DOES LOW DOSE ORAL KETAMINE HAVE OXYTOCIC EFFECT?

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ABSTRACT

Objectives: To evaluate if low dose oral Ketamine has oxytotic effect on term pregnant uterus.

Methodology: This is a cross sectional double blind placebo control prospective study. A total of 745 parturients were studied, 261 had low dose oral Ketamine in active phase of labour (group A), 227 had Oxytocin augmentation (group B) and 257 had none of these medication (control group C). Their age, parity, gestational age, duration of labour and APGAR score were determined and all data analyzed using Epi Info.

Results: The parturients were predominantly within the age group 26 – 35 years and their mean gestational age at delivery was 39.1weeks. The mean (± S.D.) duration of labour (first stage of labour) was found to be shortest in group A 5.80 ± 2.06 hours, while it was 8.03 ± 3.37 hours in group B and 7.01 ± 3.25 hours in group C. Foetal outcome was comparable in all the three groups.

Conclusion: Low dose oral Ketamine probably has an Oxytocic effect which needs to be explored in future research. And if this be the case, then it will be a suitable and safe single agent for labour analgesia and augmentation and for extended use in repairs of episiotomy and perineal tears.

Key words: Oral *Ketamine, low dose, oxytocic effect, labour duration, foetal outcome.*

INTRODUCTION

Ketamine is a general anaesthetic agent which over time has proven to be of great benefit in obstetric practice. Most studies conducted on the use of Ketamine in obstetrics had focused on its benefit as a potent analgesic for use in obstetric practice. From these studies, it has been established that low dose Ketamine is good for obstetric analgesia with no untoward effects to both mother and baby.[1,2,3]

The first stage of labour which refers to the onset of labour to full cervical dilatation is associated with a lot of anxiety and pain especially in the active phase, and prolonged labour may pose adverse effect on the mother and baby. There is often thus a need to ensure that parturients scheduled for vaginal delivery are successfully delivered within a specific time frame in order to avert the adverse sequelae of prolonged labour. The normal duration of active phase of the first stage of labour ranges between 8 – 12 hours. This duration can be shortened with the use of medications especially when there is a slowing

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down or some dysfunctionality in the labour process. Most widely used medication till date has remained Oxytocin, which can be used to improve the quality of uterine contractions. Oxytocin does not provide any analgesic effect. In fact most parturients in our society has the traditional belief that the use of Oxytocin in labour aggravates labour pains and sometimes may be reluctant to consent to its use.

Many methods have been tried over time for relief of labour pain, ranging from non-pharmacological methods such as water baths, continuous support in labour, transcutaneous electrical nerve stimulation (TENS), acupuncture, hypnosis and breathing exercises, and pharmacological methods such as use of parenteral narcotics (such as pethidine, fentanyl and tramadol), inhalational agents like entonox (nitrous oxide with oxygen) and servox (servoflurane and oxygen) and more recently continuous epidural infusion of dilute local anaesthetic with opioid. Each method however has its own shortfall. For instance many of the opioid analagesics have respiratory depressive effects on the fetus and thus cannot be used in advanced labour.[4] Epidural anaesthesia which has been found to be highly beneficial needs skill to administer, is expensive compared to other forms of labour analgesia, has been found to cause a delay in second stage of labour.[4] None of these methods is known to facilitate labour. This has led us to search for a single medication that is safe for use in labour, has both analgesic and oxytocic properties, cheap, readily available and easy to administer in low resource settings like ours. Ketamine, which is currently being evaluated for different purposes and is gaining greater popularity in obstetric practice, has been established not to cause respiratory depression in the baby when administered in anaesthetic doses and this has led to the evaluation of its benefit in obstetric practice using low (sub-anaesthtic) doses in most studies.

A number of authors have found Ketamine to increase uterine tone in animal studies with no significant effect on uterine blood flow.[5,6] It has also been established that anaesthetic doses of Ketamine increase the intensity of uterine contractions.[7] Most studies conducted evaluated the use of continuous intravenous infusion of Ketamine[1,2,6] or its intrathecal or epidural administration[8,9] for pain relief. In an earlier study by Jagatia K et al, it was found that the use of low-dose intravenous Ketamine in labour shortened both the first and second stages of labour remarkably with no inhibition of the bearing down reflex and has no adverse effect on APGAR scores while providing excellent analgesia.[1]

The parenteral routes of administration of Ketamine require skill, expertise and close monitoring. Nigeria is a developing country where many traditional birth attendants with minimal skills reside especially in rural settings. Bearing this in mind, we decided to evaluate the use of low dose oral Ketamine for similar purposes, as it can easily be administered. Ketamine is tasteless, colourless and odourless and can thus be taken orally in fruit juice without being noticed.

The aim and objective of this study is thus to evaluate the effect of low dose oral Ketamine on duration of active phase labour and to assess its safety for use in labour.

METHODOLOGY

This study was conducted at the Ebonyi state University teaching hospital Abakaliki and Lagos University Teaching Hospital, Idi-araba, Lagos, Nigeria. Ethical clearance was given by the ethical clearance committee of Ebonyi state university teaching hospital for the administration of oral ketamine to parturients in active phase of labour and consent was obtained from the parturients before administration of the oral ketamine. It is a follow up of our earlier studies on low dose Ketamine for use

in labour analgesia and for repair of episiotomy and perineal tears.[3,10] Here we decided to compared the duration of labour in three (3) groups of parturients viz those who received low dose oral Ketamine in labour (group A), women who had their labour augmented with Oxytocin (group B) and the control, that is those who did not receive any of these medications (group C).

Parturients who presented in labour at term (37 – 42 weeks gestational age) were studied. Women who had multiple pregnancy, congenital anomaly and hypertensive disorders were excluded.

A total of 745 parturients at term were studied. Of these 261 (35.0%) had low dose oral Ketamine primarily for labour analgesia, 227 (30.5%) had Oxytocin for augmentation of labour while 257 (34.5%) had none of these two medications.

Data was obtained from the case note recordings using a proforma designed for this study. Information obtained included age, parity, gestational age, duration of labour and APGAR score. Foetal outcome was assessed using the one-minute APGAR score. Baby is said to be normal if APGAR score is 7 or more at 1 minute, considered to have mild birth asphyxia if 1-minute APGAR score is 6, moderate birth asphyxia if it is 4 or 5 and severe birth asphyxia if it is 3 or less. Data analysis was done using Epi Info statistical version 3.5.1. ANOVA, Chi square and Kruskal-Wallis tests were used to assess statistical significance where applicable. A p-value of <0.05 was considered to be statistically significant.

RESULTS

A total of 745 parturients at term were recruited for this study. Of these 261 (35.0%) had low dose Ketamine primarily for labour analgesia, 227 (30.5%) had Oxytocin for augmentation of labour while 257 (34.5%) had none of these two medications.

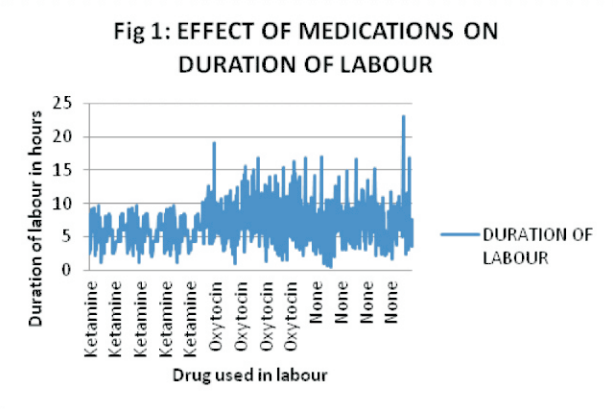
The parturients were predominantly women between the age groups 26 – 35 years, comprising 65.2% of the total population studied, while minority (1.9%) were in extremes of reproductive age groups 16 - 20 and 41 - 45 years. They were mostly multiparous women (parity 1 - 4) comprising 61.7% of the study population. The mean (± SD) gestational age at delivery was 39.1 (± 1.14) weeks, with a modal frequency of 40 weeks (33.3%), *table 1*.

The mean (±S.D.) duration of labour in group A (those who had Ketamine) was 5.80 ± 2.06 hours, in group B (those who had Oxytocin) it was 8.03 ± 3.37 hours while in group C (those who had normal progression without these two medications) it was 7.01 ± 3.25 hours and this difference is statistically significant (p=0.0000), *figure 1*.

When the relationship between duration of labour and foetal outcome was compared, it was observed that there was no statistically significant relationship in this study (p=1.0000). It was also observed that there was no clinical significance in the proportion of babies who were delivered with normal APGAR score in the three groups, 88.9%, 87.6% and 92.9% in the Ketamine arm, Oxytocin arm and the control group respectively. None of the babies whose mother had low dose oral Ketamine was severely asphyxiated.

Table I: Biosocial Characteristics Of Study Population

BIOSOCIAL CHARACTERISTIC	FREQUENCY	PERCENT
Age Group (Years)		
16-20	5	0.7%
21-25	157	21.1%
25-30	1	0.1%
26-30	252	33.8%
31-35	234	31.4%
36-40	87	11.7%
41-45	9	1.2%
Total	745	100.0%
Parity		
Grandmultipara (Para 5 and above)	32	4.3%
Nullipara (Para 0)	253	34.0%
Para 1-4	460	61.7%
Total	745	100.0%
Gestational Age (weeks)		
37	77	10.3%
38	146	19.6%
39	215	28.9%
40	246	33.0%
41	54	7.2%
42	7	0.9%
Total	745	100.0%



Note the peak of the line chart which indicates the maximum duration of labour. Also note that this is generally shorter for those parturients who had low dose Ketamine in labour compared to the other two groups.

Table II: Foetal Outcome In The Three Groups Studied

DRUG USE IN LABOUR	Normal	Mild birth asphyxia	Moderate birth asphyxia	Severe birth asphyxia	TOTAL
Ketamine	216 (88.9%)	15 (6.2%)	12 (4.9%)	0 (0.0%)	243 (100.0%)
None	237 (92.9%)	3 (1.2%)	11 (4.3%)	4 (1.6%)	255 (100.0%)
Oxytocin	191 (87.6%)	10 (4.6%)	11 (5.0%)	6 (2.8%)	218 (100.0%)
TOTAL	644 (89.9%)	28 (3.9%)	34 (4.7%)	10 (1.4%)	716 (100.0%)

χ^2=15.2030, P=0.0187

DISCUSSION

This study showed that low dose oral Ketamine facilitates the progress of labour. It was found in this study that women who had low dose oral Ketamine in labour had a much shorter duration of labour than the other two groups studied with no adverse effect to the baby. Surprisingly, we also observed a much shorter duration of labour in women who had a natural progression without receiving any of the two pharmacological agents (Ketamine or Oxytocin) compared to those whose labour was augmented with Oxytocin. This might be due to the fact that labour augmented with Oxytocin is often necessitated by an initial slowing of labour or a dysfunctionality in the labour process ab initio which probably must have caused a delay in the entire process and a resultant prolongation of the duration of labour even before Oxytocin infusion is commenced for augmentation.

The overall foetal outcome in terms of the APGAR scores of the babies was comparable in all the three groups and this goes to show that Ketamine is quite safe for use in labour in carefully selected cases. Ketamine can thus be considered used as a single agent to aid labour while providing potent analgesia, as was found in an earlier study by Okorie O et al.[3]

The question now is does Ketamine have oxytocic properties or does it influence the release of oxytocin from the posterior pituitary? In one study by Zierer R on rats, it was found that a premedication with atropine and diphenylhydantoin in combination with Ketamine does not cause a change in the concentration of oxytocin, oxytocin-neurophysin and its metabolic products in the posterior pituitary and in the circulation.[11] If this be the case, then is the chemical structure of Ketamine in any way similar to that of Oxytocin? Or could it have effect on the hypophyseal-pituitary axis of the brain.This calls for further research.

CONCLUSION

If ketamine is found to shorten the duration of labour significantly then it may be used as a single agent in providing labour analgesia and also minimize the need for oxytocics with no untoward effects to both mother and baby. It is cheap, readily available and does not need skill to administer as it can be given orally. Low dose oral Ketamine probably has an Oxytocic effect which needs to be explored in future research. And if this be the case, then it will be a suitable and safe single agent for labour analgesia and augmentation and for extended use in repairs of episiotomy and perineal tears. It will be of great value in the nearest future for use in obstetric practice in low resources settings where skilled manpower is lacking.

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