazolam fentanyl combination. In dexmedetomidine fentanyl combination group, the analgesic requirement was 56% lesser and dexmedetomidine placebo group it is 31% lesser than midazolam fentanyl group.

In our study, patients belonging to dexmedetomidine group one patient needed fentanyl top up intraoperatively. However five patients in midazolam group needed fentanyl. The difference between the two groups were statistically significant.(p=0.019).

Bradycardia, hypotension, hypertension are the common side effects of dexmedetomidine.[44]

Scheinin et al have observed that patients in dexmedetomidine group required glycopyrrolate for bradycardia and fluids and vasopressors for hypotension more often than midazolam group. Intraoperatively the incidence of bradycardia in patients who received dexmedetomidine alone was 20% and in those who received dexmedetomidine-fentanyl combination was 33%. It was only in 8% of the patients in midazolam group.

In our study, 17% of patients in dexmedetomidine group, developed bradycardia(HR<50/minute) and were treated with Inj.atropine 0.6mg intravenously. Hypotension occurred in 7% of patients of patients in dexmedetomidine group and in no patients in midazolam group.

Post operative nausea vomiting is an unpleasant event for the patients. Kalkman[23] Preoperative anxiety showed statistically significant but weak correlation with increased the incidence of PONV. Laparoscopic surgeries are associated with significant post operative nausea and vomiting[24]. Hence, in our

study we had given inj.dexamethasone and inj.ondensetron for PONV prophylaxis.

Midazolam, apart from its anxiolytic effect, additionally has decreased incidence of postoperative nausea vomiting when given as intravenous premedication[33]. Dexmedetomidine, although it has numerous anesthetic adjuvant properties, it is found to increase the gastric empting time and intestinal transit time at the dose of 1 mic/kg infusion.[44]Scheinin et al observed no difference in the incidence of nausea vomiting in both dexmedetomidine and midazolam groups in their study[11].

In our study, out of sixty patients, two patients in dexmedetomidine complained of nausea immediately after extubation and two other patients had vomiting after extubation . Patients in midazolam group had no vomiting, but two patients had nausea. Thus incidence of nausea was similar in both the groups. Seven patients in dexmedetomidine group had vomiting. But incidence of vomiting is higher with patients receiving dexmedetomidine undergoing laparoscopic surgeries.

Shivering is a protective phenomenon by which our body tries to compensate for the heat lost during surgery. Postoperative shivering has number of adverse effects. It increases the risk of incidental trauma, interferes with monitoring, and increases the O2 consumption and co2 production by 200%. It increases the minute ventilation and cardiac output, which render those patients with limited reserve at and more risk of respiratory and cardiac failure.

Dexmedetomidine decreases the incidence of postoperative shivering when given at 1 mic /kg as intravenous infusion before surgery[37] as observed by sukhmindher et al. Erkola et al also in their study observed a decreased incidence of postoperative shivering in patients who received 2.5 mic/kg IM dexmedetomidine premedication[13]. The incidence of postoperative shivering was 10% after DEX and 52% after midazolam.

In our study, the incidence of shivering was 7% in midazolam group and none in dexmedetomidine group.

The mechanism by which dexmedetomidine decreases the shivering seems to be central in nature. It decreases shivering threshold and vasoconstriction. It also decreases the central thermal sensitivity by decreasing neuronal conductance[38].

In our study incidence of bradycardia was 1hour 45 minutes which corresponds to the time to peak effect of dexmedetomidine. No bradycardia was observed after 3hours of injection. No incidence of bradycardia in midazolam was observed intraoperatively and postoperatively.

This finding is similar to those by Scheinin H, Jaakola M.L [11] et al andolliErkolaet al[13.] . V.G.Yezbek.karan. (MEJ Anesth2006)[31]has clearly mentioned in his article the specific indications of dexmedetomidine premedication. Alcohol abuse, opioid tolerance, patients susceptible to the perioperative stress response and hypertensive patients are the group of patients who will specifically benefit from dexmedetomidine premedication.

SUMMARY

Dexmedetomidine, a selective alpha 2 agonist has multitude of roles in anaesthesia. Its sedative, anxiolytic and anesthetic sparing action favour its use as a premedicant. Our prospective randomized double blinded study was designed to assess whether dexmedetomidine is as efficient as midazolam in controlling anxiety and inducing sedation in patients undergoing laparoscopic abdominal surgeries.

Our observations were

- Dexmedetomidine is equally effective in inducing preoperative sedation and allaying anxiety, when compared to midazolam when given at a dose of 1 mic/kg 60 minutes before surgery.

- Oxygen saturation in the pre anesthetic room, after dexmedetomidine intramuscular premedication was well preserved above 95%, while it decreased to 93% in midazolam group.

- Intubation response in terms of heart rate is better blunted by dexmedetomidine (1 mic/kg) IM than midazolam (0.005 mg/kg). The difference between the two groups being statistically significant.

- Intubation response in terms of MAP was better blunted in dexmedetomidine group than midazolam group. Also the maximal increase in BP after intubation was less in patient who received dexmedetomidine premedication.

- Intraoperative analgesia requirement was less in dexmedetomidine group, when compared to midazolam. Only 3.33% of patients in group D required fentanyl intraoperatively. In group M, 20% of patients needed analgesia. The difference between them was statistically significant.

- The incidence of bradycardia (HR<50/min) was 17% in group D, whereas no such incidence occurred in group M.

- Hypotension was 7% with group D, whereas it occurred in none patient in group M.

- Incidence of postoperative shivering was significantly higher with group M (7%) when compared to group D where none had shivering.

- Incidence of nausea was similar in both groups. Incidence of vomiting was significantly higher with dexmedetomidine (7%) premedication, when compared with midazolam (0%).

CONCLUSION

It is concluded that premedication with a single intramuscular injection of 1micrograms/kg dexmedetomidine is as efficacious as midazolam 0.05 mg/kg given intramuscularly inproducing sedation and anxiolysis in patients undergoing laparoscopic abdominal surgeries.

It is also efficacious in blunting the hemodynamic response to intubation, reducing the intraoperative analgesic requirement. Dexmedetomidine causes significant increase in the incidence of intraoperative bradycardia and hypotension at 90 minutes after intramuscular injection in ASA physical status 1 or 2 patients undergoing laparoscopic abdominal surgeries.

PROFORMA

DATE: SERIAL NO:

Name: Lot number:

Age/Sex/Weight:

Group assigned: M/D

I.P Number:

Diagnosis:

Surgery planned:

ASA PS: Duration of Surgery

Associated medical condition:

PREOPERATIVE PARAMETERS

HR	
MAP	
SPO2	

OXYGEN SATURATION

TIME(IN MIN AFTER PREMEDICATION)	0	0	0	0	0	0
O2 SATURATION						

Induction:

Inj.thiopentone: _____ mg.

Inj.succinylcholine: _____ mg.

Intubation: _____mm ETT:

DURATION OF LARYNGOSCOPY (MIN):

PARAMETERS	R	BP	BP	AP	Analgesia
BEFORE INDUCTION					
Before intubation					
1 min after intubation					
2 min after intubation					
3 min after intubation					
5 min after intubation					
10 min after intubation					
15 min					
30min					
45min					
1 hr					
2 hr					
4hr					
6hr					
8hr					
10hr					

Sedation /Anxiety VAS score

Parameters	SSScore	VAS
Baseline	----------	
Before induction		
After extubation		
1 hour after extubation		
2 hour after extubation		

INCIDENCE OF SIDE EFFECTS:

1) BRADYCARDIA: YES/NO

TREATED WITH:

2) HYPOTENSION: YES/NO

TREATED WITH:

3) SHIVERING: YES/NO

TREATED WITH:

4) NAUSEA/VOMITING:

TREATED WITH:

5) OTHERS:

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master chart Group D (dexmedetomidine)							
Sl. No	order	Date	Name	Age	Sex	Wt	Diagnosis
1		12.6.12	Eswari	18	F	68	sub acute appendicitis
2		12.6.12	Palani	19	M	52	sub acute appendicitis
3		15.6.12	Fathima	21	F	66	sub acute appendicitis
4		19.6.12	Gopi	20	M	50	sub acute appendicitis
5		20.6.12	Devi kala	18	F	64	sub acute appendicitis
6		25.6.12	Chitra	22	F	56	sub acute appendicitis
7		27.6.12	Kanagu	16	M	48	sub acute appendicitis
8		27.6.12	Sathish	23	M	51	sub acute appendicitis
9		02.7.12	Abirami	19	F	63	sub acute appendicitis
10		04.7.12	Sundar	27	M	47	sub acute appendicitis
11		10.7.12	Sumathi	28	F	60	adhesive colic
12		12.7.12	Arokiya das	19	M	65	sub acute appendicitis
13		17.7.12	Swetha	26	F	53	sub acute appendicitis
14		17.7.12	Sultan	19	M	58	sub acute appendicitis
15		18.7.12	Anitha	25	F	62	sub acute appendicitis
16		23.7.12	Saravanan	23	M	54	sub acute appendicitis
17		25.7.12	Banumathi	22	F	57	sub acute appendicitis
18		27.7.12	Kumaran	31	M	64	sub acute appendicitis
19		30.7.12	Hema devi	30	F	55	sub acute appendicitis
20		31.7.12	Suganthi	24	F	61	sub acute appendicitis
21		31.7.12	Malliga	23	F	55	sub acute appendicitis
22		02.7.12	Padma	31	F	63	sub acute appendicitis
23		17.8.12	Murugesan	30	M	59	sub acute appendicitis
24		23.8.12	Selvam	28	M	51	sub acute appendicitis
25		25.8.12	Ram kumar	19	M	59	sub acute appendicitis
26		28.8.12	Lakshmi	25	F	61	sub acute appendicitis
27		30.8.12	Ravi	24	M	63	sub acute appendicitis
28		30.8.12	Ratha	18	F	56	sub acute appendicitis
29		31.8.12	Gopal	32	M	62	sub acute appendicitis
30		31.8.12	Usha	22	F	58	sub acute appendicitis
			Mean	23.40		23.40	
			Stdev	4.58		5.58	

			SSS		VAS	
Procedure	ASA Status	Duration	before ind	preop	PreOP	before ind
Laproscopic Appendicectomy	I	45	2		4	3
Laproscopic Appendicectomy	I	50	2		3	1
Laproscopic Appendicectomy	I	45	2		3	1
Laproscopic Appendicectomy	I	40	2		4	3
Laproscopic Appendicectomy	I	45	2		3	2
Laproscopic Appendicectomy	II	50	2		4	4
Laproscopic Appendicectomy	I	45	2		4	3
Laproscopic Appendicectomy	I	50	2		5	3
Laproscopic Appendicectomy	I	50	2		3	3
Laproscopic Appendicectomy	I	40	2		3	1
laproscopic adhesiolysis	I	45	2		3	1
Laproscopic Appendicectomy	II	50	2		4	2
Laproscopic Appendicectomy	I	60	3		3	1
Laproscopic Appendicectomy	I	50	2		3	3
Laproscopic Appendicectomy	I	50	2		4	2
Laproscopic Appendicectomy	I	55	2		3	2
Laproscopic Appendicectomy	II	45	2		4	1
Laproscopic Appendicectomy	I	45	2		5	2
Laproscopic Appendicectomy	I	45	2		3	2
Laproscopic Appendicectomy	I	40	2		5	3
Laproscopic Appendicectomy	I	40	2		3	1
Laproscopic Appendicectomy	I	44	2		3	2
Laproscopic Appendicectomy	I	45	2		3	1
Laproscopic Appendicectomy	I	40	2		5	2
Laproscopic Appendicectomy	I	45	2		5	3
Laproscopic Appendicectomy	I	50	2		4	3
Laproscopic Appendicectomy	II	50	2		6	1
Laproscopic Appendicectomy	I	50	2		6	2
Laproscopic Appendicectomy	I	60	2		5	2
Laproscopic Appendicectomy	I	65	2		3	2
		47.80	2		3.87	2.07
		6.13	0.18		0.97	0.87

	o2 saturation										
Intubation	preop	10min	20min	30min	40min	50 min	1 HR	Preop	BI	BIN	1 min
20	100	98	100	97	98	95	96	66	55	55	88
25	100	98	99	99	99	97	95	84	65	64	73
15	100	99	98	98	99	97	95	65	56	62	65
18	99	99	99	98	99	99	96	79	58	66	63
16	100	98	100	99	99	98	99	74	60	64	67
10	99	99	99	99	99	98	99	66	55	58	68
15	100	98	98	98	99	97	98	89	60	66	76
12	99	99	99	98	98	96	97	73	64	72	74
18	99	98	98	98	98	98	96	82	66	70	75
18	99	99	99	99	97	97	96	88	59	66	85
15	100	98	99	99	99	98	95	93	56	65	76
20	99	99	100	99	97	99	96	85	66	62	69
18	99	99	99	98	99	97	97	84	71	78	71
20	100	100	99	98	99	99	98	88	60	67	70
20	99	99	98	98	98	97	99	88	66	62	78
20	99	99	100	99	99	99	98	74	58	63	75
18	99	99	98	99	99	99	99	92	55	52	67
15	100	99	99	98	99	97	98	99	52	66	68
15	99	99	100	100	98	98	99	88	53	56	77
16	100	98	99	99	99	98	98	93	62	70	76
20	99	99	98	98	97	99	98	90	58	62	77
18	100	98	99	99	97	98	99	85	51	59	76
15	99	99	100	100	99	99	99	89	69	75	70
15	100	99	99	99	97	96	98	82	62	70	78
25	99	99	98	98	99	96	98	80	69	68	88
18	100	99	99	99	99	96	98	91	64	69	85
20	99	98	98	98	99	98	99	89	56	59	78
18	99	98	99	99	98	99	98	84	62	68	87
18	99	99	99	99	99	96	98	90	76	79	88
25	100	98	100	99	99	98	99	88	73	74	79
17.87	99	99	99	99	98	98	98	83.93	61.23	65.57	75.57
3.45	#REF!	#REF!		#REF!	0.50	0.55	0.72	0.67	8.53	6.35	6.47	7.13

Pulse rate														
2 min	3 min	15 min	30min	45min	1hr	2hr	4hr	6hr	8hr	10hr	Preop	BI	BIN	1min
87	61	65	68	58	88	68	88	76	66	77	123	109	116	132
96	74	76	78	48	90	86	86	86	86	90	132	112	110	140
88	65	48	80	62	88	76	94	82	84	86	124	100	120	155
95	60	78	76	64	82	70	82	84	88	86	98	124	116	145
79	70	76	72	46	78	80	80	80	82	82	109	126	120	137
96	62	66	49	52	80	70	84	82	84	86	122	108	106	128
89	69	88	78	58	90	86	99	96	100	103	110	124	122	140
90	68	88	78	62	88	82	82	85	90	88	132	124	120	150
98	78	69	54	55	58	48	64	59	56	68	116	108	104	142
90	58	46	86	56	78	68	74	78	76	78	128	98	114	132
72	62	90	86	66	80	72	78	80	80	78	132	95	116	132
68	60	78	62	64	98	73	94	95	96	98	98	114	106	142
91	60	80	59	68	64	83	62	66	62	66	111	118	114	138
72	72	80	61	44	84	87	84	85	88	84	115	116	112	121
70	72	50	65	62	78	77	72	72	72	74	136	108	104	116
58	70	72	66	61	68	70	72	72	74	72	112	118	112	138
69	84	86	45	68	66	76	59	67	69	78	130	102	116	130
61	76	60	56	54	80	68	84	83	84	82	138	108	104	122
69	72	78	54	52	68	72	70	66	68	68	128	118	116	132
68	65	84	64	60	82	73	82	84	84	82	120	108	104	128
78	73	88	59	65	88	74	72	70	84	90	128	124	112	130
88	68	86	55	58	77	80	74	76	99	87	112	119	114	122
72	66	98	66	62	73	80	65	74	93	89	116	124	114	150
68	68	83	69	66	71	75	89	93	73	95	128	119	116	140
66	58	83	62	66	66	75	63	74	73	96	120	107	120	147
56	64	86	58	60	92	58	63	74	76	70	117	107	121	139
66	63	100	65	62	83	66	74	73	66	80	132	130	112	138
76	64	91	72	70	79	67	74	81	90	75	126	116	113	146
67	69	78	80	71	76	67	72	84	100	77	118	107	113	133
72	75	80	65	63	70	80	72	86	88	83	132	110	116	140
77.17	67.53	77.70	66.27	60.10	78.77	73.57	76.93	78.77	81.03	82.27	121.43	###	###	####
12.36	6.36	13.46	10.62	6.84	9.47	8.34	10.35	8.74	11.53	9.21	10.38	8.95	5.37	9.29

Systolic Blood Pressure														
2min	3min	15min	30min	45min	1hr	2hr	4hr	6hr	8hr	10hrs	Preop	BI	BIN	1 min
122	110	90	126	116	124	118	112	108	114	110	88	72	94	93
124	108	89	98	126	104	110	108	102	108	112	82	70	86	84
129	120	102	115	100	112	108	106	112	108	104	86	68	92	94
132	112	112	129	118	108	120	116	106	120	110	90	64	82	80
101	122	119	140	130	114	116	110	98	116	108	84	82	82	84
98	106	94	134	125	100	98	100	110	104	109	80	78	84	87
129	122	119	140	126	108	112	118	116	118	115	84	77	96	100
99	110	118	89	135	118	116	122	98	116	115	80	74	90	86
132	100	135	102	140	98	100	102	104	104	103	84	76	80	83
142	112	134	118	144	114	110	108	110	110	107	80	65	80	91
98	100	142	100	124	94	106	110	114	108	112	74	69	86	90
125	100	148	128	115	98	100	102	116	104	115	80	69	96	92
134	112	139	129	148	110	112	108	99	108	109	84	63	65	68
109	108	129	104	144	100	98	102	110	108	103	78	75	83	80
130	100	138	135	160	96	98	100	110	100	110	70	61	76	87
99	102	129	104	89	110	108	114	108	112	113	84	63	74	80
135	118	119	110	98	112	110	114	103	110	111	82	58	90	87
128	98	137	94	98	102	100	100	106	104	111	78	54	82	86
124	114	148	119	150	104	102	108	114	110	110	74	66	70	74
122	106	142	120	133	92	108	104	117	108	109	76	64	82	85
125	113	148	140	145	104	102	102	102	109	114	80	77	96	92
124	112	135	135	145	110	114	102	114	115	107	83	76	90	83
122	112	137	100	140	118	110	108	100	115	105	83	66	86	100
130	100	129	94	129	100	96	106	100	104	108	74	66	76	80
132	109	145	129	144	100	109	100	109	106	110	80	69	90	87
110	108	128	122	138	96	112	120	105	112	113	80	69	90	83
134	120	140	110	99	107	110	115	97	115	114	84	69	83	87
131	120	142	140	127	114	100	122	106	108	109	82	76	76	69
125	107	127	130	148	98	108	110	110	103	104	77	73	81	95
110	112	129	128	139	105	116	105	115	110	111	80	75	88	84
####	109.77	128.10						107.30		###	80.70	69.47	84.20	85.70
12.66	7.10	16.75	15.94	18.19	7.95	6.72	6.72	6.02	4.92	3.51	4.36	6.48	7.68	7.53

Diastolic Blood Pressure															
2 min	3 min	15 min	30min	45 min	1 HR	2 HR	4 HR	6 HR	8 HR	10 HR	Preop	BI	BIN	1 min	2 min
92	64	48	55	88	92	76	70	76	77	74	100	84	101	106	102
88	78	60	56	84	94	82	78	66	80	66	99	84	94	103	100
92	76	55	60	86	90	68	72	88	79	60	99	79	101	114	104
83	85	57	67	88	88	84	78	70	72	68	93	84	93	102	99
86	80	48	59	92	78	74	72	76	82	66	92	97	95	102	91
90	58	55	59	90	78	64	72	66	68	58	94	88	91	101	93
102	96	58	64	94	88	80	76	72	76	60	93	93	105	113	111
84	54	68	72	88	87	70	67	70	67	65	97	91	100	107	89
88	80	66	62	78	68	74	76	71	76	70	95	87	88	103	103
92	88	72	74	88	67	68	57	68	58	66	96	76	91	105	109
94	88	60	78	87	73	74	66	70	60	64	93	78	96	104	95
94	76	57	67	85	75	74	67	76	68	58	86	84	99	109	104
70	56	50	58	76	66	72	68	67	65	64	93	81	81	91	91
84	66	90	78	96	65	68	59	68	65	63	90	89	93	94	92
90	76	88	82	69	62	68	74	86	85	88	92	77	85	97	103
82	86	65	67	79	76	74	70	74	80	73	93	81	87	99	88
98	68	56	69	78	75	76	78	78	76	67	98	73	99	101	110
90	65	58	56	85	82	74	72	68	66	68	98	72	89	98	103
78	70	76	74	80	78	68	72	68	70	64	92	83	85	93	93
88	84	75	55	82	66	68	69	65	64	72	91	79	89	99	99
103	80	46	56	64	88	70	76	72	79	80	96	93	101	105	110
88	78	55	64	86	87	70	76	68	60	72	93	90	98	96	100
84	75	47	67	79	68	72	60	67	59	75	94	85	95	117	97
102	84	44	79	85	67	68	68	60	72	65	92	84	89	100	111
100	63	55	65	85	82	74	70	71	66	68	93	82	100	107	111
98	73	56	60	93	66	74	76	66	67	66	92	82	100	102	102
94	88	57	68	66	64	80	58	65	64	69	100	89	93	104	107
88	92	67	56	83	76	74	59	60	55	70	97	89	88	95	102
88	96	68	88	78	66	74	76	64	65	78	91	84	92	108	100
93	83	77	68	79	73	74	70	70	66	72	97	87	97	103	99
90.10	76.87	61.13	66.10	83.03	####	####	####	####	####	68.30	94	84	94	103	101
7.33	11.34	11.71	8.87	7.65	9.66	4.60	6.27	6.29	7.88	6.55	3.24	5.93	5.85	6.08	6.92

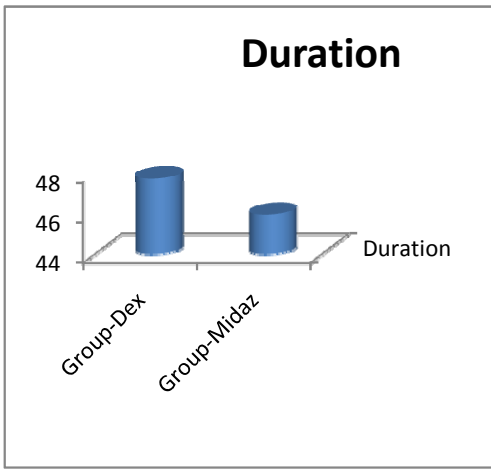
MAP											
3 min	15 min	30min	45 min	1 HR	2 HR	4 HR	6 HR	8 HR	10 HR	ANALGESIA	SIDEEFECT
79	62	79	97	103	90	84	#REF!	89	#REF!		
88	70	70	98	97	91	88	#REF!	89	#REF!		brady
91	71	78	91	97	81	83	#REF!	89	#REF!		
94	75	88	98	95	96	91	#REF!	88	#REF!		Nausea
94	72	86	105	90	88	85	#REF!	93	#REF!		brady
74	68	84	102	85	75	81	#REF!	80	#REF!		
105	78	89	105	95	91	90	#REF!	90	#REF!		
73	85	78	104	97	85	85	#REF!	83	#REF!		
87	89	75	99	78	83	85	#REF!	85	#REF!		brady
96	93	89	107	83	82	74	#REF!	75	#REF!		
92	87	85	99	80	85	81	83	76	#REF!		Vomiting
84	87	87	95	83	83	79	85	80	#REF!		
75	80	82	100	81	85	81	82	79	#REF!		
80	103	87	112	77	78	73	81	79	#REF!		brady
84	105	100	99	73	78	83	90	90	#REF!		
91	86	79	82	87	85	85	86	91	#REF!		
85	77	83	85	87	87	90	91	87	#REF!		brady
76	84	69	89	89	83	81	78	79	#REF!		
85	100	89	103	87	79	84	80	83	#REF!		
91	97	77	99	75	81	81	80	79	#REF!		
91	80	84	91	93	81	85	86	89	#REF!		
89	82	88	106	95	85	85	84	78	#REF!		Vomiting
87	77	78	99	85	85	76	78	73	#REF!		
89	72	84	100	78	77	81	77	81	#REF!		
78	85	86	105	88	86	80	84	80	#REF!		
85	80	81	108	76	87	91	80	80	#REF!		
99	85	82	77	78	90	77	78	75	#REF!		
101	92	84	98	89	83	80	75	72	#REF!		Nausea
100	88	102	101	77	85	87	81	80	#REF!		
93	94	88	99	84	88	82	86	82	#REF!		
88	83	84	98	86	84	83	#REF!	83	#REF!		
8.25	10.50	7.08	7.68	7.93	4.62	4.56	#REF!	5.84	#REF!	#DIV/0!	

#NAME?

TREATMENT	Hypotension
	79.73333333
	78.93333333
	78.93333333
	74.13333333
	73.86666667
	75.2
	74.13333333
	77.86666667
	75.73333333
	76.8
	74.66666667
	68.8
	74.4
	72.26666667
	73.6
	74.66666667
	78.4
	78.4
	73.6
	72.53333333
	76.8
	74.13333333
	75.2
	73.6
	74.66666667
	73.86666667
	80
	77.33333333
	72.53333333

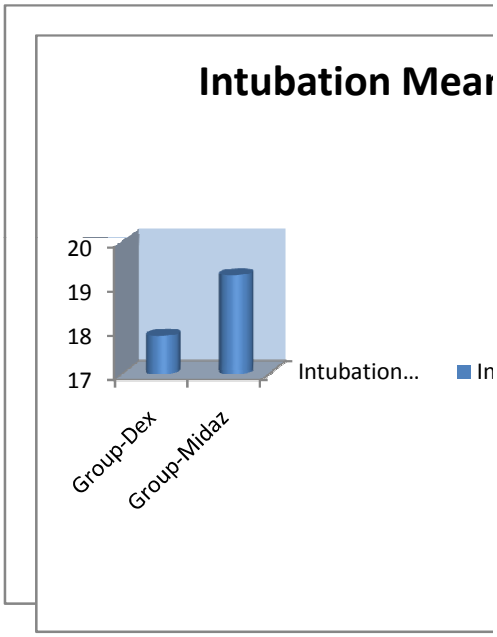
Duration

	Group-Dex	Group-Midaz
Duration	47.8	45.97
Sd	6.13	4.04
t-Value	1.37	
Df	58	
p-value	0.18 (Not Significant)	



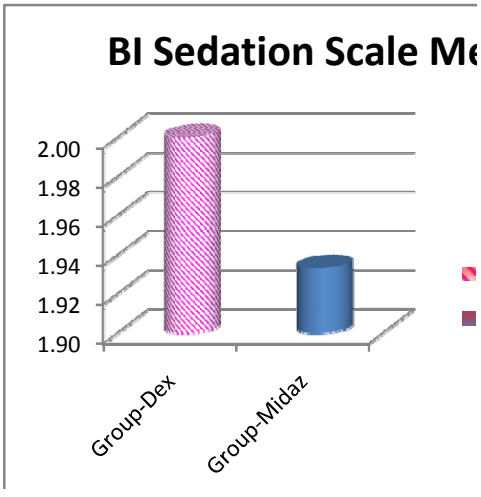
Intubation

	Group-Dex	Group-Midaz
Intubation Mean	17.87	19.23
Sd	3.45	4.09
t-Value	-1.42	
Df	58	
p-value	0.16 (insignificant)	



BI Sedation Scale

	Group-Dex	Group-Midaz
BI Sedation Sca	2.00	2
Sd	0.59	0.35
t-Value	1.07	
Df	58	
p-value	0.29 (Not Significant)	



AE Sedation Scale

	Group-Dex	Group-Midaz
AE Sedation Sca	2.4	2.8
Sd	0.62	0.41
t-Value	2.95	
Df	58	
p-value	0.01	

	Group-Dex	Group-Midaz
VAS	2.4	2.8
Sd	0.62	0.41
t-Value	2.95	
Df	58	
p-value	0.01	

MAP

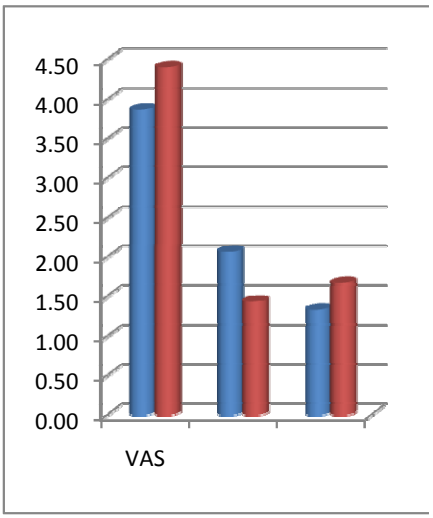
	Preop	BI	BIN	1 min	2 min	3 min	15 min
DEX	94	84	94	94	92	88	80
MID	91	86	92	104	100	95	100

O2 SATURATION

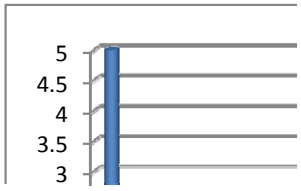
	Preop	10min	20min	30min	40min	50min	1hr
DEX	99	99	99	99	98	98	98
MID	99	99	99	97	96	97	97

VAS

DEX	3.87	2.07	1.33
MID	4.40	1.43	1.67



Side Effects		



	GROUP - D	GROUP - M
Bradycardia	5	0
Hypotension	0	1
Shivering	0	2
Nausea	2	2
Vomiting	2	0

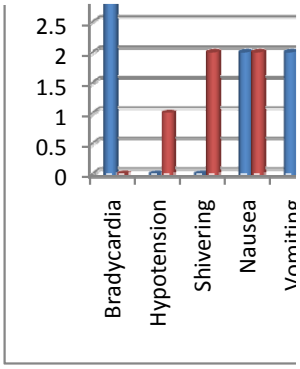


Table-1

Sex distribution of the Sample

Sex	Group-Dex N=30		Group-Midaz N=30		Total N=60	
	N	%	N	%	N	%
Male	14	46.7	19	63.3	33	55
Female	16	53.3	11	36.7	27	45
Chi-square value	**1.68**					
Df	**1**					
p value	**0.19 (Not Significant)**					

Table-2

Age Distribution of the Study Sample

	Group-Dex		Group-Midaz		Total	
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE
≤ 20	6	4	6	2	12	6
21-30	6	11	12	7	18	18
31-40	2	7	1	2	3	9
Mean (sd)	**23.40 (4.58)**		**24.03 (4.59)**		**23.72 (4.56)**	
T-value	**0.54**					
Df	**58**					
p-value	**0.60 (Not Significant)**					

Weight

	Group-Dex	Group-Midaz
Mean	58.03	58.03
Sd	5.58	5.58
t-Value	0	
Df	58	
p-value	1.000 (Not Significant)	

Height

	Group-Dex	Group-Midaz
Mean	158.43	158.43
Sd	5.01	5.01
t-Value	0	
Df	58	
p-value	1.000 (Not Significant	

ASA_Status

	Group-Dex		Group-Midaz	
	N	**%**	**N**	**%**
I	26	86.7	27	90
II	4	13.3	3	10
Total	**30**	**100**	**30**	**100**
Chi square Value *	**0.16**			
Df	**1**			
Significant	**0.69 (Not Significant)**			

Duration

	Group-Dex	Group-Midaz
Mean	47.8	45.97
Sd	6.13	4.04
t-Value	1.37	
Df	58	
p-value	0.18 (Not Significant)	

Intubation

	Group-Dex	Group-Midaz
Mean	17.87	34.83
Sd	3.45	5.94
t-Value	13.52	
Df	58	
p-value	0.0001 (Significant)	

Pulse Rate

Pulse Rate at	Group –Dex Mean ± sd	Group-Midaz Mean ± sd	t-value	p-Value df=58
Pre OP	83.70 ± 8.59	82.50 ± 7.58	0.57	0.57 *
Intra OP	60.97 ± 6.57	69.10 ± 7.42	4.45	0.0001
Bin	65.57 ± 6.48	74.53 ± 8.81	4.49	0.0001
Mint 1	75.57 ± 6.47	100.80 ± 8.66	12.33	0.0001
Mint 2	77.17 ± 12.36	95.13 ± 9.26	6.37	0.0001
Mint 3	67.53 ± 6.36	73.93 ± 7.30	3.62	0.001

Mint 15	81.23 ± 8.39	80.23 ± 6.65	0.511	0.61*
Mint 30	67.27 ± 9.40	79.07 ± 6.54	5.65	0.0001
Hour 1	78.77 ± 9.47	82.60 ± 8.01	1.69	0.096*
Hour 2	74.10 ± 7.07	76.57 ± 6.32	1.43	0.160*
Hour 4	76.93 ± 10.35	82.37 ± 11.28	1.95	0.057*
Hour 6	78.77 ± 8.74	81.70 ± 8.45	1.32	0.19*
Hour 8	81.03 ± 11.53	83.90 ± 10.40	1.01	0.32*
Hour 10	82.27 ± 9.21	85.77 ± 10.65	1.36	0.18*

* - Not Significant

Systolic Blood Pressure

Blood Pressure at	Group –Dex Mean ± sd	Group-Midaz Mean ± sd	t-value	p-Value df=58
Pre OP	120.93 ± 11.05	121.00 ± 5.55	0.03	0.98 *
Intra OP	113.37 ± 8.95	118.13 ± 5.75	2.46	0.017
Bin	113.43 ± 5.37	113.43 ± 5.37	0	1.000*
Mint 1	136.17 ± 9.29	143.37 ± 6.18	3.53	0.001
Mint 2	121.83 ±12.66	120.90 ± 13.93	0.27	0.79*
Mint 3	109.77 ± 7.10	110.63 ± 6.95	0.48	0.63*
Mint 15	128.10 ± 16.75	134.60 ± 9.30	1.86	0.07*
Mint 30	118.73 ± 15.94	127.87 ± 15.40	2.56	0.03
Mint 45	129.10 ±18.19	131.40 ± 15.53	0.53	0.60*
Hour 1	105.67 ± 7.95	105.67 ± 7.95	0	1.00*
Hour 2	107.57 ± 6.73	107.57 ± 6.73	0	1.00*

Hour 4	108.47 ± 6.73	108.47 ± 6.73	0	1.00*
Hour 6	109.30 ± 6.24	109.30 ± 6.24	0	1.00*
Hour 8	107.53 ± 6.12	107.53 ± 6.12	0	1.00*
Hour 10	109.57 ± 4.93	109.57 ± 4.93	0	1.00*

* - Not Significant

Diastolic Blood Pressure

Blood Pressure at	Group –Dex Mean ± sd	Group-Midaz Mean ± sd	t-value	p-Value df=58
Pre OP	80.70 ± 4.36	80.70 ± 4.36	0	1.000*
Intra OP	69.47 ± 6.48	69.47 ± 6.48	0	1.000*
Bin	84.20 ± 7.68	84.20 ± 7.68	0	1.000*
Mint 1	85.70 ± 7.53	85.70 ± 7.53	0	1.000*
Mint 2	90.10 ± 7.33	90.10 ± 7.33	0	1.000*
Mint 3	76.87 ±11.34	87.33 ± 11.67	3.52	0.001
Mint 15	61.13 ± 11.71	**82.03 ± 8.24**	7.99	0.0001
Mint 30	66.10 ± 8.87	**85.60 ± 6.25**	9.84	0.0001
Mint 45	83.03 ± 7.65	84.63 ± 6.37	0.88	0.382*
Hour 1	76.17 ± 9.66	76.17 ± 9.66	0	1.000*
Hour 2	72.87 ± 4.60	72.87 ± 4.60	0	1.000*
Hour 4	70.07 ± 6.28	73.67 ± 3.02	2.83	0.01
Hour 6	70.20 ± 6.29	73.03 ± 4.55	1.99	0.05
Hour 8	69.57 ± 7.88	74.93 ± 3.44	3.42	0.001
Hour 10	68.30 ± 6.55	75.67 ± 2.62	5.72	0.0001

* - Not Significant

BI Sedation Scale

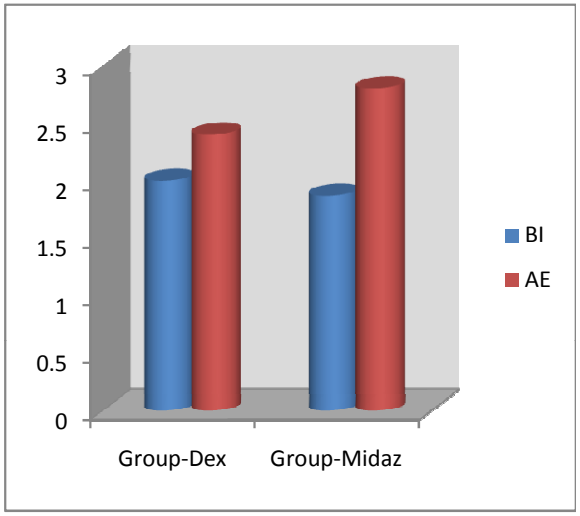
	Group-Dex	Group-Midaz
Mean	2	1.87
Sd	0.59	0.35
t-Value	1.07	
Df	58	
p-value	0.29 (Not Significant)	

AE Sedation Scale

	Group-Dex	Group-Midaz
Mean	2.4	2.8
Sd	0.62	0.41
t-Value	2.95	
Df	58	
p-value	0.01	

sedation

	Group-Dex	Group-Midaz
BI	2	1.87
AE	2.4	2.8



Graph-1

Pulse Rate

Pulse Rate at	Group –Dex	Group-Midaz
Pre OP	83.7	82.5
Intra OP	60.97	69.1
Bin	65.57	74.53
Mint 1	75.57	100.8
Mint 2	77.17	95.13
Mint 3	67.53	73.93
Mint 15	81.23	80.23
Mint 30	67.27	79.07
Hour 1	78.77	82.6
Hour 2	74.1	76.57
Hour 4	76.93	82.37
Hour 6	78.77	81.7
Hour 8	81.03	83.9

Hour 10	82.27	85.77

Graph-2

Systolic Blood Pressure

	Group –Dex	Group-Midaz
Pre OP	120.93	121.00
Intra OP	113.37	118.13
Bin	113.43	113.43
Mint 1	136.17	143.37
Mint 2	121.83	120.90
Mint 3	109.77	110.63
Mint 15	128.10	134.60
Mint 30	118.73	127.87
Mint 45	129.10	131.40
Hour 1	105.67	105.67
Hour 2	107.57	107.57
Hour 4	108.47	108.47
Hour 6	109.30	109.30
Hour 8	107.53	107.53
Hour 10	109.57	109.57

Graph-3

Diastolic Blood Pressure

	Group –Dex	Group-Midaz
Pre OP	80.7	80.7
Intra OP	69.47	69.47
Bin	84.2	84.2
Mint 1	85.7	85.7
Mint 2	90.1	90.1
Mint 3	76.87	87.33
Mint 15	61.13	82.03
Mint 30	66.1	85.6
Mint 45	83.03	84.63
Hour 1	76.17	76.17
Hour 2	72.87	72.87
Hour 4	70.07	73.67
Hour 6	70.2	73.03
Hour 8	69.57	74.93
Hour 10	68.3	75.67

Graph-4

	Male	Female
Group-Dex	14	16
Group-Midaz	19	11

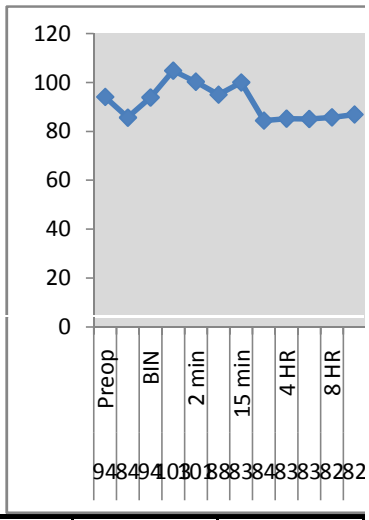
Graph-5

Age Group	Group-Dex	Group-Midaz
≤ 20	10	8
21-30	17	19
31-40	3	3

Graph-6

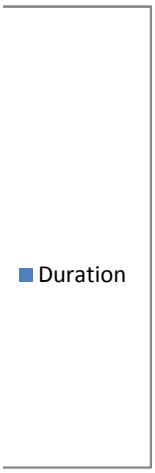
ASA Status

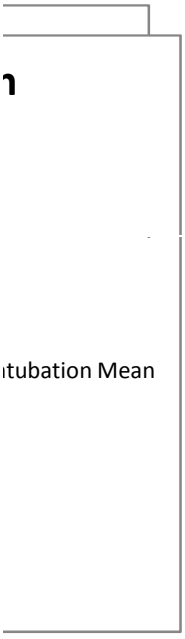
	I	II
Group-Dex	26	4
Group-Midaz	27	3



Dex	94	84	94	103			

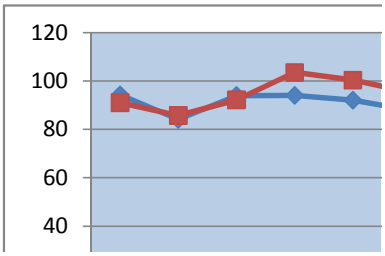
MAP	Preop	BI	BIN	1 min	2 min	3 min	15 min
MID	94	86	94	105	100	95	100

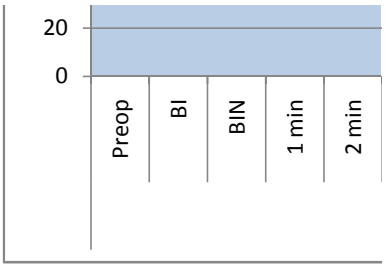

Duration

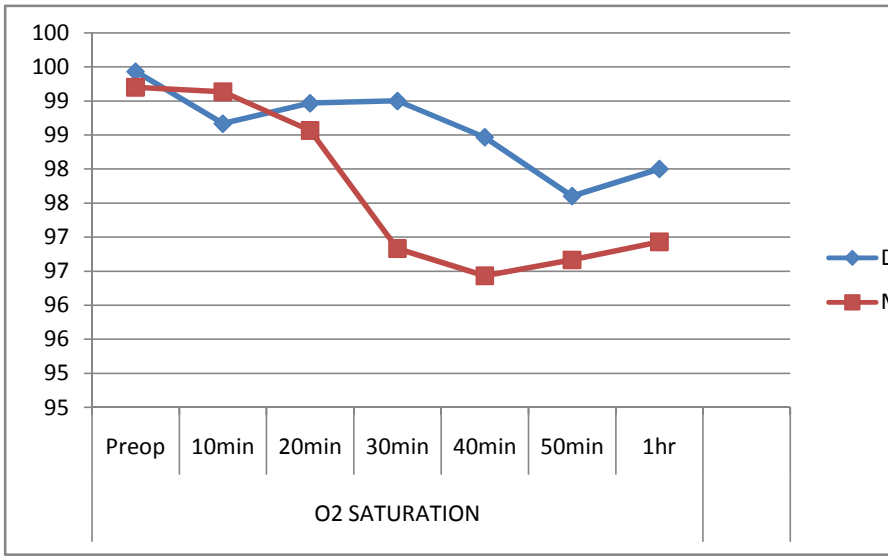

ıtubation Mean

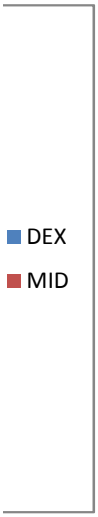

Group-Dex
Group-Midaz

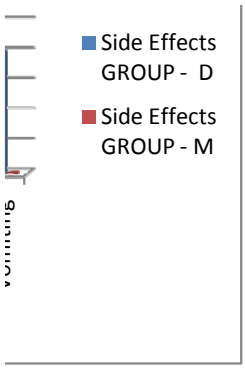
2 HR	4 HR	6 HR	8 HR	10 HR
84	83	83	82	82
84	85	85	86	87

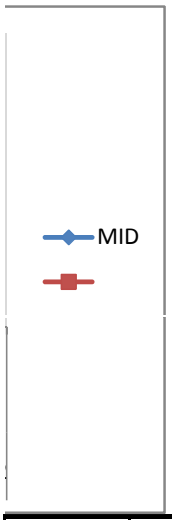



20
0
Preop
BI
BIN
1 min
2 min

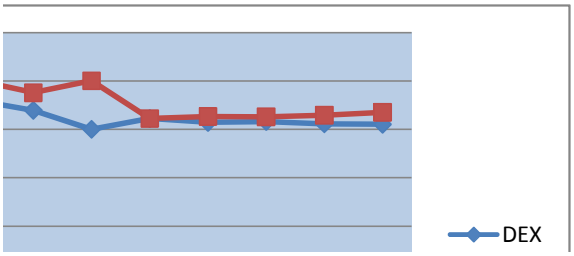

100
100
99
99
98
98
97
97
96
96
95
95
Preop
10min
20min
30min
40min
50min
1hr
O2 SATURATION


DEX
MID


Side Effects GROUP - D
Side Effects GROUP - M



	83	83	82	82
2 HR	4 HR	6 HR	8 HR	10 HR
84	85	85	86	87


DEX

MID
3 min
15 min
2 HR
4 HR
6 HR
8 HR
10 HR
MAP

DEX
MID

MASTER CHART GROUP- M (Midax)							
Sl. No	order	date	Name	Age	Sex	Wt	Diagnosis
1		19.6.12	Kalyani	28	F	50	sub acute appendicitis
2		20.6.12	prakash	19	M	48	sub acute appendicitis
3		21.6.12	yasodha	23	F	54	sub acute appendicitis
4		21.6.12	praveen	24	M	58	sub acute appendicitis
5		22.6.12	mohan	18	M	49	sub acute appendicitis
6		23.6.12	nasreen begam	22	F	60	sub acute appendicitis
7		25.6.12	Kalyani	16	M	51	sub acute appendicitis
8		25.6.12	Sukumar	21	M	59	sub acute appendicitis
9		26.6.12	Selvi	20	F	54	sub acute appendicitis
10		28.6.12	Rathinam	30	M	63	sub acute appendicitis
11		29.6.12	Balambika	28	F	60	sub acute appendicitis
12		02.7.12	Martin	22	M	57	sub acute appendicitis
13		20.7.12	Devi sree	20	F	67	sub acute appendicitis
14		21.7.12	saminathan	30	M	58	sub acute appendicitis
15		21.7.12	Prabhu	19	M	49	sub acute appendicitis
16		23.7.12	Kumari	28	F	62	sub acute appendicitis
17		23.7.12	Bakiyaraj	17	M	48	sub acute appendicitis
18		24.7.12	Senthil	31	M	66	adhesive colic
19		26.7.12	Babu sundar	22	M	51	sub acute appendicitis
20		26.7.12	Venila	25	F	47	sub acute appendicitis
21		27.7.12	Satanathan	28	M	58	sub acute appendicitis
22		10.8.12	Saraswathi	31	F	64	sub acute appendicitis
23		10.8.12	Kanan	25	M	60	sub acute appendicitis
24		11.8.12	Senthil vijay	28	M	60	sub acute appendicitis
25		14.8.12	Vignesh	19	M	51	sub acute appendicitis
26		23.8.12	Meenakshi	27	F	55	sub acute appendicitis
27		23.8.12	Ganesh	22	M	59	sub acute appendicitis
28		24.8.12	Raja	24	M	62	sub acute appendicitis
29		25.8.12	Vadivu	32	F	65	adhesive colic
30		27.8.12	Arivoli	22	M	52	sub acute appendicitis
			Mean	24.03		56.57	
			Stdev	4.59		5.92	

			SSS	VAS			
Procedure	ASA Status	Duration	BI	PreOP	BI	Intubation	Preop
Laproscopic Appendicectomy	I	45	2	5	2	15	99
Laproscopic Appendicectomy	I	50	2	3	1	15	100
Laproscopic Appendicectomy	I	45	2	4	1	22	99
Laproscopic Appendicectomy	I	40	2	5	1	23	99
Laproscopic Appendicectomy	I	45	2	3	1	20	100
Laproscopic Appendicectomy	II(old pt)	50	2	5	2	20	99
Laproscopic Appendicectomy	I	45	2	3	3	22	99
Laproscopic Appendicectomy	I	50	2	3	1	20	100
Laproscopic Appendicectomy	I	50	2	5	1	25	100
Laproscopic Appendicectomy	I	40	1	5	1	20	100
Laproscopic Appendicectomy	I	45	2	4	1	25	99
Laproscopic Appendicectomy	II(HT)	50	1	5	1	15	99
Laproscopic Appendicectomy	I	45	2	3	2	15	99
Laproscopic Appendicectomy	I	45	2	5	1	20	100
Laproscopic Appendicectomy	I	50	2	5	1	25	99
Laproscopic Appendicectomy	I	55	2	3	2	10	99
Laproscopic Appendicectomy	I	45	2	5	2	10	99
laproscopic adhesiolysis	I	50	2	3	1	15	99
Laproscopic Appendicectomy	I	40	2	5	2	20	99
Laproscopic Appendicectomy	I	40	2	4	2	20	99
Laproscopic Appendicectomy	I	40	2	4	1	20	99
Laproscopic Appendicectomy	I	44	2	5	1	25	99
Laproscopic Appendicectomy	I	45	2	5	2	20	99
Laproscopic Appendicectomy	I	50	2	5	1	18	99
Laproscopic Appendicectomy	I	45	2	5	2	18	99
Laproscopic Appendicectomy	I	45	2	5	1	16	99
Laproscopic Appendicectomy	II(obese)	50	2	3	1	25	99
Laproscopic Appendicectomy	I	50	2	6	1	22	99
laproscopic adhesiolysis	I	40	2	6	2	18	99
Laproscopic Appendicectomy	I	45	2	5	2	18	99
		45.97	2	4.40	1.43	19.23	99
		4.04	0.25	0.97	0.57	4.09	99

Oxygen Saturation						Pu						
10min20min	20min30min	30	40min	50min	ihr	Preop	BI	BIN	1 min	2 min	3 min	15 min
100	99	98	98	95	97	66	55	55	93	87	61	65
99	99	98	95	96	97	84	70	76	101	96	74	76
99	98	95	95	96	98	74	62	62	94	88	65	68
99	98	97	98	96	98	79	66	72	100	95	78	78
100	99	98	99	95	98	74	60	70	84	79	74	76
99	99	99	98	96	98	66	55	58	97	96	62	66
99	98	98	98	97	96	98	83	96	100	102	86	88
99	98	99	95	98	96	94	80	90	96	90	82	88
98	98	98	98	96	96	82	70	80	110	105	80	88
99	99	96	95	98	96	84	71	80	120	116	84	82
99	99	96	95	95	98	60	68	76	117	94	78	90
100	99	99	98	95	98	61	66	66	109	94	64	78
99	98	99	95	99	96	84	71	65	97	91	60	80
99	98	94	95	96	96	88	74	83	99	95	72	80
98	98	94	96	98	95	78	63	76	102	90	72	82
100	99	93	95	96	96	76	62	74	98	82	70	72
99	98	99	96	97	98	92	78	80	99	98	84	86
99	98	95	96	95	96	84	71	82	92	90	76	78
100	99	94	96	98	97	72	59	70	96	90	72	78
99	99	98	98	99	97	80	68	82	112	109	78	84
99	98	94	95	96	96	90	74	71	86	78	73	74
99	99	98	96	96	98	85	66	81	92	91	77	86
100	99	94	95	96	96	89	69	83	99	98	82	82
99	99	99	97	98	96	82	71	71	93	90	71	83
98	98	95	98	97	98	80	80	68	97	88	80	83
99	99	96	96	97	98	91	81	69	102	106	83	86
99	98	97	96	98	98	80	77	76	112	108	72	81
99	99	98	98	98	95	83	62	71	109	103	64	91
99	99	99	97	96	98	90	68	79	110	112	69	78
100	99	98	96	97	98	88	73	74	108	93	75	79
99	99	97	96	97	97	81.13	69.10	74.53	100.80	95.13	73.93	80.20
99	99	97	96	97	97	9.42	7.42	8.81	8.66	9.26	7.30	6.66

lse rate													
30min	45min	1hr	2hr	4hr	6hr	8hr	10hr	Preop		BIN	1min	2min	3min
68	69	88	68	88	76	101	104	128	120	116	132	122	110
78	72	90	86	86	86	86	90	116	112	110	140	124	108
70	75	88	76	94	82	84	86	124	122	120	155	129	120
76	72	82	70	82	84	88	86	130	124	116	145	132	112
72	74	78	80	80	80	82	82	128	126	120	137	101	122
78	75	80	70	84	82	84	86	110	108	106	135	98	106
78	68	90	86	99	96	100	103	124	124	122	140	129	120
78	77	88	82	82	85	90	88	126	124	120	150	99	120
90	79	84	64	80	84	84	82	112	108	104	142	105	100
86	73	78	68	74	78	76	78	124	116	114	132	142	112
86	79	80	72	78	80	80	78	126	120	116	155	98	116
80	81	98	73	94	95	96	98	120	114	106	142	125	100
78	69	64	83	62	66	62	66	128	118	114	147	134	112
76	79	84	87	84	85	88	84	120	116	112	138	109	108
89	82	78	77	72	72	72	74	114	108	104	140	130	100
79	76	80	70	72	72	74	72	122	118	112	150	99	102
77	74	96	80	92	94	92	106	130	122	116	151	135	118
73	72	80	68	84	83	84	82	116	108	104	149	128	100
66	69	68	72	70	66	68	68	120	118	116	147	135	114
89	79	82	73	82	84	84	82	110	108	104	140	128	106
80	84	88	74	72	70	84	90	119	124	112	143	125	113
76	75	77	80	98	95	99	87	116	119	114	141	134	112
76	75	73	80	98	91	93	89	120	124	114	150	109	112
100	90	71	75	98	93	73	95	120	119	116	140	130	100
83	82	92	75	63	74	73	96	120	120	120	147	128	109
81	82	92	79	63	74	76	106	119	114	121	139	99	108
90	88	83	79	74	73	66	80	124	122	112	138	134	120
91	76	79	84	74	81	90	75	126	124	113	146	131	120
74	74	76	86	94	84	100	77	118	124	113	150	125	107
108	78	91	80	98	86	88	83	120	120	116	140	110	112
80.87	76.60	82.60	76.57	82.37	81.70	83.90	85.77	121.00	118.13	113.43			
9.12	5.42	8.01	6.32	11.28	8.45	10.40	10.65	5.55	5.75				

Systolic Blood Pressure											
15min30min	30min	45min	1hr	2hr	4hr	6hr	8hr	10hr	Preop	BI	BIN
125	126	116	124	118	112	116	114	114	75	72	94
135	135	126	104	110	108	106	106	108	79	70	86
112	115	100	112	108	106	112	108	108	86	68	92
125	129	118	108	120	116	116	114	120	72	64	82
142	140	130	114	116	110	118	120	116	88	82	82
135	134	125	100	98	100	102	104	104	82	78	84
146	140	126	108	112	118	116	114	118	81	77	96
118	120	135	118	116	122	118	118	116	77	74	90
135	102	140	98	100	102	102	102	104	71	76	80
134	118	144	114	110	108	112	116	110	68	65	80
142	130	124	94	106	110	108	106	108	62	69	86
148	128	115	98	100	102	102	104	104	65	69	96
139	129	148	110	112	108	112	110	108	63	63	65
129	119	144	100	98	102	106	106	108	70	75	62
138	135	160	96	98	100	98	100	100	66	61	63
129	124	136	110	108	114	110	110	112	70	63	66
119	110	98	112	110	114	116	108	110	73	58	74
137	110	120	102	100	100	98	98	104	78	54	71
148	119	150	104	102	108	104	102	110	74	66	70
142	120	133	92	108	104	110	108	108	76	64	70
148	140	145	104	102	102	114	102	109	80	77	96
135	135	145	110	114	102	116	114	115	83	76	90
137	128	140	118	110	108	99	100	115	83	66	86
129	180	129	100	96	106	110	100	104	74	66	76
145	130	144	100	109	100	110	109	106	80	69	90
128	122	138	96	112	120	108	105	112	80	69	90
140	110	99	107	110	115	103	97	115	84	69	83
142	140	127	114	100	122	106	106	108	82	76	76
127	130	148	98	108	110	114	110	103	77	73	81
129	140	139	105	116	105	117	115	110	80	75	88
134.60	127.93	131.40	105.67	107.57	108.47	109.30	107.53	109.57	75.97	69.47	81.50
9.30	14.24	15.53	7.95	6.72	6.72	6.24	6.12	4.92	6.86	6.48	10.22

Diastolic Blood Pressure													
1 min	2 min	3 min	15 min	30min	45 min	1 HR	2 HR	4 HR	6 HR	8 HR	10 HR	Preop	BI
93	92	100	98	90	88	92	76	70	76	78	80	93	88
84	88	86	94	86	84	94	82	78	74	72	78	91	84
94	92	100	78	88	86	90	68	72	80	76	74	99	86
80	83	85	74	92	88	88	84	78	80	74	78	91	84
84	86	80	95	94	92	78	74	72	76	82	74	101	97
87	90	78	74	79	90	78	64	72	76	72	76	91	88
100	102	96	88	74	94	88	80	76	72	76	80	95	93
86	84	92	84	88	88	87	70	76	74	78	74	93	91
83	88	80	85	92	78	68	74	76	72	76	74	85	87
66	92	88	68	90	88	67	68	70	72	74	78	87	82
71	94	88	100	96	87	73	74	78	72	74	78	83	86
92	94	92	76	94	85	75	74	70	74	72	76	83	84
68	70	56	86	75	76	66	72	78	80	82	78	85	81
60	84	96	90	78	96	65	68	74	78	74	76	87	89
87	90	76	98	82	69	62	68	74	64	74	76	82	77
80	82	86	75	88	79	76	74	70	74	72	70	87	81
87	98	104	74	84	78	75	76	78	80	76	80	92	79
86	90	82	68	86	85	82	74	72	68	66	74	91	72
74	78	70	84	82	80	78	68	72	68	70	74	89	83
85	88	84	75	85	82	66	68	70	72	74	72	87	79
92	103	96	88	74	88	88	70	76	72	78	78	93	93
83	88	92	80	88	86	87	70	76	72	79	72	94	90
100	84	99	76	80	79	68	72	72	70	74	75	95	85
80	102	100	88	102	85	67	68	70	74	74	75	89	84
87	100	63	86	92	96	82	74	70	71	74	72	93	86
83	98	73	83	94	93	66	74	76	70	72	74	93	84
87	94	88	80	80	79	64	80	76	70	76	74	97	87
69	88	92	76	86	83	76	74	72	80	81	78	97	92
95	88	96	76	88	78	66	74	76	64	74	78	91	90
84	93	102	88	102	79	73	74	70	66	74	74	93	90
83.57	90.10	87.33	82.83	86.97	84.63	76.17	72.87	73.67	73.03	74.93	75.67	90.98	85.69
9.63	7.33	11.67	8.78	7.35	6.37	9.66	4.60	3.02	4.55	3.44	2.62	4.78	5.23

MAP													
BIN	1 min	2 min	3 min	15 min	30min	45 min	1 HR	2 HR	4 HR	6 HR	8 HR	10 HR	ANALGESIA
101	106	102	103	107	102	97	103	90	84	89	90	91	
94	103	100	93	108	102	98	97	91	88	85	83	88	
101	114	104	107	89	97	91	97	81	83	91	87	85	
93	102	99	94	91	104	98	95	96	91	92	87	92	
95	102	91	94	111	109	105	90	88	85	90	95	88	
91	103	93	87	94	97	102	85	75	81	85	83	85	
105	113	111	104	107	96	105	95	91	90	87	89	93	
100	107	89	101	95	99	104	97	85	91	89	91	88	
88	103	94	87	102	95	99	78	83	85	82	85	84	
91	88	109	96	90	99	107	83	82	83	85	88	89	
96	99	95	97	114	107	99	80	85	89	84	85	88	
99	109	104	95	100	105	95	83	83	81	83	83	85	
81	94	91	75	104	93	100	81	85	88	91	91	88	
79	86	92	100	103	92	112	77	78	83	87	85	87	
77	105	103	84	111	100	99	73	78	83	75	83	84	
81	103	88	91	93	100	98	87	85	85	86	85	84	
88	108	110	109	89	93	85	87	87	90	92	87	90	
82	107	103	88	91	94	97	89	83	81	78	77	84	
85	98	97	85	105	94	103	87	79	84	80	81	86	
81	103	101	91	97	97	99	75	81	81	85	85	84	
101	109	110	102	108	96	107	93	81	85	86	86	88	
98	102	103	99	98	104	106	95	85	85	87	91	86	
95	117	92	103	96	96	99	85	85	84	80	83	88	
89	100	111	100	102	128	100	78	77	82	86	83	85	30 mic FENT
100	107	109	78	106	105	112	88	86	80	84	86	83	
100	102	98	85	98	103	108	76	87	91	83	83	87	
93	104	107	99	100	90	86	78	90	89	81	83	88	
88	95	102	101	98	104	98	89	83	89	89	89	88	
92	113	100	100	93	102	101	77	85	87	81	86	86	
97	103	99	105	102	115	99	84	88	82	83	88	86	
92.14	103.50	100.37	95	100	101	100	86	84	85	85	86	87	
7.72	6.93	7.02		114									

Side effects	Treatment	Hypotension
SHIVERING		74.13333333
		73.06666667
		78.93333333
Nausea		73.06666667
		81.06666667
		73.06666667
SHIVERING		76.26666667
		74.66666667
		67.73333333
		69.33333333
		66.66666667
		66.66666667
		67.73333333
		69.33333333
Nausea		65.6
		69.86666667
		73.6
		72.53333333
		71.46666667
		69.86666667
		74.4
		75.2
		76.26666667
		71.46666667
		74.66666667
		74.4
Nausea		77.86666667
		77.33333333
		72.53333333
		74.66666667
		72.78222222
		3.821573499
		0