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CASE REPORT

A Case Report on the Anxiolytic Properties of Nitrous Oxide during Labor

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ABSTRACT

Widely used in Europe as a labor analgesic, nitrous oxide (N2O) is making a dramatic return in the United States. Valued for its analgesic properties, N2O also has anxiolytic characteristics. Fear and anxiety in childbirth have been associated with various negative effects, and N2O may have the potential to lessen these effects for some women. Women in the United States should have the option of using N2O during labor.

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Nitrous oxide (N2O) has analgesic and anxiolytic properties (Poorsattar, 2010). In countries such as Norway, New Zealand, Sweden, Australia, and England, usage rates of inhalational N2O during parturition reach are as great as 70% (Likis et al., 2012; Starr & Baysinger, 2013). Though widely used in Europe for more than 100 years, N2O has only recently become an option in the United States. As the moderator of the N2ODuringLabor listerv, I polled members at the time of this publication and found that only 38 hospitals and approximately 28 birth centers in the United States are either currently offering or working on plans to implement N2O as an analgesic option. In 2010, the American College of Nurse-Midwives (ACNM) published a position statement that supported the widespread access of N2O for women in the United States and cited the fact that women in the United States have fewer choices for pain relief than women in other countries (American College of Nurse-Midwives, 2010). The key points of the ACNM statement include the following: a) women have the right to have access to all safe options for pain relief in labor and birth, b) research does support the safety and efficacy of N2O use in labor and birth, c) midwives should play a role in the administration of N2O, d) women should receive education about this viable option for pain relief, and e) where N2O is being used, there should be accompanying research and ongoing evaluation to add to the existing body of knowledge. Neither the American College of Obstetricians and Gynecologists (The College) nor the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) has issued opinion or policy statements on the use of N2O for labor analgesia.

Nitrous oxide was first produced by the English scholar, minister, and scientist Joseph Priestley in 1772 (Riegels & Richards, 2011). Stanislav Klikovich of Poland used it as a labor analgesic in 1881 (Richards, Parbrook, & Wilson, 1976). When used for analgesia during labor, N2O is blended by a specialty Food and Drug Administration (FDA) approved apparatus at a 50/50 blend of N2O and oxygen (Collins, Starr, Bishop, & Baysinger, 2012). The woman controls her intake of the gas with her respiratory efforts by inhaling through a mask containing a demand valve that releases the gas only when the individual inhales". N2O may be used throughout all stages of labor. Alternatively, it may be initiated for second stage pushing or laceration repair after an unmedicated birth; for bedside procedures such as insertion of an intracervical foley

In multiple countries outside of the United States, women are offered the use of nitrous oxide for pain relief in labor.

bulb, or intravenous (IV) line; during manual removal of the placenta; or during placement of an epidural catheter (Stewart & Collins, 2012).

The exact mechanism of how analgesia or anesthesia from N2O is obtained is not fully understood (Schallner & Goebel, 2013). The prevailing theory for the anesthetic action of N2O is inhibition of excitatory glutamatergic neurotransmission via noncompetitive inhibition of the N-Methyl-D-aspartic acid (NMDA) subtype of glutamate receptors (Sanders, Weimann, & Maze, 2008). Ohashi, Guo, Orii, Maze, and Fujinaga (2003) suggested that the mechanism of N2O may be via stimulation of endogenous opioid release. They purported that nitrous exerts its analgesic effect by prompting opioid peptide release in the brain stem, which then stimulates the descending noradrenergic inhibitory neurons, moderating the processing of pain impulses in the spinal cord. The exact nerve pathways utilized in this process have not been clearly identified. Gillman and collegues noted increased prolactin levels and decreased cortisol levels among male participants who were administered N2O (Gillman, Katzeff, Vermaak, Becker, & Susani, 1988). The anxiolytic effect may be of significant use to laboring women, particularly in the transition stage of labor when self doubt, trepidation over one's ability to complete the birth, and decreased ability to cope can occur.

Literature Review

In a recent Cochrane review of 26 studies involving 2959 women, authors noted that inhaled analgesia appears to be effective as a labor analgesic without increasing women's risk for operative delivery or causing adverse neonatal effects (Klomp et al., 2012). No information regarding the women's sense of control in labor while using N2O or satisfaction with the childbirth experience was included; thus, further research on these two issues was suggested (Klomp et al., 2012).

In a 2012 Agency for Healthcare Research and Quality (AHRQ) review on N2O use for labor analgesia, the authors noted that in comparison to epidural analgesia, N2O is less costly and less invasive (Likis et al., 2012). Epidural analgesia has greater efficacy than N2O, and N2O appears to have greater efficacy than systemically administered opioids (Rosen, 2002). N2O offers enough relief to satisfy most women who attempt its use (Rooks, 2007).

Other benefits of N2O include a swift onset of action (within 1–2 minutes) and offset of action (within 1–2 breaths) (Akerman & Dresner, 2009). Additionally, if women find that they do not like N2O once they begin using it, it is easy to cease use and choose an alternative method of pain relief. This is a clear advantage over other pain relief methods in labor that are not as easily changed without a waiting period. Further, with regional anesthesia in particular, a woman's labor and birth positions are limited due to decreased limb strength and concern for dislodgement of anesthesia catheters. Women using N2O maintain a greater degree of mobility and freedom of movement (Stewart & Collins, 2012). Lastly, one of the most important features separating N2O from other alternatives is that it is self-administered (Likis et al., 2012). The degree of empowerment associated with the self-administration is one factor that may be important in promoting and enhancing women's satisfaction.

Although there is a paucity of literature documenting the anxiolytic benefit of N2O in the labor setting, N2O has long been useful in dental care for its analgesic and anxiolytic benefits (Poorsattar, 2010). Numerous researchers have demonstrated the positve anxiolytic effect in adult and pediatric populations (Adams, Eberhard-Gran, & Eskild, 2012; Bar-Meir et al., 2006; Bessière, Laboureyras, Ben Boujema, Laulin, & Simonnet, 2012; Byrne, Hauck, Fisher, Bayes, & Schutze, 2013; Chan, Wan, Gin, Leslie, & Myles, 2011; Ekbom, Jakobsson, & Marcus, 2005; Gillman et al., 1988; Lowe, 2007; Luhmann, Kennedy, Porter, Miller, & Jaffe, 2001; Nilsson, Bondas, & Lundgren, 2010; Rouhe, Salmela-Aro, Halmesmaki, & Saisto, 2009). In a prospective study, Ekbom et al. (2005) compared topical anesthetic cream to N2O prior to IV cannulation among children aged 6–18 years who had a history of difficulty with IV cannulation, were extremely anxious, or were required to undergo repetitive procedures. They noted that among children with a history of difficult IV cannulation and those who were undergoing repetitive procedures, the use of N2O was significantly associated with an overall decrease in the time required to gain IV access and fewer cannulation attempts. Higher satisfaction scores were also noted among the children, parents, and the nurses attempting cannulation. Similar positive effects of

N2O in pediatric populations have been noted in studies by Bar-Meir et al. (2006) and Luhmann et al. (2001). In an interesting study by Bessière et al. (2012), a single dose of 50% N2O was effective in negating the effect of fentanyl-induced anxiety-like behavior in adults. The agent has therefore been postulated to be effective for the treatment of post-opioid syndrome, with its accompanying hypersensitivity to pain and anxiety (Chan et al., 2011).

Administration of N2O is not complicated. The woman should meet unit-based specific criteria for use, provide informed consent (which may be verbal or written), and be shown how to use the apparatus. At my institution, contraindications include inability to hold the facemask/mouthpiece, impaired consciousness, documented vitamin B12 deficiency, or oxygen impairment.

Informed consent should be obtained prior to initiation and should include a discussion of risks and benefits to the woman and her fetus. Consent should also acknowledge that the gas may make one unsteady and that assistance should always be available in the room when the woman is out of bed when using the gas. Assistance can be provided by family/support persons; N20 use does not require constant staff presence. The most common side effects of dizziness, nausea or vomiting, and drowsiness should be noted within the consent (Likis et al., 2014). The woman should acknowledge that she alone will hold the mask to her face and will not allow anyone else to do so. Individual institutions may also choose to include that although N2O has been used as a labor analgesic for many decades, there is little high quality data on fetal safety beyond anecdotal evidence (American College of Nurse-Midwives, 2010). Women using N2O have not been shown to display hypoxia, thus oxygen saturation monitoring is not indicated (Carstoniu et al., 1994). Hospital staff are not required to be present in the room throughout the duration of the woman's use, though either a staff person or support person should be in the room when the woman desires to get out of bed in case of unsteadiness (Starr et al, 2011).

A woman using N2O should be instructed that when using the face mask, she must form an adequate seal with the mask on inhalation to allow the negative pressure valve to open and release the gas stream. She should also be instructed to exhale back into the mask so that the scavenging system may gather gaseous waste. If using the mouthpiece rather than the mask, she must close her lips snugly around the apparatus and inhale deeply to allow the negative pressure valve to open. She should likewise be instructed to exhale back into the mouthpiece. For optimal effect, women should be instructed to begin inhaling approximately 30 seconds prior to the onset of a contraction (Rosen, 2002).

The degree of empowerment associated with the self-administration of nitrous oxide is one factor that may be important in promoting and enhancing women's satisfaction.

Case

A 30-year-old gravida 3 para 2002 woman began labor at 40.6 weeks gestation. She received prenatal care at a facility in the United States. Her obstetric history included two prior spontaneous vaginal births with birth weights of 2551g and 3119g. An ultrasound for size/dates discrepancy at 37.0 weeks gestation revealed an estimated fetal weight of 3341g. Estimated fetal weight on admission was 3700g by Leopold maneuvers. Other than a positive Group B strep (GBS) culture, her pregnancy was unremarkable. The woman had used an epidural during her first birth and had an unmedicated second birth; she was currently planning an unmedicated labor and birth.

The woman began labor spontaneously at 0200 and was evaluated at the clinic at 0900, at which time her cervix was soft, anterior, 2.5 cm dilated, 75% effaced, with fetal vertex at -2 station. Contractions were mild to moderate, two to three minutes apart, lasting 60 to 90 seconds. The woman was using breathing techniques to manage some of the more strong contractions but could talk through the majority of uterine activity. She and her husband were encouraged to go to a nearby park and ambulate with instructions as to when to return to the clinic.

When the woman returned four hours later, her contractions were 3–5 minutes apart and moderate to strong. At sterile vaginal examination, she was 4 cm dilated, 80% effaced, with fetal vertex at -1 station. She was notably more uncomfortable than at the previous evaluation and was unable to talk or walk through contractions. During the period of observation, the fetal membranes spontaneously ruptured. She proceeded to the medical center for admission to begin GBS antibiotic prophylaxis. Once admitted, she was tolerating contractions very well using position changes and breathing techniques.

In the first four hours following admission, her uterine activity became irregular with a contraction frequency of 5–7 minutes and mild to moderate to palpation. A sterile vaginal examination performed four hours after admission revealed no change in cervical status from prior examination. The woman expressed frustration at the lack of progress. Given the late hour and that she had been awake and laboring since 0200, she elected to have labor augmented with oxytocin. She also chose to use N2O, which she had learned about and discussed with her midwife at prenatal appointments, to help her cope with the anticipated increased pain of her contractions once oxytocin was initiated. She did not have any contraindication to N2O use according to the specific unit policy, which included being unable to hold the face mask, having impaired consciousness, having a documented B12 deficiency, or being oxygen impaired.

Prior to initiation of N2O, she was counseled about the risks of the modality that include nausea, vomiting, vertigo, fatigue, and unsteadiness when upright (Bishop, 2007). Written consent was obtained and anesthesia personnel were summoned to the bedside to initiate N2O administration. Because N2O administration does not necessitate any heightened physiologic monitoring (Likis et al., 2012), no alterations were made in the monitoring of her physiologic parameters or in the mode or frequency of the intermittent fetal monitoring that had been in use for her. Per unit policy, an oxygen saturation reading was obtained prior to use, although this is not accepted as a standardized practice in either the United States or Europe.

The woman was advised to form an adequate seal with the mask over her mouth and nose and begin inhaling approximately 30 seconds prior to the onset of the contraction. Women in labor generally have a sense when contractions are coming, either by the uterine cadence or a physiologic clue such as a lower back ache. N20 is self-administered, so the woman was instructed on how to hold the mask and breathe the gas, rather than having the mask held to her face by someone else. Before the nurse had the opportunity to initiate the oxytocin infusion, the woman had taken several breaths of the N2O. Within approximately five minutes of initiating N2O, she burst into tears and exclaimed, “This baby can’t come out; he’s too big!” Prior to this point, she had been well composed and interestingly had not expressed any concern about the size of the infant or her ability to give birth. After this exclamation, with reassurance from her midwife and husband, she quickly calmed. Within another few minutes, her contractions suddenly increased to a frequency of 2–3 minutes and lasted 60 to 90 seconds (of note, the oxytocin that had been ordered at the same time as the N2O had not yet been initiated and never was). Within 30 minutes while continuing to use the N2O, the woman verbalized the urge to bear down and was noted to be 8 cm, 100% effaced, and 0/+1 station. She continued using the N2O and within 15 minutes was completely dilated and effaced, with the fetus at +2 station”. Pushing ensued and she gave birth vaginally to a male infant who weighed 3800g after an approximate four-minute second stage. She experienced none of the potential side effects of N2O use.

After the birth, the woman recalled the events of her labor:

> I don’t think I could have done it without the N2O. I thought I was doing a good job of relaxing and tolerating everything well, but until I started using N2O and was able to let go of the fear I had about the baby’s size, I realized I really was not.

She also mentioned that she was concerned about the size of the infant and her ability to give birth to an infant estimated to be much larger than her prior two children, but she had not shared this concern with anyone including her husband. She acknowledged that even she did not realize the anxiety she had been suppressing over the infant’s weight.

Discussion

Implications for Practice, Research, and Policy

Considering the analgesic and anxiolytic properties of N2O, broadened considerations for its use should include offering the option to women in early labor who exhibit significant anxiety or fear. Women particularly at risk to be affected by anxiety and fear in labor include adolescents, women with histories of trauma, or those from other cultures who face giving birth in unfamiliar cultures.

Another important consideration for use is in the case of limited or no availability of other options for pain relief. Community hospitals that do not have 24/7 anesthesia coverage and birth centers where epidural anesthesia is not administered are ideal places for N2O to be offered. The multiple applications of N2O are also important to consider. It may be thought of only in terms of analgesia relative to uterine contractions; however, it may be equally useful for laceration repair, IV start (particularly

for those women with intense fear of needles), and procedures that occur after the birth of the infant (e.g., manual removal of the placenta, uterine exploration, or bedside dilation and curettage). Preferably, women would be educated on N2O use by their providers at some point during the prenatal period so that they enter labor well versed on this and all viable options for labor analgesia.

Ideally, N2O will one day be available at every institution where birth occurs, but historically, change has been slow to come to many obstetric settings. New practice initiation fundamentally requires research underpinnings. Though N2O has been used for many decades in other countries with a great deal of anecdotal support, there is a lack of research in many aspects of its use (Likis et al, 2012). Opportunities for research related to N2O include occupational exposure and effects on those caring for women using N2O; fetal/neonatal effects; maternal satisfaction; institutional and system factors that may act as an impedance to initiation; and initiation by nursing staff versus other types of providers (respiratory therapy or anesthesia, for example).

As has been the case with other maternity issues (such as insurance coverage for home birth providers, for example), it is the often the consumer voice that influences clinical practice. An understanding of individual scope of practice (labor and delivery nurses, advance practice nurses, respiratory therapists, and physicians) is imperative for the use of N2O to go forward. New programs may be thwarted by misunderstanding of the role of the various team members, so that initiation of N2O is limited to only anesthesia personnel when, in fact, it does not require initiation by anesthesia personnel.

Legislation mandating the widespread availability of all safe and viable analgesia options for labor and birth would certainly increase the opportunity for the growth of this modality. Such a policy would go far to override initiation efforts thwarted due to reasons unrelated to the best interest of the childbearing women, such as possible concern over decline in institutional epidural rates and resultant loss of income to the anesthesia services.

Conclusion

Although researchers have not documented the anxiolytic effect on laboring women, for the woman highlighted in this article, it was the anxiolytic effect of N2O that was most helpful. She had fear and anxiety about giving birth, and although it is unclear whether this was the cause of her stalled labor, this may have been the case. Whether N2O is equally effective at decreasing fear and anxiety is an area for further study. The adverse effects of fear on labor have been well documented (Adams et al., 2012; Byrne et al., 2013; Nilsson et al., 2010). Fear in childbirth has also been associated with an increased risk for protracted labor and labor dystocia via fear activation of the catecholamine response (Lowe, 2007; Rouhe et al., 2009). The woman in this case experienced labor stalling that might have been associated with her unspoken and unresolved fear of giving birth to a child anticipated to be significantly larger than her previous two children. Inhalation of N2O with its resultant anxiolytic effect causes a decreased catecholamine response (Gillman et al., 1988), and in this case the woman's stalled labor was quickly resolved. N2O is a valuable option for labor analgesia, with notable anxiolytic effects that may prove as important as its analgesic effects. Women should have access to this safe and efficacious method of analgesia. A call for research involving N2O, particularly examining its utility in addressing the psychosocial aspects of labor, is a crucial future imperative.

Women should have access to this safe and efficacious method of analgesia.

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