Mahin Najafiyan. *et al.* / *International Journal of Pharmacy & Therapeutics*, 4(4), 2013, 242-246.

e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

IJPT

THE EFFECT OF NITROUS OXIDE (ENTONOX) ON LABOUR PAIN RELIEF DURING DELIVERY STAGES

Mahin Najefian[1], Maria Cheraghi[2,3*], Zahra Pourmehdi[4] , Alireza Dadgari Nejad[5]

[1,4]Department of Obstetrics & Gynecology Medical School, Ahwaz Jundishapur University of Medical Sciences, Ahwaz, Iran.
[2]Department of Public Health , Health School, Ahwaz Jundishapur University of Medical Sciences, Social determinant of Health Research Center, Ahwaz, Iran.
[3]Social Determinant of Health Research Center, Ahwaz Jundishapur University of Medical Sciences, Ahwaz, Iran.
[5]Department of Accounting, Masjed-Soliman Branch, Islamic Azad University, Masjed-Soliman, Iran.

ABSTRACT

We aimed to evaluate the effect of Entonox on the intensity of labor pain during delivery stages. A clinical trial study was conducted among 200 pregnant women with the gestational age of (37-41 weeks) who referred to a medical center, obstetric and gynecology ward in Ahwaz during year 2011. The subjects were equally and randomly divided into two Entonox (trial) and Oxygen (control) groups by a coin. Mean duration of active phase in the Entonox and control groups was 4.07± 3.2 and 5.28 ± 4.7 hours respectively. The association was significantly different between two groups (p= 0.03). The mean of pain severity during three consequent contractions in the trial and control groups was 5.18± 1.29 and 8.99 ± 1.98 respectively which was significantly different (p < 0.005). Entonox is more effective to reduce pain during labor and delivery. Entonox is cheap, safe and easily available for pain relieving labor. It has no severe side effect on mother and not any side effect on neonate.

Key Words:- Entonox, Labor pain, Nitrous Oxide, Vaginal delivery.

INTRODUCTION

Labor pain is one the most severe types of pain ever to be experienced. Between 35 to 58% of women in labor describe the pain as being either severe or intolerable. Pain in labor has not been demonstrated to have beneficial effects on the mother or baby, only deleterious physiological or psychological effects (May-A, 2001). Several routs for labor analgesia had been investigated as intravenous analgesics, inhalation therapy, acupuncture, and local anesthesia but the anesthesia should be safe either for mother or fetus. Of these, Entonox is analgesia gas which is a pre-mixed homogenous gas mixture of 50:50 Nitrous oxide and oxygen compressed in a cylinder. It is used all over Europe and Asia since last 50 years. It was introduced for labour analgesia in early 60's in United Kingdom and commercially it was accepted by Central Midwives Board-UK in 1965. In a systemic review by Rosen in 2002 showed that nitrous oxide is used in the United Kingdom by approximately 50 to 75 percent of women and in Finland by approximately 60 percent of women (Rosen MA, 2003).

Another study also found that 65 percent of women in Sweden received nitrous oxide for labor pain relief in 1991 (Irestedt L, 1994) and a 1995 survey of hospitals in Ontario, Canada, found that nitrous oxide was available for labor pain analgesia in 75% of responding hospitals (Oyston J,1995) Nitrous oxide is also commonly used for

Corresponding Author
Maria Cheraghi
Email:- mariacheraghi@gmail.com

labor analgesia in Australia and New Zealand (Rosen MA, other countries suggests it is an effective labor pain relief method. Entonox is an ideal choice for obstetrics analgesia as labour pains during contractions are intermittent. It can be inhaled accordingly to synchronise the contractions. It is a well proven safe and effective analgesia for obstetrics use due to its ideal properties of rapid onset, short duration and rapid offset characteristics. Side effects are minimal and gets withdrawn once gas inhalation is stopped. There is no remarkable side effect on cardiovascular, respiratory or neurological system of the mother and the fetus. Intermittent pain during uterine contractions goes well with short duration and rapid recovery characteristics of Entonox gas. Short half-life of N2O permits that the side effects immediately disappear once Entonox inhalation discontinue and less affected delivery (Nourouzinia Sh,2005).

Recent studies have helped to clarify the analgesic mechanisms of N2O, but the mechanisms involved in its anxiolytic and anesthetic actions remain less clear. It has analgesic and anxiolytic properties. The analgesic effect of N2O is opioid in nature, and, like morphine, may involve a myriad of neuromodulators in the spinal cord. The anxiolytic effect of N2O, on the other hand, resembles that of benzodiazepines and may be initiated at selected subunits of the γ-amino butyric acid type A (GABAA) receptor.Similarly, the anesthetic effect of N2O may involve actions at GABAA receptors and possibly at N-methyl-D-aspartate receptors as well (Ommanouil DE, 2007). A critical aspect of the use of N20 during labor is that the woman administers the gas to her and therefore controls when and how much she uses. A part of this effectiveness may rest in the woman's senses of being able to control not only the Nitrous Oxide but also the pain and herself (Rooks J, 2007). Therefore, we aimed to evaluate the effect of Entonox on severity of labor pain during delivery stages.

METHODOLOGY

Study design and location

A clinical study was conducted at obstetrics and gynecology department, Razi Hospital, Ahwaz, Iran, during year 2011. The study was approved by Ahwaz Jundishapur University of Medical Sciences and Ethics Committee.

Subjects

Total number of 200 women with term pregnancy was recruited and randomly divided into two groups [i.e., Entonox (trial) and Oxygen (control) groups]. Randomization was performed by a coin. The gestational age was between 37 to 41 weeks. The inclusion criteria were those with first to third parity regardless to maternal age, and agree to participate. The exclusion criteria were polyhydramnios or oligohydramnios, multiple fetus and meconium discharge. The informed consent was obtained from each subject.

Methods

The indications for both trial and control groups were cervical dilation between 3 to 4 cm and effacement of 40 to 50% in an active phase. Pulse oximetry was used for both groups to monitor O_2 saturation. To get desired analgesic effect of Entonox, patients were advised to inhale and exhale deeply and uniformly through the mask. Synchronisation of uterine contraction and analgesic effect was a key to get desired analgesic effect. The patient herself administered gases via a face mask connected to the uni- directional valve which enables the patients to breathe gas in each inspiration. The gas administration was continued to the end of contraction pain at which the patient breathed the room air. Entonox usage was continued till the bearing down stage, and thereafter, continued for pain relied during cleaning and suturing. The questionnaires were filled up by the trained midwives.

Measurements

The outcomes measurement was number of pregnancy, gestational age (weeks), pain severity, pain duration (hours), blood pressure (mm/Hg) and Entonox complications (i.e., lethargy, dry mouth, vertigo, vomiting and uncomfortable feeling). The pain severity was measured according to the pain scale. The scale was numbered from zero to 10. The highest score considered as severity of the pain.

STATISTICAL ANALYSIS

Data was analysed using SPSS, version 16. The entire test was 2 sided significant at the level of 0.05 by estimating power of 95%. Normality test was performed and all variables were normally distributed. Descriptive analysis was performed to descript characteristics of subjects. To compare mean of two normal continuous variable independent samples T- Test was conducted. The Chi- square (χ^2) test with considering odds ratio (OR) was performed.

RESULTS

The results revealed that thirty (n=30) women were excluded from the both study groups. In the trial group, 18 women were candidate for the cesarean section due to failure to fetal descending. Four women had vertigo after Entonox inhalation and other two subjects had low

O_2 saturation. Six women from the control group were excluded and candidate for the cesarean section due to failure to fetal descending. There was no significant association between numbers of pregnancy [Table 1], gestational age [Table 2] in the study groups. Mean of maternal age was 22.67 ± 3.6 years. There was significant association between mean of duration of first stage of labor (hours) in the Entonox and Oxygen groups (4.07 ± 3.2 vs 5.28 ± 4.7) (p = 0.03) [Table 2]. The second stage of labor in the trial group was longer than control group (32.19 ± 30.75 minutes vs 29.70 ± 18.60 minutes) but not significant (Table was not shown). Mean of severity of pain during three consequent uterine contractions was 5.18 ± 1.29 compared to control group (8.99 ± 1.98). The association was significant (p < 0.002) [Table 2]. There was not significant association between systolic and diastolic blood pressure before and after labor pain [Table 2]. Entonox complications were shown in Table 3. Lethargy was the highest Entonox complications (40.1%) and uncomfortable feeling was the lowest complications (1.2%).

Table 1. Comparison of Number of Pregnancy between Trial and Control Groups [Data presented as number (n) and frequency (%)]

Number of pregnancy	Entonox (Trial group) (n=76)	Oxygen (Control) group (94)	p-value
Nulliparity	61%	63%	0.25
Multiparity (2-3 gravid)	39%	37%	0.17

P is not significant using Chi- square

Table 2. Comparison of Mean and Standard Deviation between Trial and Control Groups

Variables	Entonox (Trial) group (n=76)		Oxygen (Control) group (n=94)		
	mean	Sd	mean	Sd	p
Pain severity (scale 0-10)	5.18	1.29	8.99	1.98	0.002*
Pain duration (hours)	4.17	3.2	5.28	4.7	0.03*
Systolic blood pressure (mmHg)	10.7	1.3	10.9	1.08	0.65
Diastolic blood Pressure (mmHg)	6.9	1.3	7.1	1.3	0.34
Gestational age (weeks)	39.2	1.4	38.9	1.5	0.27

*p < 0.05 is significant using Independent sample T- Test

Table 3.Frequency of Entonox Complications in the Trial Group (n=76)

Variables	Number (n)	Percentage (%)
Lethargy	80	40.1
Dry mouth	60	31
Vertigo & headache	39	20
Sickness & vomiting	17	11
Uncomfortable feeling	3	1.2

DISCUSSION

This study was demonstrated the effect of nitrous oxide (Entonox) for analgesia and pain relief during labor. Inhalation of mixture of 50% nitrous oxide in oxygen was safe and effective labor analgesia. There was not seen severe side effect on mother and neonate. The analgesic effect and mechanism of nitrous oxide in the brain is still unknown. There is hypothesis on this view that nitrous oxide stimuli release of Androgen and may be dopamine in the brain which causes pain relief in the brain (Rosen MA, 2003).

The current study showed that intensity of labor pain in Entonox group was significantly lower than oxygen group. This result was comparable with the study by Teimoori *et al.,* in 2011 that showed pain severity according to VAS score was significantly lower in patients received nitrous oxide (P = 0.0001) (Teimoori B, 2011). Another study also supported our results that the mean labor pain intensity was decreased significantly after inhaled Entonox compared with control group (4.17 vs. 6.78, p < 0.01) (Iravani, M,2008). Reductions in pain scores with inhaled nitrous oxide seem similar to that of systemic opioid (Olofsson C, 1996) which some authors suggest have little effect on labor pain (Yentis SM, 2011). The result of our study showed that mean duration of active phase of labor significantly was lower in the

Entonox group compared to the control group. Similar result was noted by Tazarjani et al. in 2010 that duration of active phase of labor in the Entonox group was shorter than control group (4.17 hr vs. 5.07 hr, $p < 0.05$) (Zare Tazarjani F, 2010).

Other study also showed that active phase of labor in the Entonox group was shorter than oxygen group significantly (153 min vs. 187 min, $P < 0.05$) (Su f, 2002). Despite these findings, some studies reported that there was not significantly difference between the two groups in mean duration of active phase of labor (Iravani, M,2008) and also in duration of second stage of labor between Entonox group and control group (33.19 min vs. 26.70 min (Zare Tazarjani F, 2010).

The current study we pointed out that, there were not significant association between systolic and diastolic blood pressure of both Entonox and oxygen groups during active phase of labor. This result of this study was in agreement with study that has done by Teimoori et al. (Teimoori B, 2011). Whist it was in contrast that the mean arterial blood pressure was comparable between Entonox and oxygen groups except two first measurements in which the control group was higher (Talebi H, 2009).

The maternal side effect of Entonox was observed in the study which showed the highest adverse effect was lethargy (40.1%) and the lowest was uncomfortable feeling (1.2%). Vertigo (20%), vomiting (11%) and dry mouth (31%) also was observed after inhalation of Entonox. The direct respiratory depressant effect of nitrous oxide such as oxygen desaturation was not observed. One small study reported that the rate of maternal desaturation was higher with nitrous oxide administration when compared to epidural analgesia (Arfeen A, 1994). Maternal drowsiness was reported to occur in 0 – 24% of laboring women. The rates of maternal unconsciousness appeared to increase in a dose dependent fashion from approximately 1% to 5% when 50% to 80% nitrous oxide was used respectively (Yentis SM, 2001). These rates would be expected to be higher during the continuous administration of nitrous oxide (Yentis SM, 2001). Others side effect induced by nitrous oxide was nauseas and vomiting reported 5% and 36% respectively (Yentis SM, 2001; McGyuinness C, 2007). Dizziness, dreams and drowsiness were reported 0% to 24%. Dry mouth due to breathing dry gas, buzzing in the ears and rarely numbness were also reported (Yentis SM, 2001; McGyuinness C, 2007; Bishop JT, 2007).

CONCLUSION

Inhalation of Entonox for labor analgesia shortens the duration of active phase of labor but has no effect on second stage of labor. Nitrous oxide administration does not affect uterine activity and thus would not be expected to affect the course of the first and second stages of labor and rates of cesarean delivery. The measure of relieving labor pain may increases the vaginal birth rate.

REFERENCES

Arfeen A, Armstrong PJ, Whitfield A. The effects of Entonox and epidural analgesia on arterial oxygen saturation of women in labour. *Anaesthesia,* 49, 1994, 32-4.

Bishop JT. Administration of nitrous oxide in labor. Expanding the options for women. *J midwifery & Women's Health,* 52, 2007, 308-309.

Iravani, M. the efficacy of entonox inhalation on pain Intensity and duration of delivery. *Iranian J obstet Cynecol infertile,* 2(11), 2008, 7-13.

Irestedt L. Current status of nitrous oxide for obstetric pain relief. *Acta Anaesthesiol Scand,* 38 (8), 1994, 771-2.

May-A, Mushamb MC. Recent advances: In obstetric anesthesia. *Bulletin, the Royal College of Anesthesia*, 6, 2001, 266-8.

McGyuinness C, Rosen M. Enflurane as analgesic in labor. *Anesthesia,* 39, 1984, 24-26.

Nourouzinia SH, Noroozinia H, Mahoori AR, Jamshidi K, Kakay Afsher M, Tahoori R. the effect of continuous inhalation of Entonox on labor pain relief. *J Iranian soc Anaesth intensive care*, 27(51), 2005, 57-62.

Olofsson C, Ekblom A, Ekman-Orderberg G, Hjelm A, Irestedt L. Lack of analgesic effect of systemically administered morphine or pethidine on labour pain. *Br J Obstet Gyencol*, 103, 1996, 968-972.

Ommanouil DE, Quock RM. Advances In understanding the action of nitrous oxide. *Anesh Prog,* 54(1), 2007, 9-18.

Oyston J. Obstetrical anaesthesia in Ontario. *Can J Anaesth,* 42 (12), 1995, 1117-25.

Rooks J. use of Nitrous oxide In midwifery practice Complementary, synergistic, and needed in the united states. *Journal of Midwifery & women's health*, 3, 2007, 186-9.

Rosen MA. Relief of labor pain. *J University of California*, 186(5), 2003, 110-111.

Su F, Wre X, Chen X, Huz, Xu H. Clinical study of efficacy and safety of labor analgesia with inhalation of Nitrous oxide In oxygen. *Zhonghua fu chan Ke Za Zhi,* 37(16), 2002, 584-7.

Talebi H, Nourozi A, Jamilian M, Baharfar N, Eghtesadi-Araghi P. Entonox for Labor Pain: A Randomized Placebo Controlled Trial. *Pakistan Journal of Biological Sciences,* 12, 2009, 1217-1221.

Teimoori B, Sakhavar N, Mirteimoori M, Narouie B, Ghasemi-rad M. Nitrous Oxide versus Pethidine with Promethasine for Reducing Labor Pain. *Gynecol Obstetric,* 1, 2011, 1.

Yentis SM. The use of Entonox for labour pain should be abandoned. Proposer. *Int J Obstet Anesth,* 10, 2001, 25-29.

Zare Tazarjani F, Sekhavat L, Karimzadeh Mibodi M.A. The Effect of Continuous Entonox Inhalation on the Length of Labor in Duration of Active Phase of Labor. *Journal of Babol*. University of Medical Sciences (JBUMS), 11(6), 2010.