COMPARISON OF EFFICACY OF ORAL CLONIDINE AND ORAL MIDAZOLAM AS PREMEDICATION IN CHILDREN

A STUDY OF 100 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE
BRANCH – X (ANAESTHESIOLOGY)

MARCH - 2010

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"COMPARISON OF EFFICACY OF ORAL CLONIDINE AND ORAL MIDAZOLAM AS PREMEDICATION IN CHILDREN"** a bonafide record work done by **Dr. G. ANGEL VELLUT** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch X –Anaesthesiology.

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DECLARATION

I **Dr. G. ANGEL VELLUT** solemnly declare that this dissertation titled **"COMPARISON OF EFFICACY OF ORAL CLONIDINE AND ORAL MIDAZOLAM AS PREMEDICATION IN CHILDREN"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D. degree Branch –X (Anaesthesiology) to be held in March 2010.

Place : Madurai **Dr. G. ANGEL VELLUT**

Date :

ACKNOWLEDGEMENT

I am greatly indebted to **Dr. I. Chandrasekaran,, M.D., D.A,** Professor and Head of the Department of Anaesthesiology, Madurai Medical College, Madurai for his guidance and encouragement in preparing this dissertation.

My heartful thanks to **Dr. SP. Meenakshi Sundaram, M.D., D.A,** Additional Professor of Anaesthesiology, Madurai Medical College, Madurai for his guidance in doing this work.

My sincere thanks to **Dr.S.C.GaneshPrabhu, M.D., D.A,** Additional Professor of Anaesthesiology, Madurai Medical College, Madurai for his able assistance in completing this study.

I also thank my Additional Professors**, Dr.T.Thirunavukarasu, M.D., D.A, and Dr. P. Shanmugam, M.D.,DCH.,** for their constant support and guidance in performing this study.

I also thank my Guide and Assistant Professor **Dr. C.Vairavarajan, M.D.,** and all Asst. Professors and postgraduate colleagues, Department of Anaesthesiology, for their kind cooperation for helping me in doing this study.

My profound thanks to **DEAN,** Madurai Medical College and Government Rajaji Hospital, Madurai for permitting to utilize the clinical materials of this hospital in the completion of my dissertation.

I gratefully acknowledge my patients who gave their consent and co-operation for this study.

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INTRODUCTION

I would like to give a teaspoonful of brandy, without water, a few minutes before hand, but not so much as a tablespoonful. If wine be given or if the patient must have some water in brandy then they should be given half an hour before inhaling, to allow time for absorption.

- Clover JT 1874

The practice of medicine fluctuates with time and such changes in practice have affected premedication, not only in the type and amount of premedication but even in its use also.

Preanaesthetic medication refers to the administration of drugs before the induction and maintenance of anaesthesia.

The term premedication was first used in the 1920s. The work itself just appeared in print in an article by the American Editor, Anaesthetist Frank Hoeffer Mcmechan in 1920. In paediatric anaesthesia, Midazolam is a commonly used premedicant drug world wide and clonidine an alpha 2 agonist entered into anaesthesia practice recently. So we decided to study the efficacy of Midazolam and clonidine as oral premedication in children.

AIM OF THE STUDY

To compare the clinical effects of oral Midazolam and oral clonidine as premedicant in children. The effects of premedication were assessed with regard to drug acceptance, preoperative sedation, anxiolysis, acceptance of mask for induction of anaesthesia and intravenous cannulation and recovery profile.

PREMEDICATION

The aims of premedication are

1. To allay anxiety and fear
2. To produce amnesia, sedation and analgesia
3. To facilitate rapid and smooth induction of anaesthesia
4. To reduce salivary secretions and secretion of the respiratory tract.
5. To reduce the volume of gastric contents and raise the pH for prevention of aspiration pneumonitis.
6. To minimize the undesirable effects of anaesthetic agents and surgical procedures like bradycardia and vomiting.
7. To attenuate the sympathetic nervous system reflex activities.
8. To reduce the requirement of anaesthetic agents
9. To reduce the possibility of awareness during light anaesthesia
10. To protect the patient against the toxic effects of anaesthesia.

Properties of an ideal premedicant drugs :

1. It should fulfill the aims of premedication
2. It should be easily administered
3. It should be safe for the patient
4. It should not prolong the recovery from anaesthesia
5. It should not produce undue depression of cardiovascular, respiratory and central nervous systems.

Various routes of administration of premedication :

1) Intramuscular administration

   e.g. opioids, benzodiazepines, anticholinergics, H_2 blockers

2) Intravenous administration

   e.g. opioids, benzodiazepines, anticholinergics, antiemetics

3) Oral administration

   e.g. clonidine, midazolam, triclofos, ketamine

4) Intra nasal administration

   e.g midazolam, ketamine, sufentanil

5) Rectal

   eg. Methohexital, thiopentone sodium

6) Oral transmucosal administration

   eg Midazolam, oral transmucosal fentanyl citrate (lollipop)

Depending on the time available and the action required, the route of premedication may vary from an intravenous injection given seconds before induction to oral drugs or intramuscular or subcutaneous injection given two hours preoperatively or at an appropriate time.

Choice of premedicant drugs depends on the following factors.

1. Patient, age, body weight, physical condition, psychological status.
2. Proposed Surgery: Nature of procedure, site of surgery, posture during surgery and duration of surgery.
3. Availability of preoperative and post operative nursing care
4. Surgical and anaesthetic management available.

Commonly used routes of administration of premedication drugs are intravenous, intramuscular and oral.

Oral premedication :

Advantages :

1. Most commonly employed route
2. Easiest route
3. Convenient
4. Economical
5. Very safe

Disadvantage :

1. Slow onset of action of drug
2. Irregularity in absorption in the presence of food or other drugs.
3. Reduced absorption of some drugs because of their physical characteristics.
4. Irritation of the gastro intestinal mucosa may cause emesis.
5. This route cannot be employed in an unconscious patient and uncooperative patient.

Special care is required in administering premedication in certain disease states. Drug sensitivity is increased in conditions like adreno cortical, thyroid and pituitary insufficiency, hepatic or renal dysfunction and myasthenia gravis. Porphyria is a special condition in which barbiturates cause acute exacerbation resulting in abdominal pain, vomiting, haematuria, paralysis and even respiratory failure.

Premedication in children :

The goal of the premedication in pediatric surgery is the safe induction of anaesthesia with minimum stress and risk to the child. However the pediatric patient differs from the average adult who desires mainly lack of recall (amnesia) and relief of anxiety. Children's anxiety may focus on major issues such as separation from parents, fear of needles, a concern of change in bodily image or not

awakening at end of an anaesthetic or secondarily minor issues such as taste, odour of medication and size of tablets or capsules.

Special concern in paediatric population :

1. Increase in vagal activity
2. Vomiting and aspiration
3. Secretion
4. Overdose of medication
5. Respiratory depression

Dr. Abraham Jacobi, the father of American paediatrics wrote "Paediatrics does not deal with miniature men and women, with reduced doses and same class of disease in smaller bodies, but each has its own independent range and horizon."

During administration of preanesthetic medication to child, four main principles need to be addressed.

1. Children fear needles and intensely dislike injections
2. It is essential that the anaesthesiologist deal openly and honestly with the child's fear and concerns.
3. Timing of premedication is essential.
4. Children remember past experiences and children know what they like and donot like.

Thus preanaesthetic medication and their routes of administration need to be individualized to the patient.

PHARMACOLOGY OF CLONIDINE

Clonidine is a centrally acting alpha-2 agonist commonly known as anti hypertensive. Because of its sedative, hypnotic and analgesic properties it is used in anaesthesiology.

Structure Activity Relationship

It is an imidazoline derivative related to alpha – adrenergic agonist naphazoline and antagonist tolazoline and H_1 antagonist antazoline with the properties of all these three.

It is a selective agonist for alpha2 receptor with a ratio of 200 : 1 (alpha2 : alpha 1) and it is a partial agonist. The molecular weight of clonidine is 266.56 Clonidine hydrochloride is an odourless, bitter, white, crystalline substance soluble in water and alcohol.

It was introduced in the early 1960's as a nasal decongestant. It was during its use as nasal decongestant that the antihypertensive property of the drug was found out.

PHARMACOKINETICS

It is rapidly and almost completely absorbed after oral administration and its bioavailability is nearly 100%. Peak plasma concentration is reached with in 60-90 minutes and maximal effects

are observed 1-3 hours after an oral dose. The elimination half life is between 6-24 hours (mean 12 hours) and 50% of the drug is metabolized in the liver into active metabolites while the rest is excreted unchanged by the kidney.

MECHANISM AND SITE OF ACTION

Undesirable side effect of clonidine when administered to patients with hypertension is sedation. It has been used to great advantage as premedication in anaesthesia.

Major site of action for this sedative / hypnotic drug is locus ceruleus situated in the upper brainstem in the floor of the fourth ventricle. It has major afferent connection from the rostral ventrolateral medullary nuclei. It has three important sets of efferent connections.

1. Noradrenergic fibres which connect with the sub thalamic nuclei and the thalamus with consequent effects on cortical activity.
2. Fibres to the descending reticular formation with connections to the pressor and depressor areas of vasomotor centres.
3. Descending fibers to the reticulospinal tracts which inhibits pain transmission at a spinal level.

Alpha-2 agonist hyperpolarize the neurons of locus ceruleus via potassium channels.

PHARMACO DYNAMICS

Central nervous system :

Clonidine produces sedation and anxiolysis by acting on locus ceruleus. The sedative effect is potentiated by benzodiazepines.

Anxiolysis is comparable to that produced by benzodiazepines. However in larger doses, it may produce anxiogenic responses through nonselective activation of alpha -2 receptor.

It produces a potent analgesic response involving both supraspinal and spinal sites.

Most impressive action in the central nervous system is reduced anaesthetic requirement. It reduces the minimum alveolar concentration of halothane by 20-50% in dose dependent fashion.

Clonidine can reduce intra ocular pressure by acting on imidazole preferring receptor (IPR) by reducing the production of aqueous humour.

Cerebral protective effect against cerebral ischemia results from action on imidazole preferring receptor (IPR) than alpha-2 receptor.

It decreases the cerebral blood flow.

Cardiovascular system :

Cardiovascular effects are due to peripheral and central action of clonidine.

Peripheral :

Clonidine inhibits noradrenaline release from the peripheral prejunctional nerve endings and this property, in part, contributes to the bradycardiac effects. At present, there is no evidence to support the existence of post synaptic alpha 2 receptor in the myocardium, therefore direct effect on heart is doubtful. Clonidine releases endothelial derived factor (EDRF) in coronary arteries which enhances coronary blood flow. (Cocks TM ANGUS JA 1983)

When given intravenously there will be initial transient hypertension due to stimulation of post synaptic alpha -2 receptors.

Central

Clonidine produces hypotension and bradycardia due to inhibition of sympathetic outflow and potentiation of parasympathetic activity by acting on a-2 receptor present over tractus solitarius. Other nuclei like locus ceruleus, dorsal motor nucleus of vagus, nucleus reticular lateralis and imidazole preferring receptor also play an important role in the hypotensive effect.

Respiratory system

In clinical doses clonidine produces less respiratory depression than opioids. Also there is no potentiation of opioid induced respiratory depression. In addition, nebulized clonidine attenuated bronchoconstriction in asthmatic patients.

Endocrine system

Clonidine inhibits steroidogenesis. However at clinical doses, this effect is not likely to have serious consequences. It potentiates the secretion of growth hormone. Its attenuation of stress response is mediated by the attenuation of central sympatho adrenal flow. It also inhibit the release of insulin from the pancreatic beta cells.

Gastrointestinal system

Antisialagogue effect is one advantages of the use of clonidine as premedication.

It modulates release of gastric acid via presynaptic mechanism.

It enhances salt absorption in gut mucosa. So it is useful in diarrohea due to diabetic neuropathy in particular.

Renal system

Clonidine has diuretic effect because it inhibits the release of anti diuretic hormone (ADH), antagonizes the action of anti diuretic

hormone at tubular level, increases the glomerular filtration and recently it has been identified that clonidine releases atrial natriureteric factor.

Hematological system :

It enhances the platelet aggregation. But in clinical setting, this is largely offset by the decrease in circulating catecholamines. It causes thrombocytopenia rarely.

Uses

Preanesthetic medication

Clonidine was various properties like sedation, anxiolysis, antisialogogue, potentiates the anaesthetic action of the drugs and reduces their requirements during surgery and attenuation of stress response to noxious stimuli on tracheal intubation. It is used as a pre anaesthetic medication.

It also has an anaesthesia sparing effect. Alpha-2 adrenergic agonists reduce the dose of intravenous hypnotics and also reduce the MAC of the volatile anaesthetic agents. It has been recommended in a dose of 4 ug/kg as a premedicant.

Its uses as a premedicant is particularly useful in certain subgroup of patients like

a) Drug addicts and alcoholics who exhibit withdrawal symptoms and risk of increased sympathetic activity especially in cocaine users.

b) Chronic pain and palliative care patients who often receive large doses of opiods and therefore have large perioperative opioid needs which can be reduced with clonidine premedication.

c) Hypertensive patients who are particularly vulnerable to blood pressure swings.

Other uses :

Control of Haemodynamics :

- Clonidine is used in moderate hypertension generally combined with diuretics. Higher incidence of side effects, impairment in quality of life, risk of withdrawal hypertension limit the use of clonidine as a first line antihypertensive.

To prolong the duration of Post operative analgesia and regional anaesthesia

a) Central neuraxial blocks b) Peripheral nerve blocks

Opioid withdrawal :

- Clonidine suppresses the sympathetic overactivity of opioid withdrawal syndrome and reduces craving to some extent.

Dose : 0.3 mg / kg 2 to 4 times a day

- Clonidine is also useful for alcohol withdrawal and smoking cessation. Clonidine has analgesic activity. It has been used to substitute or supplement opioid for intrathecal / epidural analgesia.
- Clonidine attenuates vasomotor symptoms of menopausal syndrome. Clonidine has been used to control diarrohea due to diabetic neuropathy.
- Clonidine suppression test for pheochromocytoma : Clonidine reduces plasma noradrenaline concentration to < 0.5 ng/ml in patients of essential hypertension but not in those with pheochromocytoma.
- Clonidine can be used as an adjunct to opioids in pain relief.
- Clonidine can be used to control tics in tourette syndrome (tics, coprolalia.)

DRUG INTERACTION :

When clonidine is given with nonselective beta blockers, hypertension increases due to unopposed alpha action leading to vasoconstriction.

Tricyclic antidepressants and chlorpromazine abolish the anti hypertensive action of clonidine probably by blocking alpha receptors on which clonidine acts.

Atropine is the treatment of choice for clonidine induced bradycardia, but it should be noted that large doses of oral clonidine 5ug/kg attenuate the effect of atropine. On the other hand, clonidine potentiate the pressor effect exerted by ephedrine.

Rebound hypertension that occurs when clonidine is stopped, is because of increase in nonadrenaline release which is inhibited by these agents owing to their agonist effect on presynaptic alpha receptor.

PHARMACOLOGY OF MIDAZOLAM

HISTORY :

It is the first clinically used water soluble benzodiazepine. Fryer and Walser synthesized it in 1976. It was the first benzodiazepine that was produced primarily for use in anaesthesia.

STRUCTURE :

Midazolam is a water soluble solution containing 1 or 5 mg / ml of midazolam with benzylalcohol as preservative. Preservative free midazolam is also available. Imidazole ring of its structure, accounts for its stability in solution, rapid metabolism and water solubility. pH of the parenteral form of midazolam is 3.5. It has pH dependent solubility i.e. if pH is more than 4 it is lipid soluble and if pH is less than 4 it is water soluble. Molecular weight of midazolam is 362.

pKa : 6.2

METABOLISM :

In liver midazolam is biotransformed to 1 and 4 hydroxy midazolam by oxidative pathway by cytochronic P 450 (cyp 3A4 enzymes). These metabolites are active ones. 1 hydroxy midazolam is the principal metabolite and has half the activity of parent compound. But these are rapidly conjugated to glucuronic acid and excreted in

urine more rapidly than midazolam. So there will be no prolonged sedation on single dose.

PHARMACOKINETICS :

Midazolam is extensively bound to plasma protein, about 95% bound to albumin.

Its volume of distribution is 1.1 - 1.7 L/kg

Elimination half life is 1.7 - 2.6 hour

Clearance is 6.4 – 11 ml / kg / min

Plasma level required for hypnosis and amnesia during surgery are 100 – 200 ng/ml

Awakening usually occurs at a level lower than 50 ng/ml.

Increasing age and obesity prolong the elimination half life.

Pharmacokinetics of Oral midazolam :

It is rapidly absorbed from gastro intestinal tract and only 50% reached the circulation reflecting substantial hepatic first pass effect.

MECHANISM OF ACTION :

Midazolam, interaction with $(GABA)_A$ BZD receptor γ subunit, causes chloride channel opening which increases chloride ion conductance which causes hyperpolarization and therefore resistance to neuronal transmission.

Various effects of benzodiazepines is related to amount of receptor occupancy which corresponds to plasma concentration.

If receptor occupancy is 20%, it causes anxiolysis

If receptor occupancy is 30-50%, it causes sedation

If receptor occupancy is > 60%, it causes unconsciousness.

PHARMACOLOGICAL ACTION :

Onset	:	Intravenous	:	30 – 60 sec
	:	Oral	:	15 – 30 min
Duration	:	Intravenous	:	30 – 60 min
	:	Oral	:	45 – 90 min

Effect on Central nervous system :

Midazolam produces sedation, anxiolysis, anticonvulsant effect, muscle relaxation and unconsciousness. These effects are dose dependent according to percentage of receptor occupancy. It produces both anterograde and retrograde amnesia, dose related reduction in cerebral blood flow and CMRO2. Its cerebral protective effect is superior to diazepam but inferior to barbiturate. Cerebral vasomotor response to CO2 is preserved. It does not prevent increases in intracranial pressure following tracheal intubation. It's a potent anticonvulsant.

Effect on respiratory system :

Midazolam produces dose related ventilatory depression which is greater than with other benzodiazepines. It is more pronounced by intravenous route following fast administration along with opioids but insignificant when given through other routes (oral).

Onset of respiratory depression is rapid within 3 minutes and the action lasts longer for even 60-120 minutes on intravenous administration.

Slope of ventilatory response curve to carbondioxide are flatter than normal.

Incidence of apnoea induction is similar as with thiopentone which is greater in old age, debilitated state, COPD patients and in presence of other respiratory depressants drugs.

Effect on cardiovascular system :

It decreases arterial pressure by decreasing systemic vascular resistance which is dose dependent and greater than with other benzodiazepines but similar to thiopentone.

It produces variability in heart rate changes because it impairs baroreceptor and also decreases the vagal tone.

Effect on Fetus :

Midazolam has less placental transfer than other benzodiazepines but produces greater neonatal depression than thiopentone and propofol.

DRUG INTERACTION :

Erythromycin inhibits the metabolism of midazolam and causes two to three fold prolongation and intensification of its effects.

Antifungal agents like itraconazole, ketaconazole increases the serum concentration of midazolam.

Calcium channel blockers inhibit cytochrome P450 enzymes leading to central nervous system depression.

Clonidine inhibits metabolism of midazolam, but it is greater with diazepam than midazolam.

Ethanol, barbiturates and other central nervous system depressant drugs potentiate the sedative effects of midazolam.

It reduces the minimum alveolar concentration of volatile agents as much as 30%.

Hepatic clearance is inhibited by fentanyl

Hepatic clearance is 5 times greater than lorazepam and 10 times greater than diazepam.

ROUTES OF ADMINISTRATION :

Commonly used route is intravenous. Other available routes are intramuscular route for sedation, oral route for premedication, intra nasal and rectal routes for premedication in children.

DOSAGE :

Oral	:	0.5 - 0.7 mg/kg
Rectum	:	0.25 – 0.5 mg/kg
Intranasal	:	0.2 – 0.5 mg / kg
Intramuscular	:	0.05 – 0.15 mg/kg
Intravenous	:	0.05 – 0.15 mg /kg
Sublingual	:	0.1 mg / kg

SIDE EFFECTS :

Major side effect is respiratory depression which is more pronounced following intravenous route and fast administration of drug along with opioids. So constant monitoring of respiration is essential.

CLINICAL USE : Premedication :

Midazolam is an useful premedicant because of various available routes of administration and its sedative anxiolytic amnestic action.

Midazolam is an useful premedicant in children, especially in the oral formulation which was approved by the US food and drug administration in 1998.

Oral route of administration in children is very popular because of its easy administration, but the problem is its bitter taste, which can be minimized by adding sugar solution.

Intravenous sedation :

Midazolam is an effective intravenous sedative for therapeutic procedures and regional anaesthesia

It is also useful in painless procedures like cardioversion and electroconvulsive therapy.

Its advantages over other benzodiazepines are : it is water soluble, has less or no venous irritation, rapid onset, short duration and less postoperative sedation.

Induction and maintenance of anaesthesia :

It is the benzodiazepine of choice as an induction agent.

Intravenous administration of midazolam in doses of 0.2 – 0.3 mg / kg over 30 – 60 sec will produce induction of anaesthesia which is 50-100% slower than with thiopentone.

It is used to supplement opioids or inhaled anaesthetics during maintenance of anaesthesia. It reduces the anesthetic requirement of halothane by 30%.

Other Uses :

Paradoxical vocal cord motion (non organic upper airway obstruction & stridor) dose : 0.5 to 1 mg iv midazolam is an effective treatment.

Treatment of grandmal seizures which occurs with systemic toxicity due to local anaesthetics.

REVIEW OF LITERATURE

PREMEDICATION IN CHILDREN : A COMPARISON OF ORAL MIDAZOLAM AND ORAL CLONIDINE

NCBI;pubmed.gov paediatric anesthesia 2007 dec 17(12)1143-9

Almenrader N. Passarietto M, Coccetti B, Halberger R, Pietropaoli P.

The aim of the study was to compare clinical effects of oral midazolam and oral clonidine.

Methods :

They performed a prospective open study in 64 children who were randomly assigned to receive either oral midazolam 0.5 mg /kg (group M) or oral clonidine 4 microg/kg (group C) prior to mask induction. Drug acceptance, preoperative sedation and anxiolysis, quality of mask acceptance, recovery profile and parental satisfaction were evaluated.

Results :

The task of oral clonidine was judged as significantly better ; 14% of children rejected oral midazolam. Onset of sedation was significantly faster after premedication with midazolam (30$\pm$13.1min) than with clonidine (38.5+/- 14.6min) but level of sedation was significantly better after premedication with clonidine. Quality of mask induction was equally successful in both groups. They observed a trend towards an increased

incidence of emergence agitation after premedication with midazolam. Parental satisfication was significantly higher in group C.

Conclusion :

In this study, premedication with oral clonidine appeared to be superior to oral midazolam. Quality of mask acceptance was comparable between groups, but oral clonidine was better accepted by this child, produced more effective preoperative sedation, showed a trend towards better recovery from anesthesia and had a higher degree of parental satisfaction.

EFFICACY OF ORAL MIDAZOLAM PREMEDICATION IN CHILDREN

Anesthesiology 1990 nov ,73(5)

Feld ,Lawrence H,Negus,Jean B,White ,Paul F

Efficacy of oral midazolam premedication in children was compared with different doses of midazolam, 0.25mg, 0.75 and placebo. It was concluded that oral midazolam 0.5 to 0.75 mg/kg is an effective premedication for children undergoing out patient surgery. Midazolam when administered orally should be mixed with a sweetener such as oral acetaminophen because it is bitter.

PREMEDICATION OF CHILDREN WITH ORAL MIDAZOLAM

Can journal of anesthesia 1992jan 29,39(6),545-550

Co Mc millan, IAspahr-Schopfer N Sikick E Hartiey

In a randomized double blind placebo controlled study, the safety and efficacy of different doses of oral midazolam 0.5, 0.75, 1mg/kg given orally as premedication in children were compared. From this study, it was concluded that Oral midazolam 0.5mg/kg is a safe and effective premedication and 0.75 and 1mg/kg doses while offering no additional benefit may cause more side effects.

ORAL MIDAZOLAM IS AN EFFECTIVE PREMEDICATION FOR CHILDREN HAVING DAY-STAY ANAESTHESIA

NCBI , PUBMED GOV.Anesthesia intensive care 1992 feb ,20(1) ,9-14

Parnis SJ,foote JA,Vander walt JH,short T,crowe CE

The effect of oral premedication was studied in a double-blind, randomised trial of 200 children undergoing day-stay anaesthesia.

The study showed that a high proportion of unsedated children are calm at induction of anaesthesia and that oral midazolam is an effective premedication in children for day-stay anaesthesia.

ORAL MIDAZOLAM IN CHILDREN: EFFECT OF TIME AND ADJUNCTIVE THERAPY

Anesthesia analgesia 1992 , 75, 51-55

B craig Weldon MD, mehernoor F watha MD,paul Fwhite Phd,MD

To determine the influence of timing and concomitant administration of atropine and/or meperidine on the perioperative effects of oral midazolam in children. It was concluded that Midazolam (0.5 mg/kg) given orally 30-45 min before induction of anesthesia is safe and effective without delaying recovery after ambulatory surgery.

EFFICACY OF ORAL CLONIDINE PREMEDICATION IN CHILDREN

Mikawa. K, Maekawa N, Nishina K, Takao Y, Yaku H, Obara H

NCBI;pubmed .gov.1993 nov ,79(5) 926-31

In a prospective, randomized, double blind controlled clinical trial, 105 children, aged 4-12 yrs undergoing elective ophthalmological surgery received 2 μg/kg or 4 μ/kg of oral clonidine or 0.4mg/kg oral diazepam given 105 min prior to induction of anaesthesia and were followed by treatment with 0.03 mg / kg oral atropine 60 min before anaesthesia. A blinded observer had noted the children's level of sedation, quality of separation from parents, and degree of acceptance of mask application during inhalation of nitrous oxide used for establishment of venous assess.

Anaesthesia was induced with 5 mg/kg thiopentone and tracheal intubation was facilitated with 0.2 mg / kg vecuronium. These data indicate that even in pediatric anaesthesia, the combination of 4 μg / kg oral clonidine and 0.03 mg/kg atropine is an effective premedication.

MIDAZOLAM AND LORAZEPAM AS PREMEDICATION. A RANDOMIZED DOUBLE-BLIND STUDY

Ncbi ,pubmed.gov 1994 june 27;156(26) 3897-900

Bredhl C,Knudsen L,stjernholm PH,mandoe H,Grevy C,Kirkengard L,Jensen S

Oral administration of midazolam and lorazepam as premedication was compared in a double-blind randomized clinical. In the general anaesthesia group midazolam caused less postoperative sedation, less postoperative amnesia and cognitive function returned more rapidly. In the spinal anaesthesia group cognitive function returned more rapidly after midazolam. It was concluded that Midazolam should be preferred for premedication if rapid recovery is desired.

ORAL CLONIDINE PREMEDICATION REDUCES VOMITING IN CHILDREN AFTER STRABISMUS SURGERY

NCBI;pubmed.gov can journal of anesthesia 1995,nov ;42(17)977-81

Katsuya Mikawa[1] ,Kahoru Nishina[1],Nobuhiro Maekawa[1],

Migiwa Asano[1] and Hidefumi Obara[1]

A prospective randomized double-blind trial was conducted to determine whether preoperative orally administered clonidine causes or potentiates postoperative vomiting in 140 children (3–12 yr) undergoing strabismus surgery. They concluded that preanaesthetic medication with clonidine 4 $\mu g \cdot kg^{-1}$ may be useful for preventing emesis following strabismus surgery. This property of clonidine indicates that it may be superior to other sedative premedicants such as diazepam and midazolam.

ORAL PREMEDICATION WITH MIDAZOLAM IN PAEDIATRIC ANAESTHESIA. EFFECTS ON SEDATION AND GASTRIC CONTENTS

Ncbi ;pubmed .gov paediatric anesthesia 1997;7(3) 191-6

Riva j,Lejbusiewicz G,papa M,Lauber C,Kohn W,dafonte M

It was suggested that Midazolam given by mouth is an efficient and safe drug for premedication in paediatric anaesthesia.

COMPARATIVE STUDY OF ORAL CLONIDINE AND DIAZEPAM AS PREMEDICANTS IN CHILDREN

NCBI;pubmed .gov international journal of anesthesiology 1997,may

75(5) 218-21

Ramesh VJ, Bhardwaj N, Batra YK (May 1997) Department of Anaesthesia, PGI, Chandigarh

In a prospective, double blind, controlled study the comparative efficacy of clonidine and diazepam as oral premedication in children, with respect to sedation, intubation response and recovery in 50 children, aged 4 – 12 years, undergoing general anaesthesia was studied. Clonidine 3 ug/kg produces sedation comparable to diazepam 0.2 mg/kg and also attenuates the intubation response without increasing the incidence of complications.

EFFECTS OF ORAL CLONIDINE PREMEDICATION ON PLASMA GLUCOSE AND LIPID HOMEOSTASIS ASSOCIATED WITH EXOGENOUS GLUCOSE INFUSION IN CHILDREN.

Nishina, K : Mikawa, K : Maekawa, N : Shiga, M : Obara, H

Anesthesiology. 1998 Apr; 88(4): 922-7

The effect of oral clonidine premedication on plasma glucose and lipid homeostasis associated with exogenous glucose infusion were investigated in children undergoing minor surgery. They concluded that Oral clonidine premedication attenuated the hyperglycemic response, probably by inhibiting the surgical stress-induced release of catecholamines and cortisol. Infusion of 2% of glucose maintained plasma glucose concentrations within physiologic ranges in children receiving clonidine.

A COMPARISON OF ORAL CLONIDINE AND ORAL MIDAZOLAM AS PREANESTHETIC MEDICATIONS IN THE PEDIATRIC TONSILLECTOMY

Anesthesia analgesia 2001,92;56-61

Lisa Fazi, MD, Ellen C. Jantzen, MD, John B. Rose, MD, C. Dean Kurth, MD, and Mehernoor F. Watcha, MD

Department of Anesthesiology and Critical Care Medicine, The University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania They compared the effects of oral clonidine (4 ug/kg) and midazolam (0.5mg/kg) on the preanesthetic sedation and postoperative recovery profile in children during tonsillectomy with or without adenoidectomy. In a double-blinded, double-dummy study design, 134 ASA physical status I-II children aged 4-12 yr were randomized to receive a combination of either clonidine and placebo (Group A), or placebo and midazolam (Group B) at 60-90 min and 30 min, respectively, before the induction of anesthesia Midazolam was superior to c1onidine as oral preanesthetic medication for these patients.

A COMPARISON OF THE ANXIOLYTIC EFFECT OF CLONIDINE AND MIDAZOLAM AS A PREMEDICATION DRUG

Frank T, Wehner M, Heinke W, Schmadicke I (Feb 2002)

NCBI ;PUBMED .gov 2002 feb 37(2) 89-93**:**

To compare the anxiolytic effect of clonidine with midazolam

50 patients (ASA I, II, III) were included in the double blinded, prospective study. These patients got an oral premedication with 1 mg flunitrazepam in the evening before surgery and 5 ug/kg clonidine or 100 ug/kg midazolam 60-90 minutes before surgery. They registered the degree of state anxiety before and after premedication. In addition to the higher up listed effects clonidine showed a anxiolytic effect which is comparable to midazolam. Therefore clonidine is an interesting alternative to benzodiazepines which are commonly used drugs for premedication.

EFFECTS OF CLONIDINE ON POSTOPERATIVE NAUSEA AND VOMITING IN BREAST CANCER SURGERY, OCTOBER 2009
NCBI ;Pubmed.gov anesthesiology 2002,may 96(5)1109-14

Sixty-eight women premedicated with midazolam were randomly allocated to coinduction with intravenous clonidine (group C) or placebo (group P) in this prospective, double-blind study. Anesthesia was standardized (laryngeal mask airway, fentanyl, propofol, sevoflurane, nitrous oxide, and oxygen). Haemodynamic parameters and the requirements for propofol, sevoflurane, and the postoperative need for ketobemidone were noted. The primary endpoints studied were the number of PONV-free patients and patient satisfaction with respect to PONV.

Coinduction with clonidine significantly increased the number of PONV-free patients after breast cancer surgery with general anesthesia.

EVALUATION OF ORAL OR RECTAL MIDAZOLAM AS CONSCIOUS SEDATION FOR PAEDIATRIC PATIENTS IN ORAL SURGERY

Military Medicine, Apr 2004 by Okcu, Kemal Murat, Guner, Aydintug, Yavuz Sinan, Gunaydin, Sencimen, Metin .

Oral (0.5 mg/kg) and rectal (0.35 mg/kg) midazolam was compared in view of acceptance of the mode of treatment and local anesthesia, level of amnesia, and adverse effects. There were significant differences between the acceptance of the oral and rectal administration of midazolam. A significantly higher number of children exhibited acceptance of the oral administration of midazolam.

ORAL CLONIDINE PREMEDICATION REDUCES MINIMUM ALVEOLAR CONCENTRATION OF SEVOFLURANE FOR LARYNGEAL MASK AIRWAY INSERTION IN CHILDREN.

Cat.inist pediatric anesthesia ISSN 1155-5645

2006 VOL 16,834-839

KAHORU NISHINA MD, KATSUYA MIKAWA MD, TAKANOBU UESUGI MD AND HIDEFUMI OBARA MD.

The aim of the study was to determine whether oral clonidine premedication can reduce MAC of sevoflurane for laryngeal mask airway insertion in children. They suggested tha**t** Oral clonidine premedication reduced the MAC (EC50) and EC95 values of sevoflurane for laryngeal mask airway insertion by 38% and 28%, respectively.

PAEDIATRIC DAY-CASE ANAESTHESIA AND PAIN CONTROL Lonnqvist, Per-Arne; Morton, Neil S, Dec 2006

Research gate scientific work ,current opinion anaethesiolgy

01/01/2007 ;19(6) 617-21.

Oral clonidine premedication, new, safer local anaesthetic agents, ultrasound guidance for blocks and prolongation of single-injection caudal blocks with clonidine or ketamine are recent developments. Guidelines for safe sedation and analgesia for procedures are available. Behavioural and cognitive changes can be seen in children after anaesthesia and surgery and parents should be informed of this possibility.

ORAL MIDAZOLAM PREMEDICATION FOR PAEDIATRIC DAY CARE PATIENTS

Pediatric anesthesia 2007,jan 30 ,6(4),265-270

SH cray MBBS FRCA,JL Dixon MBBS FRCA,C M B Heard MBBS FRCA ,SELSBY MBBS FRCA

This study was conducted to assess the efficacy of oral midazolam premedication for paediatric day case surgery

It was concluded that Oral midazolam is useful in producing calm behaviour in those children with high observer anxiety scores.

CLONIDINE REDUCES POSTOPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC GYNECOLOGICAL SURGERY

pak medi net ,Pakistan journal medical science October – Dec 2009

25(5) 782-5*:*

In this prospective double blind study, 86 patients in ASA class one or two were selected. The study group (n=43) received clonidine 0.2mg tablet with 50ml water 60–90 minutes before surgery while control group (n=43) received placebo (the tablets were made at Ahwaz Pharmaceutics Department). All patients were monitored for 24 hour post-operatively for presence of PONV. Hemodynamic changes after intubation between these groups were compared. Sedation and pain scores were also recorded during recovery using Ramsay score and by visual analogue scale respectively. Clonidine had statistically significant effect in reducing incidence of both nausea and vomiting. In addition it has favorable outcome on post operative pain score.

MATERIALS AND METHODS

A double blinded randomized study was done to evaluate the efficacy of clonidine and midazolam as an oral premedication in children.

The clinical study was carried out in 100 patients who came to Government Rajaji Hospital, Madurai for minor elective surgeries like inguinal herniorraphy, hydrocele repair, urethroplasty, orchidopexy, (approximately 30-45 minutes duration) in the year 2009. The age group of children selected for this study was 1-10 years. Only patients belonging to ASA I were chosen to avoid the influence of the associated diseases on the observation. Patients on other sedative, neuroleptic drugs, and barbiturates were also excluded from the study for fear of their possible influence on the effects of the premedicant drug. Children from both the sexes were included in the study.

Exclusion Criteria :

ASA III & IV

Children who refused to take the premedication or spit it out.

PREANAESTHETIC EVALUATION

1. History
2. Clinical examination
3. Relevant investigations : Hb%, Urinalysis, Bleeding time, Clotting time, if needed blood urea, sugar, serum creatinine.

Informed consent was obtained from the parents.

All the children were kept starved for 4-6 hours prior to surgery

The sedation on the night before surgery was avoided.

Clinical study

The anaesthetic procedure and surgery was discussed with the parents. All the children were anaesthetized in the sequence of preoxygenation, induction with thiopentone and atropine, intubation by using succinylcholine and maintenance with oxygen, nitrous oxide, analgesics and nondepolarizers. Neuromuscular blockade was reversed at the end of the procedure with injection neostigmine and atropine.

The children were divided into two groups randomly as per premedication given

Group I - Clonidine 4 µg/kg body weight, 45 minutes prior to surgery

Group II - Midazolam 0.5mg/kg body weight 30 minutes before surgery

In Group - I (Clonidine) :

Clonidine is available as a tablet, in the strength of 100 µg/tab. In our study we made clonidine into powder, dissolved in water and gave to the patients in the dose of 4µg/kg, 45 minutes prior to surgery. 100µg/ tablet was dissolved in 10ml of water and the dose calculated as per weight of children was given through mouth after getting consent from the older children and from the mother of smaller children.

In Group II (Midazolam) :

As per British Pharmacopeia, Midazolam is practically insoluble in water and freely soluble in acetone, ethanol and methanol. Preservative free parenteral form of midazolam in the strength of 5 mg/ml in dose of 0.5mg/kg was given orally 30 minutes prior to surgery.

In our study none of the children vomited or spit out the drug during administration.

The reaction to drug administration was evaluated.

Scores :

1. Crying

2. Not crying.

After 45 minutes in Group I and after 30 minutes in Group II sedation level was graded by evaluating the child's appearance with the help of three point sedation score described as below.

Sedation Score :

1- awake,

2- drowsy,

3 – asleep

After that, anxiety or emotional state of children while separating from mother, was assessed by using four point anxiety score described as below.

Anxiety Score :

1. Crying
2. Anxious
3. Calm, but not cooperative
4. Calm, cooperative or asleep

Then we also observed the level of anxiety on application of mask (acceptance of mask), graded by using the following scores.

Mask acceptance :

1. Combative crying
2. Moderate fear of mask
3. Cooperative with assurance
4. Calm, cooperative
5. Asleep

In all children prior to induction preoxygenation was done for 3 minutes through face mask. The child's acceptance of mask was recorded. Mask acceptance scores of 3,4,5 were regarded as successful response to premedication. Then intravenous cannulation was done and response to intravenous cannulation was recorded.

Reaction to intravenous cannulation :

1. Crying
2. Withdrawal of hand
3. Grimace
4. No response

After intravenous cannulation injection atropine 0.02 mg/kg was given intravenously and patient induced with injection thiopentone

2.5% 5mg/kg followed by injection succinylcholine 2 mg / kg given to facilitate tracheal intubation. Patient was maintained with oxygen, nitrous oxide, analgesic and nondepolarizers. At the end of surgery neuromuscular blockade was reversed with injection neostigmine and injection atropine in titrated doses. Any side effects in the perioperative period were noted.

Thirty minutes after, the child's level of agitation was assessed according to a 3 point scale.

Post operative Agitation :

1. Agitated, crying
2. Crying but easily consoled
3. Calm or asleep

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Statistical Programme for Scientific Student (SPSS 16^{th} version).

Using this software, frequencies, percentage, range, mean, standard deviation, x^2 and 'p' values were calculated. Kruskul Wallis chi square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATION AND RESULTS

Table -1 pH of drugs

Group	pH
Clonidine solution	6.5
Midazolam	3.5

pH was measured by using Merck pH indicator paper and confirmed by pH meter.

pH of these drugs were more than 2.5 Lung damage after aspiration of gastric contents does not occur (Teabeut et al).

Table -2 Demographic profile of the patients

Criteria	Clonidine Group I	Midazolam Group II	Test of Significance p value
Age (Yrs)	5.040	4.72	0.580
Sex (M/F)	44 / 6	45 /5	0.749
Weight (kg)	16.3	17.16	

Significance of 't' test 0.580 = insignificant

Significance by chi square 0.749 = insignificant

All groups were comparable in age, sex and weight

Table –3 Comparison of Surgeries underwent

Surgery underwent	Group		Total
	Clonidine Group	Midazolam group	
Circumcision	5	3	8
Excision of processes	8	13	21
Herniotomy	24	20	44
Orchidopexy	3	5	8
Urethroplasty	9	8	17
Ureterolithotomy	0	1	1
Others	1	0	1
Total	50	50	100

Chi square test is in significant (p= 0.692)

Both the groups are comparable by type of surgery

Table –4 Reaction to Drug Administration

Count		Group		Total
		Clonidine group	Midazolam group	
Reaction to Drug Administration	Crying	28	26	54
	Not crying	22	24	46
Total		50	50	100

Table -5 intensity of sedation

Score	Grade	Clonidine Group I	Midazolam Group II
1	Awake	5	23
2	Drowsy	40	26
3	Asleep	5	1

Mean value for clonidine group is 2.0 ± 0.452.

Mean value for midazolam is 1.56 ± 0.541

Students 't' test is Highly significant ($p=0.000$)

So, the clonidine group has better score than midazolam group

Table –6 anxiety level on separation from mother

Score	Grade	Clonidine Group I	Midazolam Group II
1	Crying	0	14
2	Anxious	5	21
3	Calm, Uncooperative	21	14
4	Calm, co operative/ asleep	24	1

Mean value for Clonidine group - 3.38 + 0.69

Mean value for Midazolam group - 2.04 + 0.8

Students 't' test is highly significant (p= 0.000)

So, the clonidine group has better score than midazolam group

Table –7 anxiety level on acceptance of mask

Score	Grade	Clonidine Group I	Midazolam Group II
1.	Combative / crying	9	28
2.	Moderate fear of mask	17	18
3.	Cooperative on assurance	14	4
4.	Calm / cooperative	10	0

Mean / S.D value for Clonidine group - 2.5 / 1.015

Mean value for Midazolam group - 1.52 / 0.646

Student 't' test is highly significant (p= 0.000)

So, the clonidine group has better score than midazolam group

Table –8 Reaction to intravenous cannulation

Score	Grade	Clonidine Group I	Midazolam Group II
1.	Crying	3	24
2.	Withdrawal of hand	21	23
3.	Grimace	26	3

Mean value for Clonidine group - 2.46 + 0.61

Mean value for Midazolam group - 1.58 + 0.609

Student 't' test is Highly significant (p= 0.000)

So, the clonidine group has better score than midazolam group

Table –9 - Post operative status

Score	Grade	Clonidine Group I	Midazolam Group II
1.	Agitated / crying	6	13
2.	Crying, Consolable	12	34
3.	Calm / asleep	32	3

Mean value for Clonidine group - 2.5 + 0.71

Mean value for Midazolam group - 1.8 + 0.54

Students 't' test is Highly significant (p= 0.000)

So, the clonidine group has better score than midazolam group

DISCUSSION

In this study we compared the efficacy of clonidine, midazolam as oral premedicants in children.

In preanaesthetic days both wine and opium were given to mitigate the terror of surgery. Claude Bernard observed that use of morphine before chloroform in a dog resulted in achieving anaesthesia in a smooth, rapid manner and with lesser dosage of chloroform. Ever since the realization of the importance of giving drugs before the induction of anesthesia, the search for an ideal premedicant has been going on.

Anaesthesia and surgery constitute great psychic stress in any patient. The overall frequency of anxiety before anaesthesia is 40 – 60% in older children (Norris and Davis 1967). Using an extensive psychological questionnaire as many as 80% of patients were found to be anxious (Corman et al 1958). A greater frequency has been found in females than in males.

Premedication was considered necessary in children. A pilot study using unpremedicated patients resulted in an unaccepted frequency of vaso vagal attacks following lumbar puncture. The pilot study shows that premedicated children show better value of arterial

oxygen saturation than unpremedicated anxious and apprehensive children. A positive correlation between anxiolysis and ease of induction of anaesthesia has been reported (Lindgren, Saarni Vaara, Himberg 1980) which support the importance of the anxiolytic components of premedication. Relief of apprehension may reduce excessive hormonal and circulatory responses to anaesthesia and may reduce the minimum effective dose of anaesthetic agents (Male et al 1980). Sedation has been considered an useful property of premedicant drug (Collins 1976).

In our study we used powder form of clonidine which was dissolved in water and given to the patient, since clonidine is available as uncoated non dispersible tablet.

The pH of reconstituted clonidine solution is 6.5, which is more than conservative pH limit of 2.5 thought to promote lung damage after aspiration of gastric contents. (Teebeut et al).

All the children accepted the drug very well without spitting (or) vomiting. Mikawa et al compared the two doses of oral clonidine (2μg and 4 μg) and concluded that 4 μg/kg is an effective dose for premedication. So we decided to use 4 μg/kg of clonidine in our study.

According to British Pharmacopeia, midazolam is practically insoluble in water, freely soluble in acetone, ethanol and methanol.

In our study we used parenteral form of preservative free midazolam in the strength of 5 mg/ml in the dose of 0.5 mg/kg.

Mcmillan et al compared different doses of midazolam (0.5mg, 0.75mg and 1 mg/kg) and used the parenteral form of midazolam and concluded that 0.5mg/kg is safe and effective premedication. So we decided to use parenteral form of 0.5mg/kg.

In our study, we decided not to administer oral atropine along with test drug because it also imparts bitter taste and delays gastric emptying. So we decided to give atropine 0.02 mg/kg intravenously just prior to intravenous thiopentone which is also useful in preventing clonidine induced bradycardia during intra operative period.

Nicole Almenrader et al performed a prospective open study in 64 children who were randomly assigned to receive either oral midazolam 0.5 mg / kg or oral clonidine 4µg/kg as premedication. This study demonstrates clinical advantages of oral clonidine, in both the preoperative period and during recovery compared with oral midazolam. Clonidine produced effective sedation in 100% of

patients in their study population. In their study higher sedation scores were achieved after clonidine premedication as 90% of children were asleep before mask induction compared with only 10% after midazolam administration. Clonidine causes sedation similar to natural sleep where the patient can be easily aroused to perform cognitive tests. This effect is thought to result from inhibition of spontaneous and evoked activity of central monoaminergic systems involved in modulation of sleep and cortical arousal.

In our study, 90% of the patients in clonidine group has sedation scores of 2 and 3 compared to 54% of patients in midazolam group of the same scores.

In our study, regarding anxiety level on separation from parents, 48% of patients in the clonidine group are calm/cooperative but only 2% of patients in the midazolam group are calm / cooperative.

In our study, level of mask acceptance when compared 48% of patients in clonidine are cooperative and only 8% of patients in the midazolam group were cooperative.

On comparing response to intravenous cannulation, In our study 48% of patients in midazolam group are crying but only 6% of patients in clonidine are crying.

52% of clonidine group showed only grimace to intravenous cannulation but only 6% of the patients in midazolam group has grimace.

In their study, emergence from anesthesia was comparable within the two groups (p=0.13). There was a trend towards an increased incidence of emergence agitation in midazolam group compared with clonidine group.(p=0.04).

In our study, the postoperative agitation is higher in midazolam group compared to clonidine group. 64% of patients in clonidine group are calm / asleep while only 6% of the patients in midazolam group are calm / asleep.

SUMMARY

In summary we found that both the test drugs produced significant sedation, clonidine produced better sedation than midazolam. Both the drugs provided statistically significant reduction of anxiety level on intravenous cannulation. Children accepted the technique well and parents were satisfied with the outcome. We were able to use this technique effectively in a busy government hospital with the co-operation of our nurses in the preoperative area.

CONCLUSION

It was concluded from this study that oral clonidine and midazolam can be used as better premedicants to produce optimal sedation and emotional state.

Clonidine 4 μg / kg has been shown to be a more effective premedication for children undergoing elective surgeries than midazolam 0.5mg / kg.

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PROFORMA

Name : Age : Sex : IP No.:

Weight :

Case : Plan :

ASA Risk:

Pre-medication Drug : Dose :

Reaction to Drug Administration :

Score	Reaction
1	Crying
2	Not crying

Sedation Score :

Score	Sedation level
1	Awake
2	Drowsy
3	Asleep

Anxiety Score :

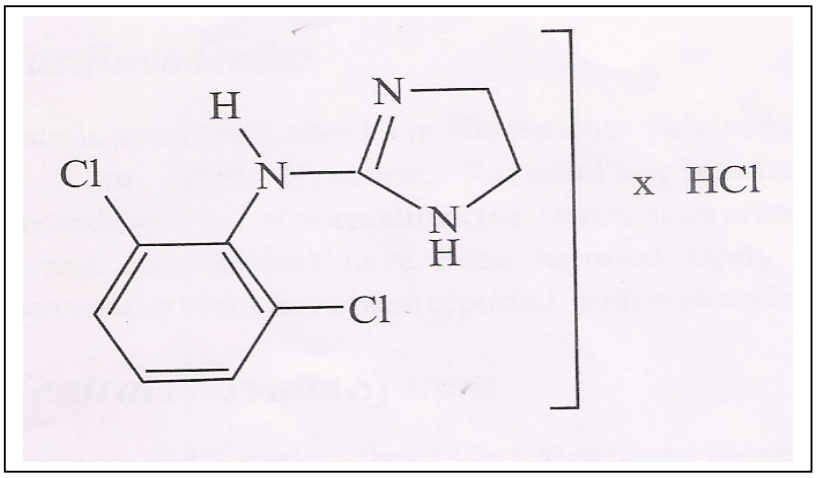
Score	Anxiety level
1	Crying
2	Anxious
3	Calm, uncooperative
4	Calm, cooperative / asleep

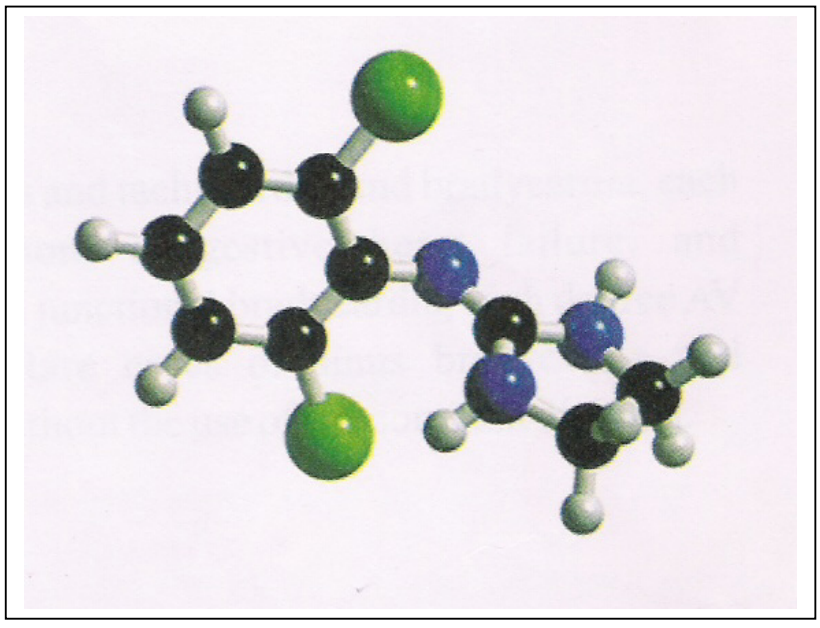
Mask Acceptance :

Score	
1	Combative / crying
2	Moderate fear of mask
3	Cooperative on assurance
4	Calm / cooperative

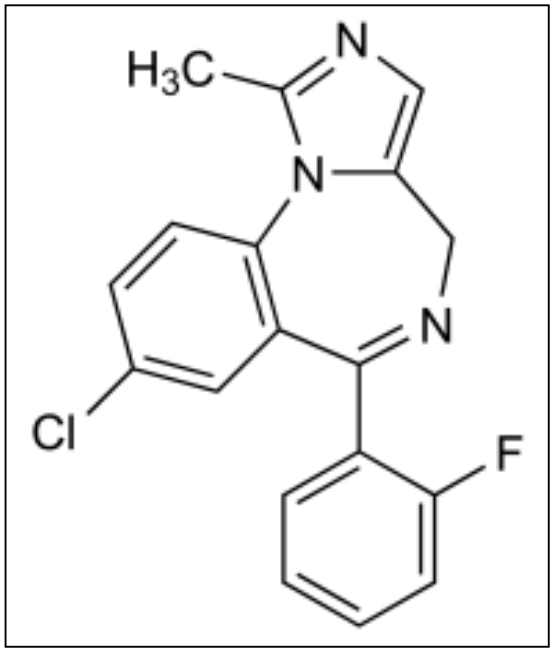
Intravenous cannulation	
Post operative status	

CLONIDINE HYDROCHLORIDE

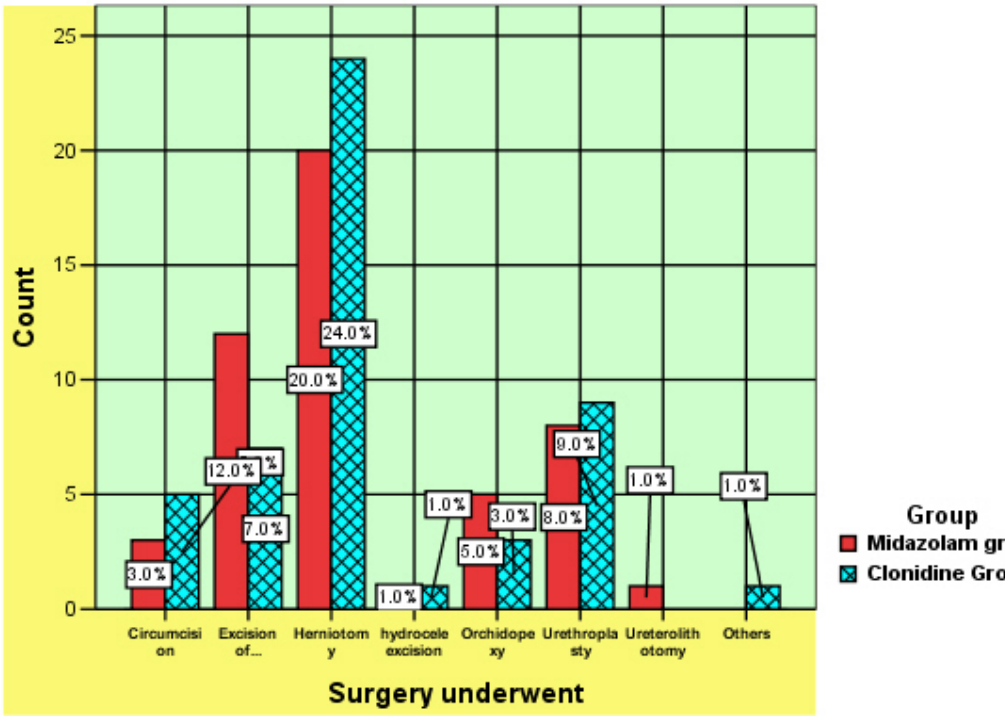




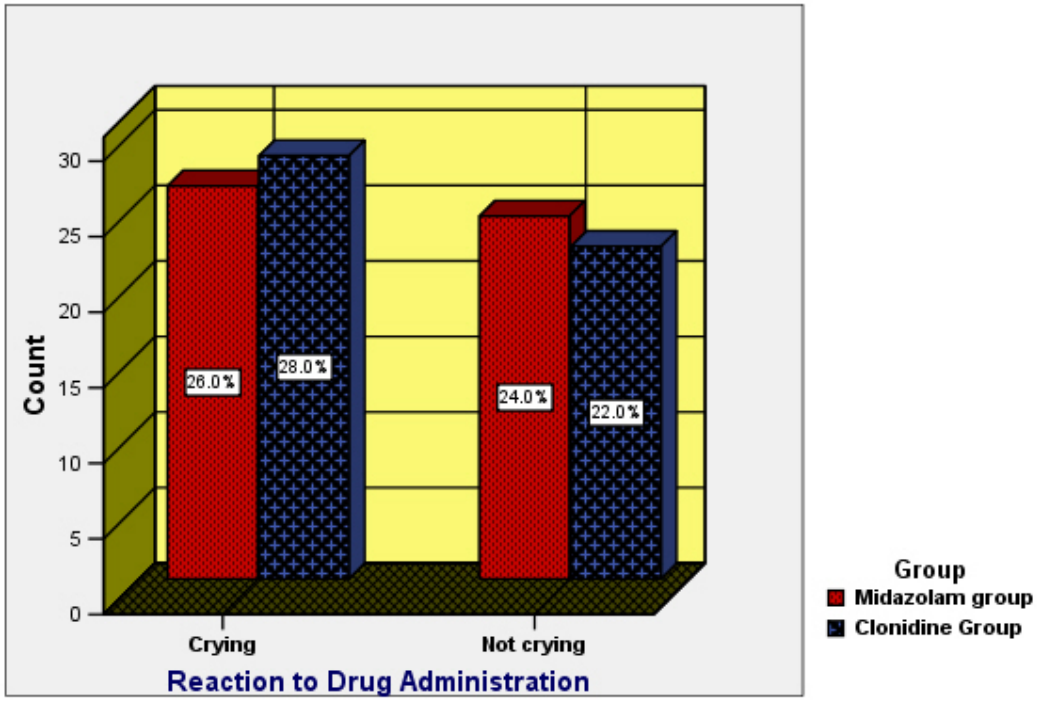
MIDAZOLAM



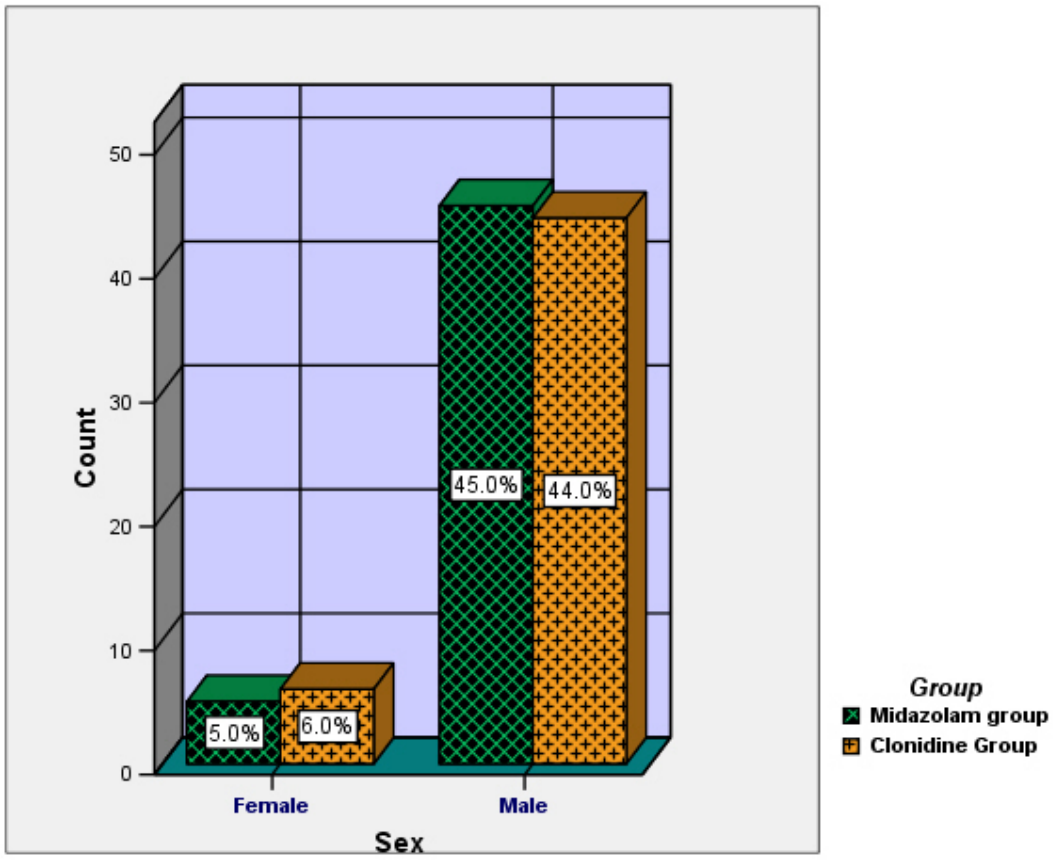
COMPARISION OF SURGERIES UNDERWENT



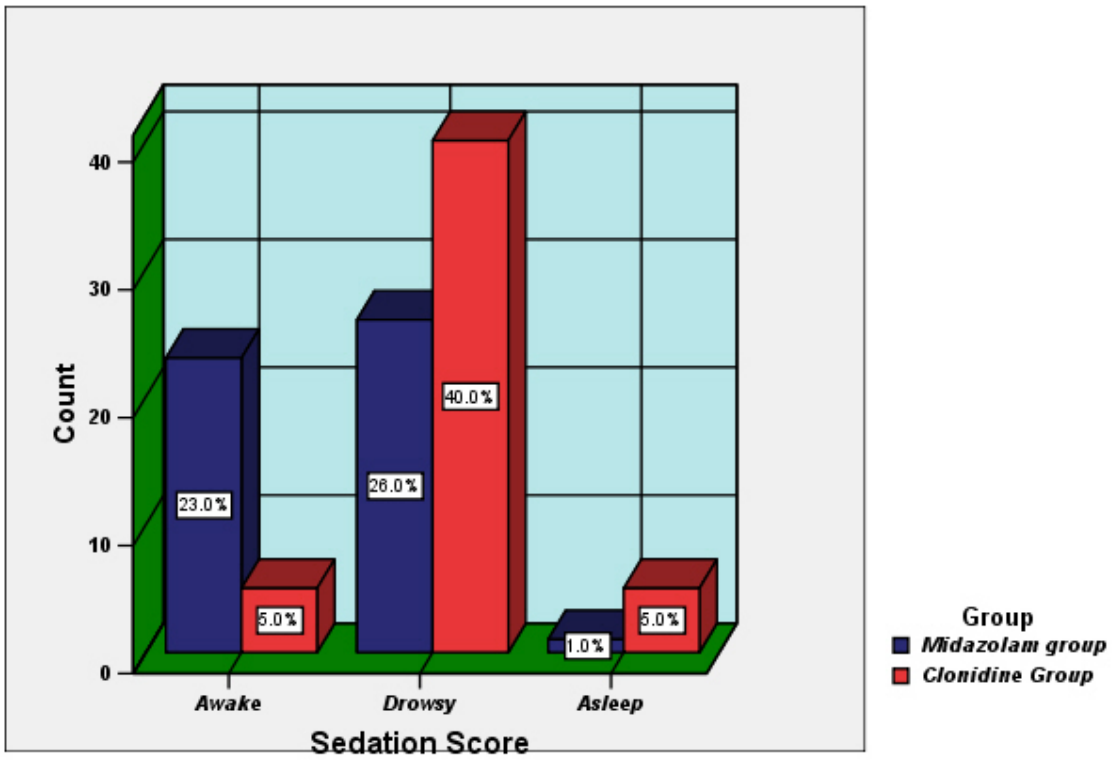
REACTION TO DRUG ADMINISTRATION



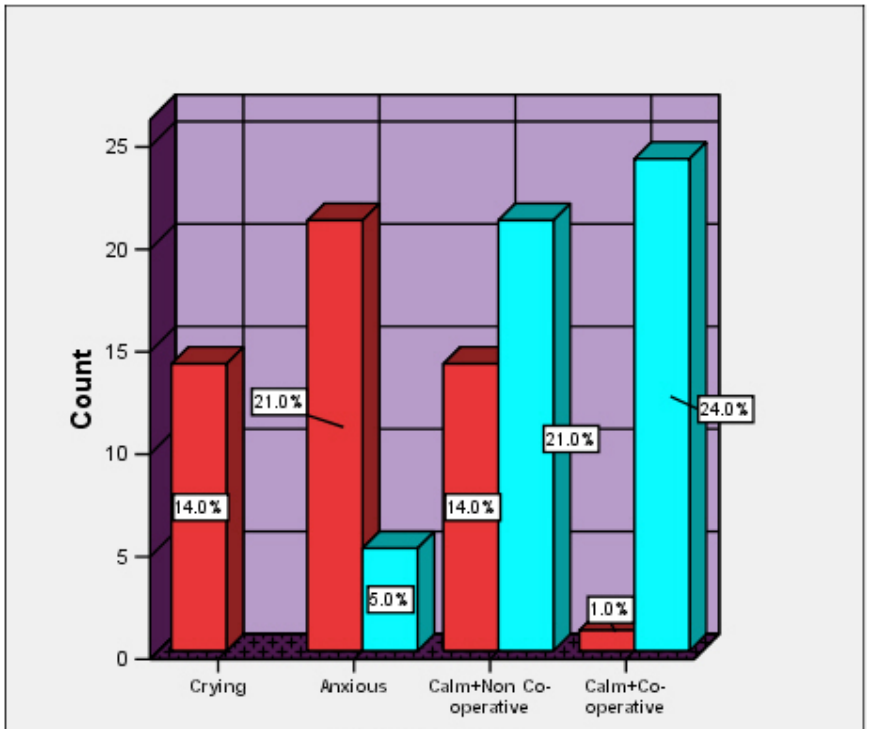
Demographic Profile



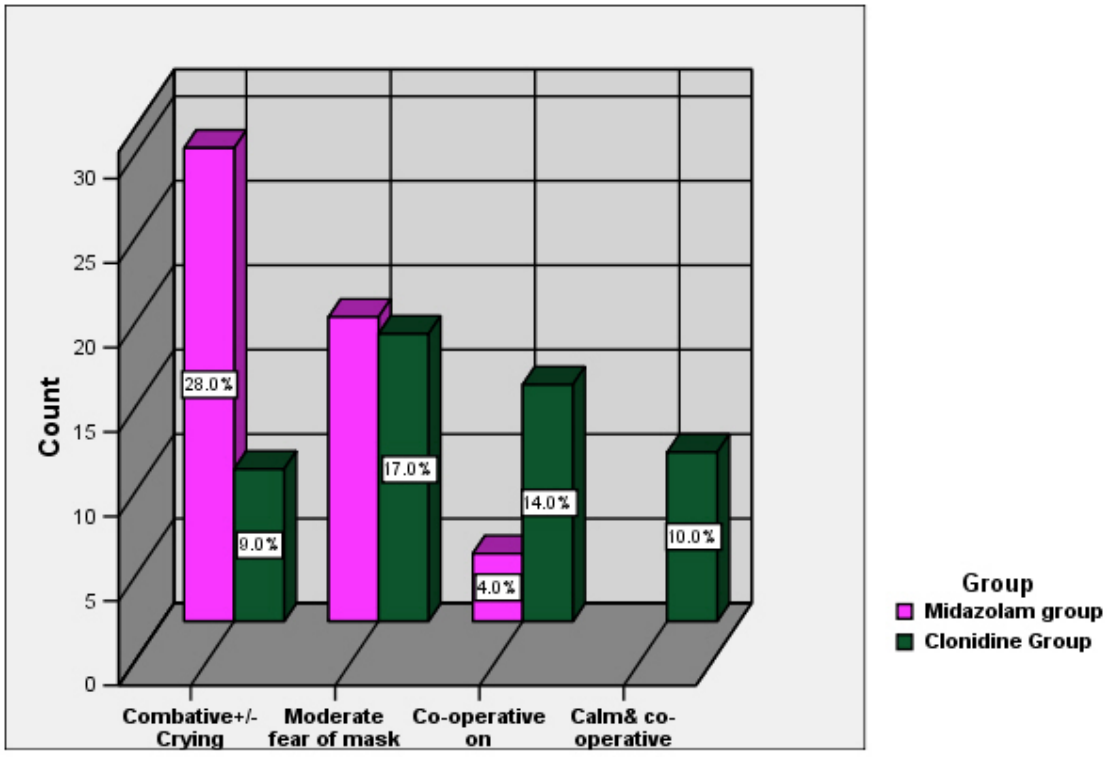
Distribution of sedation scores



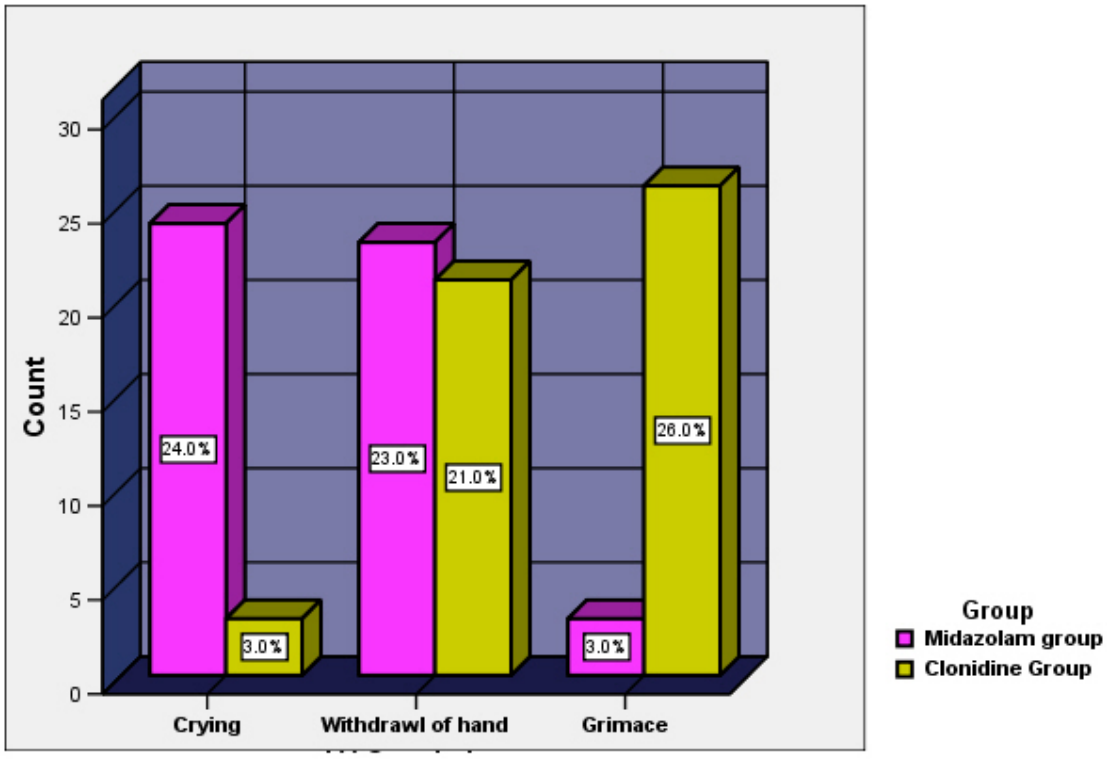
Distribution of Anxiety Score



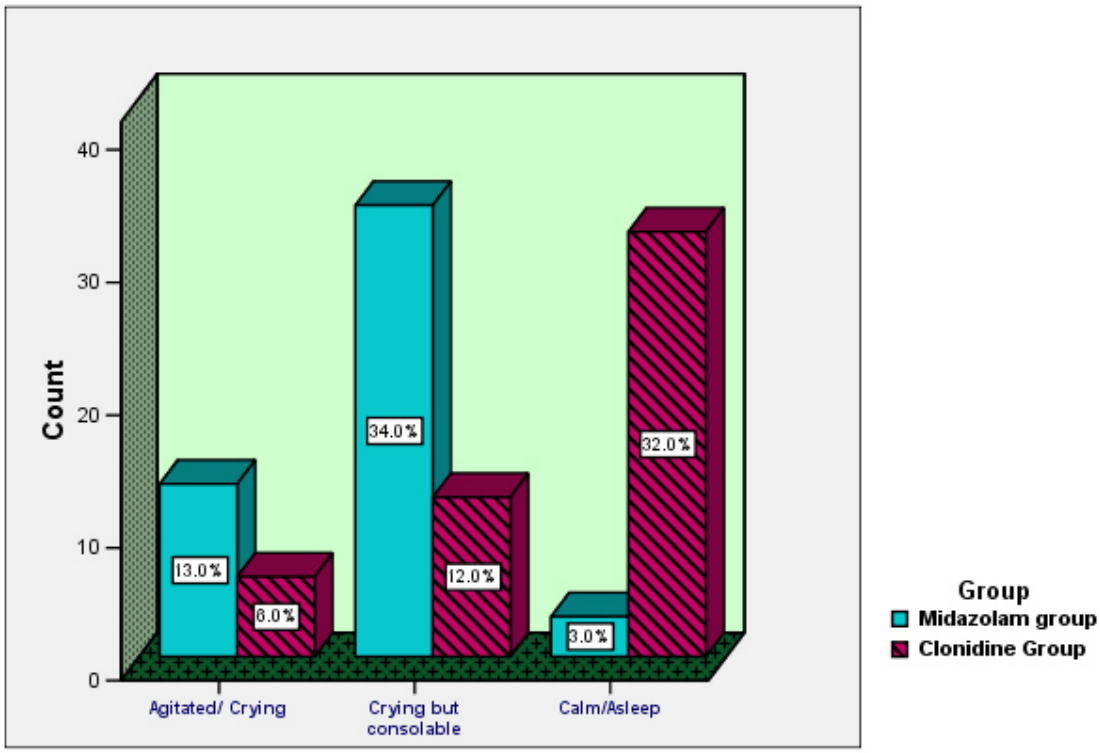
Evaluation of Mask Acceptance



Reaction to IV Canulation



Post operative status



GROUP -2 MIDAZOLAM

Sno	Name	Age	Sex	Weight	Operation	Reaction to drug	Level of Sedation	Level of anxeity	Reaction to IV cannula	Mask acceptance	Post operative status
1	jeyaraj	10	Male	27	Herniotomy	2	1	1	1	1	3
2	kailash	3	Male	8	Herniotomy	1	2	3	2	2	2
3	sulthan	2	Male	8	Orchidopexy	1	2	3	2	2	2
4	venugopal	2	Male	9	Circumcision	1	2	2	2	1	2
5	harish	6	Male	14	Herniotomy	2	1	2	2	1	3
6	pal pandi	3	Male	10	Excision of processes	1	1	1	1	1	2
7	dinesh	2	Male	9	Excision of processes	1	1	1	1	1	1
8	ragavendaran	6	Male	15	Urethroplasty	2	1	2	1	1	2
9	veerananan	7	Male	20	Excision of processes	2	1	1	1	1	2
10	yogesh	2	Male	9	Circumcision	1	1	3	2	2	2
11	vishwa	3	Male	10	Circumcision	1	1	2	1	1	2
12	vishal	3	Male	9	Orchidopexy	1	2	2	2	2	1
13	sundhara pandi	6	Male	16	Urethroplasty	2	2	2	2	2	3
14	dinesh	2	Male	8	Herniotomy	1	2	2	2	2	2
15	muralidharan	3	Male	9	Herniotomy	1	2	3	1	3	2
16	sowmya	10	Female	25	Ureterolithotomy	2	2	3	2	3	2
17	mariraja	7	Male	18	Urethroplasty	2	1	1	1	1	1
18	lakshmi	8	Female	18	Ureterolithotomy	2	2	2	2	2	2
19	radhika	4	Female	12	Ureterolithotomy	1	1	1	1	1	2
20	manoj kumar	5	Male	14	Excision of processes	2	1	2	1	2	2
21	hemalatha	5	Female	15	Ureterolithotomy	1	1	1	1	1	1
22	ranjithkumar	2	Male	8	Urethroplasty	1	2	2	1	1	1
23	muniyandi	3	Male	10	Herniotomy	1	2	1	1	2	2
24	sanjay	5	Male	14	Excision of processes	2	2	1	1	1	2

25	hari krishnan	6	Male	16	Orchidopexy	2	1	2	2	1	2
26	sreekanth	5	Male	12	Herniotomy	2	1	1	2	1	2
27	naval khan	3	Male	9	Excision of processes	1	2	2	2	1	1
28	jeyaseelan	2	Male	8	Urethroplasty	1	2	2	2	2	2
29	ram gowtham	4	Male	15	Urethroplasty	2	2	1	1	1	1
30	rafeeq md	3	Male	13	Excision of processes	1	2	3	1	1	2
31	raveendran	2	Male	8	Excision of processes	1	2	3	1	1	2
32	kandhaselvam	2	Male	8	Urethroplasty	1	2	3	2	2	1
33	nandhakumar	8	Male	17	Excision of processes	2	1	2	2	1	2
34	mahathi kumar	2	Male	9	Excision of processes	1	1	2	1	1	2
35	pandi	8	Male	24	Herniotomy	2	2	1	1	1	2
36	vignesh	3	Male	11	Excision of processes	2	2	3	2	2	2
37	praveen kumar	2	Male	9	hydrocele excision	1	2	2	1	1	1
38	harish	3	Male	12	Herniotomy	1	2	2	2	1	1
39	vasanthan	2	Male	10	Herniotomy	1	1	1	1	1	2
40	ganesan	7	Male	20	Herniotomy	2	1	1	1	1	1
41	md asir	12	Male	20	Urethroplasty	2	1	2	2	2	2
42	manoj	4	Male	14	Herniotomy	2	1	2	2	2	1
43	ambalam	7	Male	20	Herniotomy	2	2	2	2	2	2
44	prakash	5	Male	15	Herniotomy	1	2	3	1	3	2
45	akash raj	2	Male	8	Herniotomy	1	2	3	2	2	2
46	deepika	5	Female	14	Herniotomy	2	1	3	3	1	2
47	neethish	2	Male	8	Herniotomy	1	1	3	2	3	2
48	rajamohan	11	Male	13	Herniotomy	2	2	2	3	2	1
49	dileep	6	Male	16	Orchidopexy	2	3	4	3	2	2
50	albert	11	Male	36	Herniotomy	2	1	3	1	1	2

MASTER CHART

					GROUP -1 CLONIDINE						
Sno	Name	Age	Sex	Weight	Operation	Reaction to drug	Level of Sedation	Level of anxeity	Reaction to IV cannula	Mask acceptance	Post operative status
1	bharath	11	Male	28	Herniotomy	2	2	4	3	4	3
2	sudheer	6	Male	16	Herniotomy	2	2	4	3	3	3
3	thirumalai	10	Male	22	Circumcision	2	2	4	2	4	2
4	satheesh kumar	6	Male	18	Circumcision	2	2	3	3	3	3
5	siva prakash	7	Male	20	Circumcision	2	2	3	2	2	3
6	anand kumar	6	Male	15	Urethroplasty	2	2	3	2	2	2
7	vignesh	5	Male	13	hydrocele excision	1	3	4	3	4	3
8	karthik	5	Male	14	Orchidopexy	1	3	4	3	4	3
9	saravanan	5	Male	14	Herniotomy	2	2	3	2	3	3
10	bharath kumar	2	Male	9	Herniotomy	1	3	3	1	2	2
11	sweetha	10	Female	25	Herniotomy	2	2	3	3	2	3
12	velmurugan	4	Male	12	Orchidopexy	1	2	3	2	2	3
13	senthil kumar	2	Male	9	Excision of processes	1	2	4	3	4	3
14	viha moorthy	7	Male	18	Circumcision	1	1	2	2	1	1
15	veeramani	8	Male	20	Circumcision	2	1	2	2	1	2
16	iyappan	7	Male	16	Herniotomy	2	2	3	2	2	1
17	ammai appan	2	Male	8	Herniotomy	1	2	4	3	4	3
18	rajkumar	10	Male	24	Urethroplasty	2	2	3	3	2	3
19	chella pandi	10	Male	26	Urethroplasty	2	2	3	2	1	3
20	rogesh	2	Male	8	Excision of processes	1	2	4	3	4	3
21	sankariah	9	Male	28	Excision of processes	2	1	3	3	2	3
22	praveen kumar	3	Male	10	Urethroplasty	1	2	4	2	4	3
23	aravindhan	3	Male	11	Excision of processes	1	2	4	3	4	2

24	meenakshi	2	Female	9	Herniotomy	1	2	4	3	3	3
25	dhanin	2	Male	10	Herniotomy	1	2	4	3	4	1
26	deepak raja	10	Male	30	Herniotomy	2	2	2	2	1	3
27	naveen	5	Male	14	Herniotomy	2	2	2	3	2	1
28	gopala krishnan	2	Male	9	Urethroplasty	1	2	3	3	2	1
29	pavithra	3	Female	11	Others	1	2	4	2	3	2
30	sundharapandi	2	Male	10	Herniotomy	2	1	2	3	1	2
31	kishore kumar	2	Male	8	Excision of processes	1	2	4	2	3	2
32	muruganandham	2	Male	8	Herniotomy	1	2	4	3	3	3
33	gowri	3	Female	12	Urethroplasty	1	2	4	3	3	3
34	nageshwaran	7	Male	14	Urethroplasty	2	2	4	2	2	3
35	hari das	3	Male	11	Herniotomy	1	2	3	3	2	3
36	mugilan	4	Male	10	Herniotomy	2	3	3	2	1	2
37	karthikeyan	2	Male	10	Excision of processes	1	2	4	3	3	3
38	arjun	2	Male	10	Excision of processes	1	3	3	1	2	3
39	mari vignesh	6	Male	20	Herniotomy	2	2	3	3	1	3
40	raja	10	Male	23	Herniotomy	2	2	3	2	2	3
41	bharath	3	Male	10	Urethroplasty	1	2	4	3	3	3
42	naga nikila	6	Female	14	Herniotomy	1	2	3	2	2	2
43	sabari	3	Male	8	Herniotomy	1	2	4	3	3	3
44	raja shreeman	3	Male	10	Herniotomy	1	2	4	3	3	3
45	rangaswami	11	Male	26	Herniotomy	2	2	3	2	2	3
46	yogalakshmi	5	Female	16	Herniotomy	1	2	4	3	3	2
47	manzoor rehman	4	Male	12	Orchidopexy	1	1	3	2	2	1
48	anbuselvam	6	Male	15	Herniotomy	2	2	4	2	3	2
49	sanjay	2	Male	10	Urethroplasty	1	2	4	1	1	3
50	sudharshan	2	Male	10	Herniotomy	1	2	3	2	1	3