INTRAVENOUS LOW DOSE KETAMINE INFUSION

FOR LABOUR ANALGESIA

A Prospective Interventional Clinical Trial

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF

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TO BE HELD IN FEBRUARY 2007

CERTIFICATE

This is to certify that the dissertation entitled, "**INTRAVENOUS LOW DOSE KETAMINE INFUSION FOR LABOUR ANALGESIA "**is the bonafide original work done by Dr. **ANITA SHIRLEY JOSELYN**. This study was undertaken at the **Christian Medical College and Hospital, Vellore** from the year 2005-2006 under my guidance and supervision, in partial fulfillment of the requirement for the award of the **M.D Degree (Branch –X) Anaesthesiology** of the **Tamilnadu Dr.M.G.R Medical University.**

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CONTENTS

		Page No.
Introduction	…	1
Aim	…	3
Review of Literature	…	4
Patients and Methods	…	22
Results	…	26
Discussion	…	42
Conclusion	…	51
Bibliography	…	52

Appendix

i. Proforma
ii. Patient information & consent
iii. Master Chart

INTRODUCTION

Pain during labour and delivery is intense, although there is considerable variability in its perception. (1) The commonly employed methods of pain relief in labour include systemic analgesics, inhalational anaesthetics, and regional techniques. Pethidine is the most commonly used systemic analgesic which provides moderate analgesia, but it causes sedation, nausea and vomiting in the mother and respiratory depression in the neonate. (2) Inhalation of a mixture of nitrous oxide and oxygen (Entonox) provides analgesia, but it requires good maternal co-operation to be effective. (3) An epidural local anaesthetic with opioids provide good relief of pain during labour, but is associated with prolongation of the second stage of labour and an increased incidence of instrumental vaginal delivery. (4) It is also relatively expensive and needs an expert to initiate the block.

Ketamine is a short acting anesthetic with excellent analgesic property, and has been widely used for short surgical procedures like wound suturing and dressing in the out patient department. It has been safely used in obstetrics as an induction agent for caesarean section, manual removal of placenta, and for forceps delivery. (5) It has been shown that in low doses, intravenous ketamine provides good intraoperative and postoperative analgesia. (6, 7)

This prospective interventional study was an effort to evaluate the efficacy of low dose ketamine as a labour analgesic, thereby providing a safe and inexpensive alternative, especially for the developing countries with limited resources and economical constraints.

AIM

The aims of this study are:

1. To evaluate the efficacy of low dose intravenous ketamine in providing analgesia during labour.
2. To assess the safety of low dose intravenous ketamine on the parturient and the fetus, and its effect on the progress of labour.
3. To standardise a “low dose ketamine” regimen for labour analgesia.

REVIEW OF LITERATURE

To the woman He (God) said, “I will greatly increase your pains in childbearing, with pain you will give birth to children.” Genesis 3:16

SEVERITY OF LABOUR PAIN

Pain during childbirth may be the most painful experience for a woman. Melzack et al, using the McGill pain questionnaire, tried to assess the pain during the first stage of labour. Sixty percent of the women described the pain of uterine contractions as being extremely severe and unbearable, while the rest described it as being moderately severe. (1) Pain during labour was graded higher than that during several pain syndromes like backache, phantom limb, fracture and deep laceration. It just falls short of the pain experienced during amputation of a digit without anaesthesia. (Figure - 1)

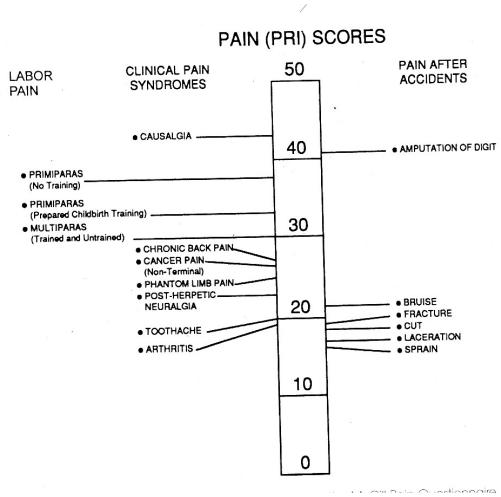


Figure 1- Comparison of pain scores, using the McGill Pain Questionnaire. (PRI - pain rating index)From Ward ME, Cousins MJ: Pain Mechanisms in Labor. In Birnbach DJ, Gatt SP, Datta S (eds): Textbook of Obstetric Anesthesia. New York: Churchill Livingstone; 2000:3-30.

PATHWAY OF LABOUR PAIN

Pain during the first stage of labour is primarily due to the uterine contraction and cervical dilatation. These visceral pain sensations are conveyed by the Aδ and C fibers that accompany the thoracolumbar T_{10} –L_1 sympathetic outflows. (9)

The second stage of labour pain is due to dilatation of the cervix and stretching of the perineum and the birth canal. This somatic sensation is conveyed by the pudendal nerves (S2-4) and is intense and sharply localized. (Figure -2)

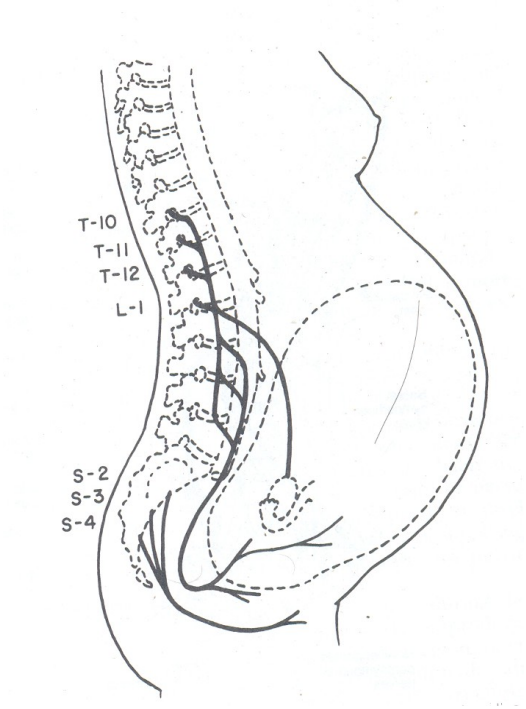
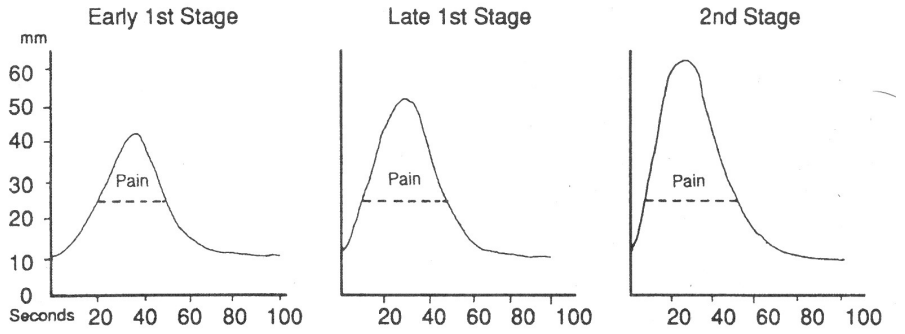


Figure 2- Schematic of the peripheral nociceptive pathways involved in the pain of child birth. (From Ward ME, Cousins MJ: Pain Mechanisms in Labor. In Birnbach DJ, Gatt SP, Datta S (eds): Textbook of Obstetric Anesthesia. New York: Churchill Livingstone; 2000:3-30)

CHARACTERISTICS OF LABOUR PAIN

There is a lag period between the start of the uterine contraction and the perception of pain, which heightens to a peak before the uterus relaxes.(1) This lag period is around 20sec in the early first stage, which gradually reduces to about 5sec during the second stage. (Figure-3) The frequency of the uterine contraction and the pain increases with the progress of labour.



	Early 1st Stage	Late 1st Stage	2nd Stage
Contractions:			
Duration	70 seconds	75 seconds	80 seconds
Intensity	40 mmHg	50 mmHg	50-60 mmHg
Pain:			
Lag	20 seconds	10 seconds	5 seconds
Duration	30 seconds	40 seconds	50 seconds

Figure 3- Relation between duration of uterine contraction and duration of pain associated with the contraction. (From Ward ME, Cousins MJ: Pain Mechanisms in Labor. In Birnbach DJ, Gatt SP, Datta S (eds): Textbook of Obstetric Anesthesia. New York: Churchill Livingstone; 2000:3-30)

EFFECT OF PAIN ON THE MOTHER AND FETUS

The pain during labour evokes a generalized neuroendocrine stress response that has widespread physiological effects on the parturient. These include delayed gastric emptying, un-coordinated uterine contractions, increased oxygen consumption and anaerobic metabolism. The sequelae of hyperventilation, increased oxygen consumption, secretion of stress related hormones can lead to metabolic acidosis in the mother and the fetus with resultant fetal hypoxia and abnormal fetal heart rate patterns. Effective pain relief has been shown to prevent, obtund or abolish these effects. (11)

METHODS OF PAIN RELIEF

Non-pharmacological techniques such as TENS, acupuncture, massage, aromatherapy and hypnosis have been used but the pharmacological methods are the main stay of labour analgesia.(3)

The ideal labour analgesic technique should dramatically reduce the pain during labour, while allowing the parturient to actively participate in the experience. In addition, it should have minimal effect on the fetus or the progress of labour. Even though a well conducted epidural blockade tends to nearly achieve this, it can be associated with problems and needs expertise to site it, which may not be readily available. Hence, systemic narcotics are still the main stay for labour analgesia in many parts of the third world where there is an acute shortage of trained anesthetists.

SYSTEMIC ANALGESICS

Pethidine is the most widely used parenteral opioid for labour analgesia. It is a synthetic, weakly basic, phenylpiperidine derivative and is 28 times more lipid soluble than morphine. The onset of action is 45 minutes after an intramuscular injection and the elimination half life is 2.5 -3 hours in the mother (12) and 18 - 23 hours in the neonate. (13) Nor-Pethidine, an active metabolite of pethidine, is a potent respiratory depressant. Pethidine and nor-pethidine, cross the placenta by passive and active diffusion and achieves equilibrium in the fetus

within 6 hours after maternal administration. Since pethidine is a weak base and gets more ionised in an acidic medium, the fetal concentration is higher than maternal levels. (3) Pethidine causes delay in uterine contraction when given in the early phase of labour, but has no effect on the progress of labour when administered in the active phase. (14) It decreases fetal heart rate variability and the residual depressant effects are demonstrated by low Apgar scores and decreased oxygen saturation in the new born, which persists for several hours after delivery. (2) Pethidine causes nausea, vomiting, confusion and sedation in the mother while nor-pethidine, which has convulsant properties may be contraindicated in those with severe pregnancy induced hypertension. (3) However, pethidine is still popular as it is inexpensive, readily available, easy to administer and has reasonable analgesic effect.

Morphine and fentanyl has also been used for labour analgesia but they cause increasing sedation with repeated doses. It has been argued that narcotics merely provide sedation rather than analgesia in labour. (15)

INHALATIONAL ANAESTHETICS

Subanaesthetic concentration of an inhalational anesthetic agent, (trilene, nitrous oxide, isoflurane) can relieve pain during the first and second stage of labour. Entonox, a mixture of 50% nitrous oxide in oxygen has been used since 1990. (3) Nitrous oxide has a low blood gas solubility coefficient and it equilibrates rapidly with blood. The technique of use is important for entonox to be effective. It takes approximately 10 breaths or 50 seconds to achieve a near maximal effect.(3) Therefore the parturient needs to be trained to time the maximum effect to peak contraction pain. There are conflicting reports concerning the efficacy of entonox as a labour analgesic. Apart from effective blood gas concentration, other factors such as distraction, relaxation, and sense of control derived from self administration, may explain why a small randomised control trial by Carstoniu showed no difference between entonox and compressed air in early labour (16) However, prolonged use of entonox can cause disorientation and headache in the mother. Some women may try hyperventilation to improve analgesia, resulting in maternal alkalosis which can reduce uterine blood flow.

REGIONAL TECHNIQUE

Epidural and combined spinal epidural analgesia perhaps, provides the most effective pain relief among the currently available techniques and its use has been increasing dramatically over the last 20 years. However, epidural analgesia has been associated with a number of side effects during labour and delivery. Liebermann et al, did a systematic review of literature examining the maternal and fetal effects of epidural analgesia. They concluded that there is sufficient evidence to show that epidural is associated with a lower rate of spontaneous vaginal delivery, a higher rate of instrumental vaginal delivery and a longer duration of labour, particularly in nulliparous women.(4)

Howell et al, in a systemic review of 21 studies, to assess the effects of epidural analgesia on the mother and the baby, when compared to non-epidural analgesia, have concluded that parturients in the epidural group had good pain relief, but were exposed to an increased risk of instrumental vaginal delivery. They did not find any significant difference in the rate of cesarean section or Apgar scores. (17)

The practical problems with epidural analgesia are that, it needs an expert to initiate the block and the kit is expensive. Close hemodynamic monitoring of the mother and the fetus is required especially during the initiation and subsequent bolus top-ups.

KETAMINE

Ketamine is a short acting intravenous anesthetic agent with good analgesic property. It does not cause cardiovascular or respiratory depression, and it preserves pharyngeal and laryngeal reflexes. It is readily available and is relatively inexpensive. It is being widely used for short procedures such as dressings and suturing in the outpatient department. (5)

Ketamine, a phencyclidine derivative was synthesized in 1962, by Stevens, and first used in 1965, by Corssen and Domino. (18) Ketamine causes dissociative anesthesia by depressing the cerebral cortex and activating the limbic system and the brainstem.(19, 20) It acts at multiple sites namely, N-Methyl D-Aspartate (NMDA), opioid, adrenergic, and serotonergic receptors. The profound analgesic action appears to be due to NMDA receptor antagonism. (21, 22)

N-Methyl D-Aspartate (NMDA) receptor is an ionotropic receptor that is activated by glutamate which is the most abundant excitatory neurotransmitter in the central nervous system. (Figure-4) It requires glycine as a co-agonist and is inhibited by Mg^{2+} in a voltage dependant manner. The receptor channel is permeable to Ca^{2+} and to a lesser degree to Na^{+} and K^{+}. Ketamine binds to the

phencyclidine receptor in the NMDA channel and inhibits its activation by glutamate, in a competitive manner (21)

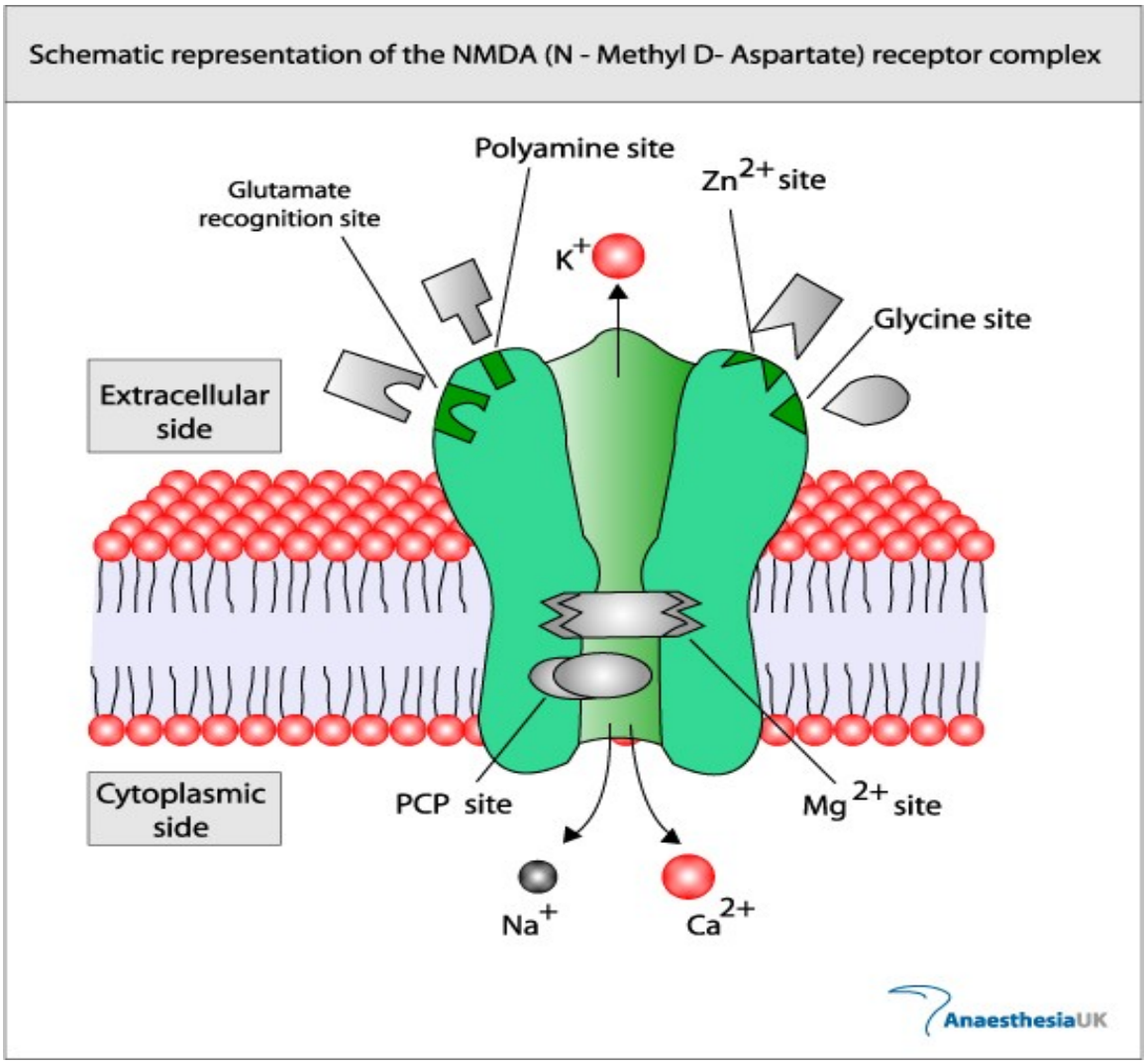


Figure-4 Structure of N-Methyl D Aspartate receptor

Ketamine contains a chiral centre, producing two optical isomers or enantiomers. The racemic mixture, which is currently available, contains equal amounts of the two isomers. (Figure-5) The analgesic potency of the S-form has been shown to be 2-3 times more than the R-form while the psychomimetic side effects are seen more with the R-ketamine. (21, 23) However, S- ketamine is currently not available in India.

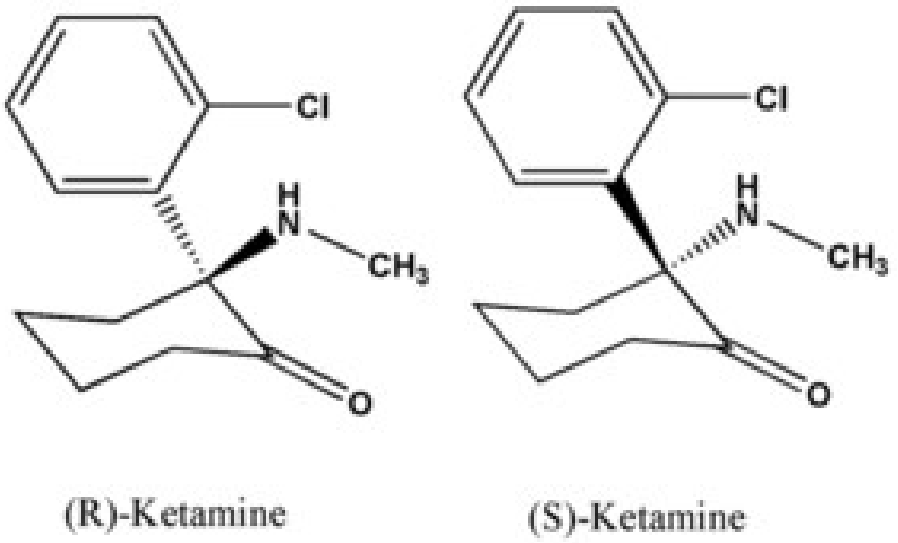


Figure – 5 Isomers of ketamine

Ketamine in anaesthetic doses (2-2.5 $mg.kg^{-1}$ intravenously) causes tachycardia, hypertension, increased salivation and emergence phenomena which includes unpleasant dreams, delirium and hallucinations. (5) These psychomimetic side effects can be minimised by the administration of a benzodiazepine. In sub-anaesthetic doses (less than $0.25mg.kg^{-1}$`) it is a potent analgesic, while the above mentioned side effects are less.

Ketamine has a relatively short distribution and elimination half life. The α elimination phase lasts for few minutes and the β elimination phase for 2-3 hours. It is metabolized extensively in the liver by the hepatic cytochrome P450 enzyme system. Its primary metabolite, nor-ketamine, is only one third as potent as the parent drug, and the metabolites are excreted by the kidney. (5, 18)

KETAMINE IN OBSTETRICS

Ketamine has been used in obstetrics for manual removal of placenta, instrumental delivery, breech delivery and as an induction agent for caesarean section. It has been reported that Chodoff and Stella (24) were the first to introduce ketamine as a labour analgesic. They used a bolus dose of $0.15mg.kg^{-1}$over 1 minute followed by an intravenous infusion.

Downing et al, studied 50 full term parturients planned for elective caesarean section. Anaesthesia was induced with ketamine $2mg.kg^{-1}$ and

maintained with nitrous oxide and oxygen. The maternal and fetal cord blood samples were analyzed for pH and PO_2 values. The anaesthesia was satisfactory, with no hemodynamic changes and without undue depression of the new born. The short duration of action, apparent lack of accumulation and satisfactory anesthetic effect suggest that ketamine is a safe alternative as an induction agent for caesarean section. (25)

Bernstein et al, compared thiopentone and ketamine ($1mg.kg^{-1}$) as an induction agent for caesarean section. Maternal pH was found to be higher in the ketamine group compared to the thiopentone group. There was no difference in the neonatal pH and PCO_2 values, or the Apgar score in both the groups. They concluded that ketamine can be safely used as an induction agent in the recommended dose of $1mg.kg^{-1}$ and is a good alternative to thiopentone. (26)

Dieh – Nielson and Holasek used $1.2mg.kg^{-1}$ of ketamine as an induction agent in 100 term parturients undergoing caesarean section. They found excellent Apgar scores in all neonates and only 3 mothers had unpleasant dreams. (27)

KETAMINE AND UTERINE TONE

Marx et al studied the effect of 4 different doses (25, 50, 75, 100 mg) of ketamine on postpartum uterine pressures. In twenty two women, who had normal vaginal delivery, a baseline uterine pressure was measured after the expulsion of the placenta. The four different doses of ketamine were given intravenously at intervals, and the intrauterine pressure was measured after each dose. Ketamine in the dose of 25mg (0.3 -0.5 $mg.kg^{-1}$) did not alter the contractile pattern, whereas, 50mg (0.6-1$mg.kg^{-1}$) caused an increase in the intensity of individual uterine contractions similar to oxytocin. Doses of 75mg (1.0-1.2$mg.kg^{-1}$) and 100mg (1.3-1.8$mg.kg^{-1}$) caused an increase in the intensity and frequency of contractions. There was no increase in the resting uterine tone with any of the above doses. They recommended that the dose of ketamine for labour analgesia, during vaginal delivery should not exceed 0.3 - 0.5 $mg.kg^{-1}$. (28)

Craft et al investigated the effect of ketamine, on the maternal and fetal cardiovascular variables, uterine blood flow, uterine tone and the possible transfer of ketamine across the placenta. The study was done on 8 pregnant term ewes. Ketamine 0.7$mg.kg^{-1}$ was given intravenously over 30 minutes. Maternal and fetal arterial samples for blood gas analysis were taken at 1, 3, 5, 10, 15, 30, 45 and 60min after the injection. Ketamine and catecholamine levels

were also measured. Maternal ketamine values peaked after 1 minute, declined rapidly over the first 5 minutes and slowly over 60 minutes. There was no significant increase in nor-epinephrine and dopamine levels following ketamine bolus. The mean blood pressure and the cardiac output increased by 7% and 16% respectively at 5 minutes and returned to baseline by 15 minutes. There were no significant changes in the uterine blood flow or the acid base values. Fetal ketamine levels peaked within 1 minute and declined within 30minutes. There was no significant change in the hemodynamics, blood gas values or the catecholamine levels in the fetus. (29)

Strumper et al studied the effect of S (+) Ketamine on the uterine blood flow. Equianalgesic doses of S (+) ketamine ($10mg.kg^{-1}.hr^{-1}$) or racemic ketamine ($20mg.kg^{-1}.hr^{-1}$) were infused into 12 pregnant sheep. The maternal and fetal vital signs, blood gases and uterine blood flow were recorded over 2hours. The uterine perfusion and the maternal and fetal hemodynamics were not affected by either compound. Racemic ketamine increased the maternal and fetal PCO_2, while S- ketamine did not. The authors have suggested the use of S- ketamine as an analgesic adjuvant in the obstetric setting. (30)

KETAMINE FOR LABOUR ANALGESIA

Galloon et al conducted a study to evaluate the oxytocic effect of ketamine on pregnant uterus. The study was done on 5 ASA–1 patients having abdominal

hysterotomies for termination of pregnancies. Once the uterus was exposed, a trochar was inserted into the amniotic cavity and the baseline uterine pressures were measured. Four different doses of ketamine were administered-0.275mg.kg^{-1}, 0.55mg.kg^{-1}, 1.1mg.kg^{-1}, 2.2mg.kg^{-1}. Ketamine in doses of 1.1 mg.kg^{-1} or less increased the intensity of uterine contractions, while larger doses, in addition to increasing the intensity of uterine contractions, increased the basal uterine tone in between contractions.(24)

Sarkar and Sahu used ketamine as a continuous intravenous infusion for labour analgesia in 50 pregnant women. A bolus of 0.2 to 0.4 mg.kg^{-1} of ketamine at the onset of active labour was followed by an infusion of 0.5-1.0mg.min^{-1}. The total dose used was 220-540mg in the primigravida women and 100-320mg in the multigravida women. 35 women had excellent analgesia while 7 had hallucinations. The progress of labour was unhampered and the mean 1min Apgar score was more than 8. (31)

Gangla et al used boluses of ketamine in 50 full term pregnant women. The initial loading dose was 0.5mg.kg^{-1} followed by 0.25mg.kg^{-1} every 20-30minutes. The average total dose used was 200mg and they reported satisfactory analgesia in 72 % of parturients. All the neonates had an Apgar score of more than 8 and 98% of patients delivered within 5hrs. However, fifty four percent of the parturients had hallucinations. (32)

KETAMINE FOR POSTOPERATIVE PAIN

Ketamine has been administered as a low dose infusion for its analgesic effect during various surgical procedures and in the post operative period. Snijdelaar et al used S (+) ketamine in patients undergoing radical prostatectomy. The patients were randomized to receive either ketamine in a dose of 0.1mg.kg^{-1} bolus intravenously followed by an infusion of 0.002mg. kg^{-1}. min^{-1} or saline as placebo. Postoperatively, the patients in the ketamine group received patient controlled analgesia containing morphine (1mg per bolus) combined with ketamine (0.5mg per bolus), while the patients in the saline group received patient controlled analgesia containing only morphine. Patients in the ketamine group demonstrated a significant drop in opioid requirement during the postoperative period. The pain scores at rest were significantly lower in the ketamine group across the 48hr study period. (6)

Guignard et al studied 50 patients scheduled for colorectal surgery under remifentanil based anesthesia. They were randomly assigned to receive either intraoperative ketamine in a dose of 0.15mg.kg^{-1} followed by an infusion of 0.002mg.kg^{-1} or saline as placebo. Remifentanil infusion was used for intraoperative analgesia. All patients were given morphine for post operative analgesia. The dose of remifentanil that was required in the ketamine group was

less compared to that in the control group. Patients in the ketamine group received less morphine compared to those in the control group during the first 24 hours of the post operative period. (7)

PATIENTS AND METHODS

This interventional study was a prospective evaluation conducted in the labour room of a tertiary referral hospital after obtaining approval from the Research and Ethics committee of the institution.

METHODOLOGY

Parturients with no antenatal risk factors and expected to have normal vaginal delivery were eligible to be included in the study. Women with known cardiac disease, gestational hypertension, epilepsy or known psychiatric disorder were excluded, as were parturients with multifetal pregnancy, suspected cephalopelvic disproportion and those who have had previous caesarean section.

STUDY INTERVENTION

All the parturients eligible for the study were explained about the procedure and a written consent obtained from the volunteers.

A 20G intravenous cannula was inserted into the forearm which was used only for the infusion of ketamine. Racemic ketamine (Aneket®, Neon Laboratories) was loaded in a 50ml syringe in a concentration of $2mg.ml^{-1}$and connected to this intravenous cannula. A bolus dose of $0.1mg.kg^{-1}$ of ketamine was administered. This was followed by an infusion of ketamine at the rate of $0.2mg.kg^{-1}.hr^{-1}$ .The rate of the infusion was adjusted according to the pain

perceived by the parturient during the uterine contraction and was altered as and when required. The infusion was stopped after the baby was delivered.

MONITORING

The baseline parameters of the parturient such as the heart rate, the systolic and diastolic blood pressure, the pain score, the sedation score, the duration and frequency of uterine contractions and the fetal heart rate were recorded. These parameters were continuously recorded at regular intervals during the study period.

The patients were asked to grade the severity of their pain during contractions, on a Visual Analogue Scale from 0-10, with 10 being severe.

The sedation was graded on a 4 point scale as,

0 - Awake

1- Drowsy, but responsive to verbal stimuli

2– Drowsy, but responsive to physical stimuli

3– Unresponsive to physical and verbal stimuli

The duration of the second stage, the type of delivery, the amount of blood loss and any complications during the third stage were noted. Side effects like vomiting, hallucinations, unpleasant dreams, nystagmus and light headedness were also looked for and recorded.

The newborn was clinically assessed by a neonatologist. The Apgar score at 1 and 5 min after birth, and the pH of the umbilical cord blood were recorded.

The parturients were interviewed by the investigator a couple of hours after the delivery and were asked to grade their perception of the pain relief and their satisfaction with the overall care on a scale 0-10, with 10 being excellent.

The obstetricians were asked to comment on this study intervention, with regard to efficacy of ketamine as a labour analgesic, its affect on the progress of labour and maternal co-operation during delivery. The mother and the baby were observed for 48hrs after delivery or till the time of discharge from hospital.

The following variables were recorded during the study period and analysed.

Total duration of labour, duration of second stage

Total dose of ketamine required and the rate of infusion per hour

Pain score

Type of delivery

Side effects in the parturient such as, sedation, nausea and vomiting, unpleasant dreams, nystagmus and light headedness

Maternal hemodynamic parameters such as the heart rate and blood pressure and their fluctuations from the baseline

Neonatal assessment

Patient's satisfaction with regard to relief of pain and the overall care

Obstetrician's comments.

STATISTICS

Since, continuous infusion of low dose ketamine has not been used during labour before, this pilot study was undertaken to assess its efficacy as a labour analgesic and to standardise a regimen. It was decided to do the initial evaluation on 30 parturients, and then ratify the dose regimen in a larger population, if ketamine was found to be effective. The results of the pilot study on 30 patients are presented.

The statistical analysis was done using the Statistics Package for Social Sciences (SPSS® version 11).

RESULTS

Thirty parturients in active labour were consented to participate in the study. The characteristics of the patients are described in Table -1.

Table -1 The demographic details of the patients in the study population

Age (yrs) Mean ± SD	24.5 ± 4.0 (Range 17 – 31)
Weight (kg) Mean ± SD	65.1 ± 8.7 (Range 51 – 85)
Gravida	Primigravida – 12 Multigravida - 18
Onset of labour	Spontaneous – 16 Induced - 14

DURATION OF LABOUR

The duration of labour for each parturient was recorded, as the time from the onset of active labour to the delivery of the baby. This was 260 ± 167min in the study group, with it being longer in the primigravida (307 ± 150min) as compared to the multigravida (200 ± 175min). This difference was statistically significant (p =0.005). The duration of labour was shorter in those parturients who had a spontaneous onset of labour(239 ± 160min) as compared to those who had to have their labour induced (304.35 ± 163.5min) although, this was not statistically significant (p=0.166).

DURATION OF SECOND STAGE

The duration of second stage namely, the time from the full dilatation of the cervix to the delivery of the baby was 38 ± 35.2min. This was longer in the primigravida women (46.2 ± 33.2 min) as compared to the multigravidae (29.5 ± 36.9 min) and was statistically significant (p= 0.037)

TYPE OF DELIVERY

Of the 30 women who participated in the study, 21 (70 %) had normal vaginal delivery, 6 (20%) had assisted delivery and 3 (10%) had to be delivered by caesarean section. The indications for caesarean section were arrest of cervical dilatation in one and non-reassuring fetal status, in the other two. Of the women who had assisted delivery, 2 had prolonged second stage (145 and 116min), while the others had non-reassuring fetal status.

All the 3 women who had caesarean section and 5 out of 6 women who had assisted delivery were primigravida.

BLOOD LOSS

The average blood loss during delivery in the study group was 184.17 ± 85 ml with it being 206.9 ± 86.5ml in the primigravida and 150.0 ± 73.8ml in the multigravida. This was statistically significant (P = 0.007). None of the parturients, included in the study had postpartum hemorrhage.

PAIN SCORE

During the course of labour the parturients were asked to grade the severity of their pain on a visual analogue scale with scores from 0-10 and this was recorded at hourly intervals. All the parturients experienced adequate analgesia within 1-2hrs of administration of ketamine infusion as shown in figure -6.

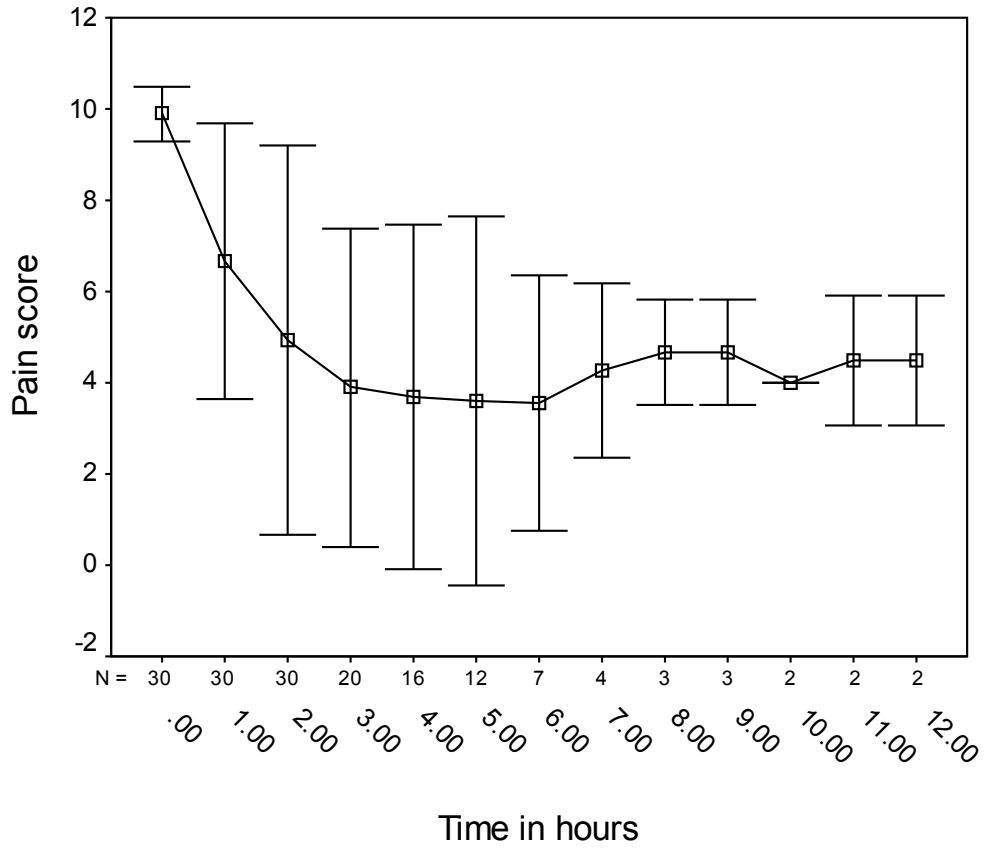


Figure – 6. Pain score at hourly intervals during the study. N denotes the number of patients at each hour.

INTRAPARTUM REQUIREMENT OF KETAMINE

The total dose of ketamine required by each parturient was calculated and the average dose was found to be 57 ± 37.5mg (range 18-160mg). The infusion rate of ketamine during the course of labour was also calculated and the average infusion required was 0.17 ± 0.06mg.kg^{-1}.hr^{-1} (range 0.08-0.32).

Table –2 The dose of ketamine and gravida

Gravida	**Primigravida**	**Multigravida**	**p value**
Total (mg)	68.5 ± 35.9	39.6 ± 34.2	0.002
Average (mg.kg^{-1}.hr^{-1})	0.18 ± 0.06	0.16 ± 0.05	0.5

Although the total dose of ketamine required among the primigravida was significantly more than that required for the multigravida, this was not so when the infusion rates were compared. (Table -2)

Table –3 The dose of ketamine and onset of labour

Onset of labour	**Spontaneous**	**Induced**	**p value**
Total (mg)	45.5 ± 33.1	70.14 ± 39.1	0.02
Average ($mg.kg^{-1}.hr^{-1}$)	0.16 ± 0.06	0.19 ± 0.06	0.20

The parturients who had a spontaneous onset of labour required a lower dose of ketamine when compared to those who had induction of labour (p=0.02) However, the rate of infusion, did not differ between these two groups. (Table -3)

INFUSION RATE OF KETAMINE

The infusion of ketamine was started immediately after the bolus dose. The infusion was initially started at the rate of $0.2mg.kg^{-1}.hr^{-1}$ and was adjusted

based on the pain perceived by the parturient. The infusion rate had to be increased in the initial couple of hours and was reduced by the third hour. (Figure-7)

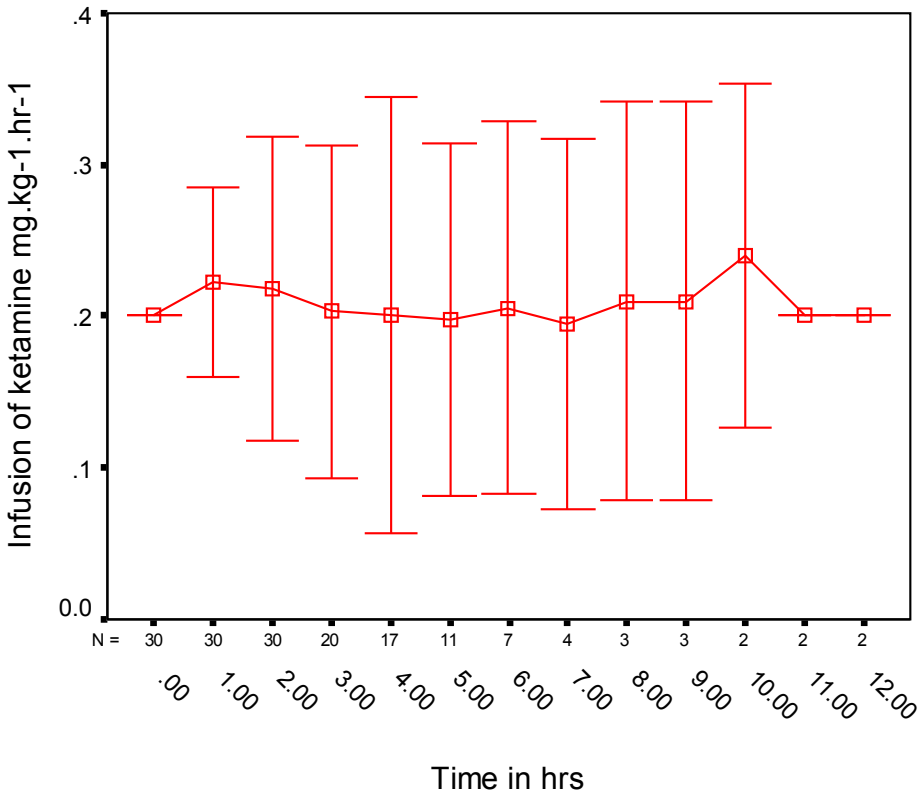


Figure -7 The infusion rate of ketamine at hourly intervals. N denotes the number of parturients at each hour.

RESCUE ANALGESIC

According to the study protocol, any parturient who did not achieve adequate analgesia with ketamine were to be administered an intramuscular

dose of Pethidine (50mg) and Promethazine (25mg). This rescue analgesic was needed in only one parturient.

COMPLICATIONS

Ketamine is known to cause side effects such as hallucinations, unpleasant dreams, nystagmus, light-headedness, nausea and vomiting. Therefore, these complications were looked for in all the parturients in the study.

None of the women had hallucinations or unpleasant dreams. 2 women had vomiting but they had episodes of vomiting before the ketamine administration was started, and there was no worsening of symptom.

Immediately following the administration of the bolus dose of ketamine, 16 women complained of light headedness which lasted for about 3-5min, and 7 women had jerky, to and fro movement of their eyeballs (nystagmus) which lasted for nearly a minute. These findings did not recur during the study period when the ketamine infusion was being administered.

Since ketamine causes sedation, the level of wakefulness was graded on a four point scale during the study period. All the women were awake during labour, except for 8 women who were drowsy but responded to verbal stimuli (Grade 1).

HEMODYNAMIC CHANGES

Since intravenous administration of ketamine causes transient sympathetic stimulation, the heart rate and the blood pressure were monitored during the first one hour after the administration of the bolus dose of ketamine.

CHANGES IN THE HEART RATE

The baseline heart rate was 84.56 ± 4.6 beats per minute and there was a clinically insignificant increase in heart rate (4.96%) above the baseline value and this was seen within 10min after the bolus dose. (Figure – 8)

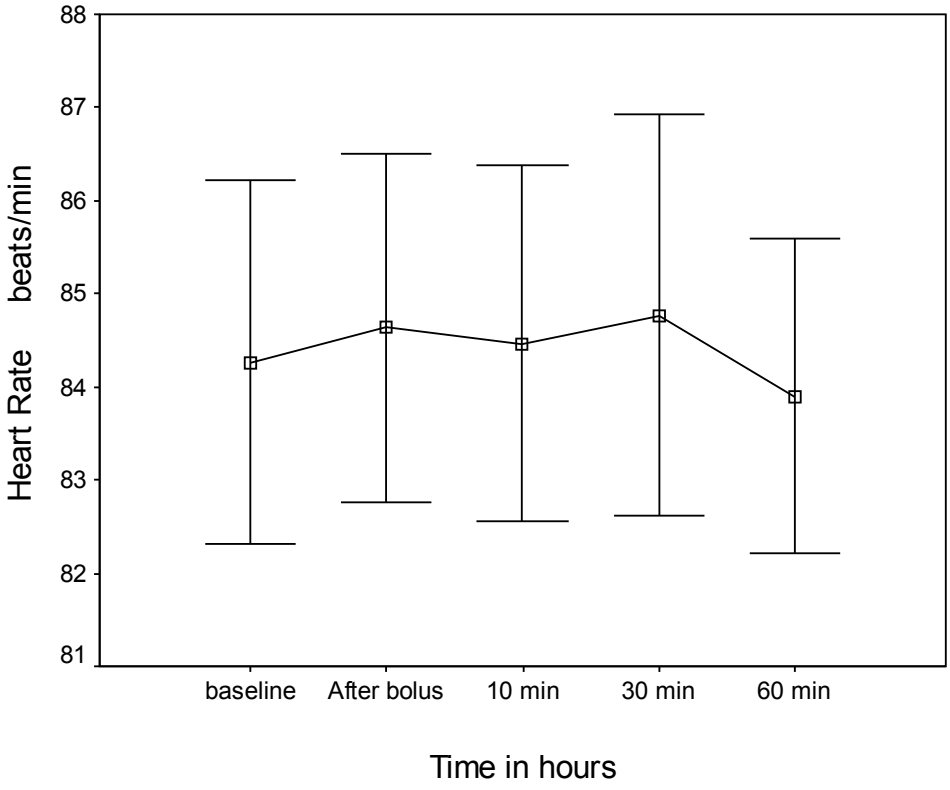


Figure – 8 The heart rate (mean and 95% Confidence interval) during the initial one hour of study intervention.

CHANGES IN THE BLOOD PRESSURE

The baseline systolic and diastolic blood pressure was 118.4 ± 8.9mmHg and 76.8 ± 6.8mmHg respectively. There was a clinically insignificant increase in the systolic (5%) and diastolic (6.3%) blood pressure above the baseline and this was observed soon after the bolus dose. (Figure-9)

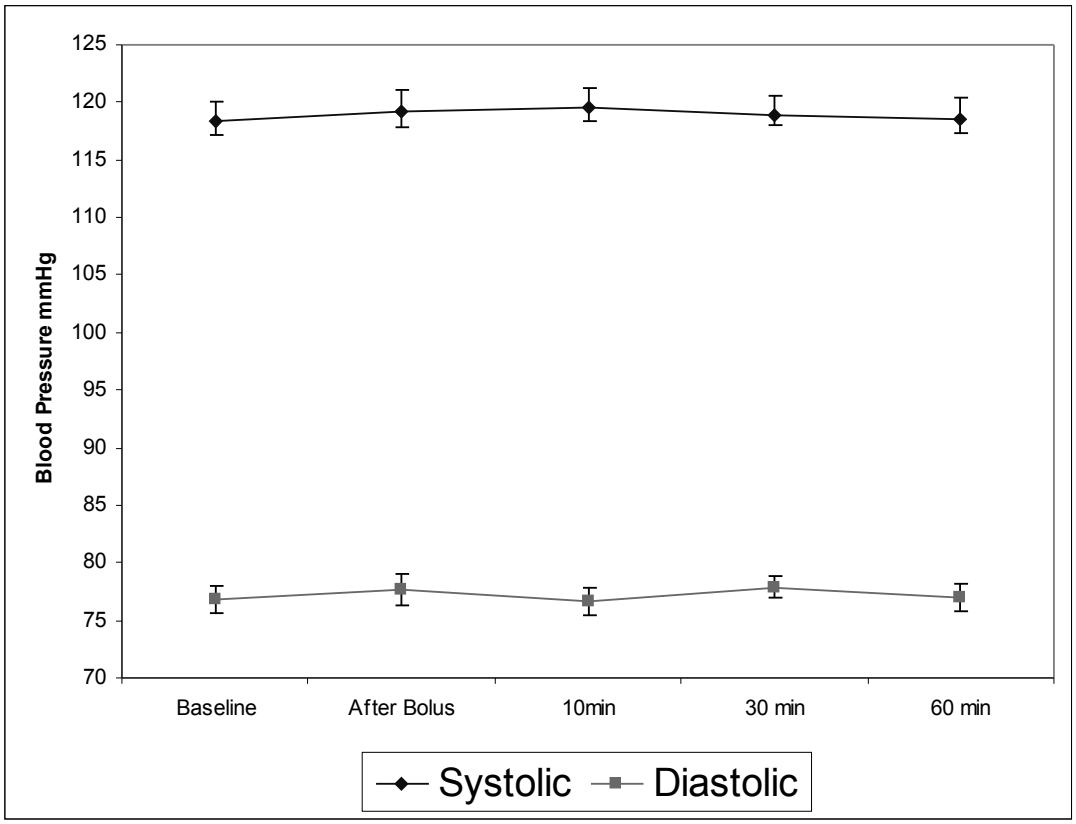


Figure - 9 Systolic and diastolic blood pressure (mean and 95% confidence interval) during the initial one hour after the bolus dose of ketamine.

FETAL HEART RATE

The fetal heart rate was monitored throughout the study period. There was a drop in the fetal heart rate of about <5 beats per minute after the bolus dose of ketamine. However, this was not clinically significant. (Figure -10)

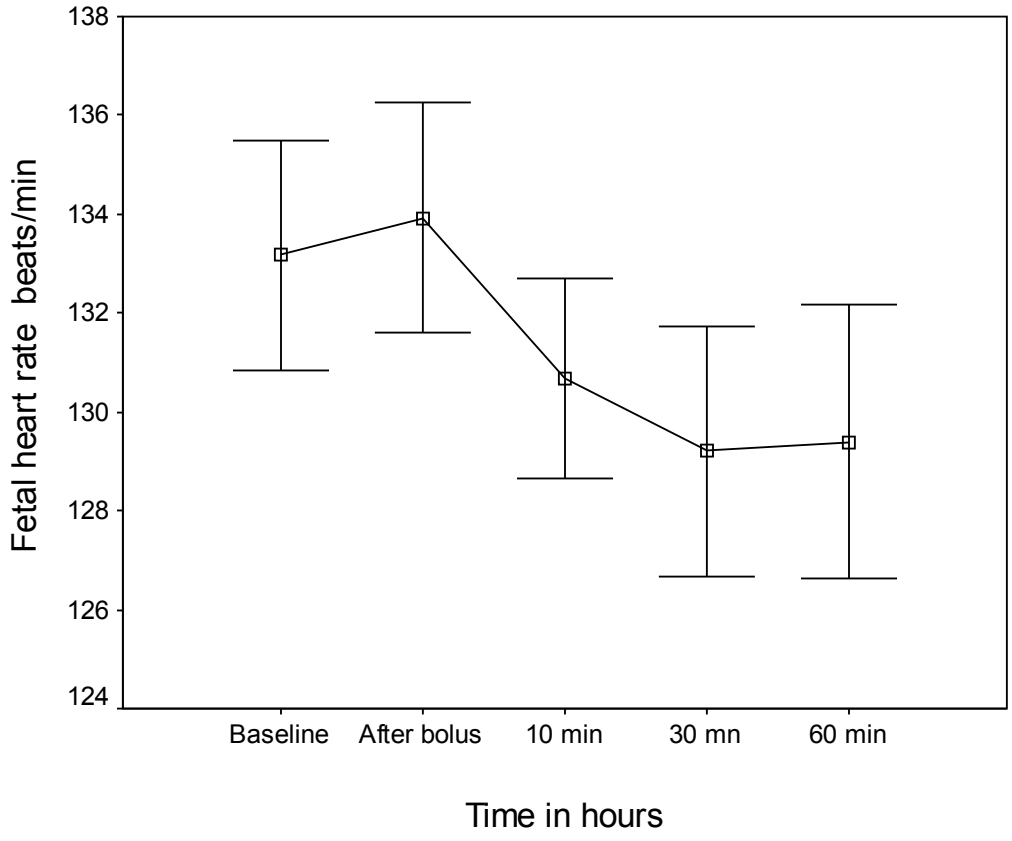


Figure – 10 The fetal heart rate (mean and 95% confidence interval) during the initial one hour after the bolus dose of ketamine.

ASSESSMENT OF THE NEW BORN

All the neonates were assessed by a neonatologist at birth. The Apgar score at the first and fifth minute of birth, and the pH of the cord blood were recorded.

NEONATOLOGIST'S ASSESSMENT

Three babies were found to be clinically depressed at birth. Two of them had irregular respiratory efforts which improved with gentle throat suctioning and mask ventilation with oxygen. One neonate was floppy at birth with severe respiratory depression and required intubation and assisted ventilation for 1min, after which the respiratory efforts became regular and was extubated. Five neonates were transfered to the nursery for observation. Of these, 3 were delivered by caesarean section, one had an Apgar score of 1 at the first minute of birth but recovered later, and the mother of the fifth neonate had an altered glucose tolerance test and a history of early neonatal death during previous pregnancy.

APGAR SCORE

The Apgar score of two neonates were less than 8 at the first minute but they improved, and all had a score of more than 8 at 5 minutes. (Table-4)

Table – 4 Apgar score at 1min and 5min

Score	<8	≥8
1 min	2	28
5 min	0	30

pH OF CORD BLOOD

A sample of blood was taken from the umbilical artery of the neonate for blood gas analysis. The pH ranged from 7.05–7.35 with a mean of 7.207 ± 0.007.

PATIENT'S SATISFACTION

The parturients were interviewed within couple of hours of delivery and asked to comment on their perception of the degree of pain relief and their satisfaction with the overall care.

All the parturients graded the level of analgesia as a percentage relief of pain. Twenty seven (90%) graded the level of pain relief as more than 50%. However, when asked about their satisfaction with the overall care, on a scale of 0-10, 25(83.3%) graded it as good while 5 (16.6) were moderately satisfied. (Table-5)

Table – 5 Satisfaction score

Score	0-3 (Poor)	4- 6 (Average)	≥7 (Good)
No. of Patients	0	5	25

OBSTETRICIAN'S COMMENT

The obstetrician was asked to comment on various aspects of the study such as, the adequacy of pain relief, the effect on the progress of labor, maternal co-operation during delivery and any side effects.

They were satisfied with the relief of pain in 26 of the 30 women. They did not feel that the progress of labour was affected in any way except in 2 women who had prolonged second stage. All the mothers co-operated well during the second stage and all of them were fully awake except two who had to be called to awaken.

DISCUSSION

Pain during childbirth is graded as severe by most women, although there is a considerable variation in its perception. The characteristic of labour pain is that it is intermittent and it increases in intensity and frequency as the labour progresses. An ideal labour analgesic should be safe to the parturient and the neonate, easy to administer, readily available, inexpensive and with no untoward effect on the progress of labour.

Ketamine is a short acting intravenous anaesthetic with excellent analgesic property. It has been widely used in outpatient departments for short and painful procedures like wound suturing, change of dressing in patient with burns, and short surgeries such as incision and drainage of abscess. Perioperative use of low dose ketamine infusion has been shown to provide analgesia and reduce the intraoperative and postoperative narcotic requirement. (6, 7)

Ketamine has been safely used in obstetrics since 1966. (24) It's been recommended as an analgesic for forceps delivery, manual removal of placenta and as an induction agent for cesarean section. Ketamine, when used in the dose of less than $1mg.kg^{-1}$ over 30min, was shown to have no effect on the progress of labour, the intra-uterine pressures, the oxygenation and the acid base status of the fetus. (24, 28, 29, 30)

ANALGESIA AND PATIENT SATISFACTION

This study has shown that low dose intravenous ketamine infusion at the rate of 0.17 ± 0.06mg.kg^{-1}.hr^{-1} provides acceptable labour analgesia in 90% of the study patients. The pain score was decreased to an acceptable level within 2hrs of starting the infusion. (Figure-6) Of the 3 women who graded low on analgesia, one was a primigravida who was induced for post dates and was on a oxytocin infusion for augmentation of labour. Ketamine, at the rate of 0.2-0.25mg.kg^{-1}.hr^{-1} was infused, but she had only 20% pain relief. Five hours into labour, the fetal heart monitor showed a loss of beat to beat variability, and therefore the oxytocin and the ketamine infusion were stopped. One hour later, an intramuscular injection of pethidine (50mg) was given. Five hours following this, she delivered normally and the baby had an Apgar score of 9 at the first minute and 10 at the fifth minute of birth. The other two patients were multigravidae at term with spontaneous onset of labour. They delivered within two and a half hours of starting the ketamine infusion. This short duration of labour could have been the cause for them not having had good analgesia, as it takes an average of 2hours to achieve good analgesic effect with this infusion rate. However, this lack of pain relief did not reflect on their rating of satisfaction with the overall care. This could be due to the concern of the investigator during labour and the joy of having a healthy baby in their arms.

OBSTETRICIAN'S COMMENTS

The obstetricians felt that out of the 30 women, 26 had good analgesia while 4 had incomplete pain relief. They also felt that the second stage was prolonged in 2 of the parturients, both of whom needed outlet forceps to assist delivery. Two women were drowsy but arousable on calling their names (sedation score -1). This low dose infusion of ketamine seems to be acceptable to the obstetricians since it provided adequate analgesia in most of the parturients, with them being co operative during delivery and without interfering with the progress of labour.

DOSE OF KETAMINE

The dose of ketamine was found to be 57 ± 37.5mg and the average infusion rate was 0.17 ± 0.06mg.kg^{-1}.hr^{-1}. This translates to a dose of only 10-15mg per hour. This is much lower than that used in the previous studies (31, 32). The total dose of ketamine was more in the primigravida women, since the duration of labour was longer, but the infusion rate per hour was similar, thereby suggesting that the analgesic requirement is similar in both. The parturients who had a spontaneous onset of labour required less ketamine when compared to the women who had their labour induced. Augmentation of the uterine contractions with oxytocin could be the reason for this.

EFFECT ON THE PROGRESS OF LABOUR

Although the obstetricians commented that two patients had prolonged second stage, the average duration of second stage was 46.2 ± 33.2min for primigravida women and 29.5 ± 36.9min for multigravida which is within the acceptable limits. (33) Similarly, the duration of labour was 307 ± 150min in primigravida and 200 ± 175min in multigravida which are also within the acceptable limits. (33) Ketamine is shown to have oxytocic effect and in low doses, it increases the intensity of uterine contractions while maintaining the basal uterine tone (24, 29). This could theoretically shorten the duration of labour and this was evident in this study population. This is in contrast to epidural analgesia, which has been shown to prolong the second stage. (4)

In this study, the incidence of caesarean section was 10% which is less than the prevailing incidence of 25-30% among the population attending this tertiary referral institution. The indication for caesarean section were, arrest of cervical dilatation in one and non-reassuring fetal status in the other two parturients. Of the 6 parturients who had assisted delivery, 2 of them had prolonged second stage (140 and 116 min) and the rest had non-reassuring fetal status. The incidence of assisted delivery in this study was 20% which is within the current incidence of instrumental delivery of this institution.

The blood loss in the study group was minimal (184.17 ±85ml). None of the women had postpartum hemorrhage probably reflecting the oxytocic action of ketamine.

SIDE EFFECTS OF KETAMINE

Intravenous administration of a bolus dose of ketamine causes sympathetic stimulation with an immediate increase in heart rate and blood pressure. This was not observed in the study population possibly due to the low dose of ketamine used.

The use of a larger dose of ketamine ($2mg.kg^{-1}$) causes emergence phenomena. (16) Sarkar et al (31) used the dose of $0.2\text{-}0.4mg.kg^{-1}$ as bolus, followed by an infusion of $0.5\text{-}1.0mg.min^{-1}$ which approximated to $1mg.kg^{-1}hr^{-1}$. and they reported 14% of their study patients to have hallucinations. Gangla et al (32) although having used only $0.5\text{-}0.6mg.kg^{-1}.hr^{-1}$, had high incidence (54%) of hallucinations, thereby suggesting that emergence phenomena could be related to peak levels of ketamine. This was not observed in this study population as a lower dose was given as an infusion rather than as bolus. Benzodiazepine was avoided in the study for the fear of sedation and non-participation of the mother during labour. None of the women were sedated to be un-cooperative during the second stage.

However, the administration of the bolus dose did cause a sensation of light headedness in 16 patients lasting for less than five minutes and seven parturients had a vacant gaze with a slow nystagmic movement of the eyeball which lasted for about a minute. This may suggest that these side effects could be avoided or minimised if this dose was administered over a period of 15-30minutes.

Sarkar et al (31) have described an incidence of 14% of nausea and vomiting with the use of ketamine for labour analgesia. In this study it was seen that 2 women had vomiting, but they had these episodes before the study intervention and there was no worsening of the symptom.

EFFECT ON THE NEW BORN

Of the 30 babies, 28 had a Apgar score of more than 8 at 1min and all of them had a score of 9 and above at 5minutes. Of the two babies who had less Apgar score at the first minute, one was born to a primigravida at 40^{+3} weeks, who had her labour induced and was on an infusion of oxytocin for augmentation of labour. She had ketamine infusion at the rate of 0.2mg. $kg^{-1}.hr^{-1}$ and experienced good analgesia within 1hr of the infusion. After 3hrs of the study period she had variable decelerations of the fetal heart rate and per vaginal examination revealed meconium stained amniotic fluid and ketamine infusion was stopped. The infusion of oxytocin which was also stopped was restarted after 2 hrs and she continued to have variable decelerations of the fetal heart

rate and was delivered by outlet forceps (4hrs after stopping the ketamine infusion).The baby was floppy and cyanosed at birth, and needed intubation suctioning and ventilation. However, after 1 min the respiratory efforts became regular and the endotracheal tube was removed. The Apgar score at the fifth minute was 9 and pH of the cord blood was 7.053. The second neonate was born to a multigravida at term, by normal vaginal delivery and had an Apgar score of 6 at the first minute. Throat suctioning and mask ventilation were done after which the respiratory efforts became regular and the Apgar at the fifth minute was 10 and cord blood pH was 7.084.

The pH of the cord blood was analysed for all neonates and it ranged from 7.05-7.35 with a mean of 7.20 ± 0.07 which is within the normal recommended range, (34) suggesting adequate fetal oxygenation.

All the babies were examined by the neonatologist and 3 of them were found to be clinically depressed at birth. Two babies had irregular respiratory efforts which improved with gentle throat suctioning and mask ventilation with oxygen. The third neonate who had severe respiratory depression as described earlier, was intubated and ventilated for 1min. Five babies were shifted to the nursery. Three of them were babies born by caesarean section and are routinely kept for observation for 24 hrs. The other 2 babies included, the one with severe respiratory depression at birth (described earlier) and a neonate born to a mother with impaired glucose tolerance test and previous early neonatal death

Therefore, ketamine, which is inexpensive and readily available, can provide good pain relief to the parturients when administered intravenously at the rate of 0.15- 0.2mg.kg^{-1}.hr^{-1}. The minor side effects observed, were in relation to the bolus dose of 0.1mg.kg^{-1} given as a loading dose prior to initiation of the infusion. Despite this bolus dose, effective analgesia was established only by 2hours. Therefore, it seems that a higher loading dose should be administered, possibly, 0.2-0.4mg.kg^{-1} but this should be given over a period of 15-30 minutes. This would mean starting the infusion at a higher rate of 0.4mg.kg^{-1}.hr^{-1} and reducing it to 0.15-0.2mg.kg^{-1}.hr^{-1} within 30minutes.

This study has shown that, intravenous low dose ketamine can provide effective labour analgesia. However, this dose regimen should be ratified on a larger population before being recommended as a standard technique of labour analgesia.

CONCLUSION

Although, systemic opioids, inhalational analgesia and regional techniques are widely used, effective control of labour pain with a technique which has minimal side effects on the parturient, the fetus and the progress of labour is yet to be found. Ketamine, a NMDA receptor antagonist, is shown to be an excellent analgesic. Although it is associated with unpleasant side effects, these can be minimised when ketamine is administered slowly in very low doses ($0.1\text{-}0.2 mg.kg^{-1}.hr^{-1}$) while retaining its analgesic property.

In this study, ketamine was administered as a bolus of $0.1 mg.kg^{-1}$, followed by an infusion of $0.2 mg.kg^{-1}.hr^{-1}$ to parturients in active labour and was found to provide effective analgesia with minimal side effects. This technique was found to be acceptable both to the parturient and the obstetrician. However, minor modification to this technique, namely, a loading dose of $0.4 mg.kg^{-1}.hr^{-1}$ given over a period of 30minutes followed by an infusion of $0.15\text{-}0.2 mg.kg^{-1}.hr^{-1}$, would ensure rapid onset of analgesia while minimizing the side effects due to the bolus administration of the loading dose.

Since, the efficacy and safety of low dose intravenous ketamine as a labour analgesic has been established, a regimen, with slight modification, would be ratified on a larger population, before being recommended as a standard technique of labour analgesia.

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KETAMINE IN LABOUR ANALGESIA

PROFORMA

NAME		**SERIAL NO:**	
HOSPITAL NO:		**DATE**	
AGE		**OBST.SCORE**	
WEIGHT		**GEST. AGE**	

TIME OF ONSET OF LABOUR: **SPONTANEOUS / INDUCED**

DOSE OF KETAMINE BOLUS:

TIME OF THE PRIMING DOSE:

TIME OF STARTING INFUSION:

VARIABLE	BASELINE	10MIN	20MIN	30MIN	45MIN	1HR	1.5 HR	2 HR	2.5 HR	3 HR	3.5 HR	4 HR	4.5 HR	5 HR
PULSE														
B.P														
R.R														
F.H.R														
CX DILATION														
STATION														
DUR OF CONTRACTn														
INFUSION RATE														
PAIN SCORE														
SEDATION														
INFUSION RATE (MG/KG/HR)														

RESCUE ANALGESIA ADMINISTERED-

TIME OF DELIVERY

TYPE OF DELIVERY- NORMAL/ ASSISTED/ LSCS

BLOOD LOSS –

SIDE EFFECTS

-VOMITING YES/ NO

-HALLUCINATIONS YES/NO

-DREAMS YES/ NO

TIME OF DISCONTINUING INFUSION –

NEONATE --APGAR SCORE 1min 5min

-CORD BLOOD PH –

-NEONATOLOGIST OPINION-

PATIENT'S RESPONSE –

- PAIN 0----------10
- SATISFACTION 0----------10

OBSTETRICIAN'S COMMENT -

VISUAL ANALOGUE SCALE 0----------10

SEDATION SCORE:

0-Awake
1-Responds to verbal call
2-Responds to tactile stimulus
3-Unresponsive

MASTER SHEET

Name	Hosp.no	age	Weight	Gravida	Geat. Age	Onset	Bolus	
Poomagal	645286C	27	60	M		1	1	6
Priya	728565 C	20	51	P		1	1	5
Rathna	683453 C	27	75	P		2	2	7
Kannaki	754478 C	21	60	P		1	1	6
Sumathi	671342 C	21	55	P		1	1	5.5
Komathi	450375 C	27	55	M		1	1	5
Mohana	377570 C	18	67	M		1	1	7
Parveen	183803 C	25	60	P		1	1	6
Selvi	729490 C	29	74	M		1	1	7
Vanitha	776893 C	21	70	P		2	2	7
Lakshmi	748107 C	23	60	P		1	2	6
Shanthi	215279 C	23	62	M		1	1	6
S.Laksmi	737563 C	30	75	P		1	2	6
Selvi	031652 C	19	72	M		1	1	7
Rekha	728756 C	23	55	M		1	1	6
Syeeda B	863619 B	25	78	M		1	1	8
A. Selvi	784390 C	30	70	P		1	1	7
Deepa	208655 C	21	60	M		2	1	6
Usha	824861 C	23	65	P		2	2	6
Padma	442551 C	30	60	M		2	1	6
M.Megalai	742716 C	29	55	P		2	2	5
jothi	784107 C	25	85	P		2	2	8
T.Sundari	816922 C	27	53	P		1	2	5
Ramya	726882 C	17	80	P		1	2	8
Nazeema	727570 C	28	65	P		1	2	6.5

Malathi	303233 C	31	60	M	1	2	6
Nalini	234340 C	21	65	M	1	1	6
Suguna	832293 C	24	70	P	2	2	7
Tamil	741871 C	20	75	P	1	2	7.5
Tasneem	832297 C	30	62	P	2	2	6

1 stage	2-Stage	3-Stage	Cerv. Dilat	Inf_0.5hr	Inf_1hr	Inf_2hr	Inf_3hr	Inf_4hr	Inf_5hr
30000.00%	30	5	4	0.2	0.2	0.2	0.2	0.2	0.
300	75	4	3	0.2	0.3	0.3	0.3	0.3	0.
300	35	7	3	0.2	0.2	0.3	0.3	0.4	0.
240	50	4	4	0.2	0.2	0.16	0.1	0.1	0.
360			3	0.2	0.27	0.29	0.21	0.2	0.
90	20	4	5	0.2	0.25	0.3			
80	5	3	5	0.2	0.23	0.2			
155	88	5	4	0.2	0.26	0.26	0.13	0.13	
560	145	3	3	0.2	0.2	0.27	0.28	0.28	0.2
220	10	4	3	0.2	0.3	0.3	0.2	0.2	
120	25	4	3	0.2	0.2	0.1			
100	20	4	3	0.2	0.2	0.2			
660	40	5	3	0.2	0.2	0.3	0.3	0.23	0.2
215	25	5	3	0.2	0.23	0.23	0.2	0.2	
120	16	3	4	0.2	0.2	0.2			
90	25	6	4	0.2	0.2	0.2			
285			4	0.2	0.26	0.2	0.2	0.2	
70	13	3	3	0.2	0.2	0.2			
135	40	6	4	0.2	0.2	0.18	0.18		
160	23	4	4	0.2	0.23	0.2	0.2		
150	100	4	3	0.2	0.21	0.18	0.18	0.14	
160	11	4	5	0.2	0.2	0.18			
240	14	4	3	0.2	0.2	0.18	0.18	0.18	
435	116	3	3	0.2	0.25	0.2	0.15	0.15	0.1
420			3	0.2	0.2	0.18	0.15	0.15	0.1
120	20	3	3	0.2	0.2	0.2			
97	13	3	3	0.2	0.2	0.18			
150	28	2	3	0.2	0.25	0.2	0.2		
320	34	2	3	0.2	0.24	0.24	0.2	0.16	0.1
280	27	3	4	0.2	0.21	0.21	0.2	0.2	0.

Inf_7hr	Inf_8hr	Inf_9hr	Inf_10hr	Inf_11hr	Inf_12hr	Sta_inf	Pain_0hr	Pain_1hr	Pain_2hr
						0.2	9	8	6
						0.3	10	8	8
						0.2	10	8	9
						0.1	9	3	1

							10	8	6
						0.3	10	8	8
						0.2	10	7	3
						0.13	10	6	3
0.28	0.28	0.28	0.28	0.2	0.2	0.2	10	8	8
						0.2	10	8	4
						0.1	10	6	2
						0.2	10	5	3
0.2	0.2	0.2	0.2	0.2	0.2	0.2	10	8	5
						0.2	10	8	6
						0.2	10	6	4
						0.2	10	6	4
							10	6	4
						0.2	10	6	6
						0.18	10	3	1
						0.2	10	5	3
						0.14	10	5	3
						0.18	10	6	6
						0.18	9	8	4
0.15	0.15	0.15				0.15	10	8	7
0.15							10	7	5
						0.2	10	6	4
						0.18	10	5	5
						0.2	10	8	5
						0.16	10	8	8
						0.2	10	8	7

Pain_5hr	Pain_6hr	Pain_7hr	Pain_8hr	Pain_9hr	Pain_10hr	Pain_11hr	Pain_12hr	Sed_0hr
1								0
4	4							0
8								0
1								0
1	1							0
								0
								1
								0
5	5	5	5	5	4	5	5	1
								0
								0
								0
4	4	4	4	4	4	4	4	0
								0
								0
								0
3								0
								0
								1
								0

									0
									1
									0
5	5	5	5	5					0
3	3	3							0
									0
									0
									0
4	3								0
4									0

Sed_1hr	Sed_2hr	Sed_3hr	Sed_4hr	Sed_5hr	Sed_6hr	Sed_7hr	Sed_8hr	Sed_9hr	Sed_10
1	1	0	0	0					
0	0	1	1	0	0				
0	1	1	0	0					
0	0	0	0	0					
1	1	0	0	0	0				
1	1								
1	1	1							
1	1	0	0						
1	0	0	0	0	0	0	0	0	
1	1	0	0						
1	0								
0	0								
1	1	1	1	1	1	0	0	0	
0	1	1	0						
1	0								
0	1								
0	1	0	0	0					
2	1								
1	0	0							
1	0	0							
1	1	0	0						
1	1								
1	1	0	0						
0	1	1	0	0	0	0	0	0	
1	1	1	1	0	0	0			
0	0								
1	0								
0	0	0							
1	1	1	1	1	1				
0	0	0	0	0					

Sed_11hr	Sed_12hr	TOT_KET	RESCUE	TYPE DEL	Bld loss	Vomit	Hallucin	Dreams	Nystagmus
		66	1	1	100	2	2	2	1
		100	1	1	200	1	2	2	2
		120	2	1	350	2	2	2	1
		50	1	2	200	2	2	2	1
		40	1	3	250	2	2	2	2
		20	1	1	100	2	2	2	1
		28	1	1	50	2	2	2	2
		32	1	2	150	2	2	2	2
0	0	140	1	2	300	2	2	2	2
		40	1	1	200	2	2	2	2
		22	1	2	200	2	2	2	2
		18	1	1	150	2	2	2	1
0	0	90	1	1	100	2	2	2	2
		30	1	1	100	2	2	2	2
		18	1	1	150	2	2	2	2
		38	1	1	200	2	2	2	2
		60	1	3	350	2	2	2	2
		20	1	1	100	2	2	2	2
		44	1	1	250	2	2	2	1
		36	1	1	200	2	2	2	2
		46	1	2	150	2	2	2	1
		52	1	1	200	2	2	2	2
		56	1	2	200	1	2	2	2
		160	1	1	150	2	2	2	2
		92	1	3	400	2	2	2	2
		30	1	1	250	2	2	2	2
		32	1	1	100	2	2	2	2
		44	1	1	100	2	2	2	2
		100	1	1	175	2	2	2	2
		86	1	1	100	2	2	2	2

Giddiness	Sedation	APG-1	APG_-5	Cord-Ph	Aver inf mg/kg/hr	Satis scor	BS_SYST	AB_SYS	10ms

2	2	9	10	7.249	0.21mg/kg/hr	8	110	110
1	2	9	10	7.235	0.28	7	110	116
1	2	9	10	7.195	0.32	6	136	136
2	2	9	10	7.094	0.15	9	126	130
1	2	9	10	7.236	0.09	8	116	120
2	1	9	10	7.351	0.14	4	120	124
2	1	9	10	7.184	0.25	8	130	130
2	2	9	10	7.109	0.11	8	106	100
1	2	1	9	7.052	0.18	4	116	120
1	2	9	10	7.222	0.12	9	124	124
1	2	9	10	7.237	0.15	9	120	120
1	2	9	10	7.154	0.08	6	124	120
2	1	9	10	7.121	0.09	7	126	125
1	2	9	10	7.162	0.08	6	122	126
1	2	9	10	7.234	0.09	8	120	120
1	2	9	10	7.177	0.21	8	130	130
2	1	9	10	7.258	0.16	9	110	116
2	1	9	10	7.206	0.16	7	110	110
1	2	8	10	7.21	0.19	8	118	120
2	2	6	10	7.084	0.17	8	118	120
1	2	9	10	7.187	0.18	9	120	126
2	1	9	10	7.257	0.29	8	126	130
1	2	9	10	7.288	0.15	9	126	126
1	2	9	10	7.195	0.23	8	100	96
2	1	8	10	7.214	0.18	7	112	110
1	2	9	10	7.297	0.17	8	126	126
1	2	9	10	7.348	0.21	7	110	108
2	2	9	10	7.289	0.17	7	112	110
2	1	9	10	7.189	0.2	8	128	130
2	2	9	10	7.172	0.24	8	100	98

30min_sys	60min_sys	BS_DIA	AB_DIA	10min_dia	30min_dia	60min_dia	BS_RR	AB_
116	110	76	80	76	76	80	22	
110	116	66	70	70	70	66	70	
135	136	86	90	90	90	90	22	
126	120	70	76	76	78	72	20	
116	120	88	86	80	80	86	18	
120	120	80	80	86	82	80	18	
130	128	78	82	76	70	76	17	
108	110	72	70	70	72	74	19	
120	110	70	80	76	76	78	21	
118	120	76	72	72	80	72	15	
120	120	72	80	80	80	76	18	
130	128	90	92	86	86	86	21	
130	130	88	86	86	84	84	20	
120	120	72	76	70	72	70	16	
120	124	84	84	80	80	86	18	
136	136	70	70	78	78	70	16	
110	110	72	68	68	70	74	15	

110	100	80	76	76	82	80	18
110	110	76	70	70	76	72	18
116	120	72	70	70	78	70	17
120	124	74	70	78	74	74	16
126	126	80	80	82	80	80	15
120	120	74	70	70	80	80	16
100	100	78	80	80	80	80	16
110	110	86	90	80	86	86	17
130	130	80	82	80	76	76	16
110	118	70	72	70	76	76	14
116	110	72	72	70	76	70	18
130	130	86	86	86	80	80	15

30min_RR	60min_RR	BS_HR	AB_HR	10min_HR	30min_HR	60min_HR	BS_FHR	AB_FHR
23	22	82	84	84	80	80	126	130
23	22	76	80	76	76	80	132	134
24	22	86	85	86	84	86	132	133
19	18	79	82	82	86	82	146	142
18	16	82	82	88	89	86	136	132
20	18	76	72	76	76	80	140	132
15	14	86	80	84	88	89	126	128
17	17	86	79	78	78	82	135	139
20	20	88	86	86	90	87	124	130
15	14	92	88	90	95	92	120	116
19	19	84	88	84	84	84	129	127
20	20	92	90	93	92	90	133	136
20	20	88	88	88	86	88	138	138
17	16	82	86	86	85	80	140	128
16	19	86	86	82	90	82	139	140
19	19	88	92	88	86	80	129	132
15	16	86	90	88	88	82	130	139
20	15	90	88	88	94	88	136	138
16	18	78	82	76	76	78	134	133
16	16	89	90	88	86	86	139	143
15	14	78	82	82	80	80	131	136
15	14	72	73	79	72	72	132	138
17	16	86	80	80	89	88	132	134
16	16	82	86	80	80	79	128	130
18	15	76	80	80	80	80	126	128
17	14	88	90	90	88	86	142	143
15	15	90	90	96	90	90	130	125
15	18	88	90	88	88	86	129	130
16	14	84	84	80	80	86	135	141
14	14	88	86	88	87	88	146	143

10mn_FHR	30min_FHR	60mn_FHR
128	132	126
132	130	125
132	1140	139
139	142	147
136	133	134
136	135	139
130	126	130
128	132	130
130	128	124
130	125	124
127	130	128
132	130	129
140	141	143
142	129	129
132	129	125
130	128	122
132	129	128
129	116	120
135	128	120
128	115	136
125	132	130
120	126	126
130	128	118
128	129	120
120	119	122
128	136	140
126	129	130
122	125	129
135	138	129
138	116	140

MASTER SHEET

List of Abbreviations:

1	age	- Age
2	WT	- Weight
3	GR	- Gravida
4	GA	- Gestational age 1 = term, 2= post term
5	onset	- Onset of labour1 = spontaneous, 2= induced
6	Bolus	- Bolus dose of ketamine
7	1_stage	- duration of first stage of labour
8	2_stage	- duration of second stage
9	3_stage	- duration of third stage of labour
10	cerv.dil	- cervical dilatation at the start of study
11	inf_0.5hr	- infusion rate at half an hour
12	inf_1hr	- infusion at one hour
13	inf_2hr	- infusion at second hour
14	inf_3hr	- infusion at third hour
15	inf_4hr	- infusion at fourth hour
16	inf_5hr	- infusion at fifth hour
17	inf_6hr	- infusion at sixth hour
18	inf_7hr	- infusion at seventh hour
19	inf_8hr	- infusion at eight hour
20	inf_9hr	- infusion at ninth hour
21	inf_10hr	- infusion at tenth hour
22	inf_11hr	- infusion at eleventh hour
23	inf_12hr	- infusion at twelfth hour
24	sta_inf	- second stage infusion
25	pain_0	- pain score at 0 hour
26	pain_1hr	- pain score at 1 hour
27	pain_2hr	- pain score at 2 hour
28	pain_3hr	- pain score at 3 hour
29	pain_4hr	- pain score at 4 hour
30	pain_5hr	- pain score at 5 hour
31	pain_6hr	- pain score at 6 hour
32	pain_7hr	- pain score at 7 hour
33	pain_8hr	- pain score at 8 hour
34	pain_9hr	- pain score at 9 hour
35	pain_10hr	- pain score at 10 hour
36	pain_11hr	- pain score at 11 hour
37	pain_12	- pain score at 12 hour
38	sed_0hr	- sedation score at 0 hour
39	sed_1hr	- sedation score at 1 hour
40	sed_2hr	- sedation score at 2hour
41	sed_3hr	- sedation score at 3 hour
42	sed_4hr	- sedation score at 4 hour

43	sed_5hr	- sedation score at 5 hour
44	sed_6hr	- sedation score at 6 hour
45	sed_7hr	- sedation score at 7 hour
46	sed_8hr	- sedation score at 8 hour
47	sed_9hr	- sedation score at 9 hour
48	sed_10	- sedation score at 10 hour
49	sed_11hr	- sedation score at 11 hour
50	sed_12hr	- sedation score at 12 hour
51	TOT KET	- total ketamine used in mgs
52	RESCUE	- rescue analgesia administered 1 = no, 2 = yes
53	TYPE DEL	- type of delivery 1 = normal vaginal delivery 2 = assisted delivery 3 = caesarean section
54	bld loss	- blood loss
55	vomit	- vomiting present 1 = yes, 2 = no
56	hallucin	- hallucinations present 1 = yes, 2 = no
57	dreams	- dreams present 1 = yes, 2 = no
58	nyst	- nystagmus present 1 = yes, 2 = no
59	giddiness	- giddiness present 1 = yes, 2 = no
60	sedation	- sedation present1 = yes, 2 = no
61	APG_1	- apgar score at 1 minute
62	APG_5	- apgar score at 5 minutes
63	cord-ph	- cord blood pH
64	aver inf	- average infusion rate
65	satis score	- satisfaction score
66	bs_syst	- Baseline systolic blood pressure
67	ab_syst	- Systolic blood pressure after bolus of ketamine
68	10min_sys	- systolic blood pressure 10 minutes after ketamine bolus
69	30min_sys	- systolic blood pressure 30min after ketamine bolus
70	60min_sys	- systolic blood pressure 60min after ketamine bolus
71	bs_dia	- Baseline diastolic blood pressure
72	ab_dia	- diastolic blood pressure after ketamine bolus
73	10min_dia	- diastolic blood pressure 10 minutes after ketamine bolus
74	30min_dia	- diastolic blood pressure 30 minutes after ketamine bolus
75	60min_dia	- diastolic blood pressure 60minutes after ketamine bolus
76	bs_hr	- baseline heart rate
77	ab_hr	- heart rate after ketamine bolus
78	10min_hr	- heart rate 10 minutes after ketamine bolus
79	30min_hr	- heart rate 30 minutes after ketamine bolus
80	60min_hr	- heart rate 60minutes after ketamine bolus
81	bs_fhr	- baseline fetal heart rate
82	ab_fhr	- fetal heart rate after ketamine bolus
83	10min_fhr	- fetal heart rate 10minutes after ketamine bolus
84	30min_fhr	- fetal heart rate 30minutes after ketamine bolus
85	60min_fhr	- fetal heart rate 60minutes after ketamine bolus