

## Comparison of Epidural versus Entonox for Labor Analgesia in Nulliparous Women

Nayereh Khadem<sup>1</sup>, Nahid Zirak<sup>2✉</sup>, Ghasem Soltani<sup>3</sup>, Nahid Sahebdelfar<sup>4</sup>, Alireza Sepehri Shamloo<sup>5</sup>, Saeed Ebrahimzadeh<sup>6</sup>

<sup>1</sup>Associate Professor, Department of Obstetrics and Gynecology, Women's Health Research Center, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran;

<sup>2</sup>Associate Professor, Department of Anesthesiology, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran;

<sup>3</sup>Associate Professor, Cardiac Anesthesia Research Center, Anesthesia Department, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran;

<sup>4</sup>Gynecologist, Department of Obstetrics and Gynecology, Mashhad, Iran;

<sup>5</sup>Students Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran;

<sup>6</sup>Instructor of Statistics, Health Faculty, Mashhad University of Medical Sciences, Mashhad, Iran.

Received: 19 July 2013

Revised: 23 October 2013

Accepted: 30 October 2013

### Abstract

**Introduction:** The aim of this study is to compare the efficacy of epidural versus entonox methods for labor analgesia in nulliparous women.

**Methods:** This randomized controlled trial was performed on 84 nulliparous women with - pregnancy admitted to Imam Reza Hospital in 10 May 2010- 10 May 2011.

They were randomly divided into two groups; 42 women inhaled entonox in active phase at the beginning of each contraction, and for 42 cases, epidural catheter was inserted and analgesic substance was injected and it was increased adjusted with contraction progressing by bupivacaine combined with fentanyl. The rate of pain was measured with pain scores (minimum pain 0 and maximum pain 10).

**Results:** In epidural analgesia, pain score was lower in all stages of labor than entonox analgesia; 42% of cases had no pain, while as in entonox group, pain has been decreased 4 scores in 7% of cases and there was no complete analgesia. Duration of different stages of labor was not statistically different between two groups ( $P=0.89$ ). Cesarean rate was similar in two groups. First and five minute Apgar were not statistically different between two groups ( $P=0.87$ ,  $P=0.75$ , respectively).

**Conclusions:** Epidural analgesia with more relief in labor pain is the desired method. This method doesn't cause more cesarean rate or prolonged labor duration. Although Entonox decreases labor pain in first stage, but doesn't affect on second stage and fetus Apgar.

**Key Words:** Entonox; Epidural analgesia; Labor pain

©2013 Journal of Surgery and Trauma  
Tel: +985614443041 (636)  
Fax: +985614440488  
Po Box 97175-379  
Email: jsurgery@bums.ac.ir



✉ Correspondence to:

Nahid Zirak, Department of Anesthesiology, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran;  
Telephone Number: +985118525209  
Email Address: ZirakN@mums.ac.ir

## Introduction

Nowadays, painless delivery is a necessity for mothers' health. Unmodified 'natural' labor produces maternal changes that are followed by adverse fetal effects [1]. There are many debates over the choice and safety of the different types of analgesia for labor pain [2]. Although, epidurals are well-established techniques to relief pain in labor, but their

effects on the progress of labor and cesarean delivery is rem

ained controversial [3]. A study showed that inhalational analgesia using Entonox is more effective and, being rapidly exhaled by the newborn, it is less likely to produce lasting depression [4]. On the other hand, the other study showed that spinal anesthesia is the preferred method for cesarean, because of performance simplicity, being economical and producing rapid onset of anesthesia and completing muscle relaxation. It carries high efficiency, involving less drug doses, minimal neonatal depression; awaken mother and lesser incidences of aspiration pneumonitis [5]. Despite the safety and acceptability of regional analgesia, a study performed in 2002-2003 showed that only a third of all deliveries took place under regional analgesia [6]. In the US, 60% of pregnant women choose epidurals for labor analgesia [7].

Entonox, a 50:50 mixture of nitrous oxide and oxygen, is the only self-administered inhalation analgesic [8]. Using nitrous oxide 50% provides significant pain relief. Nonetheless, it is associated with few side effects; nitrous oxide can be quickly implemented during advanced labor pain [9]. The efficacy and safety of entonox is under debates, because of maternal respiratory depression especially when it is combined with opioids [10]. Moreover, another study reported that Epidural analgesia in primigravidae in spontaneous labor led to an increased instrumental delivery rate, prolonged duration of labor, greater rate of fetal malpositions in the second stage, increased oxytocin requirements but with no difference in fetal outcomes, with happier mothers as compared to the inhalation group [11].

The aim of this study is to compare the efficacy of epidural versus entonox methods for labor analgesia in nulliparous women.

## Methods

This randomized controlled trial was performed on 86 nulliparous women with pregnancy admitted to Imam Reza Hospital in 10 May 2010- 10 May 2011 for vaginal delivery. They were randomly divided into two groups by means of random numbers of calculator; 44 women used inhaled entonox, and for 42 cases, epidural catheter was inserted. Two cases from entonox group were excluded from the study because they didn't have consent for participating in the study. Finally, 42 cases in the entonox group entered to the study.

Inclusion criteria were nulliparous women, patients' consent for analgesia, no contraindication for vaginal delivery, single pregnancy, gestational age  $\geq 37$  weeks, cephalic presentation, active phase of labor (cervical dilatation 3-5 cm with contractions occurring at least once every 3 minutes), no contraindication for regional analgesia (coagulopathy disorder, infections in the site of catheter insertion, and hemodynamic instability). Exclusion criteria were labor arrest, maternal or fetal problems which need cesarean, previous cesarean experience, morbid obesity, and lack of mother cooperation. This study was approved by the Ethics Committee of Mashhad University of Medical Sciences. A written consent was filled by all the women.

First, bishop score of cervix was determined and recorded when dilatation was 3-5 cm. Before analgesia, pain score was recorded by pain ruler (0-10) through questioning mother. After analgesia through entonox or epidural, again pain score was recorded. Duration of first stage labor, cesarean rate and fetus Apgar were recorded for both groups. Pain score was again recorded when cervical dilatation was 5 and 8 cm and also when cervical dilatation was completed. Second stage labor duration, pain intensity in second stage and during delivery were also recorded.

The entonox group inhaled entonox by a mask simultaneously with beginning of feeling contraction by mother. Painless rate was recorded in any stage of labor. In pain intervals, mask was removed and room air was inhaled by mother. 2 mothers didn't continue the study due to giddiness and they were excluded from the study. Epidural group were placed in sterile conditions, and after hydration by 500 ml ringer lactate, epidural was entered to epidural space from lumbar site L3-L4 or L4-L5 with Tuohy needle size 18, then it was entered 4-6 cm into the space and then epidural needle was exited and catheter was fixed in the site

using suture. The patient was controlled in the view of labor development and fetal heart monitoring. When dilatation was 5 cm, first dose including bupivacaine 0.125%, fentanyl 1  $\mu$ g/ml in volume of 8-10 ml was injected at the beginning. Then dilution solution was infused with speed of 8-15ml/h related to the patient's need. If it was required, the concentration of Bupivacaine was increased to 0.25%. Monitoring included controlling mother's blood pressure, the rate of oxygen in blood by pulse oxymeter, and continuous controlling fetal heart rate through external monitoring that was maintained on abdomen (fondus of uterus) by a belt. No local anesthetic drug was administered for episiotomy.

Data was analyzed by SPSS software version 11.5. T-student, Smirnov-kolmogorov, and Mann-Whitney tests were used for comparison between the two groups. Confidence coefficient was 95% and  $P \leq 0.05$  was considered statistically significant.

## Results

A total of 84 nulliparous women with pregnancy completed this randomized controlled trial. These women were placed into two groups; entonox group (42 patients) and epidural group (42 patients).

Distribution of maternal age, BMI, newborn weight, pain score at beginning of the study and Bishop score in two groups is presented in (table 1).

Mean pain score at analgesia in the beginning of first stage labor was 5.8 in entonox group and 1.2 in epidural group ( $P=0.960$ ). The difference shows that epidural is more effective in pain relief at first stage ( $P=0.00$ ). Mean pain score at the end of first stage labor was 7.7 in entonox group and 1.5 in epidural group ( $P=0.00$ ). The difference shows that epidural is also more effective in pain relief at this stage ( $P=0.00$ ). Moreover, mean pain score during delivery was 9.5 in entonox group and 1.6 in epidural group ( $P=0.00$ ). The difference shows that entonox had no effects on pain relief in this stage ( $P=0.00$ ).

Mean time duration of uterine dilatation from 3 cm to 5 cm was 1.5 h in entonox group and 1.4 h in epidural group. The difference was not statistically significant ( $P=0.89$ ). Also, mean duration of uterine dilatation from 5 cm to complete dilatation was 3.4 h in entonox group and 3.7 h in epidural group. Two groups were similar in this view ( $P=0.25$ ).

Mean duration of second stage labor was 48 min in entonox group and 54 min in epidural group. No

significant differences were observed in terms of mean duration of second stage labor ( $P=0.28$ ).

In entonox group, cesarean was performed for 5 cases and in epidural group for 3 cases, but no significant differences were observed between the two groups in terms of C/S rate ( $P=1$ ).

Mean of neonatal first minute Apgar was 8.4 in entonox group and 8.5 in epidural group. Mean of neonatal five minute Apgar was 8.8 for both groups. The two groups were not different in terms of first and five minute Apgar ( $P=0.87$ ,  $P=0.75$ , respectively).

In entonox group, 13 cases had complete satisfaction of entonox method and in epidural group, 27 cases were completely satisfied from epidural method for analgesia. The difference was statistically significant between the two groups ( $P=0.002$ ).

## Discussion

Epidural was more effective in pain relief at the beginning of first stage labor than entonox, epidural was also more effective for decreasing pain at the end of first stage labor, entonox had no effects on decreasing the pain of second stage labor, but epidural affected the pain relief of second stage labor, and cesarean rate was not statistically different between two groups. Theoretically, if epidural is used in high volume and concentration, it can block labor pain as 100%, but high concentration is not used because the aim is pain relief with no motor block in first stage of labor, pushing in second stage and decreasing the fetal outcomes [12].

Some studies reported that nitrous oxide is a commonly available option for labor pain relief in several countries outside the U.S. 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 [12].

Bhattacharya et al. in their study reported that the rate of epidural analgesia has changed very little over a period of 16 yrs study [7]. But, the rate of epidural analgesia has increased from 12.35% in 1987 to 18.27% in 2001; the rate of increase was about 5.92% [13]. Moreover, Marmor et al. in the study performed in 2002 reported that the rate of epidural analgesia has increased up to 50% in the

**Table 1: Comparison of two groups in terms of different factors effective on delivery pain and delivery duration**

variables	Entonox group (N=42)	Epidural group (N=42)	P-value
Maternal age (yrs)	22.3	22.5	0.818
BMI (kg/m <sup>2</sup> )	28.3	28.2	0.887
Newborn weight (gr)	3164	3215	0.506
Pain score at beginning of the study	7.6	7.6	0.960
Bishop score	8.5	8.6	0.596

US [14]. A survey performed in Germany in 1996 showed that the rate of epidural analgesia was greater than 70% in larger units with more than 1000 delivery per year [15]. In addition, Goldberg et al. in the study performed in America reported that epidurals are the analgesia of choice for nulliparous women [16]. On the other hand, Bhattacharya et al. showed that the most popular analgesia in the labor ward of the Aberdeen Maternity Hospital was opioids analgesia with or without entonox and this was the analgesia of choice throughout the study both in primi and multigravidae [7]. This finding is in contrast with the finding of our study. The preferred analgesia method in the present study was epidural analgesia.

In this study demographic characteristics of the patients in the two groups were similar, but Bhattacharya et al. found that the women who had received different types of analgesia had different characteristics [7]. They reported that patients in epidural group were younger, shorter, heavier, and delivered larger babies.

The present study found no differences between the two groups in terms of cesarean rate. This result is in accordance with the findings of a meta-analysis that reported the rate of cesarean was not different between the groups of receiving different types of analgesia [6]. Although, some studies have found an increase in cesarean rate with epidural analgesia [8], but some others have shown that the cesarean rate is not increased with the use of epidural analgesia [2, 3].

This study showed that epidural was more effective in pain relief of labor in first and second stage than entonox; entonox had no effect on decreasing the pain of labor second stage. In the study performed by Loughman et al., women who received epidural analgesia were more likely to grade their pain relief as good or excellent (83% in the first stage and 85% in the second stage) compared to those who received pethidine (56% in the first stage and 64% in the second stage) [17].

In the current study, no differences were observed in terms of neonatal outcomes between

the two groups. This finding is in accordance with the result of Lui et al. study [18]. They found no statistical differences in the Apgar scores of neonates born from mothers in epidural group as compared to opioids group. Mansoori et al. reported that there was no relation between type of analgesia and neonatal outcomes, although neonates born from epidural group had worse Apgar score compared to those using no analgesia [19].

Generally, 30.9% of patients from entonox group and 64.2% of epidural group were completely satisfied with their analgesia methods. This difference between the two groups was statistically significant. The choice of analgesia is influenced by the information provided [13]. For example, some health care providers reported that there is an association between epidural analgesia and increased rate of cesarean despite some other researchers who denied this relation. However, further studies with more volume samples are needed to better clarify the choice of analgesia and the factors influencing these preferences.

The limitations of this study were as follow: it was better to have a third group (for example intravenous analgesia) and we could compare our two groups with this group in order to obtain more close results. Also, most of the patients would like to receive analgesia through intravenous catheter and no other intervention to be performed for them.

Therefore, it seems that more studies with higher population and more studied groups are required to be sure about the results.

## Conclusions

The results of the present study showed that epidural was more effective in first stage labor than entonox; epidural also was effective in decreasing pain of second stage labor, but entonox had no effect in this stage. Moreover, the rate of patients satisfied of epidural analgesia was higher than entonox analgesia. Therefore, epidural analgesia is recommended as a desirable method for painless delivery. Entonox analgesia should be

considered as a method of analgesia when regional analgesia is not performed due to different causes.

### Acknowledgments

The authors would like to thank Women's Health Research Center of Mashhad University of Medical Sciences who supported this paper financially. Also, we thank Atefeh Akbarabadi who helped us in recording pain scores.

### Reference

- Hugh R. Maternal hyperventilation and fetus. *Journal of Perin Medicine*. 1986; 14: 3-17.
- Howell CJ. Epidural versus non-epidural analgesia for pain relief in labour. *Cochrane Database of Systematic Reviews* 2005; 3.
- Leighton BL, Halpern SH. The effects of epidural analgesia on labor, maternal, and neonatal outcomes: A systematic review. *American Journal of Obstetrics & Gynecology* 2002; 186(5): S69-77.
- Reynolds F. The effects of maternal labour analgesia on the fetus. *Best Practice and Research Clinical Obstetrics and Gynecology* 2010;24(3):289-302.
- Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section. *BMC Anesthesiology* 2005; 5: 5.
- Department of Health Hospital Episode Statistics: NHS Maternity Statistics. England: 2002-03 2004. Bulletin 2004/10.
- Bhattacharya S, Wang T, Knox F. Analgesia for labour pain--analysis of the trends and associations in the Grampian region of Scotland between 1986 and 2001. *BMC Pregnancy Childbirth* 2006; 6: 14.
- Yeo ST, Holdcroft A, Yentis SM, Stewart A, Bassett P. Analgesia with sevoflurane during labour: ii. Sevoflurane compared with Entonox for labour analgesia. *British Journal of Anaesthesia* 2007; 98(1): 110-5.
- Talebi H, Nourozi A, Jamilian M, Baharfar N, Eghbesadi-Araghi P. Entonox for Labor Pain: A Randomized Placebo Controlled Trial. *Pakistan Journal of Biological Sciences* 2009; 12(17):1217-21.
- Yentis SM. Controversy: the use of Entonox for labour pain should be abandoned. *The International Journal of Obstetric Anesthesia* 2001; 10: 25-7.
- Leong EW, Sivanesaratnam V, Oh LL, Chan YK. Epidural analgesia in primigravidae in spontaneous labour at term: a prospective study. *Journal of Obstetrics and Gynaecology Research* 2000; 26(4):271-5.
- Caton D, Frölich MA, Euliano TY. Anesthesia for childbirth: controversy and change. *American Journal of Obstetrics & Gynecology* 2002; 186 (5): S25-30. Review.
- Khor LJ, Jeskins G, Cooper GM, Paterson-Brown S. National obstetric anaesthetic practice in the UK 1997/1998. *Anaesthesia* 2000; 55(12): 1168-72.
- Marmor TR, Krol DM. Labor pain management in the United States: Understanding patterns and the issue of choice. *American Journal of Obstetrics & Gynecology* 2002; 186 (5): S173-80.
- Zhang J, Yancey MK, Klebanoff MA, Schwarz J, Schweitzer D. Does epidural analgesia prolong labor and increase risk of cesarean delivery? A natural experiment. *American Journal of Obstetrics & Gynecology* 2001; 185(1): 128-34.
- Goldberg AB, Cohen A, Lieberman E. Nulliparas' preferences for epidural analgesia: their effects on actual use in labor. *Birth* 1999; 26(3): 139-43.
- Loughnan BA, Carli F, Romney M, Doré CJ, Gordon H. Randomized controlled comparison of epidural bupivacaine versus pethidine for analgesia in labour. *British Journal of Anaesthesia* 2000; 84(6): 715-9.
- Liu EHC, Sia ATH. Rates of caesarean section and instrumental vaginal delivery in nulliparous women after low concentration epidural infusions or opioid analgesia: Systematic review. *British Medical Journal* 2004; 328(7453): 1410-2.
- Mansoori S, Adams S, Cheater FM. Choice of analgesia in labour on neonatal outcomes, delivery and maternal satisfaction with pain relief. *Clinical Effectiveness in Nursing* 2000; 4(1): 11-9.