Nitrous Oxide During Labor: Maternal Satisfaction Does Not Depend Exclusively on Analgesic Effectiveness

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BACKGROUND: Evidence on the analgesic effectiveness of nitrous oxide for labor pain is limited. Even fewer studies have looked at patient satisfaction. Although nitrous oxide appears less effective than neuraxial analgesia, it is unclear whether labor analgesic effectiveness is the most important factor in patient satisfaction. We sought to compare the relationship between analgesic effectiveness and patient satisfaction with analgesia in women who delivered vaginally using nitrous oxide, neuraxial analgesia (epidural or combined spinal-epidural [CSE]), or both (neuraxial after a trial of nitrous oxide).
METHODS: A standardized survey was recorded on the first postpartum day for all women who received anesthetic care for labor and delivery. Data were queried for women who delivered vaginally with nitrous oxide and/or neuraxial labor analgesia over a 34-month period in 2011 to 2014. Parturients with complete data for analgesia quality and patient satisfaction were included. Analgesia and satisfaction scores were grouped into 8 to 10 high, 5 to 7 intermediate, and 0 to 4 low. These scores were compared with the use of ordinal logistic regression across 3 groups: nitrous oxide alone, epidural or CSE alone, or nitrous oxide followed by neuraxial (epidural or CSE) analgesia.
RESULTS: A total of 6507 women received anesthesia care and delivered vaginally. Complete data were available for 6242 (96%) women; 5261 (81%) chose neuraxial analgesia and 1246 (19%) chose nitrous oxide. Of the latter, 753 (60%) went on to deliver with nitrous oxide alone, and 493 (40%) switched to neuraxial analgesia. Most parturients who received neuraxial analgesia (>90%) reported high analgesic effectiveness. Those who used nitrous oxide alone experienced variable analgesic effectiveness, with only one-half reporting high effectiveness. Among all women who reported poor analgesia effectiveness (0–4; n = 257), those who received nitrous oxide alone were more likely to report high satisfaction (8–10) than women who received epidural analgesia alone (OR 2.5; 95% CI 1.4–4.5; $P = .002$). Women who reported moderate analgesia (5–7) and received nitrous oxide only were more likely to report high satisfaction compared with the other groups. Among women who reported a high level of analgesic effectiveness, satisfaction with anesthesia was high and not different among groups.
CONCLUSIONS: Patients who received nitrous oxide alone were as likely to express satisfaction with anesthesia care as those who received neuraxial analgesia, even though they were less likely to report excellent analgesia. Although pain relief contributes to the satisfaction with labor analgesia care, our results suggest that analgesia is not the only contributor to maternal satisfaction. (Anesth Analg 2017;124:548–53)

Evidence regarding analgesic effectiveness of nitrous oxide for labor pain is limited. Two systematic reviews,[1,2] which included a total of 14 studies published from 1961 to 2007, deemed the trials insufficient to draw conclusions concerning analgesic effectiveness, citing unsatisfactory study design and variations in methodology. Most of the studies included subsets of women who chose nitrous oxide and appeared to experience benefit, with some reporting significant analgesic effectiveness and many stating that they would choose it again for a future delivery. Likewise, few studies have examined patient satisfaction with nitrous oxide during labor, and it is unclear whether labor analgesic effectiveness is the most important dimension influencing a parturient's satisfaction with analgesic modality during her labor and birth experience.[2–5]

The 2014 review by Likis et al[2] identified only 3 randomized trials assessing patient satisfaction, but all were performed by the same investigators, who compared the effects of nitrous oxide with subanesthetic concentrations of volatile anesthetic drugs.[6–8] Study design prevents drawing meaningful conclusions—an anesthesiologist administered inhaled agents continuously using an anesthesia machine, briefly, only for delivery, and half of the parturients in 2 studies received various other analgesics,[6,7] whereas subjects in the third study received no analgesia during the first stage.[8] Four of 6 nonrandomized cohort[9–11] and survey[12–14] studies included in the same review were deemed of poor quality.[2] In those comparing nitrous oxide and epidural analgesia, women selecting the latter more commonly reported greater satisfaction, consistent with greater reported effectiveness.[9–11,13] In a large cross-sectional survey

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study, nitrous oxide was an independent predictor of lower maternal satisfaction.[12]

Beginning in June 2011, the anesthesiology department at Vanderbilt University Medical Center has offered the option of self-administered 50% nitrous oxide in 50% oxygen (Porter Nitronox, Porter Instrument, Parker Hannifin, Hatfield, PA) to all laboring parturients.[a] We routinely survey patient's pain relief and overall satisfaction with labor analgesia when performing postpartum postanesthesia assessments. We analyzed these prospectively gathered data obtained during a 34-month period (June 2011 to March 2014) to compare parturient-reported analgesic effectiveness and overall analgesic satisfaction among women who delivered vaginally using nitrous oxide, neuraxial (epidural or combined spinal-epidural), or both (neuraxial after a trial of nitrous oxide) to test the hypothesis that maternal satisfaction with analgesic care depends on effectiveness of labor analgesia.

METHODS

A standardized survey is used during the follow-up visit with all parturients who have received intrapartum anesthetic care at Vanderbilt University Medical Center. The visits are conducted by anesthesiology staff on the first postpartum day for all women who have delivered between midnight and midnight on the previous day. Patient identifiers, date and time of delivery and of follow up, obstetric procedure(s), and anesthetic technique(s) are recorded. Patients are asked about neuraxial block placement problems, problems during vaginal delivery, and side effects. They are asked specifically about headache, back pain, nausea, and itching. They use a 0- to 10-point scale to rate the effectiveness of their labor pain relief, and they also use a 0- to 10-point scale to rate their overall satisfaction with analgesia care. Finally, they are asked to provide any additional clarifying comments.

Each patient's responses are entered into her medical record and into a secure database for quality improvement purposes. We queried and evaluated the quality improvement database for all parturients who received nitrous oxide and/or neuraxial analgesia for labor and who subsequently delivered vaginally during a 34-month period, from June 1, 2011 (the date nitrous oxide labor analgesia was first offered), to March 31, 2014 (after which postdelivery quality data were no longer systematically collected in a readily accessible database). Parturients whose medical records included both analgesia quality and patient satisfaction scores were included. The study protocol was reviewed by Vanderbilt University institutional review board. Because the purpose of this project was to compare relative benefits of nitrous oxide analgesia and those of neuraxial analgesia alone to improve the quality of care, the requirement for written informed consent was waived by the institutional review board

Statistical Analysis

Patients were assigned to 3 study groups according to their labor analgesic choices—nitrous oxide alone, neuraxial (epidural or combined spinal-epidural) analgesia alone, and nitrous oxide followed by neuraxial analgesia. Analgesic effectiveness and satisfaction scores, the 2 primary outcomes for the study, were grouped a priori into 3 groups: 8 to 10 high, 5 to 7 intermediate, and 0 to 4 low. Analgesic effectiveness scores were compared among labor analgesia groups with the use of unadjusted proportional odds logistic regression. Anesthesia care satisfaction scores were compared among groups via the use of a similar technique, with adjustment for the level of analgesic effectiveness. The Wald method was used to compute 95% confidence intervals and statistical hypothesis tests. A P value of .05 was considered statistically significant. No a priori sample size or power analysis was performed. We analyzed every datum available to us, from the beginning of data collection to the last collected into database 34 months later. This manuscript adheres to the applicable Equator guidelines.

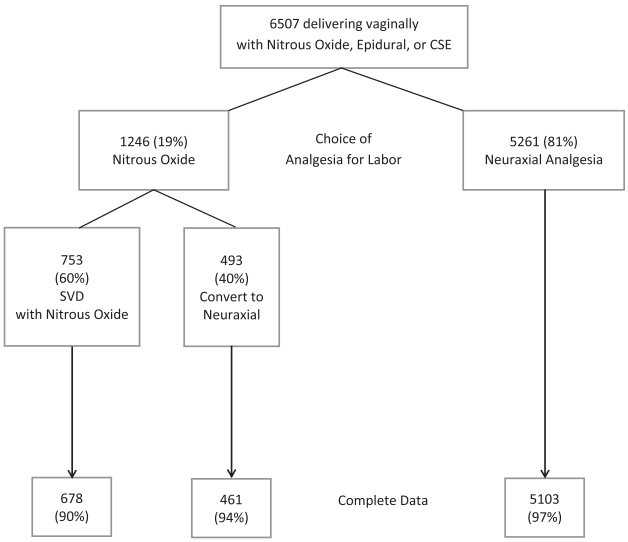

Figure 1. Patients included in the study analysis, and study group assignments. CSE indicates combined spinal epidural; SVD, spontaneous vaginal delivery.

RESULTS

Assignment to study groups is presented in Figure 1.[b] Among laboring women who ultimately delivered vaginally, 19% initially chose nitrous oxide analgesia. Of these, 40% subsequently converted to neuraxial analgesia. This compares to a 63% conversion rate for women who ultimately delivered by cesarean (data not shown). Parturients receiving neuraxial analgesia, whether as the sole modality or after a trial of nitrous oxide analgesia, rated analgesic effectiveness uniformly as high (>90%), whereas those who used nitrous oxide alone reported variable analgesic effectiveness (Figure 2). The median (interquartile range) analgesic effectiveness scores were 10 (9–10) for both neuraxial groups and 8 (5–10) for the nitrous oxide alone group. These findings were supported by ordinal logistic regression analysis. Specifically, among those who received nitrous oxide alone, the odds of high analgesic effectiveness (8–10) were 90% less (odds ratio [OR] 0.10; 95% confidence

[a]Per institution policy, nitrous oxide is not administered to parturients who received parenteral opioids during the 2 hours before the request for nitrous oxide.

[b]Excluded from analysis were 3831 women who underwent cesarean delivery during the study period and 1082 parturients who delivered vaginally without nitrous or neuraxial analgesia. Nurse-administered parenteral opioids are not administered during active labor, and patient-controlled intravenous opioids are not offered on our unit.

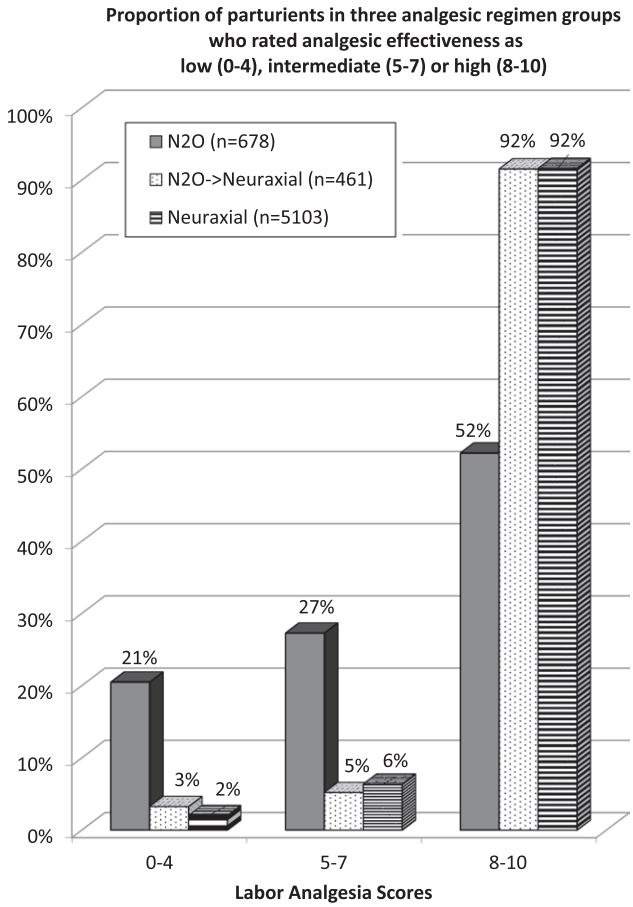

Figure 2. Proportion of parturients in 3 analgesic regimen groups who rated their analgesic effectiveness as low (0–4), intermediate (5–7), or high (8–10). Analgesia effectiveness was variable among women who received nitrous oxide alone but uniformly high among those who received neuraxial analgesia.

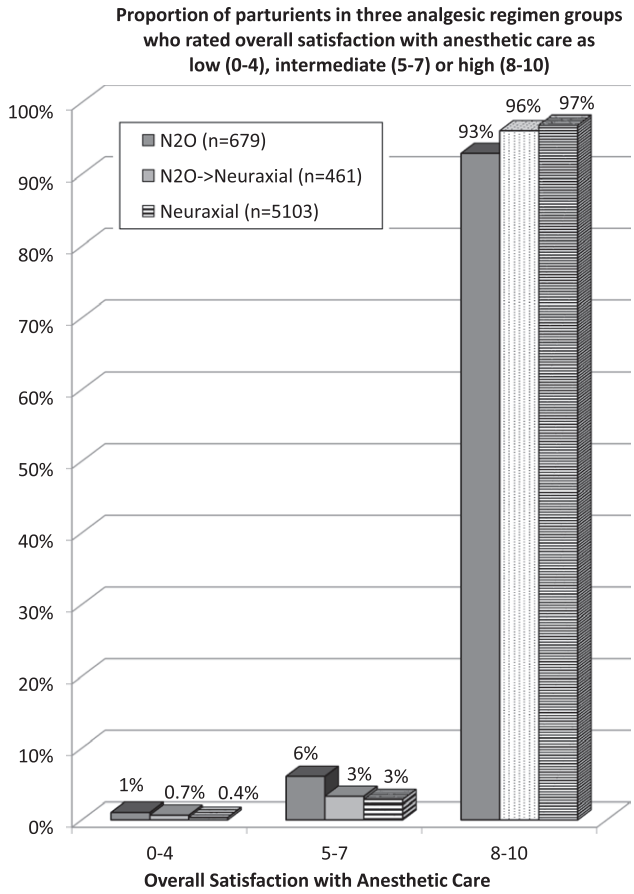

Figure 3. Proportion of parturients in 3 analgesic regimen groups who rated overall satisfaction with analgesia care as low (0–4), intermediate (5–7), or high (8–10). Satisfaction was uniformly high, despite variable analgesia effectiveness among women who received nitrous oxide alone.

interval [CI] 0.08–0.12; $P < .001$) than those who received neuraxial analgesia. There was no evidence that the effectiveness of the analgesic differed significantly across neuraxial anesthesia groups ($P = .13$).

Despite variability in the effectiveness of the analgesic, overall analgesia satisfaction scores were uniformly high (Figure 3). For all 3 groups, the median (interquartile range) satisfaction score was 10 (10–10). This finding was, again, corroborated by ordinal logistic regression analysis. Specifically, among parturients who reported poor analgesia effectiveness (0–4; n = 257), those who received nitrous oxide as the sole analgesic modality were more likely to report high overall satisfaction than those who received neuraxial analgesia alone (OR 2.5; 95% CI 1.4–4.6; $P = .002$). There was insufficient evidence to draw a similar conclusion for those who received nitrous oxide alone versus neuraxial analgesia after nitrous oxide (OR 1.6; 95% CI: 0.5–5.4; $P = .46$). Among women who reported moderate analgesia effectiveness (5–7; n = 536), however, those who received nitrous oxide alone reported high satisfaction more often than women in either neuraxial analgesia group (neuraxial only: OR 2.2; 95% CI 1.3–3.8; $P = .005$ and neuraxial analgesia after nitrous oxide: OR 4.4; 95% CI 1.65–11.6; $P = .003$). Among women who reported a high level of analgesia effectiveness, there was uniformly high satisfaction with anesthesia care, and thus no evidence of significant differences among groups. There was no evidence that women who chose neuraxial analgesia differed from those who converted to neuraxial analgesia after a trial of nitrous oxide, with regard to analgesia effectiveness or overall satisfaction.

DISCUSSION

This was a retrospective analysis of prospectively gathered patient-reported rating scores for analgesic effectiveness and overall satisfaction with analgesic care. Unlike a randomized trial, group assignment was determined by each parturient's choice of labor analgesic modality, not only initially, but through delivery. On a labor and delivery unit where nitrous oxide routinely is offered among other labor analgesic modalities, all of which are presented and discussed at the time of admission, 1 in 5 women who requested labor analgesia, and who ultimately delivered vaginally, initially chose nitrous oxide. Of these, 60% (753 of 1246) went on to deliver with nitrous oxide alone, the remainder switching to neuraxial analgesia. We introduced a nitrous oxide program in mid-2011 to meet a perceived need for systemic analgesic alternatives to neuraxial analgesia among a subset of women who desired a less invasive

modality.[3,15] The proportion of women who chose nitrous oxide remained stable over nearly 3 years, suggesting that nitrous oxide meets the pain relief needs of a subset of laboring women in this tertiary North American medical center.

Nitrous Oxide: Variable Analgesic Effectiveness

Not unexpectedly, nitrous oxide was less effective in alleviating labor pain than neuraxial modalities, the latter of which most parturients (92%) reported as very effective (scores 8–10). This finding is consistent with studies that compared analgesic effectiveness between nitrous oxide and neuraxial modalities.[9,16] In a postpartum survey study of 2482 parturients, 80% rated epidural analgesia as very effective, compared with 44% among those who were using nitrous oxide.[16] Of note, effectiveness scores reported by women in our study who delivered solely with nitrous oxide were more heterogeneous compared with those reported by the neuraxial groups. One-half of those who delivered while receiving nitrous oxide reported high analgesic effectiveness scores, the remainder split between intermediate (27%) and low (21%) scores.

Similar heterogeneity of nitrous oxide analgesic effectiveness has been observed in several nonrandomized observational studies.[6–9,14–18] In a study of 833 Finnish parturients, epidural analgesia was superior to nitrous oxide during the first stage of labor (pre- versus postintervention pain scores). On the third postpartum day, 94% of women receiving epidural analgesia reported good analgesic adequacy, 6% moderate, and 0% poor. In contrast, only 33% of women receiving nitrous oxide reported analgesia as good, 39% as moderate, and 28% as poor.[9] In an additional study of 663 women who delivered vaginally with nitrous oxide, meperidine, or both, 31% of those who received nitrous oxide alone (n = 130) reported no pain relief, 18% slight, 47% satisfactory, and 4% complete analgesia.[14] Dammer et al[15] studied 60 women who chose nitrous oxide after implementation of an inhalation analgesia program in a German hospital. Median pain scores ranged from extremely low to extremely high, and two-thirds of women reported being likely to use nitrous oxide again for labor.[15] Other randomized trials the compared the effects of nitrous oxide with those of subanesthetic concentrations of volatile agents also reported heterogeneity in analgesic effectiveness.[6–8,17,18] Factors predictive of nitrous oxide analgesic effectiveness have yet to be reported.

Of note, parturients in our study who opted for neuraxial analgesia after a trial of nitrous oxide reported labor analgesic effectiveness similar to those who chose neuraxial analgesia without a trial of nitrous oxide. Effectiveness scores were solicited from parturients on the first postpartum day, and our database did not separate scores they might assign to the nitrous oxide trial before receiving neuraxial analgesia. However, insufficient analgesia is the most common, albeit not sole, reason for switching. Some women switch because of unpleasant side effects of nitrous oxide (dysphoria, sedation, dizziness, nausea). Furthermore, the rate of conversion from nitrous oxide to neuraxial analgesia among laboring women who went on to deliver by cesarean (not included in analysis) was 62.5%, compared with 40% among nitrous oxide users who delivered vaginally. Thus, although not proven, limiting our analysis to women who deliver vaginally likely underestimates the proportion of women using nitrous oxide who experience poor analgesic effectiveness.

Nitrous Oxide: High Satisfaction, Regardless of Analgesic Effectiveness

Although nearly half of the women in our study who delivered with nitrous oxide analgesia alone reported low or intermediate analgesic effectiveness, satisfaction scores were uniformly high in this group, with only a minority (48, or 7%) reporting a satisfaction score <8. These women were as likely to express high satisfaction with anesthesia care as those who received neuraxial analgesia. Of note, they also made the choice to continue with nitrous oxide, despite the availability of neuraxial modalities on demand. Such paradoxical findings have not been reported previously.

In an observational study at a Malaysian University Center, 123 healthy women in early labor were offered epidural analgesia.[11] Those who declined (n = 68) received scheduled meperidine and self-administered 50% nitrous oxide. More women in the epidural group (69%) were satisfied with their choice and would choose it again compared with the meperidine/nitrous oxide group (35%). Dissatisfaction with pain relief was reported by 3 (5.5%) and 31 (45.6%), respectively. Analgesic effectiveness and satisfaction were not compared directly, and it is unclear whether women using nitrous oxide were allowed to subsequently switch to epidural analgesia.

Of 278 Swedish parturients (48% nullipara) experiencing labor who were surveyed 4 hours to 7 days postpartum, most reported experiencing severe pain and underestimated the intensity of labor pain.[19] Most (219, or 79%) received nitrous oxide labor analgesia, whereas fewer (95, or 34%) received epidural analgesia. Satisfaction was not measured; however, when considering a future birth, more women reported wishing to have epidural analgesia, and fewer nitrous oxide.[19] The same investigators conducted a 2-month postpartum, in-depth written survey of 1111 parturients, including the examination of hospital delivery data, to identify factors that predicted a negative overall birth experience. Nitrous oxide analgesia was an independent predictor of a less positive birth experience (OR 0.52; 95% CI 0.38–0.72), as were labor augmentation, instrumental vaginal delivery, cesarean delivery, and nulliparity. Yet, mothers in this study continued to labor using nitrous oxide, declining available neuraxial modalities.[12]

What Matters? Analgesia, Other Factors, or Both?

Pain relief clearly contributes to the satisfaction with labor analgesic care, especially with neuraxial modalities[4,9–11,13,20,21]; however, our results, and those of others[4,21–25] suggest that satisfaction with labor analgesia is not determined solely by analgesic effectiveness. In a study of women with a priori plans to use labor epidural analgesia, effective analgesia, and timely access to it, emerged as central to the birth experience, important in regaining self-control and the ability to focus, think, and participate in the birth.[4] Women identified other important factors, such as preservation of bodily sensations of labor, mobility, and strength.[4] A systematic review of reports investigating factors influencing parturients' satisfaction with childbirth experiences, identified personal expectations,

caregiver support, quality of the relationship with her caregiver, and involvement in decision making.[22] In a survey study of more than 700 European women, prelabor expectations of severe pain, experienced pain greater than expectations, and drug use (nitrous oxide, 69%; meperidine, 53%; epidural, 10%) associated with lower overall birth experience satisfaction, but independent predictive factors were not analyzed.[26] Finally, a qualitative analysis of 2005 national survey data from 1573 US parturients identified the importance of timely and effective neuraxial analgesia for those who requested it, but analgesia was only one among many other factors identified by women who were asked open-ended questions about the best and worst aspects of their birth experience.[25]

Challenges in measuring maternal satisfaction, and the paucity of standard assessment tools or validity evidence, are limitations of our and most studies to date.[27] Nonetheless, the high satisfaction reported by women who delivered with nitrous oxide alone, regardless of reported analgesic effectiveness, is striking, especially when contrasted with neuraxial groups. The unexpected high satisfaction scores may be explained by maternal expectations regarding pain relief and the relative importance they assign to it. Women who request neuraxial analgesia have high expectations regarding the analgesic effectiveness of this choice.[4,20,21] The subset of women who choose neuraxial analgesia initially but experience ineffective analgesia report low satisfaction. In contrast, women who choose to use nitrous oxide, and continue on to deliver with it despite ready availability of neuraxial analgesia, may have lesser expectations regarding analgesic effectiveness, or they may simply place greater value on non-pain-related factors. Parturients who convert from nitrous oxide to neuraxial analgesia, typically because of inadequate analgesia or side effects, also reported high levels of satisfaction. If the level of analgesic effectiveness from nitrous oxide reaches a threshold of unacceptability, the ability to choose readily available and effective neuraxial analgesia likely accounts for the observed high overall satisfaction.[4,25]

In summary, under the conditions of the present study, and in our practice and patient population, nitrous oxide was less effective in treating labor pain than neuraxial analgesic modalities. Six in 10 parturients who chose nitrous oxide for labor and who delivered vaginally did so with nitrous oxide alone, despite the availability of neuraxial analgesia. These women reported high levels of satisfaction, despite variable labor analgesic effectiveness. Nitrous oxide, offered in addition to neuraxial labor analgesia, consistently has served the needs and preferences of a small subset of parturients at this high-risk academic center.

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DISCLOSURES

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