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An Investigation into the Side Effects of Entonox on Primiparas in Painless Labor

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ABSTRACT

Introduction: Labor pain causes a great fear of vaginal delivery as well as increase of cesarean section among women. Therefore, using harmless and efficacious pain relief methods is of great significance. Entonox is an effective and popular method for labor pain relief. However, there is a dearth of research conducted to examine its efficacy and side effects.

Objectives: Accordingly, the present study aimed at investigating the side effects of nitrous oxide on the mother and fetus.

Patients and Methods: This is a randomized controlled trial [RCT] study carried out on 178 primipara candidates for natural. During the active labor phase, women were assigned to two groups: intervention group [89 women inhaling Entonox] and control group [89 women inhaling oxygen]. In addition, the required data including age, gestational age, evidence of abruption, mode of delivery, meconium staining, fetal Apgar score, side effects of drug consumption, the amount of postpartum bleeding, initial hemoglobin concentration, and its concentration 6 hours after delivery were recorded. Then, the data were analyzed in SPSS software, version 16, using t-student, and Chi-square tests.

Results: There was no significant difference between the two groups in terms of the evidence of abruption, accelerated labor, meconium staining by the fetus, mean Apgar scores at 1 and 5 min and the final mode of delivery [$P > 0.05$]. Side effects such as dizziness, dry mouth, numbness of the tongue, nausea, and drowsiness were reported in the group inhaling Entonox. In the two modes of vaginal delivery and cesarean section, the mean reduction in

hemoglobin concentration 6 hours postpartum in the group inhaling Entonox was less than that of the control group and the difference was significant [$P < 0.05$].

Conclusion: Compared to the use of oxygen, the use of Entonox gas for painless labor did not cause adverse effects on the mother and fetus; however, only minor side effects including drowsiness, dry mouth, dizziness and nausea, and numbness of the tongue were observed. Furthermore, it was observed that Entonox caused less reduction in hemoglobin concentration of the mother which might be related to its positive effects on labor progress and its duration.

Keywords: labor, pain, Entonox, oxygen

BACKGROUND

Labor pain is one of the most severe pains women experience within delivery [1]. It can lead to adverse effects on labor progress and maternal and fetal conditions. Potential physiological effects of pain and their subsequent reactions include increased rate of basal metabolic and oxygen demand, respiratory alkalosis, elevated maternal heart rate, and systolic pressure. Moreover, the side effects of labor pain on the fetus include late deceleration in the fetal heart rate as a consequence of a drop in maternal arterial oxygen pressure, a decrease in utero-placental blood flow due to intense uterine contraction during labor, and fetal metabolic acidosis [2]. The key factors in people's response and pain perception are maternal age, parity, mother's condition, bishop score at the first stage of labor, position of the fetus to the birth canal, and demographic and psychological factors [3,4]. It must be mentioned that the pain is more intense and lasts longer in primiparas. The intensity of contractions in early labor in nulliparas is higher than multiparas. However, as the labor advances, the reverse condition is the case [5,6]. According to previous studies, 77% of primiparas described labor pain as extreme and unbearable [7]. An ideal pain reliever should produce good analgesia, be safe for both mother and fetus, controllable, reversible if necessary, easy to use, can be controlled by mother, does not interfere with uterine contraction, and does not affect the mobility of the mother. Entonox is a gas which is a mixture of 50 % nitrous oxide and 50% oxygen. The use of 50% nitrogen in oxygen dates to 1961 in England, when it was known as Entonox [8]. Attempts to reduce labor pain have a long history in Asia and the Middle East and painless labor started since James Young Simpson first administered it [9,10]. Entonox is a ready-to-use mixture of 50:50 oxygen and N₂O in a single cylinder [11]. This cylinder has a mask with a valve which opens with the patient's inhalation. Compared with epidural analgesia, some of the advantages of Entonox are being non-invasive, not damaging the spinal cord and making CSF infection, quick discharge from the body, not needing complicated and expensive equipment and specialized staff as well. This gas is not metabolized in the kidney or liver and is removed from the body in the form of N₂O via the lungs. Thus, patients suffering from organ dysfunction can use it as well [12]. Nitrous oxide is itself active and doesn't require any changes in the body to become active. It has an onset roughly in the lung-brain circulation time which takes 30 seconds and, therefore, it should be inhaled 30 seconds before a contraction becomes painful. Its analgesic effect is like 15 ml subcutaneous morphine.

In a study, patients receiving nitrous oxide/oxygen [50:50] were compared with those who only received oxygen. It was finally concluded that nitrous oxide noticeably reduced labor pain and had minor side effects [6]. Labor pain has caused great fear of vaginal delivery and an increase in cesarean section among women in our society which is in turn associated with complications of anesthesia and surgery. On the other hand, nitrous oxide is an effective and popular method to reduce labor pain. Although it has been used as a pain reliever over a hundred years, few studies have examined its side effects.

OBJECTIVES

Accordingly, the current study aimed to investigate the side effects of nitrous oxide in painless labor on primiparas.

Patients and Methods

This is a randomized controlled trial [RCT] study conducted on 178 primipara candidates for natural childbirth which was carried out during 2012-2013 in Fatemeh Hospital, Iran. Inclusion criteria were being primipara, gestational age ranging between 37 and 42 weeks, being in the active labor phase [3-4 cm dilation], absence of medical problems and lack of obstetric complications in the mother and fetus. After obtaining the informed consent, the women meeting inclusion criteria were randomly assigned into experimental [89 women inhaling Entonox] and control [89 women inhaling oxygen] groups. After entering the active phase of labor, the patients could inhale 2-6 times in the face mask connected to Entonox cylinder, 30 seconds before pain started and they could breathe room air in the pain intervals. The control group used oxygen cylinders after entering the active labor phase. Then, age, gestational age, evidence of abruption and after the delivery information such as mode of delivery, meconium staining and Apgar scores at 1 and 5 min were recorded in the questionnaires. Side effects such as nausea and vomiting, dizziness, drowsiness, dry mouth, numbness of the tongue and the amount of postpartum bleeding based on the number of saturated pads during 6 hours after delivery were recorded in the questionnaires. The data as well as the initial and 6-hour postpartum hemoglobin level were recorded in the questionnaires, too. The data obtained were analyzed using SPSS software v.16, and t-student and Chi-square formulas.

RESULTS

This study was carried out on 178 primipara women who referred to Fatemeh Hospital for delivery during 2012-2013. The participants were randomly assigned into two equal groups of 89 women [experimental and control]. During the active labor phase, the experimental group was provided with Entonox, whereas the control group was provided with oxygen. The mean age of the women in the experimental and control groups was 22.7 ± 3.4 and 21.236 ± 3 and the mean gestational age was 39.3 ± 1.06 and 39.5 ± 1.14 , respectively and the difference was not statistically significant [$P > 0.05$]. Evidence of abruption during labor [increased uterine tone and severe vaginal bleeding] was observed in 4.5% of women in the experimental group and 3.4% in the control group. The mean Apgar scores at 1 and 5 min were 8.87 ± 0.36 and 9.82 ± 0.41 in the experimental group and 8.79 ± 0.48 and 9.82 ± 0.41 in the control group. The difference was not statistically significant in this case, too [$p > 0.05$]. The frequency of accelerated labor [experimental group 23.4% and control group 21.9%] and meconium staining by the fetus

[experimental group 5.6% and control group 11.2%] were recorded which did not have a significant difference after being analyzed by Chi-square test [$p > 0.05$]. However, concerning the dizziness [experimental group 29.2% and control group 0%], dry mouth [experimental group 47.2% and control group 0%], numbness of the tongue [experimental group 4.5% and control group 0%], nausea [experimental group 9% and control group 0%], drowsiness [experimental group 21.3% and control group 0%], there was a significant statistical difference between the two groups, as shown in Table 1. Dry mouth was the most common side effect reported by the mothers.

Table-1: Comparison of the two groups in terms of dizziness, dry mouth, nausea, numbness of tongue and drowsiness

P-value	Number [Percentage]	Side effects
0.000	26 [29.2]	dizziness
0.004	8 [9]	Nausea
0.000	19 [21.3]	Drowsiness
0.000	42 [47.2]	dry mouth
0.04	4 [4.5]	numbness of tongue

Due to various reasons, such as fetal heart rate drop, meconium staining and failure to progress, cesarean section was performed on 13.5% in the experimental group and on 18% in the control group. In terms of cesarean section, the difference between the two groups was not significant [$p > 0.05$]. To compare the amount of bleeding during and after labor, we used the average drop in hemoglobin level of the participants before and after delivery. The average drop in hemoglobin level in the women who had vaginal delivery [experimental group 0.79 ± 0.45 and control group 1.2 ± 0.45] and in the women undergoing cesarean section [experimental group 0.84 ± 0.48 and control group 1.5 ± 0.45] was not significantly different [$p < 0.05$] [Table 2].

Table-2: Comparison of the difference in the average drop of hemoglobin level in the two groups for different delivery types

Group		Number	Standard deviation \pm the average drop [g/dl]	P-value
Vaginal delivery	Entonox	77	0.793 ± 0.456	0.000
	Oxygen	73	0.693 ± 1.28	
Cesarean section	Entonox	12	0.483 ± 0.841	0.001
	Oxygen	16	0.454 ± 1.5	

In order to estimate the amount of postpartum bleeding, besides the drop in hemoglobin level, the number of saturated pads during 6 h after delivery was used which were 3.14 ± 1.18 and 0.9 ± 3.08 in the experimental and control group, respectively. It should be noted that the difference was not statistically significant [$p > 0.05$].

DISCUSSION

The present study was carried out on 178 primipara women referring to Fatemieh Hospital for labor. The mean age of the experimental and control s was 22.7 ± 3.4 and 21.2 ± 3.36 , respectively which are consistent with the studies conducted by Talebi and Esfandiari in terms of age range [6,14]. The mean gestational age in both groups was 39 weeks and regarding the evidence of placental abruption, there was no significant difference between the two groups. Therefore, Entonox was not recognized as a cause of placental abruption. 23.4% of women in the experimental group and 21.9% in the control group had an accelerated labor - the duration of the active labor phase was less than 3 h. Entonox was not recognized as a cause of accelerated labor because there was no significant difference between the two groups. In the study conducted by Zare, it was indicated that the duration of active labor phase in the Entonox group was shorter than that in the oxygen group. Parashi et al. also confirmed that inhaling Entonox resulted in a shorter labor [7]. According to the findings obtained in this study, Entonox did not have an effect on meconium staining and the difference between the two groups was not significant. In a study carried out on 1300 primiparas to compare the effects of Entonox and oxygen, Entonox did not have any effects on meconium staining; this is consistent with the results of the present study [16]. Concerning the Apgar score at 1 and 5 min, the two groups were not significantly different and Entonox did not adversely affect the Apgar score; this is consistent with the results of other studies [14,16].

Entonox gas did not have any effect on the increase in cesarean rate and decrease in labor progress. However, a study showed that those who used oxygen, compared with Entonox, underwent cesarean section which was due to more intense and longer-lasting pain in the active labor phase, which contradicts with the results of the present study [17]. A few side effects were reported by mothers using Entonox; however, the effects were not that much serious to cause the patient to discontinue Entonox. These side effects included dry mouth, dizziness, drowsiness, nausea, and numbness of the tongue. In their studies, Talebi and Parashi demonstrated that the side effects were more in the intervention group [Entonox] [6,7]. Mohammad Jafari draw the conclusion that drowsiness [29%], dizziness and headache [14%] were the most common side effects of Entonox, whereas the least common ones were lethargy [1%] and vomiting [2%]. In Norouzinia's study, 4 out 40 mothers who used Entonox complained of lightheadedness and dizziness [18]. Hemoglobin level in women undergoing cesarean section or vaginal delivery was measured 6 h postpartum and the drop in hemoglobin level in both groups was significant. The hemoglobin level in those receiving Entonox dropped less compared to the other group. Therefore, they lost less blood during labor which could be due to the shorter labor they experienced.

Limitations

Some of the limitations of the present study were not being double-blind and lack of similar oxygen cylinder and face masks, and lack of necessary equipment for a more accurate estimation of the amount of bleeding during and

after labor.

CONCLUSION

According to the results obtained from this study, the use of Entonox for painless labor, compared with oxygen, did not cause adverse effects on the mother and fetus; however, only minor side effects including drowsiness, dry mouth, dizziness and nausea and numbness of tongue were observed. Furthermore, it was observed that Entonox causes less reduction in hemoglobin concentration of the mother which may be due to its positive effects on labor progress and its duration. Therefore, no serious side effects were reported for this analgesic gas except for some harmless and controllable effects. Moreover, by reducing labor pain and labor duration, Entonox can help women overcome their fear of labor pain.

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