RESEARCH ARTICLE

LOW DOSE KETAMINE FOR PAINLESS LABOUR: A COMPARATIVE STUDY OF 100 PATIENTS

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ABSTRACT

Background: The phencyclidine derivative Ketamine is widely used as intramuscular and intravenous anaesthetic agent. In contrast to other anaesthetics, ketamine has potent analgesic properties in sub-anaesthetic doses. Recent studies indicate that analgesia produced by ketamine is mediated through opiate receptors and N-methyl D aspartate receptors. As systematically administered ketamine is unlikely to produce the respiratory depression, it seemed to offer an obvious advantage over the narcotics in which major drawback is respiratory depression.

Aims & Objective: (1) To study the following parameters in pregnant women given ketamine v/s pregnant women not given analgesic - (a) Maternal outcome in form of duration of labour, mode of delivery, complication of third stage of labour. (b) Foetal outcome in form of Apgar score at 1 min and 5 min. (2) To study pharmacological effect of ketamine on mother (3) To evaluate patient's satisfaction about this method.

Material and Methods: The present study was Randomized controlled trial, conducted in Department of Obstetrics and Gynaecology at Smt. SCL Municipal General Hospital affiliated to NHL Medical College Ahmedabad over a span of 3 yrs. from 2010 to 2012. Study included primigravida and multigravida. 100 women fulfilling the inclusion and exclusion criteria were taken for the study. Study population divided into Control Group (no drug administered) and Study group (intravenous ketamine administered).

Results: The duration of 1st and 2nd stage was remarkably shortened in study group. 64% of parturient in study group delivered within 3 hours of entering the active phase of labour compared to only 10% in control group. In study group 98% delivered vaginally only 2% required instrumental delivery. There was no inhibition of bearing down reflex by ketamine, no maternal exhaustion in study group. In present study ketamine had no effect on APGAR score at 1 min & at 5 min. 30% had marginal rise in pulse rate with range of 10-15 beats /min. 16% had risen in B.P. not beyond 15-20 mm of Hg. 10% cases had nausea but no vomiting. 90% of cases had excellent pain relief & 8% had satisfactory pain relief, while 2% had no pain at all.

Conclusion: The low dose intravenous ketamine suits best to this situation as it provides effective analgesia in low doses, safe without significant maternal and foetal complications, does not prolong duration of labour and there is no increase in rate of instrumental delivery or caesarean section rate. Since it reduces maternal pain thereby reducing the maternal exhaustion the patients on ketamine are very co-operative during labour, easy to administer and monitor without the help of an expertise and cost effective.

KEY-WORDS: Normal Labour; Intravenous Ketamine; Study Group; Control Group

Introduction

Giving birth is one of the most significant events in woman's life, transition from womanhood to motherhood. It initiates family life, miracle of creating life itself. Right from the beginning of human life, motherhood and pain are regarded inseparable, pain in labour is considered inevitable, it is normal and not due to some pathological condition. Effective pain relief prevent maternal exhaustion, enhance co-operation of mother. It reduces stress related elevation of catecholamine, allows smooth cervical dilatation, making labour more tolerable and enjoyable experience.[1] According to Inger Findley and Geoffrey Chamberlain, an ideal method of pain relief in labour should not interfere with uterine contraction or the progress of labour and should not increase operative intervention.[2] It should not depress the respiratory centre of new born and should be easy to administer. It should not have unpleasant side effect to mother and foetus. The phencyclidine derivative Ketamine[3] is widely used as intramuscular and intravenous anaesthetic agent. In contrast to other anaesthetics, ketamine has potent analgesic properties in sub-anaesthetic doses.[4] In recent years, epidural narcotics have been used to provide good pain relief in labour pains but this method is still subject to certain

drawbacks, the most serious of which appears to be delayed respiratory depression. Recent studies indicate that analgesia produced by ketamine is mediated through opiate receptors and N-methyl D aspartate receptors. As systematically administered ketamine is unlikely to produce the respiratory depression, it seemed to offer an obvious advantage over the narcotics in which major drawback is respiratory depression.[5]

Materials and Methods

Study Design: Randomized Controlled Trial

The present study was conducted in Department of Obstetrics and Gynaecology at Smt. SCL Municipal General Hospital affiliated to NHL Medical College Ahmedabad over a span of 3 yrs from 2010 to 2012. Women admitted in labour room were screened. Study included primigravida and multigravida. Detailed history was taken. Major medical or surgical illnesses were ruled out. General as well as obstetric examination was done in detail. The aims and objectives are: (1) To study the following parameters in pregnant women given ketamine v/s pregnant women not given analgesic- (a) Maternal outcome in form of duration of labour, mode of delivery, complication of third stage of labour. (b) Foetal outcome in form of Apgar score at 1 min and 5 min. (2) To study pharmacological effect of ketamine on mother (3) To evaluate patient's satisfaction about this method. 100 women fulfilling the inclusion and exclusion criteria were taken for the study. Procedure was explained to the parturient and informed consent obtained. Women were randomized as study and control group.

Study Groups: Control Group (no drug) and Study group (intravenous ketamine administered)

Inclusion Criteria: (1) Parturient in active phase of labour with 3 cm cervical dilatation; (2) Vertex presentation; (3) Single term pregnancy; (4) Normal blood pressure; (5) No cephalopelvic disproportion; (6) Foetus in good condition

Exclusion Criteria: (1) Parturient with Malpresentation; (2) Parturient with multiple pregnancy; (3) Parturient with high risk obstetric problems; (4) Parturient with premature rupture of membranes; (5) Parturient with IUGR; (6) Previous uterine Scar

The study stated at active phase of labour (3 cm cervical dilatation) with effective uterine contraction (3 Cont lasting for 40 to 50 sec in 10 minutes). Patients who fulfil the inclusion criteria mention above were taken for the study. Patients were premeditated with glycopyrrolate[6] 0.005 mg/kg then low dose ketamine 0.4 mg/kg body weight[7] was given slowly IV over period of 30-60 seconds. The maintenance dose was started using infusion pump at the rate of 1 mg/min in normal saline after 30 min of induction dose. Patient was monitored on one to one basis. Partogram maintained. Assessment of labour by foetal monitoring with help of NST machine, maternal monitoring with cardiac monitor measuring pulse, B.P, SPO2 was done. Respiratory rate was measured. All instruments necessary for neonatal resuscitation were kept on by stand. When the cervix reached full dilatation doses were not increased. The dose in 1st stage was continued in 2nd stage even if she perceived pain. This enable the patient to enter a light plane of analgesia when she could just about perceive a much attenuated pain of uterine contractions and the patient was made to bear down. After delivery, Infusion was continuing till the episiotomy suturing done. These obviate or decrease need for local analgesia during episiotomy suturing. In the 50 control parturient, no method of pain relief was given & monitoring was done as follows. Time of induction, induction dose, onset of analgesia, total dose of ketamine mode of delivery, duration of 1st stage (from 3cm cervical dilatation), 2nd stage, and 3rd stage was noted. Induction delivery internal was calculated. All women observed for 1 hour after delivery in labour room. The mothers were assessed to roll their overall quality of analgesia using visual analogue scale after delivery of baby.[8] Pain was measured subjectively using visual analogue sale. Visual Analogue scale is the most common form consists of 10cm horizontal line with 2 end points labelled "no pain" and "worst pain ever". The Patient is required to place a mark on the 1 cm line at a point that corresponds to her pain intensity during labour. Final assessment of analgesia was done using visual Analogue Scale Follow: Excellent (VAS 0-2) – No pain during labour, Satisfactory (VAS 2-8) –

Patient had brief period of pain but it was bearable and patient remained co-operative, Unsatisfactory (VAS 9-10) – Little/No relief of Pain and Patient become un-cooperative.[9]

Results

The duration of 1st stage was remarkably shortened in study group. The duration of 1st stage of labour in study group was less than 2hours in 40% of cases as compared to only 6% in control group (Table 1). Majority of patients in study group delivered within 30 mints while it took 40 mints for control group for the 2nd stage of labour. There was a definite reduction of 2nd stage compared to control group (Table 2). 64% of parturient in study group delivered within 3 hours of entering the active phase of labour compared to only 10% in control group (Table 3, 4). In study group 98% delivered vaginally only 2% required instrumental delivery. There was no inhibition of bearing down reflex by ketamine, no maternal exhaustion in study group. All Patients cooperated well in 2nd stage (Table 5). In present study ketamine had no effect on Apgar score at 1 min & at 5 min (Table 6). 30% had marginal rise in pulse rate with range of 10-15 beats /min.16% had risen in B.P. not beyond 15-20 mm of Hg.10% cases had nausea but no vomiting (Table 7). 90% of cases had excellent pain relief & 8% had satisfactory pain relief, while 2% had no pain at all (Table 8).

Table-1: Duration of First Stage of Labour

Group	N	Mean	SD	Z Value	Significance
Study	50	140.6	32.3	8.10	Significant
Control	50	205	46.07		

Table-2: Duration of Second Stage of Labour

Group	N	Mean	SD	Z Value	Significance
Study	50	32.04	5.37	3.15	Significant
Control	50	35.80	6.50		

Table-3: Induction Delivery Interval

Time (in minutes)	Study Group		Control Group	
	N	%	N	%
120-180	32	64	5	10
181-240	16	32	23	46
241-300	2	4	16	32
>300	0	0	6	12
Total	50	100	50	100

Table-4: Induction Delivery Interval

Group	N	Mean	SD	Z Value	Significance
Study	50	32.04	5.37	3.15	Significant
Control	50	35.80	6.50		

Table-5: Type of Delivery

Type	Study Group		Control Group	
	N	%	N	%
Normal delivery with or without episiotomy	49	98	50	100
Instrumental delivery	1	2	0	0
Caesarean section	0	0	0	0
Total	50	100	50	100

Table-6: Effect on Foetus

Apgar Score	At One Minute		At Five Minutes	
	Study Group (%)	Control Group (%)	Study Group (%)	Control Group (%)
9-10	2	0	100	96
7-8	98	98	0	4
<7	0	2	0	0
Total	100	100	100	100

Table-7: Effects on Mother

Side Effects	N	%
Rise in pulse	15	30
Rise in B. P.	8	16
Hallucination	0	0
Apnoea	0	0
nausea / Vomiting	5	10
Emergence reaction	0	0

Table-8: Degree of Pain Relief

Degree of Analgesia	N	%
Unsatisfactory	1	2
Satisfactory	4	8
Excellent	45	90
Total	50	100

Discussion

In present study, induction dose of ketamine was 0.4 mg/kg & maintenance dose was 1mg/min continuous intravenous infusion, comparing with Desai & Daftary[10] induction dose was similar but maintenance was given in form of intermittent intravenous injection instead of continuous infusion. Here was the role of infusion pump[11] which was costly but aborting the need of intravenous drip which required dose adjustment, otherwise either excess or less amount of dose accidently given lead to more toxicity or less efficacy. So every obstetrician must learn how to use infusion pump.

In present study, degree of pain relief was excellent in 90% as compared to Desai& Daftary it was 70%. These was due to continuous intravenous infusion with infusion pump.[10] In a study of Ayangade O, duration of labour was shortened from 360mins to 196mins.[12] In Leena et al duration of 1st stage was 246.5min in primi & 110.7 min in multi.[13] In Sharma et al duration of

1st stage was 192 mints in primigravida 98 mins in multigravida.[14] In present study, mean duration of 1st stage was 140.6 mins in study group & 205 mins in control group. Z value was 8.10 i.e. significant. Ketamine reduces maternal pain thereby reduces maternal exhaustion; the patients on ketamine are very cooperative during labour. It has oxytocic's property. Uterine contractions & cervical dilatation were not interfered by ketamine. So, 1st stage duration was significantly shortened.

Study by Leena et al[13] showed shortening of 2nd stage to 17.5 mins compared to normal (45 mins). In present study, mean duration of 2nd stage was 32 mins in study group & 35.8 mins in control with Z value of 3.15 i.e. significant. Bearing down reflex was not inhibited by ketamine during 2nd stage.

Chodoff & Stella found out oxytocic property of ketamine.[15] The 3rd stage of labour in this group was characterized by prompt uterine contractions with rapid expulsion of placenta. Following delivery of placenta uterus remained firmly contracted so the oxytocic were needed only in 3 patients. Average blood loss was 100 to 200 ml, much less than the use of other anaesthetics techniques. In present study, mean duration of 3rd stage was 6.08 min in study group while 6.38 min in control group. No difference in 3rd stage of labour in both groups. There were no 3rd stage complications in both groups. Sharma et al[14] have shown that there was no case of dysfunctional labour in study group. After 4 cm cervical dilatation the average duration required was 192 mins in primi, 98 mins in multigravida. Sarkar & Sahu, progress of labour was not hampered & postpartum bleeding was minimal with low dose ketamine.[16] Desai & Daftary found that duration of labour reduced on an average by 2.5 hours.[10] In present study, Induction delivery interval was 174mins in study group & 241.8 mins in control. 64% (study group) as compared to 10% (control group) delivered within 3hours. Ketamine in low dose significantly curtails duration of labour.

In Sarkar & Sahu[16], Desai & Daftary[10] and present study, large majority of patients delivered vaginally only 2-10% required instrumental delivery. In Sharma & Parekh[14], Sarkar & Sahu[16] and present study, ketamine had no effect on Apgar score at 1 min & at 5 min.

Ayangade O et al[12] reported 18% had risen blood pressure, 18% had emergence reactions. Sharma et al[14] found minor side effects[17] like dryness of mouth (80%), visual disturbances (60%), pleasant dreams (12%), nausea (4%), vomiting (4%), restlessness (2%), excessive salivation (2%), and unpleasant dreams (2%). Sarkar & Sahu noted no serious maternal complication except transient &mild rise in B.P. and pulse rate which reverted to normal after stoppage of infusion. In present study 30% had marginal rise in pulse, 16% had marginal rise in blood pressure, and 10% had nausea but no vomiting.

Conclusion

In developing countries like India where analgesia during labour is still in its infancy various techniques have been tried for pain relief during labour. Today the most popular method of pain relief during labour used worldwide is the epidural analgesia.[18] But in our countries because of financial constraints, we need simple, safe effective and economical method for pain relief. The low dose intravenous ketamine suits best to this situation since[19], (1) It provides effective analgesia in low doses; (2) It is safe without significant maternal and foetal complications; (3) It does not prolong duration of labour and there is no increase in rate of instrumental delivery or caesarean section rate. Since it reduces maternal pain thereby reducing the maternal exhaustion the patients on ketamine are very co-operative during labour; (4) It is easy to administer and monitor without the help of an expertise; (5) It is cost effective and economic.

References

1. Kilpatrick SJ, Laros RK Jr. Characteristics of normal labor. Obstet Gynecol 1989;74(1):85-7.
2. Findley I, Chamberlain G. Relief of pain. BMJ 1999;318(7188):927–930.
3. Ahmadi A, Khalili M, Hajikhani R, Hosseini H, Afshin N, Nahri-Niknafs B. Synthesis and study the analgesic effects of new analogues of ketamine on female wistar rats. Med Chem 2012;8(2):246-51.
4. Niesters M, Martini C, Dahan A. Ketamine for Chronic Pain: Risks and Benefits. Br J Clin Pharmacol. 2013 Feb 21. doi: 10.1111/bcp.12094. [Epub ahead of

print]
5. Panzer O, Moitra V, Sladen RN. Pharmacology of sedative-analgesic agents: dexmedetomidine, remifentanil, ketamine, volatile anesthetics, and the role of peripheral Mu antagonists. Crit Care Clin. 2009;25(3):451-69.
6. Abboud TK, Read J, Miller F, Chen T, Valle R, Henriksen EH. Use of glycopyrrolate in the parturient: effect on the maternal and fetal heart and uterine activity. Obstet Gynecol 1981;57(2):224-7.
7. Rasmussen KG, Lineberry TW, Galardy CW, Kung S, Lapid MI, Palmer BA, et al. Serial infusions of low-dose ketamine for major depression. J Psychopharmacol 2013;27(5):444-50.
8. DeLoach LJ, Higgins MS, Caplan AB, Stiff JL. The visual analogue scale in the immediate postoperative period: intrasubject variability and correlation with a numeric scale. Anesth Analg 1998; 86(1):102-6.
9. Bodian CA, Freedman G, Hossain S, Eisenkraft JB, Beilin Y. The Visual Analogue Scale for Pain: Clinical Significance in Postoperative Patients. Anesthesiology 2001;95(6):1356-61.
10. Dftary SN, Desai SV, Thanawala U, Bhide A, Levi J, Patki A, et al. Programmed labor- Indegenous protocol to optimize labor outcome. South Asian Federation of Obstetrics & Gynecology 2009;1(1):61-4.
11. Yeom JH, Chon MS, Jeon WJ, Shim JH. Peri-operative ketamine with the ambulatory elastometric infusion pump as an adjuvant to manage acute postoperative pain after spinal fusion in adults: a prospective randomized trial. Korean J Anesthesiol 2012;63(1):54-8.
12. Ayangade O. Microadministration of ketamine during labor and delivery of Nigerian women. Int J Gynaecol Obstet 1979;17(1):88-90.
13. Sun LS. Labor Analgesia and the Developing Human Brain. Anesth Analg 2011;112(6):1265-7.
14. Sharma SK, Sidawi JE, Ramin SM, Lucas MJ, Leveno KJ, Cunningham FG. Cesarean delivery: a randomized trial of epidural versus patient-controlled meperidine analgesia during labor. Anesthesiology. 1997;87(3):487-94.
15. Chodoff P, Stella JG. Use of CI-581-a phen- cyclidine derivative for obstetric anesthesia. Anesth & Analg 1966;45(5):527-30.
16. Sarkar P., Sahu S.P. Ketamine hydrochloride for painless labour. Ind J Anaesth 1992;40(3):120-3.
17. Rachel Q, Prommer EE, Mihalyo M, Twycross R, Wilcock A. Ketamine. Journal of Pain and Symptom Management 2011;41(3):640–9.
18. Anim-Somuah, M., Smyth, R. M., Jones, L. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev. 2011 Dec 7;(12):CD000331.
19. Little B, Chang T, Chucot L, Dill WA, Enrile LL, Glazko AJ, et al. Study of ketamine as an obstetric anesthetic agent. Am J Obstet Gynecol 1972;113(2):247-60.

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