"NEONATAL OUTCOME USING KETAMINE AS A PRE SPINAL AGENT IN CAESAREAN SECTION - A HOSPITAL BASED RANDOMIZED CONTROL TRIAL"

By

DR.ISSAC VARGHESE

Dissertation submitted to the

BLDE UNIVERSITY, BIJAPUR

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

PEDIATRICS

UNDER THE GUIDANCE OF

DR.R.H.GOBBUR **MD, DCH**

PROFESSOR

DEPARTMENT OF PEDIATRICS

B.L.D.E U'S SHRI B.M.PATIL MEDICAL COLLEGE AND HOSPITAL

BIJAPUR - 586103

2014-15

DECLARATION BY THE CANDIDATE

I here by declare that this dissertation entitled **"NEONATAL OUTCOME USING KETAMINE AS A PRE SPINAL AGENT IN CAESAREAN SECTION - A HOSPITAL BASED RANDOMIZED CONTROL TRIAL**" is a bonafide and genuine research work carried out by me under the guidance of Dr.R.H.GOBBUR MD DCH, Professor, Department of Pediatrics, BLDE University's Shri.B.M.Patil Medical College Hospital and Research Centre, Bijapur.

Date: Dr. Issac Varghese
Place:Bijapur

BLDE UNIVERSITY

BIJAPUR

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"NEONATAL OUTCOME USING KETAMINE AS A PRE SPINAL AGENT IN CAESAREAN SECTION-A HOSPITAL BASED RANDOMIZED CONTROL TRIAL"** is a bonafide research work done by **Dr. Issac Varghese** in the partial fulfillment of the requirement for the degree of M.D. in Pediatrics.

Date:
Place: Bijapur

Dr. R.H.GOBBUR MD,DCH
Professor
Department of Pediatrics
B.L.D.E.A's Shri B.M.Patil
Medical College Hospital &
Research Centre,
Bijapur-586103

BLDE UNIVERSITY

BIJAPUR

ENDORSEMENT BY THE HOD AND PRINCIPAL

This is to certify that the dissertation entitled **"NEONATAL OUTCOME USING KETAMINE AS A PRE SPINAL AGENT IN CAESAREAN SECTION-A HOSPITAL BASED RANDOMIZED CONTROL TRIAL"** is a bonafide research work done by **Dr. Issac Varghese** under the guidance of **Dr.R.H.GOBBUR$_{MD,DCH}$** Professor, Department of Pediatrics, BLDE University's Shri.B.M.Patil Medical College Hospital and Research Centre, Bijapur.

Dr.S.V.Patil $_{MD}$
Professor & Head
Department of Pediatrics
B.L.D.E.A's Shri B.M.Patil
Medical College Hospital &
Research Centre , Bijapur-586103,
Date:
Place: Bijapur

Dr.M.S.Biradar $_{MD}$
Principal,
B.L.D.E.A's
Shri B.M.Patil Medical
College Hospital & Research
Centre, Bijapur - 586103.
Date:
Place:Bijapur

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the B.L.D.E.U'S Shri B M PATIL Medical College, Hospital and Research centre, Bijapur, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic/research purpose.

Date: **Dr .Issac Varghese**
Place: Bijapur

ACKNOWLEDGEMENT

I find my words inadequate to express my most humble and profound gratitude to my eminent and esteemed teacher and guide ***Dr.R.H.Gobbur*** ***MD,DCH*** *Professor , department of Pediatrics, Shri B M Patil Medical, Bijapur. His never ending willingness to render help, guidance and encouragement coupled with his rich knowledge and keen interest were a constant source of inspiration .*

I am extremely grateful to my eminent and esteemed teacher ***Dr.S.V.Patil*** ***MD*** ***,****Professor and head of the Department, Pediatrics for his overall guidance and Inspiration without which this would not have seen the light of the day. I am grateful to him for what I have learnt from him and for his kind support.*

I specially thank my co-guide ***Dr Vijaykumar .T. Kalyanappagol*** ***MD*** *, Professor , Department of Anaesthesia for his continued support ,inspiration and help in all the steps of my research.*

I sincerely thank my learned teachers and greatly thankful to my true teachers ***Dr.A.S.Akki*** ***MD,DCH*** *Professor,* ***Dr.S.S.Kalyanshettar*** ***MD*** *Professor,* ***Dr M.M.Patil*** ***MD*** ***,****Associate Professor, Department of Pediatrics, Shri B M*

Patil Medical College, Bijapur fortheir timely suggestions and willingness to help all the time and making me understand the real Pediatrics.

I sincerely thank my ***fellow postgraduates*** *and* ***friends*** *for their support and cooperation. My sincere thanks to all* ***nursing staff*** *of department of pediatrics, Shri B .M .Patil Medical College for their kind cooperation from time to time in carrying out the study.*

I express my thanks to the ***library*** *and all* ***hospital staff*** *for their kind cooperation in my study.*

Finally I thank ***God*** *for making all these wonderful people happen to me and pray for continued blessing and success.*

Date:

Place: Bijapur **Dr.Issac Varghese**

LIST OF ABBREVATIONS USED

LSCS	Lower Segment Caesarian Section
FiO_2	Fraction of Inspired Oxygen
IM	Intra Muscular
IV	Intra Venous
CNS	Central Nervous System
NMDA	N-Methyl-D-aspartate
CSF	Cerebrospinal fluid
IVRA	Intravenous regional anesthesia
SNAPPE	Score for Neonatal Acute Physiology
IQR	Interquartile range
SD	Standard Deviation
ASA	American Society of Anesthesiologists

ABSTRACT

BACKGROUND

Studies with pre spinal ketamine have shown that even with known cases of intra uterine asphyxia, excellent APGAR scores have been achieved in neonates [11].Pre spinal Ketamine is also known to **reduce** shivering during spinal anesthesia[14], postoperative analgesic requirement, and significantly **increase** mobility post operatively and ability of mother to care for the infant

OBJECTIVE

To study advantages ,and neonatal outcome of using Ketamine as an induction agent in caesarian sections

DESIGN: Randomized case control trial

SETTING: A tertiary care, University hospital in Bijapur

PARICIPANTS: The study included 80 neonates born by elective LSCS randomly divided equally into case and control group

RESULTS

A total of 80 babies born by LSCS was included in the study ,40 babies were in case group and 40 in the control ground divided according to randomization, In the case group 20 were males and 20 were female and in the control group 22 were males and 18 were females .The APGAR scoring at 1st minute in case and control group were 7.20 ± 0.164 (Lowest 6 , Highest 8)and 6.875± 0.365 ,which by the t test had a value < 0.05 which was significant .The 5th minute APGAR scoring on the other hand was 9 , and 8.5 ± 0.358 for cases and controls respectively .This had a test value of <0.05 which was

significant . The time of onset of breast feeding in the case and control group were 98.925 ± 60 min and 113.625 ± 65 min respectively which had a significant value <0.05 .

CONCLUSION

From the above study it can be concluded that Ketamine given to the mother as a pre spinal anesthetic not only eases the induction of spinal anaesthesia but also has no adverse effect on the Apgar scoring or time of onset of breast feeding, rather it shows a significant improvement in the1st and 5th minute APGAR scoring and ease of induction of breast feeding by the mother

KEY WORDS: Ketamine ,pre spinal, neonatal outcome , caesarean section

TABLE OF CONTENTS

Sl. No	Particulars	Page. No
1.	INTRODUCTION	1
2.	AIMS AND OBJECTIVE	4
3.	REVIEW OF LITERATURE	6
4.	METHODOLOGY	39
5.	PHOTOGRAPHS	43
6.	RESULTS AND OBSERVATIONS	48
7.	DISCUSSION	59
8.	CONCLUSION	69
9.	BIBLIOGRAPHY	71
10.	ANNEXURE Ethical clearance Case Performa Consent form Master chart	78

LIST OF TABLES

TABLE. NO.	DESCRIPTION	PAGE NO.
1.	Apgar Scoring	29
2.	A S A Physical Status Classification	35
3.	Age group of mothers	50
4.	Babies sex ratio	51
5.	Apgar scoring at 1st minute	54
6.	Apgar scoring at 5th minute	55
7.	Time of onset of breast feeding	57
8.	Ebong et al - present study case group comparison	62
9.	Wahjoeningsih et al- present study case group comparison	63
10.	K Ghazi et al- present study group comparison	64
11.	Dich neilson et al- present study case group comparison	65
12.	Safety profile	67

LIST OF GRAPHS

GRAPH NO.	DESCRIPTION	PAGE NO.
1.	Age group of mothers	50
2.	Babies sex ratio	51
3.	Baby weight distribution	52
4.	Apgar scoring at 1st minute	53
5.	Apgar scoring at 5th minute	56
6.	Time of onset of breast feeding	58
7.	Apgar score comparison diagram	65

LIST OF PHOTOS

Sl. No	DESCRIPTION	PAGE NO.
1	Sterile water and ketamine	44
2	Ketamine	45
3	Sterile water	45
4	Spinal anesthesia	46
5	Apgar score at 1st min.	47
6	Apgar score at 5th min.	47

INTRODUCTION

INTRODUCTION

Ketamine (Phencyclidines) was the first drug of its class to be used for anaesthesia[1]. It is an intravenous anesthetic agent which induces so called "dissociative anesthesia", profound analgesia, immobility amnesia with light sleep and feeling of dissociation from one's own body[2,4]. Ketamine differs from most other drugs used to induce anaesthesia because it has a significant analgesic effect; the interest in Ketamine has increased because of its effect on hyperalgesia and opiate tolerance[2]. The primary site of action is cortical and sub cortical area[2]. The anesthetizing doses are (2 to 2.5mg/kg) and pre anesthetic dose 0.25mg/kg [3].

Studies have shown that even with known cases of intra uterine asphyxia, excellent APGAR scores have been achieved in neonates [11], pre spinal Ketamine is also known to reduce shivering during spinal anesthesia[14], postoperative analgesic requirement, and significantly increase mobility post operatively and ability of mother to care for the infant[13]

Inadequate pain relief following a caesarian delivery may impair the mother's ability to optimally care for her infant in the immediate postpartum period and adversely affect early interaction between mother and infant[13]. Pain and anxiety may also reduce the ability of mother to breast feed effectively. It is necessary that pain relief be safe and effective, that it does not interfere with mother`s ability to move around and care for her infant, and results in no adverse neonatal effect in breast feeding women

Ketamine is known to cross placenta but it is significant only above dosages above 1.5mg/kg [3].It can change beat to beat variability without changing fetal acid / base status[8].

There are only very few international studies demonstrating neonatal outcome in using Ketamine as a pre spinal agent in LSCS[9,10,11,12,13],

OBJECTIVES

OBJECTIVES

To study fetal outcome using Ketamine as an pre spinal agent in caesarian sections.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

In a study done by **Ebong EJ**, Mato CN, Fyneface –Ogan S, performed at an obstetric anaesthesia unit, Department of Anaesthesia, University of Port Harcourt Teaching Hospital, Port Harcourt, NIGERIA, with the aim of finding out the effect of pre – incisional administration of low dose intravenous Ketamine, on post operative analgesia demand time. This randomized hospital based control trial proved that the post operative analgesia requirement in mothers who received pre spinal Ketamine at a dose of 0.25mg/kg diluted in sterile water were longer than the mothers in placebo group , who received 10ml sterile water

Study done by **Dich – Neilson, Holasek** , on a series of 100 patients undergoing caesarian section with Ketamine 1.25 mg/kg as induction agent and atropine 0.25-0.5mg and diazepam 1mg were given intravenously as pre medication, with anaesthesia maintained at N_20 :FIO2 0.4 . Showed that despite the fact that patients with known intrauterine asphyxia were also included in the study it showed excellent Apgar scores ((9.1 at 1 min and 9.9 at 5 min. The article suggested that Ketamine can be used not only on special indications but also on routine method of induction of anaesthesia for caesarian section

In a study made by **K Ghazi– Saidi and A.Hajipour**, Department of Anaesthesia and Intensive Care ,Imam Komeini Hospital ,School of Medicine ,Tehran University of Medical Sciences showed that in a randomized double blind study of two groups of women, of them one group A received pre anesthetic Ketamine and other group B which did not receive Ketamine , group which received Ketamine showed that first request for analgesic request was longer for group A , the mean use of morphine dose required in 24 hrs was also less in group A , APGAR scores were similar

In a Case Report by **George H Bancroft and John L Lauria** published in *anesthesiology*, The official journal of The American Society of Anesthesiologists', showed that pre anesthetic induction with Ketamine in a case of acute intermittent porphyria showed good Apgar scoring in the neonate

A study conducted by **Wahjoeningsih and Widow Ati**, Department of Anesthesiology and Reanimation ,School of Medicine Airlangga University St Soetomo Hospital, Indonesia. In the retrospective study conducted on 240 patients undergoing Caesarian Section with indication of fetal distress during three year period (2002-2004) showed that the best technique of anaesthesia in fetal distress, is sub arachnoid block with Ketamine , than using thiopental

In a study done by **Shakya.S and Chaturvedi.A,** published in Journal of anesthesiology and Clinical Pharmacology 2010 Oct-Dec 465-469. This prospective , randomized and placebo controlled study conducted on 120 patients undergoing lower abdomen surgery showed that prophylactic low dose Ketamine (0.25mg kg^{-1}) showed that shivering during spinal anaesthesia was significantly reduced in Ketamine group than placebo (10 ml normal saline) group

PHARMACOLOGY

OF

KETAMINE

PHARMACOLOGY OF KETAMINE

Pharmacology of Ketamine was reported by Chen, McCarthy & Associates [43] in 1965who described it as being a compound with cataleptic and analgesic and anesthetic action without hypnotic properties.

Corssen and Domino [44] in 1966 described its effect as dissociative anaesthesia.

HISTORY: - The first agent used to cause dissociative anaesthesia was phencyclidine, also known as CI-375 ,PCP or Sernyl. Sernyl was synthesized by Maddox and after basic studies[43], the drug was clinically introduced by Grietensten and Johnstone[47] .It was associated with unacceptable high incidence of Post anesthetic hallucination and delirium reaction . This precluded further use of drug in the operating room .Sernyl is used successfully in veterinary anaesthesia and also as a street drug of abuse Cyclohexamine or CI – 400 a congener of phencyclidine was then studied clinically by Lear [33] .When compared to phencyclidine, Cyclohexamine was less effective in producing satisfactory analgesia and emergence delirium and other psychic disturbances were as serious as with phencyclidine . Cyclohexamine use too has been discontinued.

The next dissociative agent was Ketamine also known as CI – 581 Ketalar and Ketaject. Ketamine was first synthesized by Stevens of Detroit in 1963 and tested on volunteers from state prison in Michigan in 1964 . It was first used in clinical anaesthesia by Domino and Corssen of Germany in 1965. It proved a promising new agent particularly for use in developing countries or in the field situation .Since then considerable interest has developed in the compound and it has been critically evaluated by anaestheologists and other scientists around the world and vast literature has been published describing the drug as a new different and possibly safer anaesthetic agent

CHEMISTRY :- Chemically ,Ketamine is a 2(O - Chorophenyl) 2 (Methylamino) cyclohexanone hydrochloride .The Ketamine molecule has a molecular weight of 238 , is a water soluble ,has pKa of 7.5 and contains chiral center producing two resoluble optical isomers .Only the racemic mixture is available for clinical use .The positive isomer is a more potent analgesic and less likely to cause to emergence reaction than the negative isomer. [35]

PHYSICAL PROPERTIES : Ketamine hydrochloride is a white crystalline subdtance soluble in water . The base component is 86.5% of the salt .The solution is clear colourless and stable at room temperature. It forms aqueous solution of pH 3.5 to 5.5 .It is available in 10 mg and 50 mg vials .

OPTICAL ISOMERS OF KETAMINE :- Ketamine is optically active currently supplied as a racemic mixture of its component stero –isomers ie . S(+) and R(-) isomer

The work of White [35] showed that the isomer of Ketamine had different properties from eachother and formracemic mixture which is normally used .In terms of potency the S(+) isomer is 3-4 times more powerful than R(-) isomer . Quantification of verbal response in post anaesthetic period suggested that more psychic emergence reactions occurred after administration of R(-) Ketamine, than the racemic compound S(+) Ketamine .Since these individual metabolites have yet to be studied in terms of their neuropharmacological effects, it remains possible that they may be implicated in certain of CNS effects of ketamine .

PHARMACOKINETICS :-

ABSORBTION :- Absorbtion after IM injection is rapid. Apparent mean peak concentration after an IM dose of 0.5mg/kg was 240 ± 50 ng/ml occurring at 22 ± 4 min . The lag time was 1 min and mean absorption half time was 8.2 min[29.] Peak

plasma concentration of ketamine occur within 1 min following IV administration of 2mg/kg and within 5 min following IM administration 10mg/kg .

After oral administration of 0.5 mg /kg ketamine absorption was incomplete and delayed with a lag time of about 8 minutes , the mean peak plasma concentration was 45 ± 10 ng/ml at 30 ± 5 min .The mean bioavailability was 16.5 % .

DISTRIBUTION :- The initial distribution phase of intravenous ketamine from plasma to peripheral tissue compartment occurs with a half- life of 7 – 11 minutes .The elimination phase occurs with half life of 2.5 hours of 4 hours or more . Ketamine is not significantly bound to plasma protein that leaves the blood rapidly to be distributed to highly perfused tissues like brain where peak concentration may be four to five times that present in plasma .It is extremely lipid soluble and hence rapidly cross the blood brain barrier .Subsequently Ketamine is redistributed from brain to less well perfused tissues .

The concentration in the brain of the drugs administered nasally is observed to be higher than corresponding IV drugs .Intranasal administration is speculated to reach the brain through the cribriform plate.

METABOLISM :- Ketamine is metabolized extensively by hepatic drug metabolizing enzyme system . Some biotransformation pathways are well established , others remain postulates . A major pathway for biotransformation involves N – demethylation of ketamines via cytochrome P-450 enzyme to form norketamine (metabolite I) which can then be hydroxylated at one or more positions in the cyclohexanone ring to form hydroxyl- norketamine compounds which can then be conjugated to more water soluble glucuronide derivatives. The hydroxylated metabolites of norketamine are unstable at high temperature and undergo thermal dehydration to form a cyclohexanone product, dehydronorketamine (metabolite II)

.Ketamine itself may undergo ring hydroxylation directly ie. Without prior N – demethylation . Norketamine has 1/3rd potency of Ketamine and lesser side effects than ketamine. The mean peak norketamine concentration after 0.5mg/kg Ketamine IM was 90 ± 10 ng/ml at 77 ±14 min[29].

The mean peak norketamine concentration after oral Ketamine 0.5mg/kg was 200 ±44 ng /ml at 60 ± 13 min .Thus , the plasma concentration of norketamine is twice as high after oral administration of ketamine than after IM administration . This high plasma norketamine concentration accounts for analgesic effect of oral Ketamine doses of 0.5mg/kg despite a plasma Ketamine concentration of only 40ng/ ml[29]

Only 16% of Ketamine is bioavailable when administered orally . White[35] found that the same dose of Ketamine produced more rapid and greater plasma concentration after nasal than rectal administration [35].

Mean plasma concentration of Ketamine 3mg/kg intranasally peaked at 496ng/ml within 20 min , with 6mg/kg at 2104ng/ml within 21 minutes. By rectal routes peak concentration was observed at 42 minutes.

EXCRETION :-

Following its intravenous administration , less than 4% can be recovered from urine as either unchanged drug or norketamine and only 16% appears as hydroxylated derivatives .Faecal excretion accounts for less than 5 % [35].

At the termination of Ketamine induced anaesthetic state , a large fraction of Ketamine remains in body tissue in unchanged form . This is responsible for cumulative effects . Halothane and diazepam prolong the elimination half life of Ketamine and delay recovery . Nitrous oxide shortens the recovery period [35].

PHARMACODYNAMICS :-

CENTRAL NERVOUS SYSTEM :

Ketamine produces dose related unconsciousness and analgesia. The anaesthetized state is called dissociative anaesthesia[2,3,4] , because patients who receive Ketamine alone appear to be in a cataleptic state, unlike other state of anaesthesia which resemble normal sleep .The Ketamine anaesthetized patients have profound analgesia but keep their eyes open and maintain many reflexes . Corneal , cough and swallow reflex may all be present but should not be assumed to be protective. There is no recall of surgery or anaesthesia , but amnesia is not as prominent with ketamine as with benzodiazepines.

Ketamine has a low molecular weight , a pKa near the physiologic pH, and relatively high lipid solubility, it crosses the blood brain barrier rapidly and therefore has an onset of action within 30 seconds. The maximal effect occurs in about a minute .After Ketamine administration, pupils dilate moderately and nystagmus occurs. Lacrimation and salivation are common, as is increased skeletal muscle tone , often with coordinate seemingly purposeless movement of the arms ,legs , trunk and head.

Although there is great interindividual variability, plasma levels of 0.6 to 2.0 micrograms/ ml are considered minimum concentration for general anaesthesia but children may require slightly higher plasma levels (0.8 to 4.0 microgram / ml).

The duration of Ketamine after single administration of general anesthetic dose 2mg/kg IV is 10 – 15 min and full orientation to person, place and time occurs within 15 – 30 minutes.

An intramuscular dose of 10mg/kg will usually produce loss of consciousness in 2 – 4 min which lasts for 12 – 25 min.

An oral dose of 6mg/kg provides uniform predictable sedation within 20-25 minutes. Analgesia may precede the onset of anaesthesia and persist after the return of consciousness. After an oral dose of 0.5mg/kg analgesia occurs at 30 minutes after administration.

When given intramuscularly in micro doses of 0.44 mg/kg, Ketamine provides analgesia for both experimental and post operative pain[34] . This analgesia is found at 15 min after administration and lasts up to 90 min.

This CNS side effects noted with IM Ketamine 0.44mg/kg includes dizziness, blurred vision ,in coordination, agitation and difficulty in communicating. [34] All these side effects were of a mild or moderate nature . The mild degree of sedation produced was not troublesome. A definite sense of well-being has also been experienced by most of the patients. This supplements the analgesic effect of the drug and thereby proves that it has a potential for being abused[34].

Analgesia is greater for somatic than for visceral pain and can be achieved with small IV doses of ketamine that do not necessarily produce unconsciousness. Recovery from amnesia requires atleast1 hour after apparent recovery of consciousness.

MECHANISM OF ACTION :

The primary site of CNS action of Ketamine appears to be the thalamoneocortical projection system[2] .It selectively depresses neuronal function in parts of cortex (especially association areas) and thalamus , while simultaneously stimulating parts of limbic system including hippocampus .This creates what is termed “functional disorganization” of non specific pathways in brain and thalamic areas. There is also evidence that ketamine suppresses transmission of impulses in the medullary reticular formation , which is important for transmission of affective – emotional components of noiception from the spinal cord to higher brain centers [2] .

There is some evidence that ketamine occupies opiate receptors in the brain and spinal cord , which could account for some of the analgesic effects. The S(+) isomer has been found to have some opiod mu-receptor activity accounting for part of its analgesic effect [2,35] .

N- methyl D-aspertate(NMDA) receptor interaction may mediate the general anesthetic as well as analgesic actions of ketamine[2].

The spinal cord analgesic effect of ketamine is postulated to be due to inhibition of dorsal horn wide dynamic range (WDR) neuronal activity.

Although a number of drugs have been used to antagonize ketamine , no specific receptor antagonist is yet known , that reverses all the CNS effect of ketamine . Agoston[45] recently reported that 4 aminopyridine, a potent antagonist of non depolarizing myoneuronal blocking drugs enhance the recovery rate of ketamine – diazepam anaesthesia.

Ketamine increases cerebral metabolism, cerebral blood flow and intracranial pressure.

POST ANAESTHESIA EMERGENCE REACTIONS:

The psychic sensation reported during emergence from ketamine anaesthesia have been characterized as alteration in mood state and body image, dissociative or extracorporeal(out of body) experiences ,floating sensation , vivid dreams or illusion "weird trips" and occational frank delirium[5]. The vivid dreams and visual illusion usually disappear immediately upon wakening although recurrent illusion (flashbacks) have been reported several weeks after ketamine administration in adults and children.

Recent cerebral glucose utilization indicate that ketamine produces depressive action on the inferior colliculus (a primary acoustic relay nucleus). It would appear that psychic emergence reactions occur secondary to ketamine – induced depression

of these auditory and visual relay nuclei, leading to misperception of visual and auditory stimuli . Furthermore, the loss of skin and musculoskeletal sensation result in decreased ability to feel gravity , floating in space .Despite many statements in the literature to contrary[9] , there is no evidence that covering the eyes during operative and post operative periods or allowing patients to emerge in a quiet area alter the incidence of emergence reaction [11].

The psychic disturbances following ketamine vary in incidence from less than 5 per cent to greater than 30 per cent . Various factors associated with higher incidence of emergence reactions include : age (less than 10 per cent incidence of unsatisfactory anaesthesia and/or emergence reaction in patients less than 16 years old v/s 24 -34 percent in patients greater than 16 years old); sex (female greater than males); subjects who normally dream ; large use of ketamine (> 2mg/kg IV); rapid IV administration (>40 mg/min) ; or history of personality problems.

A variety of pre medicants and adjunctive agents have been evaluated in attempts to prevent the untoward emergence reactions following ketamine anaesthesia. Atropine premedication prior ketamine administration has been shown to increase the frequency of unpleasant dreams. Similarly, droperidol may increase the occurance of vivid dreams when used as a premedicant . Benzodiazepam- Diazepam 0.15-0.3mg/kg IV administered prior to induction of ketamine anaesthesia of completion of procedure . Lorazepam : 2-4 mg oral or IV is reported to be most effective in preventing emergence sequelae, it does not prolong recovery from ketamine in contrast to other benzodiazepines which prolong recovery from ketamine

.

CARDIOVASCULAR EFFECTS :

Ketamine produces dose related rise in rate pressure product with transient rise in cardiac index but without significantly altering the stroke index[35].

Initially cardiostimulatory effects of ketamine were thought to be due to increased sympathetic activity secondary to depression of baroreceptor reflux activity . Subsequent studies showed that cardiovascular response is unrelated to baroreceptor desensitization. Traber[49] suggested that sympathomimetic effects of ketamine is mediated within the CNS by ganglionic blockade and thoracias – epidural block were capable of ablating its cardiostimulatory properties.

In the absence of autonomic control of ketamine has direct myocardial depressant properties . It has been noticed that ketamine acted as an antiarrhythmic, especially digitalis induced arrhythmias. Ketamine directly dialates vascular smooth muscles while causing sympathetic mediated vasoconstriction. The net effect is that systemic vascular resistance is not much altered by ketamine.

Weiskopf found that although continuous ketamine anaesthesia was more effective in maintaining the cardiovascular system , it produces a greater base deficit and greater increase in arterial lactate concentration than the volatile anaesthetic agents[49].

Waxman observed occasional decrease in cardiac and pulmonary anaesthesia in pulmonary anaesthesia in critically ill and acutely traumatized patients . Furthermore, others have demonstrated that general anaesthetics block the cardiovascular stimulating properties of ketamine such that significant cardiovascular depression can be produced when ketamine is used during halothane or enflurane anaesthesia [36].

Ketamine produces an increase in cerebrospinal fluid (CSF) pressure which appears related to an increase in cerebral blood flow secondary to cerebral vasodilatation and rise in systemic pressure.

PULMONARY EFFECTS :

Ketamine does not produce significant respiratory depression except in those situation when it is given as rapid infusion .

Ketamine is known as a very good bronchodialator . Propanolol blocked the relevant effect of epinephrine but not that of ketamine , suggesting that ketamine acts at site other than beta receptors .

Salivary and Tracheobronchal mucus gland secretion are increased by ketamine necessitating prophylactic administration of an antisialogogue. Despite alleged retention of protective laryngeal and pharyngeal reflexes , tracheal soiling and aspiration has been reported

MISCELLANEOUS ACTIONS :

Ketamine frequently produces an increase in skeletal muscle tone and occasionally muscle spasm , although it has been used safely in patients with myopathies and malignant hyperthermia.

Corsen, Hoy, Miyaska and Domino found slightly increased intraocular pressure following administration of ketamine[44,47] .Ketamine causes slight rise in blood sugar but this effect is quite variable .It reaches the peak about 10 to 15 min after injection and has passed off within two hours . Serum free fatty acid are decreased by ketamine . Thyroxine (T4) levels are not altered by ketamine however ,T3 levels are reduced therefore dose dependent hypothermia produced by ketamine in rats at an ambient temperature may be due to decreased heat production as well as increased heat loss secondary to cutaneous vasodialatation .In addition ketamine

produces an activation of the pituitary adrenal axis ,with adrenal release of catecholamines and corticosteroids . In common with other intravenous agents ketamine causes a slight fall in the serum potassium in less than patients induced with Thiopentone . Ketamine also appeared to reduce the incidence and severity of fasciculation produced by the relaxant.

CLINICAL APPLICATION :

1) The aged and critically ill patients

- Shock or cardiovascular instability
- Severe dehydration
- Respiratory failure or bronchospasm
- Severe anemia
- Major thoracoabdominal procedures
- Cardiac tamponade and constrictive pericarditis

2) Obstetrical Anasthesia

- For rapid induction of general anaesthesia in
- Severe hypovolaemia
- Acute hemorrhage
- Acute bronchospasm

For low dose analgesia

- Supplement regional technique
- As a transient analgesia at the time of delivery or during postpartum period

3) Adjunct to local and regional anaesthetic techniques

- low dose(0.5) for sedation and analgesia during performance of nerve block procedure .
- Supplemental analgesia for inadequate block

4) Outpatient anaesthesia

- Children

Brief diagnostic and therapeutic procedures (eg cardiac cath ; endoscopy oral surgery ,head and neck surgery ;orthopedic surgery;ophthalmology; radiotherapy)

-Adults

Brief surgical procedures (eg gyenaecological ,head and neck ,arthopaedic , urologic)

-Supplement local and regional techniques

-Diagnostic and therapeutic procedures (eg endoscopy)

5) Patients with reactive airway disease

- Asthmatic with acute bronchospasm
- Chronic obstructive pulmonary disease with bronchospasm

6) For Burn Patients

- Debridement and skin grafting
- Dressing changes

7) Post operative analgesia

- Recovery room
- Intensive care units

8) As total intravenous regional anaesthesia (IVRA).

9) In field anaesthesia and in situation where there are mass casualities.

It is the anaesthetic of choice for body surface procedure and wound debridement in a military field anaesthesia since it produces minimal respiratory depression .It is used as an induction agent before spontaneous and controlled ventilation with a draw over vaporizer in such situations

10) As preanaesthetic medication

- in children by intramuscular , rectal , oral , and intranasal routes

CONTRAINDICATIONS FOR USE OF KETAMINE [3]

1) Cardiovascular disease

- Poorly controlled hypertension
- Intracranial , thoracic or abdominal aneurysms
- Unstable angina or recent myocardial infarction
- Right or left system disorders

2) Central Nervous System disorders

-Cerebral trauma

- Intracerebral mass or haemorrhage

3) Open – globe injury to eye or increased intraocular pressure

4) Thyrotoxic states

5) Otolaryngologic procedures involving pharynx, larynx or trachea

6) Psychiatric disorders (eg schizophrenia) or history of adverse effects to ketamine or any one of its congeners

COMPLICATION OF KETAMINE [2,3]

Intraoperative

1) Respiratory: inadequate exchange due to mechanical causes (salivation , obstruction) central depression , laryngiobronchospasm , coughing ,sneezing and hiccups

2) Circulatory: Blood pressure rise ,blood pressure fall , tachycardia , bradycardia

3) Others : Hypertonia due to the extent of interfering with the surgery , purposeless movements of extremities, skin rashes , flus , shivering and vomiting

Post Anaesthesia Complications

1) Respiratory : Inadequete exchange due to hypoventilation , mechanical causes (salivation), laryngiobronchospasm and hiccup

2) Circulatory: Persistent blood pressure elevation,persistent tachycardia and bradycardia

3) Others : vomiting shivering ,opisthotonus, long term repeated use may lead to development of tolerance to ketamine as proved by the decrease in duration of anaesthesia as the number of anaesthetics increase .

DOSAGE AND ROUTES OF ADMINISTRATION [2,3,4]

1) **Intramuscularly** : For anaesthesia – 10 mg / kg will produce 12-25 minutes of surgical anaesthesia . For analgesia 0.44 mg/kg action lasts upto 90 min and analgesia is found at 15 min after administration . As preinduction drug in uncooperative children 2mg/kg .For analgesia with sedation 2-4 mg /kg

2) **Intravenously** –For anesthesia 2mg /kg for induction and 1mg/kg for maintainence repeated repeated when patient shows movement in response to stimulation , nystagmus or phonation . For analgesia with sedation 0.125 – 0.25 mg/kg

As an adjuvant to regional techniques 0.5 mg/kg/min

As IV infusion for outpatient procedure 0.5 – 1.5 mg/kg bolus followed by infusion at 10 – 20 microgram/kg/minFor intravenous regional analgesia 3mg/kg.

3) **Rectally** : 8-10 mg/kg for induction in children and 5 mg/kg for preanaesthetic sedation.

4) **Intranasally** : 5-6 mg/kg for pediatric premedication ,onset within 20 min

5) **Orally** : 6mg/kg for pre anaesthetic sedation in children onset of action within 30 min

APGAR SCORE

In 1949 Dr. Virginia Apgar, an American obstetric anaesthesiologist, developed a score to quantify the physiological status (as an effect of the transitional process) of newborn infants shortly after delivery. This tool was based on simple observation, and was thought to be useful for:

1. Comparison of the results of obstetric practices
2. Evaluation of the effects of maternal anesthesia
3. Evaluation of the effects of neonatal resuscitation

The so-called Apgar score was published in 1953 [15] and since then this scoring system has been widely used as a numeric assessment of the condition of newly born infants.

The **Apgar score** is a practical method of systematically assessing newborn infants immediately after birth to help identify those requiring resuscitation and to predict survival in the neonatal period [9] . The 1-min Apgar score may signal the need for immediate resuscitation, and the 5-, 10-, 15-, and 20-min scores may indicate the probability of successfully resuscitating an infant. A low score may be due to a number of factors, including drugs given to the mother during labor and immaturity. The Apgar score was not designed to predict neurologic outcome. Indeed, the score is normal in most patients in whom cerebral palsy subsequently develops[9], and the incidence of cerebral palsy is low in infants with Apgar scores of 0–3 at 5 min (but higher than in infants with Apgar scores of 7–10). The Apgar score and umbilical artery blood pH both predict neonatal death. An Apgar score of 0–3 at 5 min is uncommon but is a better predictor of neonatal death (in both term and preterm infants) than an umbilical artery pH of 7.0 or less; the presence of both variables increases the relative risk of neonatal mortality in term and preterm infants.

The association of the 1 and 5 min Apgar score with neurological disability, as well as mortality has been confirmed in population studies, incl. one of Norwegian newborns 1983-1987 [16,18] . However, it is important to keep in mind that the use of the score alone in risk assessment and prognosis is at the statistical level; the score alone is not as useful for predicting individual outcomes. Used together with neonatal severity of illness scores, e.g.the Clinical Risk Index for Babies (CRIB) and Score for Neonatal Acute Physiology (SNAP)-II/ Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE)-II (38), the score might to some degree predict individual outcomes[18]. However, it is important to note that the CRIB score has primarily been developed for predicting outcome for preterm babies rather than asphyxiated term infants. , four out of five elements of the Apgar score are to a certain extent based on visual inspection of the infant. The fifth, the one found by Apgar to be the most valuable prognostic and diagnostic element of the score: heart rate, was defined as **good** (equals a score of 2) if over 100 beats per minute. However, as Dawson[50] recently reported that median (IQR) heart rate at 1 minute of age of healthy newborn infants was 96 (65–127) beats per minute[50] , Apgar's proposal for a cut-off might not be feasible. Current 18 international guidelines for newborn resuscitation do, like Apgar, use a heart rate of less than 100 beats per minute as a definition for which infants need intervention at birth[19]. The way the Apgar score is being assigned to preterm babies may cause uncertainty and greater degree of subjectivity of the scoring .. It has also been speculated that the element of "reflex response" often is not being formally assessed as many infants are not being actively stimulated (which must be believed to be a prerequisite for a response to occur)[20] .As recommendations for routine suctioning of infants (with or without meconium staining of the amniotic fluid) have been abandoned due to insufficient evidence for

its benefit, scoring of reflex response might no longer be justified[21]. In addition, scoring of infants being resuscitated and in particular after intubation may impose challenges and reduced reliability[22].

Despite concerns regarding subjectivity of Apgar scoring [20], equal weighting of the components, as well as clinical usefulness of the score, the Apgar score is still being used as a diagnostic criterion and in epidemiologic research. E.g. Apgar scores are being used in defining neonatal asphyxia, its severity and need for interventions. However, many argue that immediate resuscitative interventions in the delivery room should no longer be guided by the Apgar score. The American Neonatal Resuscitation Program (NRP) states that ‘‘…the Apgar score is not used to determine the need for resuscitation, what resuscitation steps are necessary, or when to use them’’[23].

This is in accordance with updated guidelines for neonatal resuscitation where the former recommendation for resuscitative interventions being guided by the colour (in addition to pulse and respiration) of the baby has been removed, as this is an unreliable parameter.

This change in guidelines is partially based on the work by O’Donnell [42]. showing that assessment of colour is highly subjective and that inter-rater variability is high . In addition, based on the natural rise in SpO2 in healthy term neonates where mean time (SD) to SpO2 > 90% is 5.8 (3.2) min (48), skin colour may not be expected to be “pink” the first minutes of life.

Table No 1 –APGAR SCORING

SIGN	0	1	2
Heart rate	Absent	Below 100	Over 100
Respiratory effort	Absent	Slow, irregular	Good, crying
Muscle tone	Limp	Some flexion of extremities	Active motion
Response to catheter in nostril (tested after oropharynx is clear)	No response	Grimace	Cough or sneeze
Color	Blue, pale	Body pink, extremities blue	Completely pink

ANESTHESIA

It is a temporary state consisting of unconsciousness, loss of memory, lack of pain, and muscle relaxation[1].

Anesthesia is a unique medical intervention which does not itself offer any particular medical benefit and instead enables the performance of other medical interventions. The best anesthetic is therefore one with the lowest risk to the patient that still achieves the end points required to complete the other intervention. There are many different needs and goals of anesthesia. The goals are traditionally described as unconsciousness and amnesia, analgesia, and muscle relaxation .To reach multiple end points one or more drugs are used (general anesthetics , hypnotics, sedatives, paralytics, narcotics and analgesics), each of which serves a specific purpose in creating a safe anesthetic.

The types of anesthesia are broadly classified into general anesthesia, sedation and regional anesthesia[3]. General anesthesia refers to the suppression of activity in the central nervous system, resulting in unconsciousness and total lack of sensation. Sedation (or dissociative anesthesia) uses agents that inhibit transmission of nerve impulses between higher and lower centers of the brain inhibiting anxiety and the creation of long-term memories. Regional anesthesia renders a larger area of the body insensate by blocking transmission of nerve impulses between a part of the body and the spinal cord[1]. It is divided into peripheral and central blockades. Peripheral blockade inhibits sensory perception within a specific location on the body, such as when a tooth is "numbed" or when a nerve block is given to stop sensation from an entire limb. Central blockades place the local anesthetic around the spinal cord (such as with spinal and epidural anesthesia) removing sensation to any area below the level of the block.

There are both major and minor risks of anesthesia[3].

The major risks include death, heart attack and pulmonary embolism whereas minor risks can include postoperative nausea and vomiting and readmission to hospital. The likelihood of a complication occurring is proportional to the relative risk of a variety of factors related to the patient's health, the complexity of the surgery being performed and the type of anesthetic. Of these factors, the person's health prior to surgery (stratified by the ASA physical status classification system) has the greatest bearing on the probability of a complication occurring.

Patients typically wake within minutes of an anesthetic being terminated and regain their senses within hours. One exception is a condition called long-term post-operative cognitive dysfunction, characterized by persistent confusion lasting weeks or months, which is more common in those undergoing cardiac surgery and in the elderly.

The first public demonstration of general anesthesia was in 1846 by a Boston dentist named William T.G. Morton at the Massachusetts General Hospital. Dr. Morton gave an ether anesthetic for the removal of a neck tumor by surgeon John Collins Warren (the first editor of the New England Journal of Medicine and dean of Harvard Medical School). About a decade later, cocaine was introduced as the first viable local anesthetic. It wasn't until the 1930s that Dr. Harvey Cushingtied the stress response to higher mortality rates and began using local anesthetic for hernia repairs in addition to general anesthesia.

Medical use

The purpose of anesthesia can be distilled down to three basic goals or end points[3,5].

- Hypnosis (a temporary loss of consciousness and with it a loss of memory)
- Analgesia (lack of sensation which also blunts autonomic reflexes)

- Muscle relaxation

Different types of anesthesia affect the endpoints in different ways[3]. The Regional anesthesia for instance affects analgesia, benzodiazepine type sedatives used in twilight sleep) favor amnesia and general anesthetics can affect all of the endpoints.

The goal of anesthesia is to achieve the necessary endpoints with the least amount of risk possible to the patient.

To achieve the goals of anesthesia, drugs act on different but interconnected parts of the nervous system. Hypnosis, for instance, is generating through actions on the nuclei in the brain and is similar to the activation of sleep. The effect is to make people less aware and less reactive to non-noxious stimuli[3].

Loss of memory (amnesia) is created by action of drugs on multiple (but specific) regions of the brain. Memories are created as either declarative or non-declarative memories in several stages (short-term, long-term, long-lasting) the strength of which is determined by the strength of connections between neurons term edsynaptic plasticity. Each anesthetic produces amnesia through unique effects on memory formation at variable doses. Inhalational anesthetics will reliably produce amnesia through general suppression of the nuclei at doses below those required for loss of consciousness. Drugs like midazolam produce amnesia through different pathways by blocking the formation of long-term memories[3].

Tied closely to the concepts of amnesia and hypnosis is the concept of consciousness. Consciousness is the higher order process that synthesizes information. For instance, the “sun” conjurers up feelings, memories and a sensation of warmth rather than a description of a round, orange warm ball seen in the sky for part of a 24 hour cycle. Likewise, a person can have dreams (a state of subjective consciousness) during anesthetic or have consciousness of the procedure despite

having no indication of it under anesthetic. It is estimated that 22% of people dream during general anesthesia and 1 or 2 cases per 1000 have some consciousness termed “awareness during general anesthesia”.

Techniques

Anesthesia is unique, in that it doesn't offer any particular benefit, rather it allows others to do things that might be beneficial. The best anesthetic, therefore is the one with the lowest risk to the patient that still achieves the endpoints required to complete the procedure. The first stage of an anesthetic is the pre-operative risk assessment made up of themedical history, physical examination and lab tests. Diagnosing a person's pre-operative physical status allows the clinician to minimize anesthetic risks. A well completed medical history will arrive at the correct diagnosis 56% of the time which increases to 73% with a physical examination. Lab tests help in diagnosis but only in 3% of cases, underscoring the need for a full history and physical examination prior to anesthetics. Incorrect pre-operative assessments or preparations are the root cause of 11% of all adverse anesthetic event.

One part of the risk assessment is based on the patients' health. The American Society of Anesthesiologists have developed a six-tier scale which stratifies the pre-operative physical state of the patient called the ASA physical status. The scale assesses a high-order of risk as the patient's general health relates to an anesthetic[3,5].

The more detailed pre-operative medical history aims to discover genetic disorders (such as malignant hyperthermia or pseudo cholinesterase deficiency), habits (tobacco, drug and alcohol use), physical attributes (such as obesity or a difficult airway) and any coexisting diseases (especially cardiac and respiratory diseases) that might impact the anesthetic. The physical examination helps quantify the impact of anything found in the medical history in addition to lab tests.

Aside from the generalities of the patients' health assessment, an evaluation of the specific factors as they relate to the surgery also needs to be considered for anesthesia. For instance, anesthesia during childbirth must consider not only the mother but the baby. Cancers and tumors that occupy the lungs or throat create special challenges to general anesthesia. After determining the health of the person undergoing anesthetic and the endpoints that are required to complete the procedure, the type of anesthetic can be selected. Choice of surgical method and anesthetic technique aims to reduce risk of complications, shorten time needed for recovery and minimize the surgical stress response.

Table -2 A S A Physical Status Classification

A S A Physical Status Classification	
ASA class	**Physical status**
ASA 1	Healthy person
ASA 2	Mild systemic disease
ASA 3	Severe systemic disease
ASA 4	Severe systemic disease that is a constant threat to life
ASA 5	A moribund person who is not expected to survive without the operation
ASA 6	A declared brain-dead person whose organs are being removed for donor purposes
E	Suffix added for patients undergoing emergency procedure

SPINAL, EPIDURAL AND CAUDAL ANESTHESIA

Central neuraxial anesthesia is the injection of local anesthetic around the spinal cord to provide analgesia in the abdomen, pelvis or lower extremities. It is divided into either spinal (injection into the subarachnoid space), epidural (injection outside of the subarachnoid space into the epidural space) and caudal (injection into the cauda equina or tail end of the spinal cord). Spinal and epidural are the most commonly used forms of central neuraxial blockade[35].

Spinal anesthesia is a "one-shot" injection that provides rapid onset and profound sensory anesthesia with lower doses of anesthetic, and is usually associated with neuromuscular blockade (loss of muscle control). Epidural anesthesia uses larger doses of anesthetic infused through an indwelling catheter which allows the anesthetic to be augmented should the effects begin to dissipate. Epidural anesthesia does not typically affect muscle control.

Because central neuraxial blockade causes arterial and vasodilatation, a drop in blood pressure is common. This drop is largely dictated by the venous side of the circulatory system which holds 75% of the circulating blood volume. The physiologic effects are much greater when the block is placed above the 5th thoracic vertebra. An ineffective block is most often due to inadequate anxiolysis or sedation rather than a failure of the block itself

RECOVERY

The immediate time after anesthesia is called emergence. Emergence from general anesthesia or sedation requires careful monitoring because there is still a risk of complication[5]. Nausea and vomiting are reported at 9.8% but will vary with the type of anesthetic and procedure. There is a need for airway support in 6.8%, there can be urinary retention (more common in those over 50 years of age) and hypotension in 2.7%. Hypothermia, shivering and confusion are also common in the immediate post-operative period because of the lack of muscle movement[3,5].

Postoperative cognitive dysfunction (also known as *POCD* and post-anesthetic confusion) is a disturbance in cognition after surgery. It may also be variably used to describe emergence delirium (immediate post-operative confusion) and early cognitive dysfunction (diminished cognitive function in the first post-operative week). Although the three entities (delirium, early POCD and long-term POCD) are separate, the presence of delirium post-operatively predicts the presence of early POCD. There does not appear to be an association between delirium or early POCD and long-term POCD. According to a recent study conducted at the David Geffen School of Medicine at UCLA, the brain navigates its way through a series of activity clusters, or "hubs" on its way back to consciousness. Recovery from anesthesia is not simply the result of the anesthetic 'wearing off,' but also of the brain finding its way back through a maze of possible activity states to those that allow conscious experience. Put simply, the brain reboots itself .

Long-term postoperative cognitive dysfunction is a subtle deterioration in cognitive function, that can last for weeks, months, or longer. Most commonly, relatives of the person report a lack of attention, memory and loss of interest in activities previously dear to the person (such as crosswords). In a similar way, people

in the workforce may report an inability to complete tasks at the same speed they could previously. There is good evidence that POCD occurs after cardiac surgery and the major reason for its occurrence is the formation of microemboli. POCD also appears to occur in non-cardiac surgery. Its causes in non-cardiac surgery are less clear but older age is a risk factor for its occurrence.

METHODOLOGY

MATERIALS AND METHODS

SOURCE OF DATA:

Elective Caesarian Section cases posted for surgery at Shri B.M.Patil Medical College, Hospital and Research center and referred to our hospital from November 2012 –November 2013

METHOD OF COLLECTION OF DATA :

After taking the informed consent from the patients and fulfilling inclusion and exclusion criteria, patients was included in the study

METHOD OF STUDY:

A case control study. 80 full term women who were undergoing caesarian section were categorized into Group A(Ketamine) and Group B (Placebo) by using simple randomization technique of consecutive numbers. Patients who had odd numbers were categorized under Group A and received low dose intravenous Ketamine 0.25mg/kg diluted to 10ml with sterile water. While those who had even numbers were Group B and received placebo

On arrival at the operating room, all the patients had their baseline vital signs (Pulse, Blood Pressure and oxygen saturation) measured and recorded

At the delivery of the baby APGAR scores were assessed at one and five minutes and later the time of onset of breast feeding was calculated in minutes.

DATA ANALYSIS :

Sample Size: 80

Determination of Sample Size :

The sample size for the comparative study of two groups for APGAR scores to be collected to the present study, may be determined at permissible error 0.074067 using the formulae [7]

$$n = \frac{z^2 \alpha / 2 \, \sigma^2}{E^2}$$

$$= \frac{3.8416 \times 0.057121}{0.074067^{\,2}}$$

= 40

Z = standard normal variable .1.96

E = Permisible error

Here $z^2 \alpha / 2$, the theoretical value of z statistic at 5 % level of significance

σ^2= (0.239) ^{2} = 0.057121 assumed as standard value

STATISTICAL DATA :

The observations for different parameters under study maybe depicted by suitable diagram and graph

Eg : Pie Chart and Multiple Bar Diagrams

SELECTION CRITERIA

INCLUSION CRITERIA:

After taking informed consent, Full term women undergoing caesarian section were taken for the randomized study.

EXCLUSION CRITERIA:

Patients Excluded from the study include

1) Refusal to Participate
2) History of Drug Abuse
3) Adverse reaction to study drugs
4) Psychiatric Disorder
5) Bleeding disorder
6) Evidence of fetal compromise
7) Mothers with hypertension
8) H\O Epilepsy

PHOTOGRAPHS

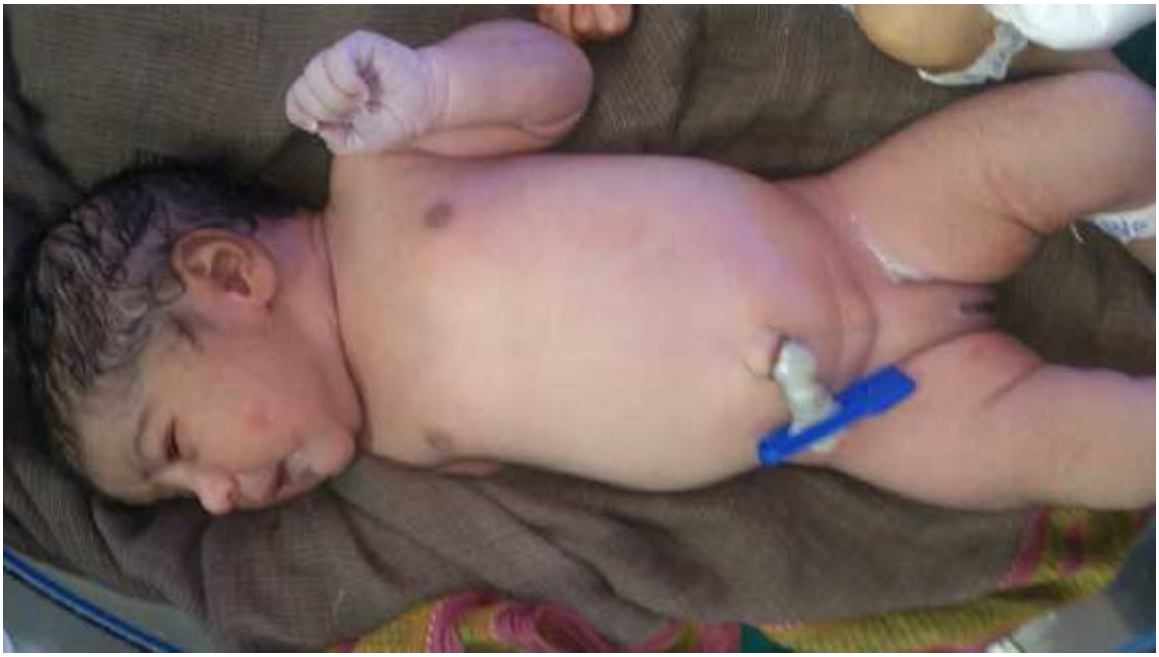
STERILE WATER AND KETAMINE

KETAMINE

STERILE WATER

SPINAL ANESTHESIA

APGAR SCORE AT 1ST MIN.



APGAR SCORE AT 5TH MIN.

RESULTS

STATISTICAL ANALYSIS :

Statistical analysis was done using and significance of APGAR scoring and time of onset of breast feeding was analysed using **t-test** in the present study.

Table -3 AGE GROUP OF MOTHERS

Age	Mothers
19-22	19
22-25	16
25-28	5

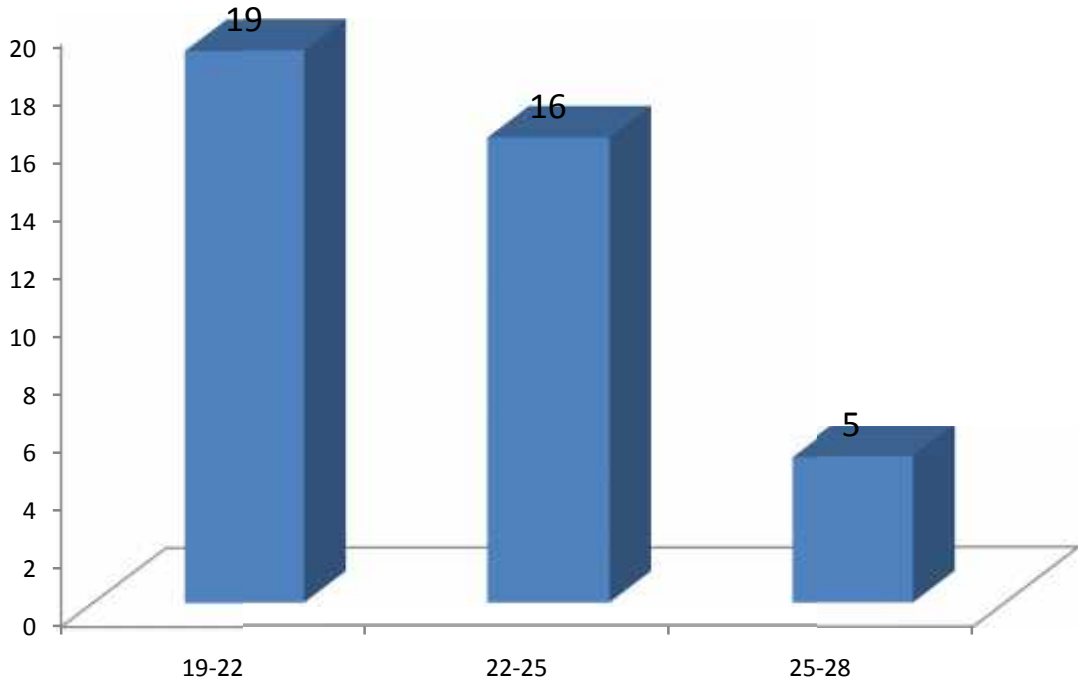
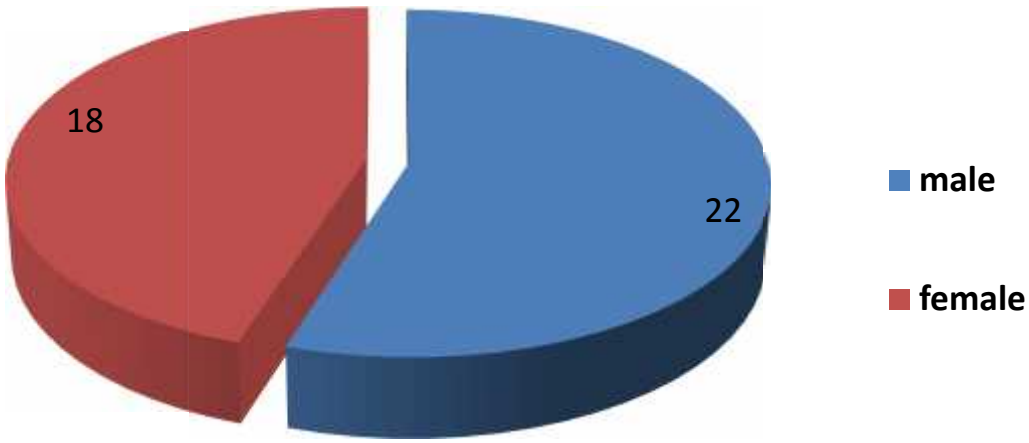
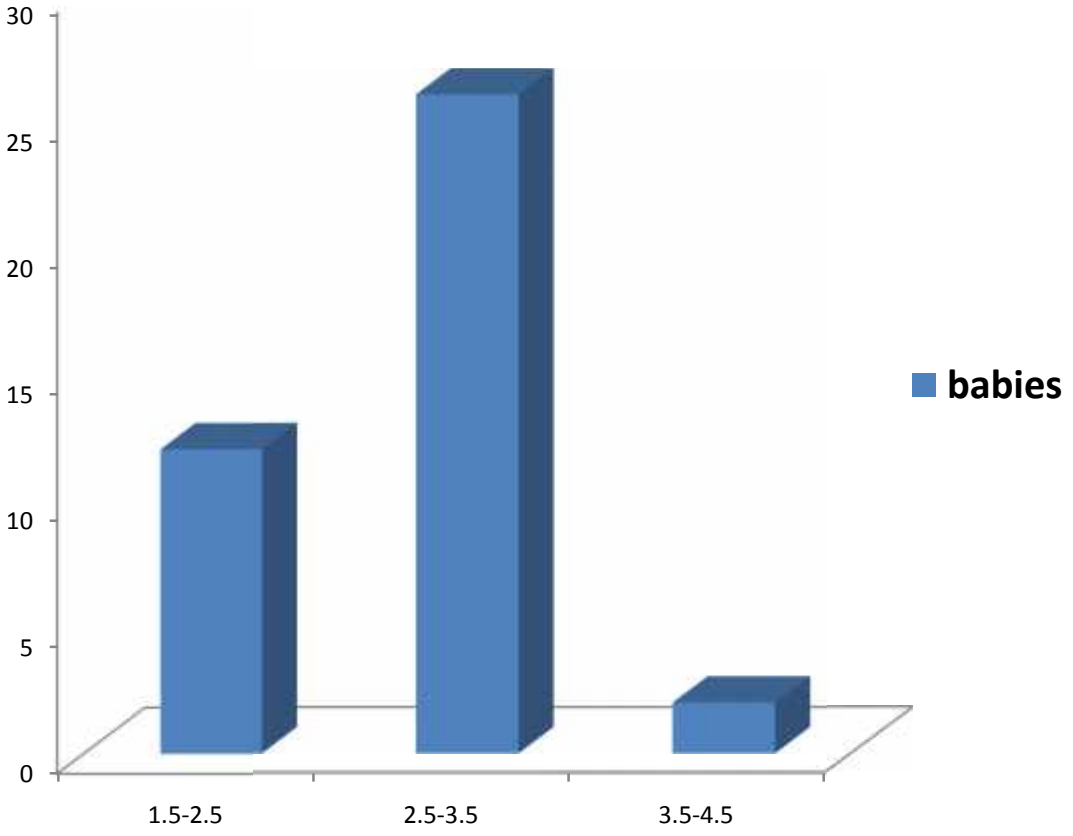


Table 4-BABIES SEX RATIO

Male	22
Female	18

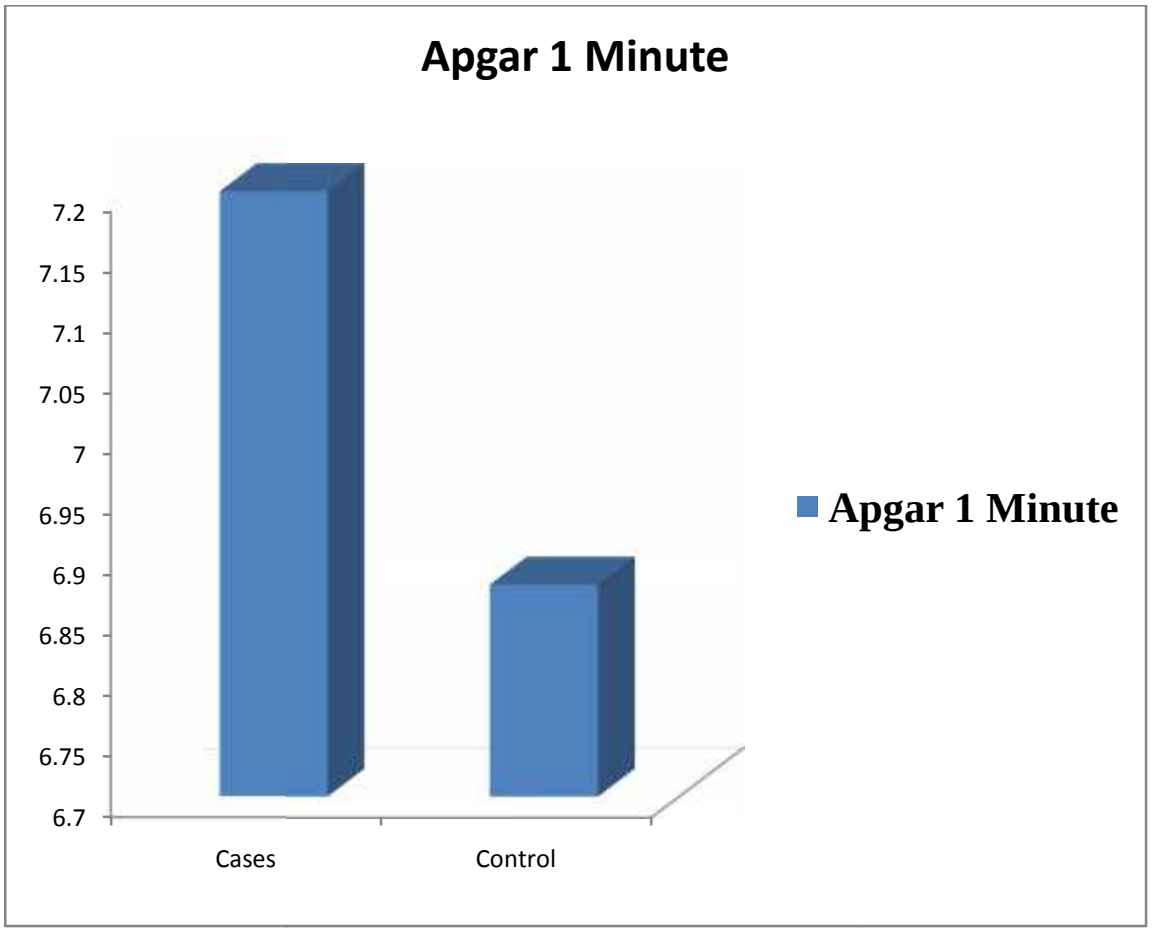


BABY WEIGHT DISTRIBUTION



Most of the babies fell into the normal birth weight range while 12 babies were in the low birth weight range

APGAR SCORING AT 1ST MINUTE



The Apgar scoring for the case group was significantly higher than the control group at 7.20 and 6.85 respectively

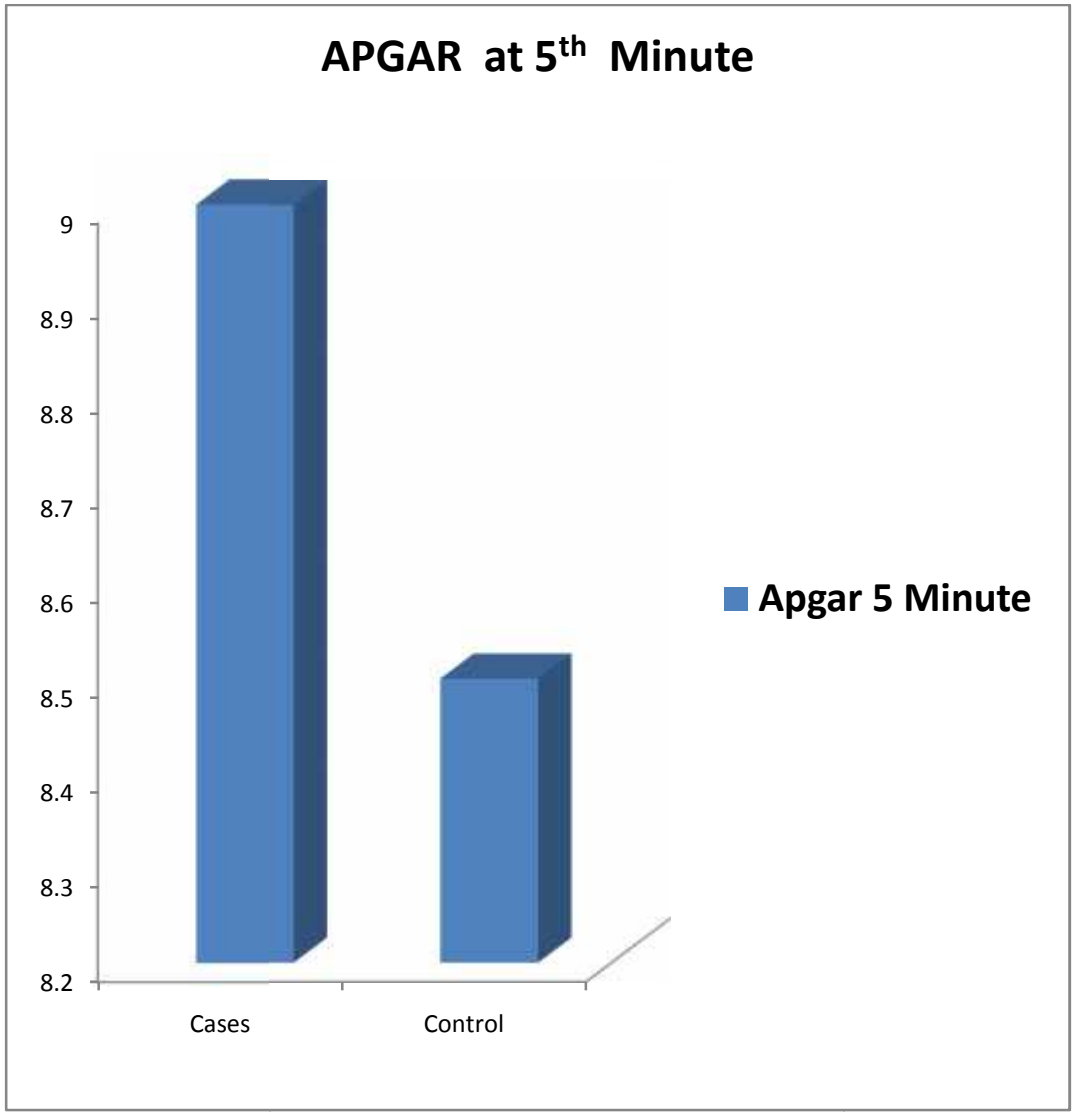
Table 5-APGAR SCORING AT 1ST MINUTE

t-Test: Two-Sample Assuming Unequal Variances			
	cases	*control*	
Mean	7.2	6.875	
Variance	0.164102564	0.368589744	
Observations	40	40	
Hypothesized Mean Difference	0		
df	68		
t Stat	2.816275544		
P(T<=t) one-tail	0.003176242	< 0.05	significant
t Critical one-tail	1.667572281		
P(T<=t) two-tail	0.006352485	< 0.05	significant
t Critical two-tail	1.995468907		

Table 6- APGAR SCORING AT 5TH MINUTE

t-Test: Two-Sample Assuming Unequal Variances					
		cases		*control*	
Mean		9		8.5	
Variance		0		0.358974359	
Observations		40		40	
Hypothesized Mean Difference		0			
df		39			
t Stat		5.277986629			
P(T<=t) one-tail		0.003659206		< 0.05	Significant
t Critical one-tail		1.684875122			
P(T<=t) two-tail		0.00318506		< 0.05	Significant
t Critical two-tail		2.022690901			

APGAR SCORING AT 5TH MINUTE

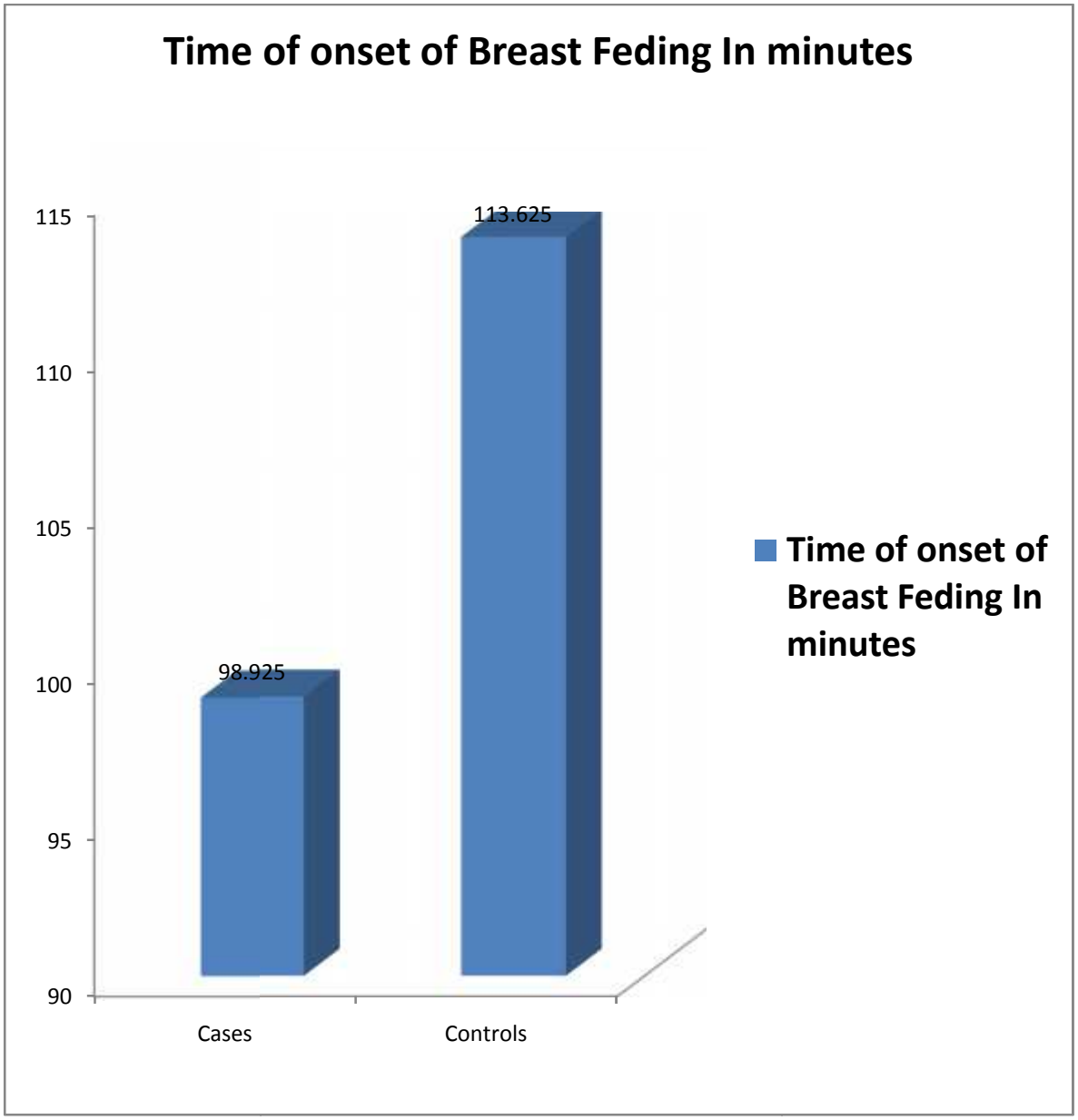


The Apgar score for the 5th Minute was higher for case than the control group at 9 and 8.5 respectively

Table 7-TIME OF ONSET OF BREAST FEEDING

t-Test: Two-Sample Assuming Unequal Variances			
	cases	*control*	
Mean	98.925	113.625	
Variance	707.7634615	1201.266026	
Observations	40	40	
Hypothesized Mean Difference	0		
df	73		
t Stat	-2.127850012		
P(T<=t) one-tail	0.018363284	<0.05	significant
t Critical one-tail	1.665996224		
P(T<=t) two-tail	0.036726567	<0.05	significant
t Critical two-tail	1.992997097		

TIME OF ONSET OF BREAST FEEDING



The time of onset of breastfeeding in case of cases were significantly lower than control group at 98.25 min and 113.625 min respectively

DISCUSSION

DISCUSSION

Ketamine (Phencyclidines) was the first drug of its class to be used for anaesthesia[1]. It is an intravenous anesthetic agent which induces so called "dissociative anesthesia", profound analgesia, immobility amnesia with light sleep and feeling of dissociation from one's own body[2,4]. Ketamine differs from most other drugs used to induce anaesthesia because it has a significant analgesic effect; the interest in Ketamine has increased because of its effect on hyperalgesia and opiate tolerance[2]. The primary site of action is cortical and sub cortical area[2]. The anesthetizing doses are (2 to 2.5mg/kg) and pre anesthetic dose 0.25mg/kg [3].

Studies have shown that even with known cases of intra uterine asphyxia, excellent APGAR scores have been achieved in neonates [11], pre spinal Ketamine is also known to reduce shivering during spinal anesthesia[14], postoperative analgesic requirement, and significantly increase mobility post operatively and ability of mother to care for the infant[13]

Inadequate pain relief following a caesarian delivery may impair the mother's ability to optimally care for her infant in the immediate postpartum period and adversely affect early interaction between mother and infant[13]. Pain and anxiety may also reduce the ability of mother to breast feed effectively. It is necessary that pain relief be safe and effective, that it does not interfere with mother`s ability to move around and care for her infant, and results in no adverse neonatal effect in breast feeding women

In our case control study. 80 full term women who were undergoing caesarian section are categorized into Group A(Ketamine) and Group B (Placebo) by using simple randomization technique of consecutive numbers. Patients who had odd numbers were categorized under Group A and received low dose intravenous

Ketamine 0.25mg/kg diluted to 10ml with sterile water. While those who had even numbers were Group B and received placebo

On arrival at the operating room , all the patients had their baseline vital signs (Pulse , Blood Pressure and oxygen saturation) measured and recorded

In this discussion we compare our study with studies done by

Ebong et al (2011), Wahjoeningsih et al (2007) K Ghazi– Saidi and A.Hajipour (2002) Dich Neilson , Holasek (1982) and A Case Report by George H Bancroft and

John L Lauria

Ebong et al [9] who compared pre incisional low dose ketamine for studying the pre emptive analgesic effect following caesarian section in 80 women for comparison of pain and neonatal outcome, the Apgar scores of the babies in either group showed not much statistical difference at p value of 0.3 but it showed that pre spinal ketamine was safe for administration as no adverse effects were noted in the babies when compared to our study we had shown a significant improvement in neonatal outcome as our apgar scores in case group were significantly improved

Table 8- **EBONG et al - PRESENT STUDY CASE GROUP COMPARISON**

STUDY		**EBONG et al**	**PRESENT STUDY CASE GROUP**
INDUCTION AGENT		KETAMINE	KETAMINE
APGAR SCORE	1 MIN	8.45 ± 0.239	7.23 ± 0.164
	5 MIN	9.45 ± 0.239	9

When we look at the study done by **Wahjoeningsih et al** [13] in which the the evaluation of best fetal outcome on basis of using ketamine and thiopental as induction agent and the babies were divided into three groups according to fetal distress as bradycardia, normal range and tachycardia , the outcome of this study showed that the group with normal heart rate had best apgar scores in both 1st and 5th minute and when the induction agent was compared for the efficacy on basis of apgar scoring the 1st minute apgar scoring showed significant higher for the ketamine group than thiopental group but not significant when 5th minute apgar scoring was taken into consideration .

The induction time for ketamine was significantly faster than thiopental at 6.35sec and 7.39sec respectively

The difference in apgar scoring for the dosage of ketamine used at <1mg/kg and >1mg/kg also did not show any statistical difference further showing that ketamine at higher doses also did not have any adverse effect on the neonates

Table -9 WAHJOENINGSIH et al- PRESENT STUDY CASE GROUP COMPARISON

STUDY		WAHJOENINGSIH et al	PRESENT STUDY CASE GROUP
INDUCTION AGENT		PROPOFOL	PLACEBO
		KETAMINE	KETAMINE
APGAR SCORE	1MIN	p value – 0.04	6.850 ± 0.365
			7.23 ± 0.164
			p value – 0.0031
	5MIN	p value – 0.65	8.5 ± 0.358
			9
			p value -0.0036

On comparison with study done by **K Ghazi– Saidi and A.Hajipour** [10] which was double blinded study for the post operative ananlgesic requirement in a double blind study for patients undergoing caesarian section with standardized general anaesthesia and other group with pre emptive low dose ketamine .The post operative analgesia requirement for the ketamine group was significantly lower in basis of first request for analgesia and mean consumption of morphine over 24 hrs. In our study we also compared the time of onset of breast feeding by the mother after extraction of the baby in both the group based on the post operative analgesia requirement statistics of this study.

Table-10 K GHAZI et al- PRESENT STUDY GROUP COMPARISON

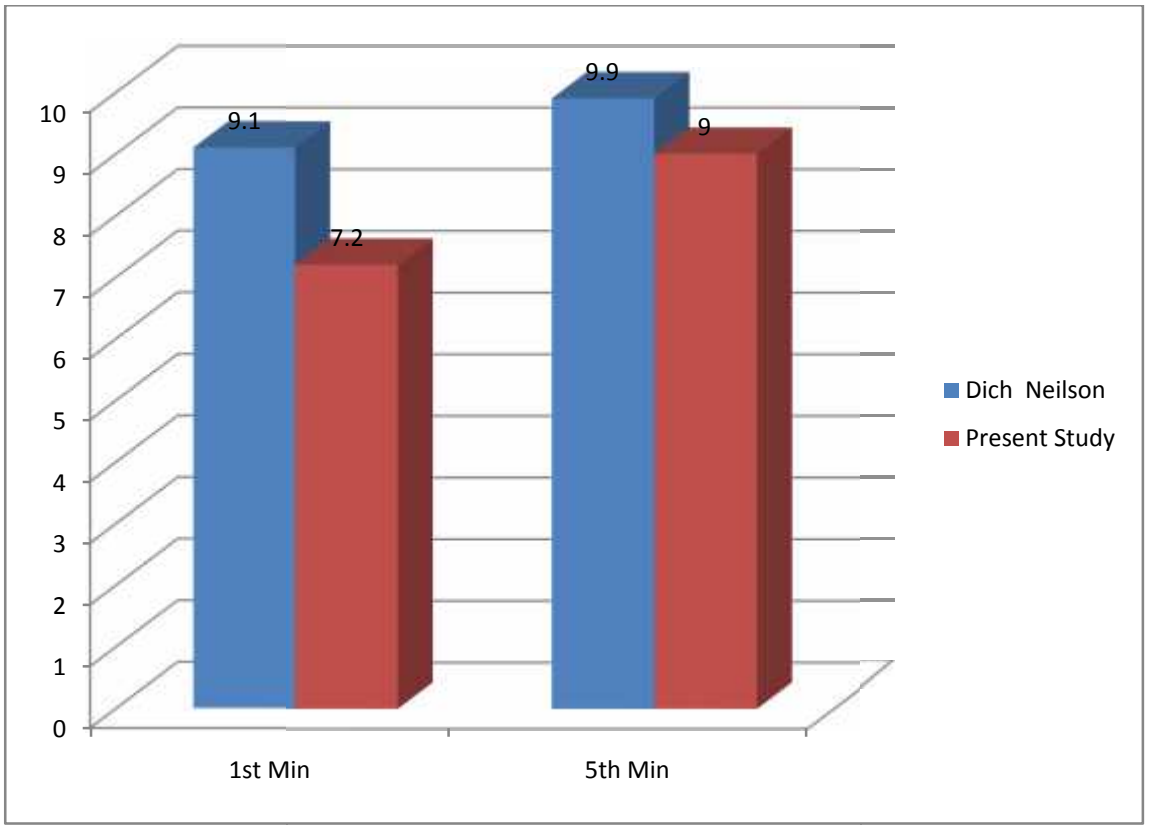
STUDY		K GHAZI et al	PRESENT STUDY GROUP
INDUCTION AGENT		GA	PLACEBO
		KETAMINE	KETAMINE
APGAR SCORE	1MIN	8.96 ± 0.625	6.850 ± 0.365
		8.48 ± 0.238	7.23 ± 0.164
		p value - 0.26	p value – 0.0031
	5MIN	9.884 ± 0.254	8.5 ± 0.358
		10	9
		p value - 0.072	p value -0.0036

The study done by **Dich Neilson , Holasek** [11] studied the effect of pre operative ketamine on 100 patients undergoing caesarian section with low dose ketamine 1.2mg/kg , the study had patients with no fetal distress and also some cases with known cases of intrauterine asphyxia before induction , despite this the results showed excellent Apgar scores at 9.1 and 9.9 at 1st and 5th minute which suggested that ketamine as an induction agent was safe as well as could be regularly used with no adverse effect on the baby and the mother also it might show improvement in Apgar scoring if used .

Table -11 DICH NEILSON et al- PRESENT STUDY CASE GROUP COMPARISON

STUDY		DICH NEILSON et al	PRESENT STUDY CASE GROUP
INDUCTION AGENT		KETAMINE	KETAMINE
APGAR SCORE	1MIN	9.1	7.23 ± 0.164
	5MIN	9.9	9

APGAR SCORE COMPARISON DIAGRAM



Lastly a Case Report by **George H Bancroft and John L Lauria**[12] published in anesthesiology ,The American Society of Anesthesiologists' .Showed that pre anesthetic induction with Ketamine in a case of acute intermittent porphyria showed good Apgar scoring in the neonate

Table -12 SAFETY PROFILE

STUDY	APGAR SCORE	ADVERSE EFFECTS
PRESENT STUDY	1^{ST} MIN 7.23 ± 0.164 5^{TH} MIN 9	NIL
EBONG et al	1^{ST} MIN 8.45 ± 0.239 5^{TH} MIN 9.45 ± 0.239	NIL
WAHJOENINGSIH et al	1^{ST} MIN 7 5^{TH} MIN 9	NIL
K GHAZI et al	1^{ST} MIN 8.48 ± 0.238 5^{TH} MIN 10	NIL
DICH NEILSON et al	1^{ST} MIN 9.1 5^{TH} MIN 9.9	NIL
GEORGE BANCROFT et al	1^{ST} MIN 7 5^{TH} MIN 9	NIL

In our study ,A total of 80 babies born by LSCS was included in the study ,40 babies were in case group and 40 in the control ground divided according to randomization, In the case group 20 were males and 20 were female and in the control group 22 were males and 18 were females .

The APGAR scoring at 1^{st} minute in case and control group were 7.23 ± 0.164 and 6.87 ± 0.368 ,which by the t test had a value < 0.05 which was significant .The 5^{th} minute APGAR scoring on the other hand was 9 and 8.9 ± 0.358 for cases and controls respectively which had a test value of < 0.05 which was significant .

The time of onset of breast feeding in the case and control group were 98.925 ± 60 min and 113.625 ± 65 min respectively which had a significant value < 0.05 .

CONCLUSION

CONCLUSION

From the above study it can be concluded that neonatal outcome in using ketamine as a pre spinal anesthetic not only eases the induction of spinal anaesthesia but also has shows a significant improvement in the 1^{st} and 5^{th} minute APGAR scoring and ease of start of breast feeding by the mother .

BIBILIOGRAPHY

BIBLIOGRAPHY

1) Andre Van Zundert , Gerad .W.Ostheimer. Pain Relief and Anesthesia in Obstetrics , Sub Arachnoid Anesthesia; 1996 : 461- 465.
2) Sean .C .Sweetman. Martin Dale Pharmacology.35th edn; 2006.General Anaesthesia:1611-1612.
3) Ronald H Miller. Millers Anesthesia ; 7th edn ;2010. Anesthetic Pharmacology.P. 742- 746.
4) Tripathi K D, Essentials of Medical Pharmacology, 5th Edition ;2003.General Anesthetics .P . 424-434.
5) Wyilie and Churchill Davidsons`s - A Practice of Anaesthesia ,6thEdition , 2002 .P. 1288-1290.
6) Atkinson RS , Rushman G B , Alfred Lee J . A synopsis of Anaesthesia , Obstetric Anaesthesia and Analgesia.10thEdn . 2002.P. 535-539.
7) Kishor Shridharbhai Trivedi . Probability and Statistics with reliability,queing, and computer science applications .10th Edition.1999.P. 485 -486.
8) John P Cloherty, Eric C.Eichenwald ,Manual of neonatal care .7th edn.2012.P.936.
9) Ebong EJ, Mato CN, Fyneface –Ogan S Pre incisional intravenous low dose ketamine does not cause Pre emptive Analgesia ; J Anesthesia Clinical Research 2011;2 (5): 100013 .
10) K Ghazi–Saidi, A.Hajipour ,Effect of PreEmptive Ketamine on Post Anaesthesia Requirement .Acta Medica Iranica. 2002; 40(2) :99 -103.
11) Dich – Neilson , Holasek , Ketamine and Postoperative pain –a quantitative systematic review of randomized trials. 2005; 113: 61-70.

12) George H Bancroft, John L Lauria. Ketamine Induction for Caesarian section in a patient with acute intermittent porphyria and achondroplastic dwarfism.A case report .The American Society of Anaesthesiologists, 1983; 59(8) :143-144.

13) Wahjoeningsih and Widow Ati,Malaysian Journal of medical sciences 2007; 14(2) : 41-46.

14) Shakya.S and Chaturvedi.A, Published in Journal of anaesthesiology and Clinical Pharmacology 2010; 26 (4) : 465-469.

15) Apgar V. A proposal for a new method of evaluation of the newborn infant. Current Research Anesthesia Analog 1953 Jul;32(4):260-7.

16) Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. N England J Med 2001 Feb 15;344(7):467-71.

17) Apgar V, Holada DA, James LS, Weisbrot IM, Berrien C. Evaluation of the newborn infant; second report. J Am Med Assoc 1958 Dec 13;168(15):1985-1988.

18) The International Neonatal Network. The CRIB (clinical risk index for babies) score: a tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. Lancet 1993 Jul 24;342(8865):193-198.

19) Perlman JM, Wyllie J, Kattwinkel J, Atkins DL, Chameides L, Goldsmith JP, et al .Part 11: neonatal resuscitation ; 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation 2010 Oct 19;122(16 Suppl 2):S516-S 538.79.

20) O'Donnell CP, Kamlin CO, Davis PG, Carlin JB, Morley CJ. Interobserver variability of the 5-minute Apgar score. J Pediatr 2006 Oct; 149(4):486-9.

21) Saugstad O, New guidelines for newborn resuscitation – a critical evaluation. Acta Paediatrica 2011, 100: 1058–1062.

22) Lopriore E, van Burk GF, Walther FJ, de Beaufort AJ. Correct use of the Apgar score for resuscitated and intubated newborn babies: questionnaire study. BMJ 2004 Jul 17; 329(7458) :143-144.

23) American Academy of Pediatrics/American Heart Assosciation. Neonatal resuscitation textbook 2006; 5 edition. IL:5 : 112-115.

24) Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, et al. Part 15: neonatal resuscitation: 2010 American Heart Association Guidelines forCardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010 Nov 2 ; 122(18 Suppl 3) : 909-919.

25) O'Donnell CP, Kamlin CO, Davis PG, Carlin JB, Morley CJ. Clinical assessment of infant colour at delivery. Archives Child Fetal Neonatal Ed 2007 Nov; 92(6) : 465-467.

26) Kamlin CO, O'Donnell CPF, Davis PG, Morley CJ. Oxygen saturation in healthy infants immediately after birth. The Journal of Pediatrics 2006 May; 148(5) :585-589.

27) Apgar V. A proposal for a new method of evaluation of the newborn infant. Current Research Anesthesia Analog 1953 Jul ; 32(4) : 260-263.

28) Sean .C .Sweetman , Martin Dale Pharmacology 35th edn ;General Anesthetic: 1611-1612.

29) Grand et al : Ketamine disposition in children and adults. Anaesthesia 1981;53 : 805-09.

30) Hollister GP ,Burn JMB :Side effects of ketamine in pediatric anaesthesia Anaesthesia Anal.1974:53:264-267.

31) Sussman D R :A comparative evaluation of ketamine anaesthesia in children and adults .Anaesthesiology 1974 ;40:459.

32) Weksler N ,Ovaida L, Muati and Stav A : Nasal ketamine for pediatric premedication.Can .J.Anae 1993; 40(2) :119-21

33) Lear E, Suntay R ,Pallin IM, ChironAE Cyclohexamine(CI-100).A new intravenous agent.Anaesthesiology 1959 ;20 : 330-334.

34) Sadove M S, Shulman M, Hantano S, Fevlod N : Anaesthetic Effect of Ketamine administered in subdissociative doses ,Anesthesia Analog, 1971;50 :452-457.

35) White P F,Way W L ,Trevor A J: Ketamine :Its Pharmacology and Therapeutic uses.Anaesthesiology,1982; 56(4) :119-136.

36) Waxman K ,Lippinman M :Cardiovascular Effect of Anesthetic induction with ketamine ,Anesthesia Analog ,1980;59 Sep :355-358.

37) Weksler N, Ovaida L, Muati G : Nasal Ketamine for pediatric premedication, Canadian Journal of Anaesthesia ,1993;40; 2 :119-121 .

38) Subrahmanyam M, Mohan S. Safety features in anaesthesia machine. Indian J Anaesth 2013; 57: 472-480.

39) Birks R J S,Gemmel L W , O`Sullivan E P Recommendations for standards of monitoring during Anaesthesia and recovery;4th Edition; 2007 : 8-10.

40) Bell RF, Dahl JB, Moore RA, Kalso EA. Perioperative ketamine for acute postoperative pain. Cochrane Database of Systematic Reviews 2006, Issue 1; Art. No.: CD004603.

41) G R Dawson, J F William Deakin ,C T Dourish .The effects of ketamine and risperidone on eye movement control in healthy volunteers; Translational Psychiatry: 2013; 3 : 334.

42) Hesser, Bohla,Muraskas.E ffect of ketamine on transmission in sympathetic ganglia;British Journal of Anaesthesia ;1980; 52 (4): 371-375.

43) Mc Carthy D A, Chen G, General anaesthetic and other pharmacological properties of 2-(0-chlorophenyl-)-2 –methylamino cyclohexanone HCL(CI -581); Journal of New drugs: 1965 ; 5: 21-33.

44) Corssen G ,DominoE .Dissociative Anaesthesia and further pharmacological studies and first clinical experience with phencyclidine derivatives; Anesthesia and alnalgesia current researches ; 1966; 45 : 29-30.

45) Agoston S,Salt J,Chair B. Antagonism of ketamine-diazepam anesthesia by 4-aminopyrindine in human volunteers ;British Journal of Anaesthesia:1980 ; 52 (4): 367-370.

46) Corrsen L, Hoy ML Grietensten G ,Johnson S, Twenty Years of Dissociative Anesthesia with Ketamine (CI-581). Its Origin and Present Significance. Survey of Anesthesiology:1987 ; 31 (1) :62-74.

47) DL Traber, RD Wilson, Ove A.Cocaine-like effect of ketamine on vascular adrenergic neurons. European journal of pharmacology .1973; 23(2) :153-161.

48) Weiskopf, Richard B.Comparison of cardiopulmonary responses to graded hemorrhage during enflurane, halothane, isoflurane, and ketamine anesthesia. Anesthesia & Analgesia.1981Dec; 60(7): 481-491.

49) Dawson JA, Kamlin CO, Wong C. Changes in heart rate in the first minutes after birth. Arch Dis Child Fetal Neonatal .2010 May ; 95(3):F177-F181

ANNEXURE

ETHICAL CLEARANCE CERTIFICATE

BIJAPUR-586 103
OUT WARD
No. C46/12
18/10/12

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 18-10-2012 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title Neonatal outcome using Ketamine as a pre Spinal agent in Caesarean Section - A Hospital based randomized control trail

Name of P.G. student Dr. Issac Varghese
paediatrics

Name of Guide/Co-investigator Dr R.H. Gobbur
prof of paediatrics

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

PROFORMA

B.L.D.E.Association's

SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR.

DEPARTMENT OF PAEDIATRICS

NEONATAL RECORD

Infant of ..... Hosp. No. ..... Mother's Hosp. No. .....
Date of Birth ..... Time ..... hrs. Sex. .....
Father ..... Age.....yrs. Occupation .....
Town/Village ..... District ..... State..... Admission date .....

MATERNAL MEDICAL HX
Age .....yrs Gravida .....Parity .....Living ..... Blood group..... Rh type.....Hb.....
Level of Education ..... Ht. .....cm. Wt. gain ..... kg.

Maternal hx	Family hx		Maternal hx	Family hx	
.....	.....	Consanguinity	.....	.....	Heart disease
.....	.....	Abortions/Still births	.....	.....	Tuberculosis
.....	.....	Neonatal deaths	.....	.....	Asthama
.....	.....	Premature labour/delivery	.....	.....	Epilepsy
.....	.....	Previous C-section	.....	.....	UTI
.....	.....	Infant with cong anomaly	.....	.....	Thyroid disease
.....	.....	Hypertension	.....	.....	Other.....

Notes .....

PRESENT PREGNANCY
LMP ..... EDD..... VDRL..... ANC..... USG..... X-ray..... NST..... OCT.....

.....	Hyperemesis	.....	Oligohydramnios/Polyhydramnios
.....	Hypertension/PIH/Eclampsia	.....	Vaginal bleeding
.....	Anemia	.....	Heart disease
.....	Infection	.....	Seizure disorder
.....	Jaundice	.....	Premature labour/ROM
.....	Diabetes	.....	Placental insufficiency
.....	Urinary infections	.....	Post term
.....	drugs	.....	Other disease .....

LABOUR
Spontaneous/Induced ..... Duration : Ist stg .....hrs 2nd stg .....mts.

Drugs		RMDI	
.....	IV fluids	.....	0 -12 hours
.....	Oxytocin	.....	12 -24 hours
.....	Pethidine	.....	>24 hours
.....	Tocolytic agents		Meconium .....
.....	Other.....		

DELIVERY Type		Presentation		Place	
.....	Normal vaginal	.....	Vertex	.....	BMP Hosp.
.....	Instrumental	.....	Breech	.....	Outreach centre
.....	C-Section	.....	Other.....	.....	Other Hosp.
				.....	Home

Mat. Indications	Fetal indications	Drugs	FHR
..... Repeat C-section	..... Fetal distress	..... Gen. anaesthesia	..... <100
..... CPD	..... IUGR	..... Spinal/epidural	 100-160
..... Prolonged labour	..... Breech/malpres	..... Pethidine	..... >160/min
..... PIH/PET/eclampsia	..... Multiple preg.	..... Other	..... declerations
..... Other	..... Other		

POST DELIVERY

Apgar score	HR	Resp. effort	Tone	Reflex response	Colour	Total
1 minute	.....	.....	.....	.....	.....	.....
5 minute	.....	.....	.....	.....	.....	.....
10 minute	.....	.....	.....	.....	.....	.....
20 minute	.....	.....	.....	.....	.....	.....

Resuscitation method :

		Drugs	
.....	Oxygen blowby	.....	Sodium bicarbonate
.....	Mask and ambu bag	.....	Dextrose
.....	Intubation	.....	Adrenaline
.....	Umbilical catheter	.....	Nalorphine
		.....	Other .....

PHYSICAL EXAMINATION

Single/twin .....1st/2nd twin ..... EGA : by dates ..... weeks; by exam..... weeks

Length ..... cms. Birth weight .....gms. MAC .....cms. Cord .....cms.

General and systemic examination : HC .....cms. AF : AP .....cms. Tr .....cms.

Vital Signs :

Skin :

Craniofacial :

Chest :

CVS :

Lungs :

Abdomen :

Genitalia :

Extremities :

Back :

CNS :

Impression : Plan

Name ..... Signature .....

PROBLEM LIST :

Date	Problem	Code No.	Treatment	Date Resolved

PROCEDURES

..... Umbilical catheter
..... Spinal tap
..... Head ultrasound
..... X'rays
..... ECG
..... Abdominal USG
..... Postmortem
..... Developmental assessment
..... Other

DRUGS/THERAPY

..... Artificial feedings
..... IV fluids
..... Phototherapy
..... Antibiotics
..... Calcium
..... Steroids
..... Diuretics
..... Blood transfusion
..... Exchange transfusion
..... Other

DISCHARGE DATE : .....

BABY : Status ..... Bed category ..... Blood Group ..... Rh type .....

Weight ..... gms. HC..... cms. Hb..... gms. Discharge date .....

Immunisation : BCG ..... OPV .....Age ..... Days .....

Course in Hospital :

Impression :

Discharge plan :

Feeding :

Medication :

Follow-up visit :

Name :

Signature :

NEWBORN MATURITY RATING AND CLASSIFICATION

ESTIMATION OF GESTATIONAL AGE BY MATURITY RATING

Symbols : X – 1st Exam O- 2nd Exam

NEUROMUSCULAR MATURITY

	0	1	2	3	4	5
Posture						
Square Window (Wrist)	 90°	 60°	 45°	 30°	 0°	
Arm Recoil	 180°		 100°-180°	 90°-100°	 <90°	
Popliteal Angle	 180°	 160°	 130°	 110°	 90°	 <90°
Scarf Sign						
Heal to Ear						

PHYSICAL MATURITY

	0	1	2	3	4	5
Skin	gelatinous red, transparent	Smooth pink, visible veins	superficial peeling & few veins	cracking pale area rare veins	parchment deep cracking no vessels	leathery cracked wrinkled
Lanugo	none	sparse	thinning	bald areas	mostly bald	
plantar Creases	no creases	faint red marks	anterior transverse creases only	creases ant. 2/3	creases cover entire sole	
Breast	barely percept.	flat areola no bud	stippled areola 1-2 mm bud	raised areola 3-4 mm bud	full areola 5-10 mm bud	
Ear	pinna flat, stays folded	sl. curved pinna; soft with slow recoil	well-curv. pinna; soft but ready recoil	formed & firm with instant recoil	thick cartilage ear stiff	
Genitals	scrotum empty no rugae		testes descending, few rugae	testes down, good rugae	testes pendulous deep rugae	
Genitals	prominent clitoris & labia minora		majora & minora equally prominent	majora large, minora small	clitoris & minora completely covered	

Gestation by Dates _____ wks

Birth Date _____ Hour _____ am / pm

APGAR _____ 1 min _____ 5 min

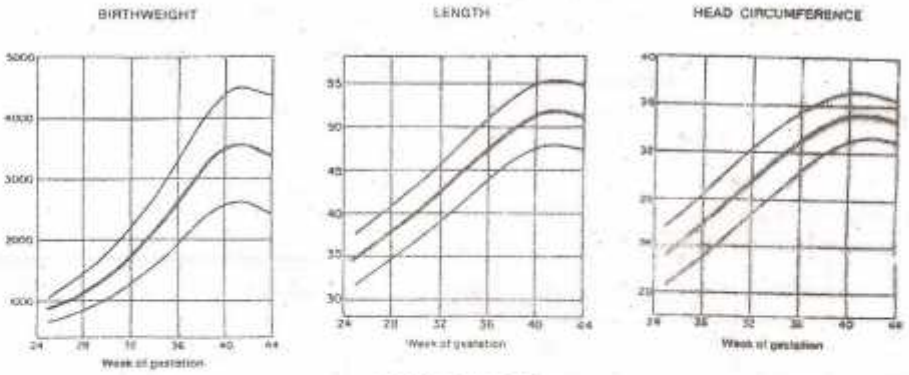
SCORING SECTION

1st Exam =X 2nd Exam=O

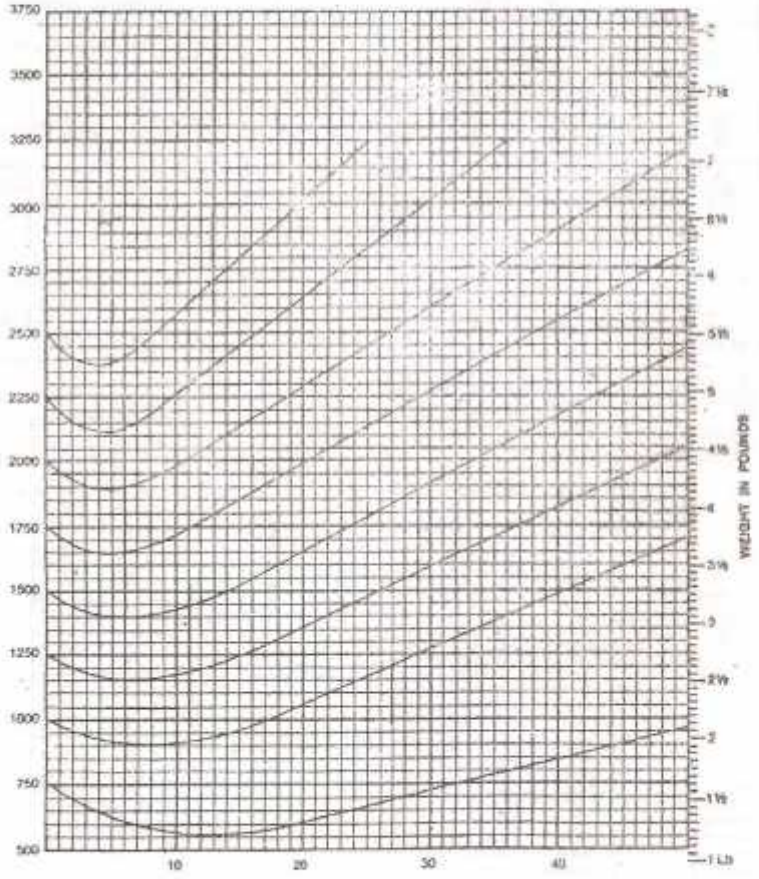
Estimating Gest Age by Maturity Rating	_____ Weeks	____ Weeks
Time of Exam	Date_____ Hour____ am / pm	Date_____ Hour____ am / pm
Age at Exam	_____Hours	_____Hours
Signature of Examiner	_____ _____M.D.	_____ _____M.D.

MATURITY RATING

Score	Wks
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44



GROWTH RECORD



AGE IN DAYS

CONSENT FORM

BLDEA`s SHRI . B.M.PATIL MEDICAL COLLEGE HOSPITAL &

RESEARCH CENTER, BIJAPUR

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT :

"NEONATAL OUTCOME USING KETAMINE AS A PRE SPINAL AGENT IN CAESAREAN SECTION - A HOSPITAL BASED RANDOMIZED CONTROL TRIAL"

GUIDE : Dr .R.H.GOBBUR , PROFESSOR ,
DEPT OF PEDIATRICS

CO – GUIDE : Dr. VIJAYAKUMAR T KALYANAPPAGOL,
PROFESSOR,
DEPARTMENT OF ANAESTHESIA

PG STUDENT : Dr. ISSAC VARGHESE

PURPOSE OF RESEARCH

I have been informed that the present study will help improve neonatal outcome in terms of apgar scoring and neonatal outcome in caesarian section.

PROCEDURE : I Understand That After Having Obtained A Detailed Clinical History,Through Clinical Examination And Relevant Investigations , A Final Work Up Of The Procedure And Its Outcome Is Planned

RISK AND DISCOMFORT : I Understand That I May Experience Some Pain And Discomfort During The Examination Or During Treatment .This Is Mainly The Result Of My Condition And Theprocedures Of This Study Are Not Expected To Exaggerate This Feeling Which Are Associated With Usual Course Of Treatment.

BENEFITS :

I Understand That My Participation In The Study Will Have No Direct Benefit To Me Other Than The Potential Benefit Of The Treatment.

CONFIDENTIALITY :

I understand that the medical information produced by this study will become part of hospital records and will be subject to confidentiality. Information of sensitive personal nature will not be part of medical record , but will be stored in the investigations research ,If data is used for publication in medical literature or for teaching purpose no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving permission.

REQUEST FOR MORE INFORMATION:

I understand that i may ask more questions about study at anytime ; Dr Issac Varghese at the department of pediatrics is available to answer my questions or concerns that I will be informed of any significant new finding discovered during the course of the study , which might influence my continued participation .a copy this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWAL FROM PARTICIPATION :

I understand that my consent is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice . I also understand that Dr Issac Varghese may terminate my participation in the study after he has explained reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me and my baby resulting directly from participation in this study ,if such injury was reported promptly , the appropriate treatment would be available to me. But , no furthter compensation would be provided by the hospital. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

SIGNATURE OF PATIENT / RELATIVE

NAME AND RELATION TO THE PATIENT

I HAVE EXPLAINED TO Shri / Smt

THE PURPOSE OF THE RESEARCH ,THE PROCEDURES REQUIRED AND POSSIBLE RISKS TO THE BEST OF MY ABILITY

_____

Dr . ISSAC VARGHESE

(INVESTIGATOR) DATE

STUDY SUBJECT CONSENT STATEMENT

I confirm that Dr Issac Varghese has explained to me the purpose of research, the study procedure, that I am willing to allow me and My baby to undergo the investigation and the possible discomforts as Well as benefits. I have been explained all the above in detail in my own language and I understand the same .therefore I agree to give Consent to participate as subject in this research purpose

(PARTICIPANT)

DATE

WITNESS TO SIGNATURE

DATE

MASTER CHART

CASES

SL NO	NAME	IP NO	SEX	WEIGHT	DOSE OF KETAMINE	APGAR	1 MIN	5 MIN	TIME OF ONSET OF BREAST FEEDING	AGE	OBSTETRIC HISTORY	INDICATION FOR LSCS
1	B/O RUKMINI	8245	FEMALE	2.28 Kg	12.5 mg		7 \ 10	9 \ 10	165 Min	26 Yrs	Primigravidae	CPD
2	B/O ANITA	8376	MALE	3.05 Kg	12.5 mg		7 \ 10	9 \ 10	80 Min	24 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
3	B/O REEMA	8351	FEMALE	3.15 Kg	12.5 mg		7 \ 10	9 \ 10	70 Min	24 Yrs	Primigravidae	CPD
4	B/O KAVITA	8687	MALE	3.5 Kg	12.5 mg		7 \ 10	9 \ 10	108 Min	25 Yrs	G3 P2 L1 D1	Repeat LSCS/ Scar Tenderness
5	B/O ASHWINI	8953	MALE	2.53 Kg	12.5 mg		7 \ 10	9 \ 10	85 Min	23 Yrs	G2 A1	Repeat LSCS/ Scar Tenderness
6	B/O VIJAYALAXMI	17183	MALE	3.6 Kg	12.5 mg		7 \ 10	9 \ 10	45 Min	20 Yrs	G3 P2 A1 L1	Repeat LSCS/ Scar Tenderness
7	B/O SHOBHA	17320	MALE	2.46 Kg	12.5 mg		7 \ 10	9 \ 10	75 Min	22 Yrs	G2 P1 A1	CPD
8	B/O RAJSHREE	18608	FEMALE	3.01 Kg	12.5 mg		8 \ 10	9 \ 10	55 Min	20 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
9	B/O ROOPA	18183	MALE	2.7 Kg	12.5 mg		8 \ 10	9 \ 10	125 Min	20 Yrs	G2 P1 L1	CPD
10	B/O JAYASHREE	18500	FEMALE	2.5 Kg	12.5 mg		7 \ 10	9 \ 10	115 Min	23 Yrs	Primigravidae	CPD
11	B/O AMBIKA	19002	MALE	2.5 Kg	12.5 mg		7 \ 10	9 \ 10	110 Min	20 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
12	B/O YASHMIN	19333	MALE	3.1 Kg	12.5 mg		7 \ 10	9 \ 10	110 Min	18 Yrs	G2 P1 L1	CPD
13	B/O ASHA	19437	MALE	2.51 Kg	12.5 mg		7 \ 10	9 \ 10	100 Min	20 Yrs	Primigravidae	CPD
14	B/O SUREKHA	19491	MALE	2.55 Kg	12.5 mg		7 \ 10	9 \ 10	100 Min	18 Yrs	Primigravidae	CPD
15	B/O INDUMATI	19952	MALE	3.1 Kg	12.5 mg		8 \ 10	9 \ 10	110 Min	28 Yrs	Primigravidae	Repeat LSCS/ Scar Tenderness
16	B/O POORNIMA	21675	FEMALE	2.51 Kg	12.5 mg		7 \ 10	9 \ 10	90 Min	20 Yrs	G5 P2 L2 A2	CPD
17	B/O SAROJA	21674	MALE	3.51 Kg	12.5 mg		8 \ 10	9 \ 10	80 Min	21 Yrs	Primigravidae	Repeat LSCS/ Scar Tenderness
18	B/O ANUPAMA	22589	MALE	3.9 Kg	12.5 mg		7 \ 10	9 \ 10	115 Min	21 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
19	B/O TAYABBA	22986	MALE	2.9 Kg	12.5 mg		7 \ 10	9 \ 10	145 Min	28 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
20	B/O SHANTABAI	23220	MALE	4.02 Kg	12.5 mg		8 \ 10	9 \ 10	90 Min	24 Yrs	G5 P4 L3 D1	Repeat LSCS/ Scar Tenderness
21	B/O VAISHALI	23444	FEMALE	3.2 Kg	12.5 mg		7 \ 10	9 \ 10	140 Min	22 Yrs	G3 P2 L2	Repeat LSCS/ Scar Tenderness
22	B/O SAHANA	26158	MALE	3.15 Kg	12.5 mg		8 \ 10	9 \ 10	140 Min	29 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
23	B/O SUMANGALA	26520	FEMALE	2.56 Kg	12.5 mg		7 \ 10	9 \ 10	75 Min	26 Yrs	G4 P2 L2 A2	CPD
24	B/O MAHADEVI	27178	MALE	2.82 Kg	12.5 mg		7 \ 10	9 \ 10	100 Min	20 Yrs	Primigravidae	CPD
25	B/O JYOTHI	27180	FEMALE	1.98 Kg	12.5 mg		7 \ 10	9 \ 10	95 Min	19 Yrs	Primigravidae	CPD
26	B/O HULIGEMA	27338	FEMALE	2.9 Kg	12.5 mg		7 \ 10	9 \ 10	180 Min	22 Yrs	Primigravidae	CPD
27	B/O SHOBHA	27507	FEMALE	2.8 Kg	12.5 mg		8 \ 10	9 \ 10	95 Min	20 Yrs	Primigravidae	CPD
28	B/O VEENA	27710	FEMALE	2.5 Kg	12.5 mg		7 \ 10	9 \ 10	110 Min	24 Yrs	Primigravidae	CPD
29	B/O SADNA	27968	MALE	2.8 Kg	12.5 mg		7 \ 10	9 \ 10	110 Min	19 Yrs	Primigravidae	CPD
30	B/O JAYASHREE	27972	FEMALE	2.6 Kg	12.5 mg		7 \ 10	9 \ 10	90 Min	27 Yrs	Primigravidae	CPD
31	B/O SRIDEVI	28153	FEMALE	2.9 Kg	12.5 mg		7 \ 10	9 \ 10	80 Min	22 Yrs	G4 P3 L3	Repeat LSCS/ Scar Tenderness
32	B/O SAVATRI	30379	FEMALE	2.73 Kg	12.5 mg		7 \ 10	9 \ 10	110 Min	24 Yrs	Primigravidae	Repeat LSCS/ Scar Tenderness
33	B/O GEETHA	30385	FEMALE	2.73 Kg	12.5 mg		7 \ 10	9 \ 10	140 Min	20 Yrs	G3 P1 L2 A1	Repeat LSCS/ Scar Tenderness
34	B/O ROOPA	17	FEMALE	3.3 Kg	12.5 mg		7 \ 10	9 \ 10	75 Min	20 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
35	B/O RAMJAANBEE	3167	FEMALE	3.14 Kg	12.5 mg		7 \ 10	9 \ 10	200 Min	21 Yrs	Primigravidae	CPD
36	B/O UMA	3189	MALE	2.9 Kg	12.5 mg		7 \ 10	9 \ 10	200 Min	23 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness
37	B/O VIDYASHREE	3282	FEMALE	3.24 Kg	12.5 mg		8 \ 10	9 \ 10	185 Min	26 Yrs	Primigravidae	CPD
38	B/O MADIINA	3592	FEMALE	2.85 Kg	12.5 mg		7 \ 10	9 \ 10	120 Min	24 Yrs	G2 P1 L1	CPD
39	B/O RENUKA	3887	MALE	2.44 Kg	12.5 mg		7 \ 10	9 \ 10	90 Min	18 Yrs	G2 P1 D1	Repeat LSCS/ Scar Tenderness
40	B/O SUNITA	4038	FEMALE	3.1 Kg	12.5 mg		7 \ 10	9 \ 10	110 Min	22 Yrs	G2 P1 L1	Repeat LSCS/ Scar Tenderness

CONTROLS

SL NO	NAME	IP NO	SEX	WEIGHT	DOSE OF STRILE WATER	APGAR		TIME OF ONSET OF	AGE (yrs)	OBSTETRIC HISTORY	INDICATION FOR LSCS
						1 MIN	5 MIN	BREAST FEEDING			
1	B/O LAXMI	1353	MALE	3.74 Kg	5cc	7 \ 10	9\10	80min	20	PRIMI	CPD
2	B/O VIJAYALAXMI	1904	MALE	2.75Kg	5cc	7 \ 10	9\10	105min	24	G3 P2 L2	Repeat LSCS/ Scar Tenderness
3	B/O LAXMI	9136	FEMALE	2.57Kg	5cc	7 \ 10	9\10	70min	28	G4 P3 L1 D1	Repeat LSCS/ Scar Tenderness
4	B/O BHARTI	12942	FEMALE	2.7OKg	5cc	7 \ 10	9\10	110min	26	G3 P2 L2	Repeat LSCS/ Scar Tenderness
5	B/O HALEEMA	17284	FEMALE	2.4OKg	5cc	7 \ 10	9\10	85min	24	G2 P1 L1	Repeat LSCS/ Scar Tenderness
6	B/O VAANI	18082	MALE	2.8OKg	5cc	6\10	9\10	210min	22	PRIMI	CPD
7	B/O SUNANDA	18184	MALE	3.05Kg	5cc	7 \ 10	9\10	140min	22	G2 P1 L1	Safe Confinement
8	B/O SRIDEVI	19353	MALE	3.1OKg	5cc	6\10	9\10	85min	24	G4 P1 L1	Repeat LSCS/ Scar Tenderness
9	B/O SWETHA	19468	MALE	2.78Kg	5cc	7 \ 10	9\10	110min	24	G3 P2 L2	Repeat LSCS/ Scar Tenderness
10	B/O PADMAVATI	18979	MALE	3.6OKg	5cc	6\ 10	9\10	80min	24	G2 P1 L1	CPD
11	B/O ABITA	18035	FEMALE	3.09Kg	5cc	6\10	7\10	100min	21	PRIMI	CPD
12	B/O BHARTI	18534	FEMALE	2.33Kg	5cc	5\10	7\10	125min	20	PRIMI	CPD
13	B/O ROOPA	18404	MALE	2.68Kg	5cc	8\10	9\10	85min	26	PRIMI	Repeat LSCS/ Scar Tenderness
14	B/O SANGEETHA	20069	FEMALE	2.3OKg	5cc	7 \ 10	9\10	75min	24	G3P2 L1 A1	CPD
15	B/O RENUKA	21681	FEMALE	3.25 Kg	5cc	8\10	9\10	100min	24	PRIMI	CPD
16	B/O RIHANBEE	21692	MALE	3.2OKg	5cc	8\10	9\10	160min	22	G2 P1 L1	Repeat LSCS/ Scar Tenderness
17	B/O GEETHA	22384	MALE	1.92 Kg	5cc	7 \ 10	9\10	100min	25	G3 P2 L2	CPD
18	B/O REKHA	22965	MALE	3.1OKg	5cc	6\10	9\10	125min	24	PRIMI	CPD
19	B/O SHOBHA	23023	MALE	2.8OKg	5cc	7 \ 10	9\10	75min	23	G2 P1 L1	Repeat LSCS/ Scar Tenderness
20	B/O BHAGAMMA	23350	FEMALE	2.7OKg	5cc	6\10	9\10	160min	24	G2 P1 L1	Repeat LSCS/ Scar Tenderness
21	B/O MAHADEVI	23477	MALE	3.2OKg	5cc	7 \ 10	9\10	80min	22	PRIMI	CPD
22	B/O BHANKARAMMA	26147	FEMALE	2.5OKg	5cc	7 \ 10	9\10	80min	24	G2 P1 L1	Repeat LSCS/ Scar Tenderness
23	B/O YALLAMMA	26485	MALE	2.19 Kg	5cc	7 \ 10	9\10	110min	24	G2 P1 L1	Repeat LSCS/ Scar Tenderness
24	B/O NINGAMMA	27179	MALE	2.7OKg	5cc	7 \ 10	9\10	150min	22	G3 P1 L1 A1	Repeat LSCS/ Scar Tenderness
25	B/O DEVAMMA	27177	FEMALE	2.51 Kg	5cc	8\10	9\10	150min	21	G4 P2 L2 A1	Repeat LSCS/ Scar Tenderness
26	B/O SUNANDA	27075	MALE	3.1O Kg	5cc	6\10	9\10	140min	21	G2 P1 L1	Repeat LSCS/ Scar Tenderness
27	B/O SARASWATI	22813	FEMALE	2.2OKg	5cc	7 \ 10	9\10	180min	22	PRIMI	CPD
28	B/O SRIDEVI	27838	FEMALE	2.52 Kg	5cc	7 \ 10	9\10	180min	20	G6 P4 L3 A1 D1	Repeat LSCS/ Scar Tenderness
29	B/O SARUBAI	27912	FEMALE	2.72 Kg	5cc	7 \ 10	9\10	110min	22	G2 P1 L1	Repeat LSCS/ Scar Tenderness
30	B/O SUJATA	28089	FEMALE	2.5OKg	5cc	7 \ 10	9\10	85min	26	G2 P1 L1	CPD
31	B/O SHANTA	28148	FEMALE	2.48 Kg	5cc	7 \ 10	9\10	85min	20	PRIMI	CPD
32	B/O NASEEMA	182	MALE	2.3OKg	5cc	7 \ 10	9\10	135min	20	G2 P1 L1	CPD
33	B/O VIJAYALAXMI	3076	MALE	3.4OKg	5cc	7 \ 10	9\10	130min	21	PRIMI	CPD
34	B/O LAXMIBAI	3187	FEMALE	2.6OKg	5cc	7 \ 10	9\10	80min	22	PRIMI	CPD
35	B/O SHOBHA	3280	MALE	3.01Kg	5cc	7 \ 10	9\10	90min	24	G4 P2 L2 A1	Repeat LSCS/ Scar Tenderness
36	B/O ANNAPURNA	3276	FEMALE	2.57 Kg	5cc	7 \ 10	9\10	160min	26	G2 P1 L1	Repeat LSCS/ Scar Tenderness
37	B/O SHASHIKALA	3586	MALE	3.18Kg	5cc	7 \ 10	9\10	80min	21	PRIMI	CPD
38	B/O BASAMMA	3937	FEMALE	3.14 Kg	5cc	7 \ 10	9\10	120min	24	PRIMI	CPD
39	B/O PRABHAVATI	4105	MALE	2.44 Kg	5cc	7 \ 10	9\10	100min	22	G2 P1 L1	Repeat LSCS/ Scar Tenderness
40	B/O SEETHA	4337	MALE	2.5OKg	5cc	7 \ 10	9\10	120min	23	PRIMI	CPD