# Introduction of Inhaled Nitrous Oxide and Oxygen for Pain Management during Labour – Evaluation of Patients' and Midwives' Satisfaction

Einführung eines Lachgas-Sauerstoff-Gemischs im Kreißsaal – Evaluation der Zufriedenheit von Schwangeren und Hebammen

**Authors** 

U. Dammer¹, C. Weiss², E. Raabe¹, J. Heimrich¹, M. C. Koch¹, M. Winkler¹, F. Faschingbauer¹, M. W. Beckmann¹, S. Kehl¹

**Affiliations** 

- <sup>1</sup> Frauenklinik, Universitätsklinikum Erlangen, Erlangen
- <sup>2</sup> Abteilung für Medizinische Statistik, Biomathematik und Informationsverarbeitung, Universitätsmedizin Mannheim, Universität Heidelberg, Mannheim

#### **Key words**

- perinatal
- nitrous oxide
- o inhaled analgesia
- pain management
- satisfaction
- labour

#### Schlüsselwörter

- perinatal
- Lachgas
- inhalative Analgetika
- Schmerzmanagement
- Zufriedenheit
- Wehen
- Geburt



received 8.5.2014 revised 20.5.2014 accepted 22.5.2014

### Bibliography

**DOI** http://dx.doi.org/ 10.1055/s-0034-1368606 Geburtsh Frauenheilk 2014; 74: 656–660 © Georg Thieme Verlag KG Stuttgart · New York · ISSN 0016-5751

#### Correspondence

#### PD Dr. Sven Kehl

Universitätsklinikum Erlangen Frauenklinik Universitätsstraße 21–23 91054 Erlangen sven.kehl@uk-erlangen.de

#### **Abstract**

Aim: Effective pain management during labour is important because pain affects the birth experience. Epidural analgesia is effective but often it may not be possible; however, inhaled analgesia offers another option. Use of inhaled nitrous oxide and oxygen for pain management in labour is well established in obstetrics but is still not used much in Germany. This study aimed to investigate the acceptance of the inhaled analgesia of inhaled nitrous oxide and oxygen by midwives and pregnant women during labour.

Material and Methods: In this observational study carried out between April and September 2013, a total of 66 pregnant women received inhaled nitrous oxide and oxygen during labour on request and after prior assessment of suitability. After the birth, all of the women and the responsible midwives were interviewed about their experience and satisfaction with the inhaled analgesia.

**Results:** A statistically significant reduction of pain was achieved with nitrous oxide and oxygen. The inhaled analgesia was mostly used by women who refused epidural analgesia. The likelihood of using inhaled nitrous oxide and oxygen again was reported as higher for patients who tolerated it well (p = 0.0129) and used it in the second stage of labour (p = 0.0003) and when bearing down (p = 0.0008).

**Conclusion:** Inhaled nitrous oxide and oxygen is an effective method for pain management during labour and is accepted well by women in labour and by midwives.

# Zusammenfassung

 $\blacksquare$ 

Ziel: Das Schmerzempfinden beeinflusst das Geburtserlebnis, weshalb die Schmerztherapie unter Geburt wichtig ist. Zwar kann die effektive Periduralanästhesie nicht immer angewendet werden, jedoch gibt es mit Lachgas-Sauerstoff-Gemischen eine weitere Alternative. Lachgasgemische sind etablierte Verfahren, finden jedoch in Deutschland noch keine breite Anwendung. Ziel dieser Arbeit ist zu prüfen, wie die Anwendung des Lachgasgemischs unter Geburt von Schwangeren und Hebammen angenommen wird.

Material und Methode: In dieser Beobachtungsstudie erhielten zwischen April und September 2013 insgesamt 66 Schwangere unter Geburt bei vorliegender Indikation und Wunsch das Lachgas-Sauerstoff-Gemisch. Alle Frauen wurden nach Geburt zu ihrer Erfahrung und Zufriedenheit mit dem Lachgasgemisch befragt. Zusätzlich dokumentierten die betreuenden Hebammen ihre Zufriedenheit mit der Wirkung des Lachgasgemischs in der entsprechenden Situation.

**Ergebnis:** Unter dem Lachgas-Sauerstoff-Gemisch konnte eine statistisch signifikante Schmerzreduktion erzielt werden. Dabei wurde das Lachgasgemisch am häufigsten bei Frauen verwendet, die eine PDA verweigerten. Die Wahrscheinlichkeit, das Lachgas-Sauerstoff-Gemisch wieder zu verwenden, war höher, wenn es von den Patientinnen besser vertragen (p=0,0129) und in der Austreibungsperiode (p=0,0003) und Pressphase (p=0,0008) angewendet wurde.

**Schlussfolgerung:** Das Lachgas-Sauerstoff-Gemisch ist eine effektive Methode zur Schmerzlinderung unter Geburt, die sowohl von den Gebärenden als auch von den betreuenden Hebammen gut angenommen wird.

#### Introduction



The pain suffered during birth has a significant impact on the experience and perception of the birth, making pain management an important aspect for women in labour [1–3].

A number of different medicinal and non-medicinal methods are available for pain management. According to the perinatal statistics of the Bavarian Study Group for Quality Assurance in In-patient Care (BAQ), epidural analgesia (EPA) is the most common analgesia in labour and it is used in around 44% of births [4,5]. However, for various reasons (e.g. clotting disorders) it is sometimes not possible to use EPA, making it difficult to provide adequate pain relief. Moreover, a number of pregnant women refuse EPA, even though it is an established method with sufficient evidence-based studies showing that it is safe [5].

In this situation, obstetricians and midwives in Germany can use LIVOPAN® (Linde AG, München), an inhaled analgesia [6]. This airgas mixture consists of 50% oxygen and 50% N<sub>2</sub>O (nitrous oxide); it has a slightly sleep-inducing and a moderately powerful analgesic effect [7]. From a medical point of view, the chief advantages of this form of pain management are its rapid onset and its fast elimination and clearance within minutes. The effectiveness and safety of inhaled analgesia for the management of pain during labour are well documented [8]. In addition to its good analgesic effect, nitrous oxide and oxygen offers additional advantages during labour: it has no effect on muscle tone and allows the patient to control the intensity of pain reduction. It is easy to use and can be administered by trained, non-medical staff [7]; side effects include dizziness, nausea, vomiting and sleepiness [5,7–9].

The use of nitrous oxide is an established method for pain management, although up to now it has not been generally used in Germany. In Scandinavia, the UK and Australia there is a long tradition of using nitrous oxide mixtures – and in some countries it is even the most common form of pain relief during labour [10]. The satisfaction of patients and their midwives with this form of pain management has been sufficiently documented in international studies [11–14]; however, data on the experience and satisfaction of patients and midwives with this type of analgesia in Germany are limited or non-existent.

The aim of this study was therefore to investigate the acceptance of inhaled nitrous oxide and oxygen by women in labour and their midwives.

# **Material and Methods**



After the inhaled nitrous oxide and oxygen was introduced in the Gynaecological Department of the University Hospital Erlangen, all pregnant women expecting singleton term pregnancies between April and September 2013 who used inhaled nitrous oxide and oxygen during labour were included in the study. Women who were ineligible for EPA due to an underlying condition or who refused EPA despite extensive information about the evidence-based efficacy of EPA were offered the option of receiving inhaled nitrous oxide and oxygen. Women were excluded from the study if a breech presentation was present. Additional exclusion criteria were primary caesarean section, intrauterine foetal death, structural or chromosomal anomalies and contraindications for nitrous oxide administration.

Gestational age was determined based on the date of the last menstruation and corrected, where necessary, using crownrump length measurements. The study was approved by the Ethics Commission of Friedrich-Alexander University of Erlangen-Nuremberg.

The study did not require any changes to normal clinical routine. If inhaled nitrous oxide and oxygen was administered by the midwife, the midwife completed a questionnaire after the birth ( • Fig. 1). Only fully trained midwives recorded the indications for inhaled analgesia, the stages of labour in which the inhaled analgesia was administered, and their own satisfaction with this method of analgesia. The satisfaction of patients was documented based on the patient's subjective statements on tolerance, side effects and whether she would chose this method of analgesia again. The pain intensity before and after receiving inhaled nitrous oxide and oxygen was assessed using a numerical rating scale (NRS, 1 = lowest pain, 10 = worst pain).

The primary outcome measure was the likelihood that the patient would use inhaled analgesia again. Additional outcome measures were satisfaction of the midwife with its use, pain reduction after receiving nitrous oxide and oxygen, and its tolerance by patients.

The following parameters were investigated to assess their potential effects on the birth and neonatal outcome: mode of birth, umbilical cord arterial blood pH, umbilical cord arterial blood base excess (BE), Apgar score, pathological CTG, foetal blood analysis, meconium-stained amniotic fluid, and transfer to the neonatal intensive care unit.

#### Statistical analysis

All statistical calculations were done using the statistical programme SAS, Release 9.3 (SAS Institute Inc., Cary, NC, USA). The median value, standard deviation and minimum and maximum sample values were calculated for quantitative analysis. Ordinal scaled variables (e.g. pain intensity) are described using median values and range. Absolute and relative frequencies are given for nominal scaled variables. Medians of normally distributed variables were compared using t-test for two independent samples. Ordinal scaled variables were compared using the Cochran-Armitage trend test. Analysis of nominal scaled variables was done using  $\chi^2$ -test or, if the criteria for this were not met, using Fisher's exact test. The values for pain intensity before and after administration of nitrous oxide were evaluated using Wilcoxon test for two related samples. Multiple logistic regression analysis was done for the primary dependent variables to analyse several potential influencing variables at the same time. Results were considered significant if p < 0.05.

#### **Results**



A total of 66 pregnant women were included in the study. The demographic data and birth parameters are given in • Table 1.

#### Why and when was inhaled analgesia used?

Inhaled nitrous oxide and oxygen was usually administered because the patient refused an EPA (n = 39, 59%). In 15 cases (23%), it was not possible to place the epidural, and in 5 cases (8%) the existing epidural analgesia was insufficient. There were various other reasons for the remaining 7 women (11%) or reasons were not specified.

Inhaled analgesia most commonly used during the dilation stage (n = 51, 77%), followed by the expulsion stage (n = 34, 52%) and the bearing-down stage (n = 33, 33%). Some of the women only used inhaled nitrous oxide and oxygen during the 1st stage

Questions put to the patient	Questions put to the midwife	
Pain prior to inhaled nitrous oxide and oxygen	How satisfied was the midwife with the effect of inhaled nitrous oxide and oxygen?	
(worst)	,,,	
1 2 3 4 5 6 7 8 9 10	not at all	
Pain after/with inhaled nitrous oxide and oxygen	not much	
(worst)	moderately	
1 2 3 4 5 6 7 8 9 10	quite	
Did the patient tolerate inhaled nitrous oxide and oxygen?	very	
poorly	When was inhaled nitrous oxide and oxygen used?	
a little	dilation stage	
moderately well	<ul><li>expulsion stage</li><li>bearing-down stage</li></ul>	
well	Why was inhaled nitrous oxide and oxygen used?	
very well	one EPA possible	
Did the patient experience any side effects?	refused EPA	
no	EPA insufficient	
yes	other reasons	
If yes, what were they?	other reasons	
How likely is it that the patient would use inhaled nitrous oxide and oxygen again?		
absolutely not		
a little	_	
omoderately likely		
o quite likely		
very likely		

**Table 1** Demographic data for the study cohort and their birth parameters.

	Study cohort (range) (n = 66)	
Age	30.6 ± 4.9 (22–43)	
Body Mass Index	23.7 ± 4.8 (18.0–39.6)	
Pregnancy	median: 2.0 (1–6)	
Parity (excluding the birth in this study)	median: 0 (0–3)	
Gestational age (in days)	279.5 ± 9.5 (238–291)	
Birth weight	3 473.2 ± 523.7 (2 980–4 950)	
Type of birth, n (%)	· ·	
Spontaneous delivery	53 (80%)	
Surgical vaginal delivery	7 (11%)	
Caesarean section	6 (9%)	
pH, arterial cord blood	7.27 ± 0.08 (7.12–7.51)	
pH < 7.10 (n, %)	0	
BE, arterial cord blood	-5.13 ± 2.95 (-12.9 - + 0.1)	
BE < -12 (n, %)	1 (2%)	
5-minute Apgar score	median: 10 (7-10)	
5-minute Apgar score < 7 (n, %)	0	
Pathological CTG (n, %)	14 (21%)	
Foetal blood analysis (n, %)	3 (5%)	
Meconium-stained amniotic fluid (n, %)	4 (6%)	
Transfer to a neonatal intensive care unit (n, %)	9 (14%)	

(n = 39, 59%), while others used it in the 2nd stage (n = 13, 20%)or in all 3 stages (n = 14, 21%); none of the stages were skipped.

# Pain reduction with inhaled nitrous oxide and oxygen

The pain intensity prior to receiving inhaled analgesia was reported as between 5-10 on the NRS (median 9). There was a significant reduction in the intensity of the pain after administration of the nitrous oxide ( Table 2).

# Tolerance of inhaled nitrous oxide and oxygen

Overall, inhaled analgesia was well tolerated: 54 (82%) women reported that they had tolerated the air-gas mixture "well to very well"; only 12 (18%) women described their tolerance as "poor to moderate".

 
 Table 2
 Pain experienced before and after administration of inhaled nitrous
oxide and oxygen (n = 66).

	Before	After	p-value
Pain	median: 9 (5-10)	median: 5 (1-10)	p < 0.0001

**Table 3** Results of the survey depending on whether the patients would be prepared to use inhaled nitrous oxide and oxygen again. The percentages refer to the size of the respective groups, n = 21 and n = 45.

	"absolutely not to moderately likely" to use inhaled analgesia again $n = 21 (32\%)$	"quite likely to very likely" to use inhaled analgesia again n = 45 (68%)	p-value
Inhaled nitrous oxide and oxygen was tolerated by the patient (n, %)	13 (62%)	41 (91%)	p = 0.0129
Midwife was "quite to very" satisfied with use of inhaled analgesia (n, %)	3 (14%)	43 (96%)	p<0.0001
No side effects (n, %)	8 (38%)	15 (33%)	p = 0.7053
When was used inhaled nitrous oxide and oxygen			
▶ dilation stage	19 (90%)	32 (71%)	p = 0.1166
expulsion stage	4 (19%)	30 (67%)	p = 0.0003
▶ bearing-down stage	1 (5%)	21 (47%)	p = 0.0008
Why was used inhaled nitrous oxide and oxygen			
▶ no EPA possible	3 (14%)	12 (27%)	p = 0.6475
▶ refused EPA	13 (62%)	26 (58%)	
► EPA inadequate	2 (10%)	3 (7%)	
► Other reasons	3 (14%)	4 (9%)	
Age (mean ± standard deviation; minimum – maximum)	31.6 ± 5.0 (22–43)	28.7 ± 4.3 (22–38)	p = 0.0253

The possible answers "poorly", "a little", "moderately", "well" and "very well" were summarised as "poorly to moderately" and "well to very well".

Reported side effects included dizziness (n = 8), nausea (n = 5), raspy/dry throat (n = 3), vomiting and "feeling woozy" (2 women, respectively) as well as feelings of euphoria and powerlessness; one of the women did not provide any details. The majority of women reported no side effects (n = 43, 65%).

# Likelihood of using inhaled nitrous oxide and oxygen again

Most of the women reported that it was "quite to very" likely that they would use inhaled analgesia again (n = 45, 68%).

To analyse the factors which could affect the probability of the patient using inhaled analgesia again, the group of pregnant women who had assessed their likelihood of using it again as "absolutely not to moderately likely" was compared to the other group ("quite to very" likely) (> Table 3). The probability that they would use nitrous oxide and oxygen again was higher if the patient had tolerated the drug well (p = 0.0129). Women who used inhaled analgesia in the expulsion stage or the bearingdown stage were also very likely to use the drug again (p = 0.0003 and p = 0.0008, respectively). The incidence of side effects was approximately the same in both groups (p = 0.7053). The midwives' satisfaction depended on how inhaled analgesia was accepted by the women; 96% of midwives were satisfied with its administration if their patients considered it "quite to very" likely that they would use inhaled nitrous oxide and oxygen again. Women who were likely to use the drug again were older on average (31.6  $\pm$  5.0 years vs. 28.7  $\pm$  4.3 years; p = 0.0253). Logistic regression analysis (which took account of patient-specific variables) showed that the variable "Use of inhaled nitrous oxide and oxygen in the bearing-down stage" (p = 0.0140), how well the patient tolerated the drug (p = 0.0241) and women's age (p = 0.0289) were the most important factors which influenced the likelihood that they would use inhaled analgesia again.

#### **Discussion**



The safety of mother and child is the highest priority in obstetrics – and this includes an optimal birth experience. In addition to other factors, adequate pain management has a significant im-

pact on the birth experience. Nitrous oxide is used all over the world in many different settings because it can be controlled extremely well and is easy to use, also in paediatrics [7]. In many countries nitrous oxide is part of clinical routine in obstetrics; however, in Germany it has not yet gained widespread acceptance. Inhaled nitrous oxide and oxygen was introduced as an analgesia on our labour wards; this observational study shows that the nitrous oxide mixture was accepted very well both by the midwives and the women in labour. The drug was tolerated well and its side effects were tolerable. We recorded no serious complications.

While the satisfaction of patients and their midwives with pain relief during nitrous oxide and oxygen administration has been proven in international studies [11–14], there is currently no data available on this for Germany. This is the first German study which has prospectively investigated the satisfaction of patients and their midwives with inhaled analgesia. The case numbers in this study are not very high, and this should prompt obstetricians to include nitrous oxide in their repertoire as an additional option for analgesia and to carry out further studies. Nevertheless, we could show that the willingness to use inhaled nitrous oxide and oxygen again was correlated with how well the patient tolerated the drug, the satisfaction of the patient's midwife and the stages of labour in which it was administered.

Epidural anaesthesia continues to be the gold standard, but often it is not possible to use this method [15]; this can sometimes result in a bad birth experience and even the necessity to convert a vaginal delivery to a caesarean section. In addition, some women are critical of EPA; in our study a significant number of pregnant women refused spinal analgesia. Fear of complications is the primary reason why pregnant women refuse EPA [16].

The use of nitrous oxide is an effective alternative option [5,8]. The pain relief obtained during delivery with nitrous oxide was confirmed in a Cochrane analysis carried out in 2012 [8]. Our study also showed that the perception of pain was significantly lower after the administration of inhaled nitrous oxide and oxygen.

Analgesia with nitrous oxide is considered safe [8,17] and can be safely administered by non-medical staff [17]. The most common side effects are of a neurological (e.g. dizziness) and gastrointes-

tinal nature (e.g. nausea and vomiting). In accordance with the literature, the most common side effects found in our study cohort were dizziness, nausea and vomiting [5,7–9,17]. But these acute side effects are reversible. The potential sequelae are controversially discussed, but high-dose administration of inhaled nitrous oxide and oxygen for less than six hours is harmless [18, 19].

There were no suspicious outcome parameters in our study (rate of secondary caesarean sections 9%; no arterial cord blood pH < 7.10; no 5-minute Apgar score < 7). This is in accordance with the results of the most recent literature, where nitrous oxide was not found to affect the course of the birth [8].

Valid information on the satisfaction with nitrous oxide are limited. In particular, the impact on the experience of the birth has not been investigated much [8]. Our study showed that patients tolerated inhaled nitrous oxide and oxygen well and would be prepared to use it again in a subsequent pregnancy. The midwives were also satisfied with the effect of the nitrous oxide.

Use of a nitrous oxide mixture represents an additional asset for pain management. Inhaled nitrous oxide and oxygen was very effective, particularly in the expulsion and bearing-down stages. Nitrous oxide can therefore be considered as an additional option to supplement existing methods such as EPA. In addition to using nitrous oxide for analgesia during labour, it can also be used successfully when treating birth-related injuries [17,19,20] – and in this context it offers additional scope for treatment in clinical practice.

### **Conclusion**



Inhaled nitrous oxide and oxygen is an effective method for pain relief during delivery; it is accepted very well by both women in labour and their midwives. This method is easy to use and is considered safe. Nitrous oxide is an important addition to other well-known methods for pain management in obstetrics and can also be used postpartum during the treatment of birth-related injuries.

#### **Conflict of Interest**



Sven Kehl: speaker's fee, travel expenses (Linde AG).

#### References

- 1 Spaich S, Welzel G, Berlit S et al. Mode of delivery and its influence on women's satisfaction with childbirth. Eur J Obstet Gynecol Reprod Biol 2013: 170: 401–406
- 2 Hodnett ED. Pain and women's satisfaction with the experience of childbirth: a systematic review. Am J Obstet Gynecol 2002; 186: S160-S172
- 3 Schwab W, Marth C, Bergant AM. Post-traumatic stress disorder post partum. Geburtsh Frauenheilk 2012; 72: 56–63
- 4 Scholz R, Voigt M, Schneider KT et al. Analysis of the German perinatal survey of the years 2007–2011 and comparison with data from 1995–1997: maternal characteristics. Geburtsh Frauenheilk 2013; 73: 1247–1251
- 5 *Jones L, Othman M, Dowswell T et al.* Pain management for women in labour: an overview of systematic reviews. Cochrane Database Syst Rev 2012; 3: CD009234
- 6 [Anonym]. Fachinformation Livopan TM, Stand Juli 2012
- 7 Staubli G. Livopan. Thieme Drug Report 2009; 5: 1-16
- 8 Klomp T, van Poppel M, Jones L et al. Inhaled analgesia for pain management in labour. Cochrane Database Syst Rev 2012; 9: CD009351
- 9 Likis FE, Andrews JC, Collins MR et al. Nitrous oxide for the management of labor pain. Rockville, MD: Agency for Healthcare Research and Quality (US); 2012
- 10 Rooks JP. Nitrous oxide for pain in labor why not in the United States? Birth 2007; 34: 3–5
- 11 Pasha H, Basirat Z, Hajahmadi M et al. Maternal expectations and experiences of labor analgesia with nitrous oxide. Iran Red Crescent Med J 2012; 14: 792–797
- 12 Rezaeipour A, Idenloo F, Khakbazan Z et al. The effects of Entonox on implication of painless labor and delivery satisfaction rate among pregnant women. Hayat 2007; 13: 45–58
- 13 Jones PL, Rosen M, Mushin WW et al. Methoxyflurane and nitrous oxide as obstetric analgesics. II. A comparison by self-administered intermittent inhalation. BMJ 1969; 3: 259–262
- 14 *Jones PL, Rosen M, Mushin WW et al.* Methoxyflurane and nitrous oxide as obstetric analgesics. I. A comparison by continuous administration. BMJ 1969; 3: 255–259
- 15 Heck M, Fresenius M. Repetitorium Anästhesiologie Für die Facharztprüfung und das Europäische Diplom. Berlin, Heidelberg: Springer; 2010
- 16 Van den Bussche E, Crombez G, Eccleston C et al. Why women prefer epidural analgesia during childbirth: the role of beliefs about epidural analgesia and pain catastrophizing. Eur J Pain 2007; 11: 275–282
- 17 Collado V, Nicolas E, Faulks D et al. A review of the safety of 50% nitrous oxide/oxygen in conscious sedation. Expert Opin Drug Saf 2007; 6: 559–571
- 18 Weimann J. Toxicity of nitrous oxide. Best Pract Res Clin Anaesthesiol 2003; 17: 47–61
- 19 Rosen MA. Nitrous oxide for relief of labor pain: a systematic review. Am J Obstet Gynecol 2002; 186: S110–S126
- 20 Berlit S, Tuschy B, Brade J et al. Effectiveness of nitrous oxide for postpartum perineal repair: a randomised controlled trial. Eur J Obstet Gynecol Reprod Biol 2013; DOI: 10.1016/j.ejogrb.2013.06.025