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Nitrous Oxide versus Pethidine with Promethasine for Reducing Labor Pain

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Abstract

Background: Systemic opioids are widely used for relief of labor pain. Self-administered nitrous oxide with concentration of 50% is a new form of analgesia. The aim of this study was to compare the analgesic efficacy and side effects of patient controlled, inhaled nitrous oxide 50% ''Entonox'' with systemic intramuscular pethidine, in reducing of pain during normal vaginal labor in Iranian population.

Materials and Methods: In a randomized controlled study the analgesic efficacy of inhaled 50% nitrous oxide (Entonox) was evaluated compared to intra muscular pethidine for reducing labor pain among 100 women undergoing normal vaginal delivery.

Results: Mean maternal age was 26.2 and 27.2 years in Entonox and Pethidine groups, respectively. Duration of first and second stages was significantly shorter in patients receiving nitrous oxide as analgesia, comparing to pethidine group (P<0.05). Pain severity according to VAS score was significantly lower in patient received nitrous oxide (P=0.0001). We also showed significantly higher satisfaction of pain reduction in nitrous oxide group during labor (P=0.01). No significant different was observed among the groups regarding infant complications.

Conclusion: Although nitrous oxide is certainly not a potent analgesic, we found that it has more beneficial effects than pethidine in parturient women which remains to be cleared.

Keywords: Entonox; Labor pain; Pethidine; Nitrous oxide

Introduction

Labor is one of the painful conditions that are considered to be the most intense and stressful experiences [1]. In the last decades, changes have occurred in the obstetric expectations and in their care. In developed countries, the number of women requesting labor analgesia is increasing, and in some communities, an effective pain relief for childbirth is in great demand [2].

As it is cheap, simple to use and readily available, systemic pethidine is widely used for relief of labor pain [3,5]. Use of parental opioids was found to be between 39% and 56% in various hospital obstetrics units, in the United States [3,6,7].

Systemic opioids lead to some adverse effects on both mother and baby. Including dysphoria, sedation, respiratory depression, nausea and vomiting and delayed gastric emptying for the mother [8]. As pethidine crosses the placenta, it may accumulate in the fetal circulation [9], causing early neonatal respiratory depression and behavioral and feeding problems for even up to six weeks after delivery [10-12].

Self-administered 50% nitrous oxide "Entonox" is an effective and safe form of analgesia, which has been used by many emergency medical services for many years. Nitrous oxide is an odorless, tasteless, inhaled analgesic, [13] and it found to be an effective analgesia for many women while also being safe for the mothers and babies.14 now a day, nitrous oxide is widely used in many countries for relieving labor pain [14].

Unlike opioids, it does not depress respiration [15]. Nitrous oxide rapidly takes effect [16] and is quickly reversible on discontinuation of therapy [16,17].

Despite its wide and popular use in many countries, nitrous oxide for the relief of labor pain is largely unknown in Iran. In present study, we aimed to compare the analgesic efficacy and side effects of patient controlled, inhaled nitrous oxide 50% "Entonox" with systemic intramuscular pethidine, the most popular drug with opioid analgesic properties, in relieving pain during normal vaginal labor in Iranian population.

Materials and Methods

In this randomized clinical trial study we evaluated the analgesic efficacy of inhaled 50% nitrous oxide (Entonox) compared to intra muscular Pethidine for relieving labor pain among 100 women undergoing normal vaginal delivery in Ali-ebne-abi-taleb hospital, in Iran, from March 2007 to March 2008. The study was reviewed and approved by the ethics committee in Zahedan University of Medical Sciences, and informed consents were obtained from all participants. Hundred pregnant women with gestational age ranging from 38-42 weeks, who referred in early phase of labor, randomly were enrolled in the study. Participants were selected among non-complicated, term pregnancies with a normal cephalic fetus, referred in active phase of labor with cervical dilation less than 7 centimeters. Women who could not keep their facial mask, have recent administration of local or systemic analgesics and opiods, patients with altered mental status, vitamin B_{12} deficiency receiving replacement therapy, any oxygenation abnormalities, hemodynamically unstable patients and women bearing any fetus abnormalities were excluded from the study.

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Patients randomly allocated in two groups. The number of nulliparous women was comparable in two groups. Participant of one group were medicated with Entonox, where women in the other group received Pethidine for relieving their labor pain. All women were trained for self administration of Entonox in group A and women in group B received 1 mg/kg slowly intra-venues injection of Pethidine combined with 25mg promethazine.

50% nitrous oxide in 50% oxygen is premixed in a single cylinder called by the trade name "Entonox" [18]. Entonox is self-administered by the laboring woman using a face mask, when she determines that she needs it, Patients were trained to administer face mask of Entonox with the initial of every uterine contraction and continue deep inspirations while the contraction and pain exists.

Entonox administration can be started and stopped at any point during labor, according to the needs and preferences of the woman. It takes effect in about 50 seconds after the first breath and the effect is transient essentially gone when no longer needed [14]. The flow of gas into the mask is initiated by the negative pressure of inhalation, which opens a demand valve. This same demand valve prevents the flow of gas when inhalation ceases, and the Entonox apparatus allows the exhaled gas to be scavenged so it is not released into the air, minimizing the exposure to others in the room.

Following different analgesic administrations, severity of labor pain was evaluated according to the VAS score, numbering from 0 to 10 (0=no pain, and 10=severe and non tolerable pain). Parturients pain scored once before any analgesic administrations, and they were requested to score their maximum pain following each contraction. Total VAS score is the mean of scores rated during labor.

Patients satisfaction of analgesia method was also evaluated by Verbal Rating Scale, scoring from 0= not satisfied to 4=complete satisfaction.

All parturients were monitored for vital signs, arterial O_2 saturation, and fetal heart rate each 30 minutes during labor, and mothers were suggested to have left lateral position during labor for prevention of supine hypotension.

Mothers' somnolence and sedation was also evaluated by a nurse in 10 minutes intervals according to Ramsy Score, from 1 to 5. 1=completely awake, 2= somnolence, 3=irritable to sound, 4= irritable to touch, and 5=non responder.

Statistical analysis

Descriptive statistics were used to report demographic characteristics with SPSS statistics package version 15. The Chi-square test and Student t-test were used to compare the groups on qualitative and quantitative variables, respectively.

Results

A total of 100 pregnant including 50 prime-gravid women were enrolled in the study. Mean maternal age was 26.2 and 27.2 in Entonox and Pethidine groups, respectively. Demographic data of the participants is summarized in Table 1. Patient's characteristics were comparable in two randomly allocated groups.

All participants underwent normal vaginal delivery and none of them needed vacuum or forceps assistant. Duration of first and second stages was significantly shorter in patients receiving nitrous oxide as analgesia, comparing to pethidine group (P<0.05) (Table 2).

VAS score before administration of any analgesic agent was statistically equal between groups; however, it shows significant difference at the end of both first and second stages of labor. Pain severity according to VAS score was lower in patient received nitrous oxide. (P=0.00)

There were no differences in blood pressure, heart rate and respiratory rate before analgesia. Where, after the end of stage 1 and 2 nitrous oxide users had significantly lower heart rate and respiratory rate. Blood pressure still remained equal in both groups (Table 2). There was no statistically significant difference in VAS score and labor duration among prime-gravid and multi gravid women (P>0.05).

There were no significant differences in Apgar scores or neonatal survival between babies born to mothers who received nitrous oxide and pethidine.

Patient's satisfaction of analgesia administered during labor was finally evaluated by the mean of verbal score. Our study showed significantly higher satisfaction of pain reduction in using nitrous oxide as analgesic agent during labor (P=0.01) (Table 3).

Discussion

This study demonstrated that, using nitrous oxide (Entonox) for analgesia causes statistically significant and clinically important

Variable	Entonox (n=50)	Pethidine (n=50)	P value
Age (year)	7.34±26.2	6.02± 27.2	NS
Weight (kg)	0.38 ±69	11.06± 73	NS
Gestation (week)	0.95 ± 38.44	0.92± 38.58	NS
Cervical dilation at Analgesic inititation (cm)	0.91 ± 4.46	0.89 ± 4.36	NS

Table 1: Descriptive data of Entonox and pethidine subjects.

	Entonox	Pethidine	P-value
Duration	3.12± 1.37 3.44±1.73	2.24 ±1.07 1.18 ±1.00	0.001 <0.001
VAS mean score			
Befor Analgesia	0.98±9.14	0.75±9.40	NS
Over first stage	1.53±6.02	1.25±7.16	0.000
Over second stage	1.82±5.70	1.05±8.22	0.000
Systolic blood pressure			
before analgesia	8.95±1.13	8.37±1.14	NS
End of stage 1	8.70±1.12	56.8±1.11	NS
End of stage 2	7.87±1.11	7.61±1.11	NS
Diastolic blood pressure			
before analgesia	9.4±6.7	8.2±66.2	NS
End of stage 1	7.87±69.6	8.65±66.6	NS
End of stage 2	7.8±70.20	8.61±68.2	NS
Heart rate			
before analgesia	6.84±81.72	12.22±84.22	NS
End of stage 1	11.81±107.1	10.14±81.9	<0.001
End of stage 2	9.87±109.90	9.24±80.40	<0.001
Respiratory rate			
before Analgesia	1.50±13.92	1.51± 14.80	NS
End of stage 1	1.65±14.16	1.37±13.52	0.03
End of stage 2	1.32±13.72	1.22±12.92	0.002

Table2: Comparison of labor out comes in patients received nitrous oxide and petheidine.

Maternal satisfaction	Entonox	pethidine	P-value
Complete n (%)	8(16%)	1(2%)	0.01
Good n (%)	15(30%)	13(26%)	
Moderate n (%)	16(32%)	18(36%)	
Slight n (%)	10(20%)	14(28%)	
No relief n (%)	1(2%)	4(8%)	

Table3: Patients satisfaction of analgesia method.

reduction in severity of labor pain during first and second stages of normal vaginal delivery, compared to Pethidine. Duration of both first and second stages of labor was also reduced in using Entonox as analgesia. Thus, Entonox led to women's higher satisfaction of their labor pain relief.

Our results were in line with previous studies [8,13,14,16,17-22]. However, in contrast, one prospective non-randomized study, labor pain was more sever in prime-gravid women administered nitrous oxide compared to Pethidine [23].

A mixtured nitrous oxide 50% in oxygen"Entonox", available in a single cylinder, is a patient controlled, inhaled analgesic [13]. It has low solubility in blood and is transported in solution without binding to protein. Nitrous oxide rapidly takes effect [16,19], because it diffuses rapidly through the alveolar– arterial membrane and is excreted unchanged, mainly through the lungs [13]. As a result, it is quickly reversible on discontinuation of therapy [16,17,19]. It has shown that recovery from sedative effects of nitrous oxide is faster compared with intravenous analgesia [13].

Rapid onset and quick reversibility, allows nitrous oxide to be administered throughout the second stage of labor without fear of effects on the newborn [19]. Supervised by physicians, nurses or midwives, nitrous oxide is widely used as a safe analgesic in many parts of the world including Canada, Australia, Finland, united kingdom and New Zealand,(43-49%) [24,25,26].

The maximum effect of nitrous oxide appears at a concentration of 70%, and it has shown to relive labor pain in approximately two-thirds of women [14].

The precise mechanism of action of nitrous oxide analgesia remains uncertain. It may induce release of endogenous opioid peptides in the periaquiducatal gray area of midbrain [27].

Among various inhalation anesthetic agents, studied for labor analgesia, only nitrous oxide is used to any great extent in modern obstetric practice. The reasons are probably related to the ease of administration of nitrous oxide, its lack of flammability, absence of pungent odor, minimal toxicity, minimal depression of cardio vascular system, lack of effect on uterine contractility, and the fact that it does not trigger malignant hyperthermia [14].

Entonox is administered either intermittently, starting with the onset of pain with each contraction and discontinuing as the contraction pain eases or abates, or continuously, by inhaling both during and between contractions [14].

Intermittent administration of Entonox, as we used, is somehow problematic. Because there is a of approximately 50 seconds lag after the onset of administration before the analgesic effect can be expected [28]. However, Entonox is significantly beneficial if administration initiates approximately 30-50 seconds before each contraction [29].

Side effects induced by nitrous oxide are nausea and vomiting reported 5%-d in 36% [14,21,22,30,31]. Dizziness, dreams and drowsiness reported in 0%-24%, dry mouth from breathing dry gas, buzzing in the ears, and rarely, numbness are also reported [14,19,21,30,31].

The greater maternal risk of inhalation nitrous oxide is loss of consciousness. It is rare with 50% nitrous oxide. The alveolar concentration for wakefulness for nitrous oxide is between 50% and 70% in non-pregnant women and probably lower in pregnant. So it is important that the agent to be self-administered and not by anyone else. It is also important that a mask is kept by parturient and not fixed to the face. If it is not strapped, her hand will fall away from her face, when she became too drowsy rendering the device nonfunctional. Therefore, the nitrous oxide concentration wills rapidly decline [14].

Nitrous oxide rapidly transfer placenta, however, as shown in our study the fetus infants are clinically unaffected. There have shown no significant differences in Apgar scores or neonatal outcomes between babies born to mothers who received nitrous oxide [14,19,21,30,31].

When used intramuscularly, analgesic effect of pethidine-one of the most frequently used opiate agonists- starts within 10–20 min, and lasts 2–4 h [34].

As it is cheap, simple to use and readily available, systemic pethidine is widely used for relief of labour pain [3]. Use of parental opioids was found to be between 39% and 56% in various hospital obstetrics units, in the United States [3]. however, many studies have suggested that intramuscular pethidine may be ineffective at relieving labor pain [4,5-7] and it has been suggested that their use may even be unethical and medically incorrect [7].

Systemic opioids lead to some adverse effects on both mother and baby. Including dysphoria, sedation, respiratory depression, nausea and vomiting and delayed gastric emptying for the mother [8] as pethidine crosses the placenta, it may accumulate in the fetal circulation [9], causing early neonatal respiratory depression and behavioral and feeding problems for even up to six weeks after delivery [10-12].

Consistent with ours, an uncontrolled, observational study on primi-gravidae, showed women judged nitrous oxide to be more effective than opiods [35]. The study suggests that, nitrous oxide is a useful method for women who wish to cope with the earlier part of labor "drug free". Consistent with ours, this study showed that labor was more rapid in the nitrous group; however, it is unlikely that nitrous oxide causes more rapid labor, and it is unlikely that opioids significantly slow labor. It may be more effective for women whose labor is shorter [35].

Although nitrous oxide is certainly not a potent analgesic, it has more beneficial effects for many parturient women compared to pethidine. It is easy to administer and safe for both mother and infant.

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