Original Article

Effect of Entonox on Pain Relief and Duration of Labour in Nulliparous Patients Presenting for Delivery at Term

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Abstract

Objective: To investigate the effect of Entonox on labor pain and labor duration in primiparous women.
Methodology: This randomized controlled trial was conducted at the Department of Obstetrics and Gynaecology, Shifa International Hospital, Islamabad, over a six-month period from 01-09-2021 to 28-02-2022, after approval by the Institutional Ethics Committee. The study population consisted of nulliparous women aged 18–40 years presenting in active labor at ≥37 weeks of gestation, with any of the following well-controlled comorbidities: pre-existing or gestational diabetes (deranged OGTT), non-proteinuric well-controlled hypertension (BP ≥140/90 mmHg), anemia (Hb <8 g/dl), and morbid obesity. A total of 60 patients (30 in each group) were included in the study. Group A received Entonox, while Group B received a placebo. The mean pain scores during the first and second stages of labor were recorded using the Visual Analogue Scale (VAS). The duration of the first and second stages of labor was also documented. Side effects were monitored. Data were entered and analyzed using SPSS version 21.
Results: Both groups were comparable in terms of age, gestational age, and BMI. Entonox inhalation resulted in a shorter duration of labor and significantly lower pain scores. The mean duration of the first stage of labor in Group A was 3.73 ± 0.45 hours, compared to 5.64 ± 0.88 hours in Group B ($p < 0.001$). Similarly, the mean duration of the second stage of labor was 1.28 ± 0.48 hours in Group A and 1.93 ± 0.87 hours in Group B ($p < 0.001$). The mean VAS pain score during the first stage was 3.07 ± 1.06 in Group A and 7.20 ± 0.66 in Group B ($p < 0.001$). During the second stage, the mean pain score was 4.23 ± 1.04 in Group A and 8.81 ± 0.50 in Group B ($p < 0.001$).
Conclusion: Entonox significantly reduced pain during both the first and second stages of labor and shortened the duration of labor. No significant complications were reported, highlighting the safety and effectiveness of Entonox as an analgesic option. Therefore, Entonox inhalation is a useful and safe method for reducing labor pain.
Keywords: Entonox, Pain relief, Duration of labour .

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Introduction

Childbirth is a natural process which is primarily either vaginal or through caesarean section.[1] For most women, vaginal childbirth is considered comparatively safer method because of lesser risk of morbidity and mortality.[1-3] The increasing Caesarean Section (CS) rates may be attributed to women's increasing requests for elective CS. High Fear of Childbirth especially among nulliparous women, may be significantly associated with CS preference without medical indications. Studies have revealed that women decline natural childbirth due to pain, fear, long duration and unpredictability of labour and their perceived loss of autonomy in decision making They also fear if their bodies are capable of birthing baby vaginally. So, researchers in recent years have made great efforts for the development of natural childbirth methods without pain.[4] The employed analgesia should be safe both for the mother and fetus. Safe method for pain relief during

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labour should not stall natural labour process, physiological functions, mobility or the mothers' consciousness.[5-8] Modalities to relieve pain during labor include natural pain relief such as massage, heat, and acupuncture. Amongst non -pharmacologic treatments; water injection for low back pain or transcutaneous electrical neuromuscular stimulation (TENS) are employed. These have variable success.[9,10,13]

Pharmacologic treatment commonly used are intravenous or intramuscular opioids as pethidine, inhalational analgesics as Entonox, and epidural blocks. Intravenous pethidine is the most commonly employed for labor pain relief. however, it can be associated with several side effects such as dysphoria, sedation, respiratory depression, nausea, vomiting and neonatal respiratory depression, which is the most serious side effect. Epidural is effective in reducing pain but its administration requires skill and intensive monitoring [9,10,11,13]

Entonox® is a mix of nitrous oxide 50% and oxygen 50%. It is a very effective analgesic agent with rapid onset and clearance.[1,7,13] It is a non-inflammable, tasteless, odorless, and colorless gas.[12,13,14] Nitrous oxide has been used for labor pain relief since 1800s, but surprisingly, it is not so popular, and the number of studies evaluating its use for pain relief in labour are limited. The review of limited available literature suggests pain relief. Studies have shown conflicting result on duration of labour. Nulliparous women have comparatively longer labours and this leads to exhaustion, anxiety and inclination towards caesarean section by both patients and care givers as a quicker method of childbirth.[7,14,18,19]

The limited use of Entonox in our country may be related to less availability in the labour rooms and unfamiliarity of use. In addition, it needs more instruction to use to avoid missed use, causing inadequate inhalation and low efficacy. The rationale of this study is to compare the outcome of Entonox versus placebo given during active labour in nulliparous females presenting for delivery at term so as to alleviate the paucity of data regarding an analgesic that can potentially shorter labour duration and encourage labour and vaginal delivery experiencing childbirth for first time.

Methodology

This randomized controlled trial was conducted at the Department of Obstetrics and Gynaecology, Shifa International Hospital, Islamabad over a period of six months from 01-09-2021 to 28-02-2022. IRB approval no: CPSP/REU/OBG-2019-043-9127. A sample size of 60 participants; 30 participants in each group was calculated with level of significance 517 power of study 80% and taking magnitude of mean pain score i.e. 5.18±1.29 with Entonox and 8.99±1.981 with placebo during active. labour. Non-probability consecutive sampling was employed. Participants included females of age 18-40 years, nulliparous, presenting at ≥37 weeks of gestation (on LMP) in active labour (5 or more cm dilatation) any of these comorbid situations with well controlled chronic or gestational diabetes (deranged OGTT), non proteinuric, well controlled hypertension, (BP≥140/90), anemia (Hb<8g/dl) and morbidly obesity. Exclusion criteria comprised patients with multifetal pregnancies, placental abnormalities (e.g., previa, accreta, abruption), cardiac disease, cervical length >4 cm, AFI <5 cm or >21 cm on ultrasound, prior caesarean deliveries, meconium stained liquor, cardiac disease. Pre eclampsia, Uncontrolled diabetes, Asthma.

After taking approval from hospital ethical committee, 60 patients fulfilling selection criteria were enrolled. After obtaining informed consent and demographic information (name, age, parity, BMI, gestational age) were recorded. All patients were randomly divided in two groups by using lottery method. In group A, Entonox was given by gas mask. In group B, patients were given simple oxygen mask. Patients were given demonstration regarding correct intended use of Inhalation anesthesia and were supported and assisted for the same throughout the labour. Patients were advised to inhale and exhale deeply and uniformly through the mask. Synchronization of uterine contraction and analgesic effect was the key to get desired analgesic effect. The patients got gases herself through face mask connected to unidirectional valve.

The gas was continued to the end of contraction pain at which the patient breathed the room air. Duration of labour was recorded. First stage duration taken here as duration from admission in active labour till full dilatation. Second stage duration measured from full dilatation to delivery of baby. Pain was assessed using visual analogue scale. The pain scale was numbered 0 to 10 with highest score depicting severity of pain. For both first and second stage of labours. Pain score was assessed every hour and mean score for each stage was noted. The monitoring of contraction frequency and intensity, foetal heart rate, and mothers` physical

signs (blood pressure, pulse, and temperature and breath rate) were done as routine for both groups by midwifery personnel. Management of labour was done according to WHO labour. All information were recorded on a standardized proforma.

Data were analyzed using SPSS v21 Continuous variables (pain score, labour duration) are presented as mean ± standard deviation. Frequency was calculated for patients in stratified age groups, gestational age groups and BMI groups. Independent samples t-tests compared mean pain scores and labour duration between both groups. Chi Square and Fischer exact test was used to compare categorical data. P-value ≤0.05 was taken as significant. Data were stratified for age, parity, BMI and gestational age, followed by post-stratification comparisons using independent t-tests.

Results

A total of 60 patients (30 in each group) were included in the study. Both groups were comparable in terms of age, gestational age and BMI as shown in table I.

Table I: Baseline Characteristics of Participants. (n=60)

Parameter	Group-A (Entonox)	Group-B (Placebo)	P value
Age (Years)			
18–30 years	18 (60.0%)	19 (63.3%)	0.87
31–40 years	12 (40.0%)	11 (36.7%)	
Mean ± SD	29.1 ± 5.3	29.3 ± 6.1	0.92
Gestational Age (Weeks)			
38–39 weeks	26 (86.7%)	23 (76.7%)	0.68
40–41 weeks	4 (13.3%)	7 (23.3%)	
Mean ± SD	38.3 ± 0.5	38.9 ± 0.8	0.98
BMI (kg/m²)			
<30	16 (53.3%)	20 (66.6%)	0.67
≥30	14 (46.7%)	10 (33.4%)	
Mean ± SD	29.5 ± 4.9	28.0 ± 4.0	0.83

Table II: Comparison of Pain Scores and Labour Duration.

Variable	Group-A (Entonox)	Group-B (Placebo)	p-value
Duration of Labour (Hours)			
1st stage	3.73± 0.45	5.64 ± 0.88	<0.001
2nd stage	1.28 ± 0.48	1.93± 0.87	<0.001
Pain Score (VAS)			
1st stage	3.07± 1.06	7.20 ± 0.66	<0.001
2nd stage	4.23± 1.04	8.81 ± 0.50	<0.001

Patients in Group A (Entonox) had shorter labours and lower pain scores as compared to Group B. (Table II) After stratification according to age, gestational age and BMI, the results consistently showed shorter labour duration and lower pain scores in patients assigned to Entonox group. (Table III). No serious maternal or fetal side effects were observed in either groups. Minor side effects were comparable in both groups (Table IV).

Table III: Stratified Analysis of Labour Outcomes.

Stratification	Group-A (Entonox)	Group-B (Placebo)	p-value
By Age (18–30 years)			
Labour duration (1st stage)	3.33 ± 0.48	5.11 ± 0.93	<0.001
Pain score (1st stage)	2.92 ± 1.07	8.58 ± 0.50	<0.001
Labour duration (2ndstage)	1.12± 0.48	1.74± 0.93	<0.001
Pain score (2ndstage)	4.11 ± 1.65	8.73 ± 0.6	<0.001
(31-40 years)			
Labour duration (1st stage)	4.13 ± 0.51	6.17 ± 0.94	<0.001
Pain score (1st stage)	3.23± 1.02	8.76 ± 0.49	<0.001
Labour duration (2ndstage)	1.45 ± 0.48	2.12± 0.93	<0.001
Pain score (2ndstage)	4.15 ± 1.65	8.9± 0.6	<0.001
By BMI (<30 kg/m²)			
Labour duration (1st stage)	4.06± 0.45	5.12 ± 1.34	<0.001
Pain score (1st stage)	3.314 ± 1.13	6.9 9 ± 1.2	<0.001
Labour duration (2ndstage)	1.35 ± 0.48	1.67 ± 0.93	<0.001
Pain score (2ndstage)	4.25 ± 1.65	8.91± 0.6	<0.001
(≥30 kg/m²)			
Labour duration (1st stage)	4.19± 0.46	6.24± 1.23	<0.001
Pain score (1st stage)	3.21 ± 1.25	6.89 ± 0.60	<0.001
Labour duration (2ndstage)	1.37 ± 0.48	1.66 ± 0.92	<0.001
Pain score (2ndstage)	4.35 ± 1.67	8.51± 0.6	<0.001
By Gestational Age (38–39 weeks)			
Labour duration (1st stage)	4.06 ± 0.46	6.23± 1.23	<0.001
Pain score (1st stage)	3.21 ± 1.25	6.89 ± 0.60	<0.001
Labour duration (2ndstage)	1.37 ± 0.48	1.87 ± 0.92	<0.001
Pain score (2ndstage)	4.35 ± 1.67	8.51± 0.6	<0.001
40-41 weeks			
Labour duration (1st stage)	4.21 ± 0.55	6.19 ± 1.27	<0.001
Pain score (1st stage)	3.21 ± 1.25	6.72 ± 0.61	<0.001
Labour duration (2ndstage)	1.4 7 ± 0.48	1.92 ± 0.92	<0.001
Pain score (2ndstage)	4.35 ± 1.67	8.51± 0.6	<0.001

Table IV: Observed Side effects. (n=60)

Variable	Group-A (Entonox) n=30	Group-B (Placebo) n=30	p-value
Nausea	2(6.7%)	3(10%)	0.92
Vomiting	2(6.7%)	3(10%)	0.45
Dizziness	3(10%)	2(6.7%)	0.8
Dry mouth	3(10%)	3(6.7%)	0.9

Discussion

The findings of this study reveal significant alleviation of labour pain and in the reduction of the duration of first and second stages of labour in nulliparous women presenting in spontaneous labour in women given Entonox. Other studies too have revealed significantly lower pain scores in patients given Entonox than those given other pain killers, non-pharmacological pain relief or placebo.[1-7] Though the precise mechanism of action of inhaled Entonox remains uncertain anaesthetic actions are related to suppression of activity of the reticuloendothelial network in the brainstem. Nitrous oxide modulates NMDA receptor activity and enhances endogenous opioid release. [7,8,17,18] This also modulates pain stimuli through the descending spinal cord nerve pathways. it also increases release of endorphins leading to analgesia, euphoria, and a relaxation effect.[7,18,19] Oxygen is added to alleviate anoxia that may result from sole Nitrous Oxide inhalation. The ability of patient to titrate against her pain severity and contractions also gives patients a sense of autonomy.[1,7,18,19] Thus the psychological aspect of pain is catered to as well. Hakemzade et al.[1] reported significantly lower pain scores in patients given Entonox 5.95±1.32 vs 8.45±1.02(p<0.001) given oxygen in placebo in first stage of labour. Similarly, in second stage of labour, patients given Entonox had score of 5.44±1.94 vs 8.12±2.16 (p< 0.001) in those given oxygens. In this study patients given Entonox had even lower pan score in both first and second stages of labour. Demonstrating to patients at study enrolment and presence of labour room staff that assists patients in correct use might have contributed to this effect.

The reduction in labour duration observed in this study adds to the evidence which supports Entonox's role in facilitating labour progression. In a systematic review of 15 trials, Jones et al.[13] suggested that effective pain management reduces maternal stress and catecholamine secretion which as a result enhances uterine contractility and cervical dilation. This hypothesis is mirrored in the results of this study where the first stage of labour in the Entonox group lasted 2.27 ± 0.45 hours as compared to 5.20 ± 0.88 hours in the placebo group. Mardani Hamule et al.[14] reported the similar findings with a 40% reduction in active labour duration with Entonox use (p = 0.01) in a cohort of 120 Iranian women. The shorter second stage in our Entonox group aligns with Masoudi et al.[16] who attributed this as an improved maternal cooperation during pushing because of reduced pain- and also related anxiety.

Stratified analysis in this study revealed consistent benefits across age, BMI and gestational age subgroups which challenges the earlier concerns about its variable efficacy in diverse populations. This contradicts the statement of Panni and Segal[17] who argued that Entonox efficacy might be diminished due to obesity-could alter pharmacokinetics and adipose tissue absorption. However improved pain relief even in women of BMI of 30 or more may be due to the fact that patients were explained the correct method of inhalation with contractions and self-administered inhalation allows patients to compensate for these factors by adjusting inhalation depth and frequency.

Further, the safety profile of Entonox in this study also reinforces its suitability for low-resource settings like Pakistan. There is no need of specialized personnel and continuous monitoring unlike epidural analgesia.[19,20,21] Entonox can be administered by midwives or nurses as demonstrated in a nurse-directed model by Pinyan et al.[19] This is particularly relevant for regions like Pakistan where inadequate trained healthcare systems is a key barrier to timely obstetric care.[4] Moreover, the absence of severe side effects like hemodynamic instability, foetal or maternal hypoxia, observed in this study suggest it to be a safe mode of analgesia. Some studies have revealed increased risk of side effects, hemodynamic instability or poor APGAR at birth.[13,17,19] Minor side effects observed were comparable in both groups and in much less frequency than other studies. This difference may be because Entonox is used only when needed like during contractions. This limits how much is taken in overall and allows the body to quickly remove it through breathing.

The impact of socio-economic implications in this study is significant. In low-income countries, Entonox offers a cost-effective strategy to promote natural childbirth because C-sections are increasingly perceived as a safer and pain-free alternative to vaginal delivery.[1,22]

Moreover, this study focus on nulliparous women who often face heightened anxiety about labour pain—highlights Entonox's potential to improve maternal satisfaction.

This study has limitations as the single-canter design and the small sample size of 60 may limit its generalizability. Additionally, the short follow-up period precluded assessment of long-term neonatal outcomes, such as neurodevelopmental effects of nitrous oxide exposure. Future research should prioritize multicentre trials with larger cohorts. Despite these limitations, the findings in this study align with global trends advocating patient-centred, non-invasive pain management in obstetrics

Conclusion

This study demonstrates that Entonox inhalation analgesia significantly reduces labour pain intensity during the first and second stages and also shortens labour duration. As Entonox have self-administered nature so it allows women to control its use in synchrony with their contractions, thereby preserving the mobility and promoting a positive childbirth experience. There were no significant complications in this study which reinforces it's suitability for diverse clinic settings particularly in resource-limited settings where access to more advanced analgesia is limited.

Further multicentre research is necessary to confirm these benefits particularly in regions with rising caesarean rates which are driven by the fear of pain. In light of the persistent high caesarean rates which are mainly linked to fear of labour pain, integrating Entonox as a cost-effective, non-invasive analgesic option could play a pivotal role in promoting natural vaginal delivery and reducing unnecessary surgical interventions.

References

1. Parsa P, Saeedzadeh N, Roshanaei G, Shobeiri F, Hakemzadeh F. The effect of Entonox on labour pain relief among nulliparous women: a randomized controlled trial. J Clin Diagn Res. 2017;11(3):QC08. https://doi.org/10.7860/JCDR/2017/21611.9362
2. Agah J, Baghani R, Safiabadi Tali SH, Tabarraei Y. Effects of continuous use of Entonox in comparison with intermittent method on obstetric outcomes: a randomized clinical trial. J Pregnancy. 2014;2014:245907. https://doi.org/10.1155/2014/245907
3. Morais Í, Lemos A, Katz L, de Melo LF, Maciel MM, de Amorim MM. Perineal pain management with cryotherapy after vaginal delivery: a randomized clinical trial. Rev Bras Ginecol Obstet. 2016;38(7):325-32. https://doi.org/10.1055/s-0036-1584941
4. Sheyklo SG, Hajebrahimi S, Moosavi A, Pournaghi-Azar F, Azami-Aghdash S, Ghojazadeh M. Effect of Entonox for pain management in labour: a systematic review and meta-analysis of randomized controlled trials. Electron Physician. 2017;9(12):6002. https://doi.org/10.19082/6002
5. Najafi TF, Bahri N, Ebrahimipour H, Najar AV, Taleghani YM. Risk assessment of using Entonox for the relief of labour pain: a healthcare failure modes and effects analysis approach. Electron Physician.2016;8(3):2150. https://doi.org/10.19082/2150
6. Foji S, Moghadam MY, Tabasi Asl H, Nazarzadeh M, Salehiniya H. Comparison of ENTONOX inhalation and spinal anesthesia on labour pain reduction and Apgar score in vaginal delivery: a clinical trial. BioMedicine.2018;8(3):17. https://doi.org/10.1051/bmdcn/2018080317
7. Najefian M, Cheraghi M, Pourmehdi Z, Nejad AD. Effect of nitrous oxide (ENTONOX) on labour pain relief during delivery stages. Int J Pharma Therap. 2013;4(4):242-6.
8. Attar AS, Feizabadi AS, Jarahi L, Feizabadi LS, Sheybani S. Effect of Entonox on reducing the need for pethidine and fetal and maternal complications in painless labour. Electron Physician. 2016;8(12):3325. https://doi.org/10.19082/3325
9. Jafarzadeh L, Shabanian SH, Jafari F, Gangi F. Effect of Entonox on severity of pain, maternal hemodynamics, and fetal Apgar in vaginal delivery. J Shahrekord Univ Med Sci. 2012;14(3):92-9.
10. Sharma SK, McIntire DD, Wiley J, Leveno KJ. Labour analgesia and cesarean delivery: an individual patient meta-analysis of nulliparous women. Anesthesiology. 2004;100(1):142-8. https://doi.org/10.1097/00000542-200401000-00023
11. Chantrasiri R, Wanapirak C, Tongsong T. Entonox versus pethidine in labour pain relief: a randomized controlled trial. Int J Environ Res Public Health. 2021;18(23):12571. https://doi.org/10.3390/ijerph182312571
12. Collado V, Nicolas E, Faulks D, Hennequin M. Safety of 50% nitrous oxide/oxygen in conscious sedation: a review. Expert Opin Drug Saf. 2007;6(5):559-71. https://doi.org/10.1517/14740338.6.5.559
13. Jones L, Othman M, Dowswell T, Alfirevic Z, Gates S, Newburn M, et al. Pain management for women in labour: overview of systematic reviews. Cochrane Database Syst Rev. 2012;(3). https://doi.org/10.1002/14651858.CD009234
14. Mardani Hamule M, Heidari H, Kiani A. Comparing the effect of Entonox and pure oxygen on pain intensity during delivery. J Crit Care Nurs. 2009;2(3):105-9.
15. Stewart LS, Collins M. Nitrous oxide as labour analgesia: clinical implications for nurses. Nurs Womens Health. 2012;16(5):398-409. https://doi.org/10.1111/j.1751-486X.2012.01763.x
16. Masoudi M, Akbari S, Tarahi MJ. Comparison of Entonox and warm water on labour pain. Yafteh. 2012;12(2):25-32.
17. Reed PN, Colquhoun AD, Hanning CD. Maternal oxygenation during normal labour. Br J Anaesth. 1989;62(3):316-8. https://doi.org/10.1093/bja/62.3.316
18. Kranke P, Girard T, Lavand'homme P, Melber A, Jokinen J, Muellenbach RM, et al. Remifentanil patient-controlled analgesia in labour may not be suited as a "poor man's epidural." BMC Pregnancy Childbirth.2013;13:139. https://doi.org/10.1186/1471-2393-13-139
19. Pinyan T, Curlee K, Keever M, Baldwin KM. A nurse-directed model for nitrous oxide use during labour. MCN Am J Matern Child Nurs. 2017;42(3):160-5. https://doi.org/10.1097/NMC.0000000000000336
20. Weimann J. Toxicity of nitrous oxide. Best Pract Res Clin Anaesthesiol.2003;17(1):47-61. https://doi.org/10.1053/bean.2002.0264
21. Parsa P, Shobeiri F, Parsa N. Effect of prenatal health care on pregnancy outcomes in Hamadan, Iran. J Community Med Health Educ.2012;2:114. https://doi.org/10.4172/jcmhe.1000114
22. Boz I, Teskereci G, Akman G. How did you choose a mode of birth? Experiences of nulliparous women in Turkey. Women Birth. 2016;29(4):359-67. https://doi.org/10.1016/j.wombi.2016.01.005