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Intranasal Ketamine *vs.* Intramuscular Pethidine in Labor Pain Analgesia

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Abstract

Background: Ketamine can give good analgesia even when given in a dose less than its anesthetic doses. No previous studies of using intranasal ketamine for labor analgesia have reported, hence the idea of this study.

Subjects and methods: In this study 105 patients attending the labor unit were included and they were randomized in 2 study groups. In group A (study group 1) the patients received an initial dose of 0.5 mg/kg intranasal ketamine, followed by a single repeat dose of 0.25 mg/kg intranasal ketamine after 1 h after the initial drug administration while in group B (study group 2) the patients received a standard 50 mg intramuscular pethidine injection, followed by a single repeat dose of 50 mg intramuscular pethidine injection 1 h after the initial drug administration. Average labor pain was assessed using Visual Analogue Scale (VAS) by direct questioning from patient in both groups and considered as the primary outcome measure.

Results: On comparing the final visual analogue score (VAS) between the two study groups it is significantly lower in the group A (Ketamine group) 49.5 ± 17.7 than in group B (Pethidine group) 52.2 ± 15.3 P value=0.008. The 5 min APGAR score is significantly higher in the group A (Ketamine group) 8.34 ± 1.31 than in group B (Pethidine group) 7.35 ± 1.74 P value=0.001. The rate of vomiting is significantly lower in the group A (Ketamine group) 3.77% than in group B (Pethidine group) 23.08% P value=0.001. The rate of hallucinations is significantly higher in the group A (Ketamine group) 33.96% than in group B (Pethidine group) 5.77% P value=0.000.

Conclusion: The use of intranasal ketamine in an initial dose of 0.5 mg/kg with supplementary dose of 0.25 mg/kg is more effective than the use of 50 mg intramuscular pethidine with supplementary dose of 50 m IM as labor analgesia with better fetal APGAR score at 5 min less vomiting incidence but with significantly higher rate of hallucinations.

Keywords: Intranasal ketamine; Labor analgesia

Introduction

The process of labor for sure is one of the most painful conditions confronted by women. Different studies showed that, the usual labor pain scores where more than that of sciatic, dental or bone fractures pain scores [1]. Cervical dilatation, ischaemia of the uterine musculature due to accumulation of lactic acid and vaginal and perineal stretching are the causes of labor pain [2,3].

Increased oxygen consumption by the uterine muscles during contractions, can also results in hyperventilation and marked respiratory alkalosis and a left shift of oxygen dissociation curve of the mother and consequently fetal hypoxemia. In responce hypoventilation and transient maternal and fetal hypoxemia may occur between contractions. These periods of hypoventilation may be exaggerated by labor analgesic which may cause respiratory depression specially opioids [3-5].

Ketamine is an N-Methyl-D-aspartate receptor antagonist. It can give good analgesia even when given in a dose less than its anesthetic doses [6]. Its availability and wide use as a sedative by non-Anesthesiologists in minor surgical procedure is a fact [7,8]. Infusion of ketamine in Low-dose preoperatively proved to produce analgesia and decrease the opioid analgesics requirements [9]. Intranasal ketamine has a bioavailability of 45% and blood levels reach the analgesic effect easily [10].

Subjects and Methods

This study was conducted in the Department of Obstetrics and Gynecology, Tanta University on patients attending the labor unit. The study was held in the period from June 1, 2016 to December, 1, 2016. The number of patients enrolled in the study was 105 patients after application of inclusion and exclusion criteria.

All women were thoroughly informed about the study aims and through discussion about the procedure, associated benefits and risks and assigned written consent.

Inclusion criteria: Age from 18 to 38 years with confirmed active first stage of labor with at least 2 cm cervical dilatation and at least 80% cervical effacement.

Exclusion criteria: Patients with any indication for caesarean section, patients with diabetes mellitus, hypertension, and abnormal liver function tests, known cardiac or renal disease, endocrinological diseases, chronic diseases, multifetal pregnancy and also patients with history of two years infertility or more.

Baseline examination

At the time of admission, age and Body Mass Index (BMI) of mother, and gestational age based on last day of period were recorded. During first stage of delivery, fetus was monitored using a non-stress test [11].

Each individual with abnormal finding of NST (late deceleration or variable deceleration) was omitted from the trial. All cases were evaluated by ultrasound in order to evaluate fetus before delivery. Baseline pain score was then determined using a standard 100 mm VAS anchored with "no pain" at 0 mm and "worst pain imaginable" at 100 mm.

The 105 patients included in the study were randomized in 2 study groups according to sequence of computer-generated block-random numbers.

In group A (study group 1) (53 patients) the patients received an initial dose of 0.5 mg/kg intranasal ketamine; this dose was based on previous studies regarding postoperative pain [12]. The patients then received a single repeat dose of 0.25 mg/kg intranasal ketamine after 1 h after the initial drug administration while in group B (study group 2) (52 patients) the patients received a standard 50 mg intramuscular pethidine injection. The patients then received a single repeat dose of 50 mg intramuscular pethidine injection 1 h after the initial drug administration.

All the patients will be offered rescue analgesia of intravenous solution infusion containing 1000 mg paracetamol.

For all the patients in both groups when the cervix was fully dilated the subject was transferred to the operation room where local perineal infiltration anesthesia with 10 ml lidocaine HCL was used if episiotomy is needed.

After child birth, average labor pain was assessed using Visual Analogue Scale (VAS) by direct questioning from patient in both groups and considered as the primary outcome measure.

APGAR score at 1 and 5 min of neonate, pH of the cord blood, duration of labor, mode of labor, the need for rescue analgesia, the occurrence of complications like hallucination and vomiting and the overall patient satisfaction; these parameters were considered as secondary outcome measures.

All statistics were performed using MinitabVer.17 (Minitab Inc., USA).

Results

Table 1 shows a comparison of age, BMI, distribution of primigravidae and multigravidae and the initial visual analogue score between the study groups. There are no statistically significant differences between the two groups regarding these variables.

Table 2 show the comparison of the final visual analogue score (VAS) between the two study groups which is significantly lower in the group A (Ketamine group) indicating less pain.

Table 3 and Figure 1 show the change of the VAS in each group which is significantly lower in both groups.

	Group A (n=53)	Group B (n=52)
Age		
Mean	28.40	30.54
SD	6.32	4.61
	Two sample T-Test P value=0.050	
BMI		
Mean	28.28	27.33
SD	4.37	5.12
	Two sample T-Test P value=0.306	
Initial visual analogue score (VAS)		
Mean	65.4	66.7
SD	19.7	20.1
	Two sample T-Test P value=0.735	
Primigravidae		
Number	33	29
Percentage	62.26%	55.77%
Multigravidae		
Number	20	23

Percentage	37.74%	44.23%
Chi Square test P value=0.498		

Table 1: Comparison of the pre-study variables.

	Group A (n=53)	**Group B (n=52)**
Mean	49.5	52.2
SD	17.7	15.3
Two sample T-Test P value=0.008*		

Table 2: Final visual analogue score (VAS) between the two groups.

Group A		**Initial VAS**	**Final VAS**	**Difference**
	Mean	65.4	49.45	15.91
	SD	19.7	17.7	21.19
Paired T-Test P value=0.000*				
Group B		Initial VAS	Final VAS	Difference
	Mean	66.67	58.15	8.52
	SD	20.07	15.34	22.10
Paired T-Test P value=0.008*				

Table 3: Difference of visual analogue score (VAS).

	Group A (n=53)	**Group B (n=52)**
Duration of labor		
Mean	4.11	4.60
SD	1.80	1.32
Two sample T-Test P value=0.120		
APGAR score 1 min		
Mean	7.04	6.77
SD	1.72	1.64
Two sample T-Test P value=0.415		
APGAR score 5 min		
Mean	8.34	7.35
SD	1.31	1.74
Two sample T-Test P value=0.001*		
Cord blood pH		
(7.18-7.38)		
Number	44	42
percentage	83.02%	80.77%

(<7.18)		
Number	9	10
percentage	16.98%	19.23%
Chi Square test P value=0.765		
Need for rescue analgesia		
Number	9	12
percentage	16.98%	23.08%
Chi Square test P value=0.434		
Complications		
Hallucinations		
Number	18	3
percentage	33.96%	5.77%
Chi Square test P value=0.000*		
Vomiting		
Number	2	12
percentage	3.77%	23.08%
Chi Square test P value=0.002*		
Mode of delivery		
Spontaneous		
Number	35	33
percentage	66.04%	63.46%
Instrumental		
Number	9	7
percentage	16.98%	13.46%
Caesarean section		
Number	9	12
percentage	16.98%	23.08%
Chi Square test P value=0.694		
Overall patients satisfaction		
Good		
Number	15	14
percentage	28.30%	26.92%
Fair		
Number	30	25
percentage	56.60%	48.08%
Poor		

Number	8	13
percentage	15.09%	25.00%
Chi Square test P value=0.434		

Table 4: Secondary outcome variables.

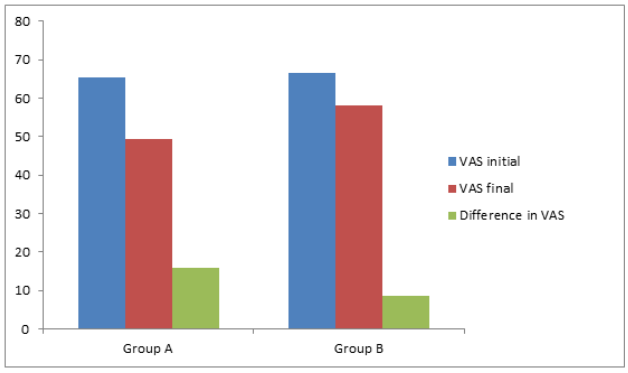

Figure 1: Visual Analogue Score (VAS).

Table 4 shows a comparison of the duration of labor, APGAR score at 1 and 5 min, cord blood pH, the number of patients who requested a rescue analgesia, rate of hallucination and vomiting, the mode of delivery and the overall patients satisfaction between the study groups. The only statistically significant difference between the groups is in the APGAR score at 5 min which is lower in the group A (ketamine group).

Discussion

Although pethidine is the standard labor analgesic used in the developing countries, its use is limited because of the "controlled drug" regulations. Also most of the obstetricians avoid using pethidine in the second stage of labor to avoid its fetal depressing effect.

Sam J, et al. [13] tried low dose ketamine infusion in a loading dose of 0.2 mg/kg delivered over 30 min followed-by an infusion at 0.2 mg/kg/h and concluded that it could provide acceptable labor analgesia.

Krishna J, et al. [14] also tried low dose ketamine for labor analgesia and concluded that It provides effective analgesia in low doses; It is safe without significant maternal and fetal drawbacks; It does not lead to labor prolongation and it doesn't increase in rate of instrumental or operative delivery.

Andolfatto G, et al. [15] used Intranasal ketamine for analgesia in the emergency department in a study and have reached a conclusion that intranasal ketamine lowered VAS pain scores to a clinically significant degree in 88% of emergency department (ED) patients

Also Roshana S, et al. [16] tried intranasal ketamine for the treatment of patients with acute pain in the ED and concluded that intranasal ketamine is an analgesic choice for acute injury patients with moderate to severe pain especially in an overcrowded and resource limited ED.

From the encouraging results of the previous studies we thought of using the intranasal ketamine for the first time in labor analgesia. The primary objective of this study was to assess the efficacy, safety and feasibility of using intranasal ketamine for labor analgesia in comparison to the standard method of using pethidine. From our results we see that intranasal ketamine is an effective method for reduction of labor pain when compared to the standard method of using pethidine with significantly lower pain scores, better fetal APGAR score at 5 min and also significantly less vomiting.

The only drawback of the use of intranasal ketamine from the prospective of this study is the rate of hallucinations reported. 33.96% of the patients in the ketamine group have experienced visual and auditory hallucinations of varying degrees; which when compared to the pethidine group only 5.77% of the patients have experienced such hallucinations and the difference is statistically significant. Sarkar and Sahu [17] used a dose of 0.2-0.4 mg/kg as a bolus followed-by an infusion of 0.5-1 mg/min and they also reported 14% hallucinations rate. Ganla et al. [18] used 0.5 mg/kg bolus, followed by 0.25 mg/kg every 20-30 min and also reported a higher incidence of hallucinations (54%).

Conclusion

The use of intranasal ketamine in an initial dose of 0.5 mg/kg with supplementary dose of 0.25 mg/kg is more effective than the use of 50 mg intramuscular pethidine with supplementary dose of 50 m IM as labor analgesia with better fetal APGAR score at 5 min less vomiting incidence but with significantly higher rate of hallucinations.

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