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Nitrous Oxide for the Management of Labor Analgesia

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This article reviews nitrous oxide and explores current practice standards for use of nitrous oxide in managing labor analgesia. Inhaled nitrous oxide is used in the labor process for analgesia as well as for anxiolysis in many countries but is rarely offered in the United States. Because of its minimal invasiveness, high safety index, effectiveness, and relatively low cost, it is reemerging as a consideration for use during labor and is worthy of further research.

Keywords: Analgesia, anxiolysis, labor, N_2O, nitrous oxide.

Objectives

At the completion of this course, the reader should be able to:

1. Describe the pharmacologic properties and effects of nitrous oxide for both mother and fetus.
2. Identify indications and contraindications for use of nitrous oxide during labor.
3. Discuss current evidence-based data regarding the safety and efficacy of nitrous oxide as an effective treatment modality in labor, specifically related to healthcare provider safety.
4. Describe safe and effective nitrous oxide administration techniques and patient education, with focus on the importance of self-administration and scavenging system use.

Introduction

Most women worldwide use some form of analgesia during labor, and different methods are widely available.[1,2] Improved methods of nitrous oxide (N_2O) administration have made this method of analgesia safe and practical. Inhaled N_2O administration is a low-risk method of pain control that is clinically effective and improves the overall labor experience for the mother. Outside the United States, inhaled N_2O is widely recognized as a valuable tool for the analgesic and anxiolytic dynamics of labor and birth plans. A study by Lindholm and Hildingsson[3] (N = 936) demonstrated N_2O was one of the most preferred pain relief methods for labor, and women who used epidural analgesia, regardless of preference of pain relief method, were 2 to 4 times more likely to have a less positive birth experience compared with other methods of pain control.

Although many countries with high-quality healthcare offer N_2O as an option for treatment of labor pain, a recent poll found that only 38 hospitals and fewer than 30 birth centers in the United States are offering N_2O as an adjunct for labor analgesia.[4] It is not surprising to find a growing interest in the United States to reconsider N_2O use in modern practice. One of the reasons for the increased interest in the United States is that staff and patient education is simple and brief while minimal resources are required to sustain N_2O administration as a practice.[4]

In 2010, the American College of Nurse-Midwives—in efforts to provide a broader range of options for laboring women—published a position statement that is strongly in favor of N_2O use in labor.[4] The statement acknowledges that the subjective experience of the labor process is unique to every parturient,[4] yet the US healthcare system provides limited options to meet the wishes and desires of the nation's women (eg, natural birth vs neuraxial anesthesia). This statement addresses a broader topic than analgesic needs alone but encompasses all that happens

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from the onset of labor through its completion. US women deserve broader treatment options such as those available in the United Kingdom, Canada, and Australia, where N_2O is recognized as a viable and valuable option.[5]

History

Nitrous oxide is an inhalational agent that has been used for its anesthetic, analgesic, and anxiolytic properties for more than 150 years.[6] This simple, inorganic molecule was discovered in 1793 by Joseph Priestley, an English scientist.[7] Sir Humphrey Davy, a Cornish chemist and inventor, first noted the analgesic effects of the agent and coined the term *laughing gas* in 1799, as cited by Emmanouil and Quock.[7] For the next several decades N_2O was used primarily for entertainment and public spectacle, but in 1844, a dentist named Horace Wells witnessed a demonstration of its use and decided to have one of his own teeth extracted under the effects of this gas. Wells was impressed with it as an analgesic and experimented with its clinical use in many patients. This led to use of the gas for anesthesia and its growth in popularity.[7]

Nitrous oxide was first used for labor analgesia in 1881, when Stanislav Klikovich studied the effects of mixed 80% N_2O with 20% oxygen on laboring women.[8] In 1934, Minnit introduced the first anesthesia machine for N_2O self-administration.[9] Subsequently, inhaled N_2O for labor analgesia has remained popular throughout Europe, with reported use in up to 60% of laboring women.[10]

In the United States, use of N_2O as an adjunct for labor analgesia has historically remained less available than in Europe, largely because of the widespread popularity of continuous labor epidural blocks ("epidurals").[9] From 1975 to 1985, N_2O was used in about 6% of laboring patients in the United States, with numbers diminishing greatly in the late 1980s.[10] Now, knowledge of and interest in N_2O-mediated labor analgesia are on the rise in the United States as a growing number of hospitals are beginning to offer it as an option for laboring women.[9]

Pharmacologic Action

Nitrous oxide is an odorless, tasteless, nonflammable gas composed of 2 nitrogen atoms and 1 oxygen atom (Figure 1).[11] Nitrous oxide is stored in pressurized gas cylinders below its critical temperature, where it exists simultaneously in gas and liquid phases.[10] With a mean alveolar concentration (MAC) of 104% in humans, N_2O exerts anesthetic, analgesic, and anxiolytic effects at subanesthetic concentrations.[12] Nitrous oxide is a low-potency anesthetic frequently used to increase the uptake of a second inhalation agent, consequently decreasing induction time. Because of its effect of decreasing the required MAC of a concurrently administered volatile anesthetic agent,[9] N_2O is commonly used to augment analgesia during surgical procedures[7] while simultaneously

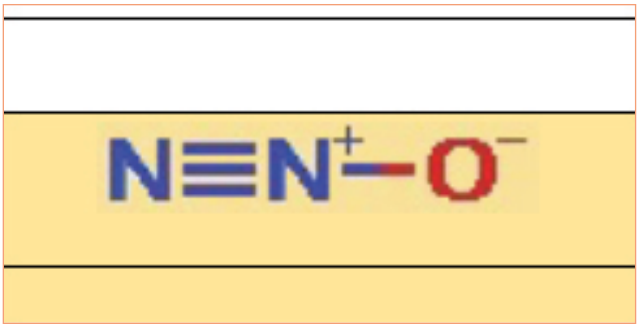

Figure 1. Nitrous Oxide Chemical Structure[3,4]

providing additional anxiolysis,[6] allowing for a dose reduction in anesthetic agents and narcotics.[7]

The mechanism of action for the anesthetic effect of N_2O is believed to predominately involve the noncompetitive inhibition of the *N*-methyl-D-aspartate subtype of excitatory glutamate receptors (Table 1). Although the inhibition of glutamate neurotransmission is the primary explanation,[8] other proposed mechanisms exist. One such alternative attributes this effect to the activation of potassium channels, increasing potassium conduction, and hyperpolarizing the neuron.[6]

Nitrous oxide elicits anxiolysis and sedation, behavioral responses similar to the effects of benzodiazepines. Animal studies have shown that both N_2O- and benzodiazepine-mediated anxiolytic behaviors were equally sensitive to flumazenil-induced antagonism. This finding indicates a possible association between the γ-aminobutyric acid (GABA) receptor mechanism of benzodiazepines and the anxiolytic mechanism of N_2O. It remains unclear how N_2O acts at the molecular level to stimulate the benzodiazepine GABA receptor binding site, but it is hypothesized to be related to a release of endogenous benzodiazepine factors that stimulate the receptor.[7]

The analgesic mechanism of action for N_2O is not completely defined, despite extensive research into the subject. One possible mechanism involves N_2O-mediated release of endogenous opioid peptides in the periaqueductal gray area in the midbrain, stimulating descending pathways, which modulate noxious stimuli via α_2 adrenoceptors in the dorsal horn.[7] It is postulated that N_2O exerts analgesic effects via supraspinal and spinal release of opioid peptides. Animal models show that the specific opioid receptor targeted is likely of the κ subtype.[9] The evidence suggests that the release of corticotropins and dopamine may also be involved in N_2O's analgesic action, and studies have shown that dopamine and norepinephrine concentrations and turnover in the brain may modulate some of the agent's effects on the central nervous system.[8]

Nitrous oxide is rapidly eliminated from the body in its original form almost entirely by the lungs. A small amount of the gas may diffuse through the skin. Nitrous oxide is not metabolized in human tissue, but rather is

Property	Description
IUPAC name	Dinitrogen monoxide
Chemical formula	N_2O
Appearance	Colorless gas
Odor	Odorless or slightly sweet
Flash point	Nonflammable; supports combustion
Onset	Rapid; 30-60 seconds
Clearance	Rapid
Metabolism	None
Excretion	Respiratory
Half-life	5 minutes
Mechanism of action	Believed to be noncompetitive inhibition of *N*-methyl-D-aspartame excitatory glutamate receptors subtype
Partition coefficients (at 37°C):	
Blood:gas	0.47
Oil:gas	1.4
Brain:blood	1.1

Table 1. Properties of Nitrous Oxide[3,5,6,19,28]
Abbreviation: IUPAC, International Union of Pure and Applied Chemistry.

reduced by intestinal bacteria to nitrogen (N_2) and free radicals, which represents a very small contribution to elimination.[11]

Efficacy

Nitrous oxide has several characteristics that makes it well suited as an analgesic for women in labor. Because of its quick onset of action and clearance, N_2O does not accumulate in maternal or fetal tissues. These pharmacologic characteristics allow N_2O to relieve pain, decrease anxiety, and provide a sensation of pain antipathy within 30 to 60 seconds.[9] As long as the patient controls the mask, the patient remains awake and alert, without loss of motor or sensory function. Additionally, the maternal laryngeal reflex is not affected, so there is no increased risk of aspiration.

Unlike the 70/30 concentration of N_2O used in the 1940s, the current practice of using a fixed 50/50 concentration of N_2O to oxygen (O_2) is associated with fewer side effects and prevents maternal desaturation. Nitrous oxide does not inhibit the release of oxytocin, infant alertness, the need for neonatal resuscitation, or breastfeeding. Other benefits of N_2O use are that laboring women can remain ambulatory and do not require intravenous access. A major advantage of N_2O is that it has a rapid onset and offset profile and can be started quickly, with the added benefit of maternal clearance within 30 to 60 seconds.[2] The rapid N_2O clearance also allows for the option to change to another form of pain management if the laboring woman is not satisfied with the analgesia provided by N_2O. Adjunct nonpharmacologic therapies to N_2O have been used and may potentiate N_2O's beneficial effect, including water immersion, psychoprophylaxis, hypnosis, and acupressure.[10]

Adverse Effects

Inhaled N_2O is associated with some negative side effects, including nausea and vomiting,[12] vertigo or lightheadedness, drowsiness,[9] subjective feelings of dysphoria and restlessness,[13] megaloblastic anemia, myocardial ischemia, hypoxia, neural toxicity, possible teratogenicity, expansion of air spaces, and increased intracranial pressure (Table 2).[14]

- ***Neuroapoptosis.*** Nitrous oxide oxidizes an active form of cobalamin (ie, vitamin B_{12}), making it inert. The adverse effects of N_2O—with the exception of consciousness, nausea and vomiting, and neuroapoptosis—are due to inactivation of cobalamin.[11] Cobalamin is an important coenzyme in the conversion of homocysteine to methionine. Methionine uses folate to synthesize myelin, DNA, and RNA.[7] This N_2O inhibition of cobalamin can lead to impaired DNA synthesis and reduced levels of methionine, possibly resulting in impaired metabolic pathways.[11]

Extremely high doses (dose is defined as concentration times duration of exposure) of N_2O and/or long-term exposure can inhibit cobalamin enough to cause adverse effects. Adverse effects of cobalamin inhibition include bone marrow depression, macrocytic (megaloblastic) anemia, and neuropsychiatric disorders. The adverse effects reverse with time except when the dose is so high that it causes cell death, which was demonstrated in rats kept under barometric pressures that caused them to inhale concentrations of N_2O for greater than 6 hours.[6] Certain conditions—including Crohn disease, celiac disease, gluten intolerance, pernicious anemia, long-term recreational abuse of N_2O, chronic malnutrition, or adherence to a strict vegan diet—reduce cobalamin function, and thus increase risks of complications from ex-

Therapeutic	Adverse	Unchanged
• Analgesia	• Nausea	• Spontaneous vaginal birth rate
• Anxiolysis	• Vomiting	• Normal uterine function
	• Megaloblastic anemia related to vitamin B_{12} deficiency	• Endogenous oxytocin levels
	• Hypoxia, diffusion hypoxia	• Progression of labor
	• Decreased hypoxic drive	• Apgar scores
	• Expansion of air fills spaces (eg, bowels)	• Maternal-newborn bonding (eg, breastfeeding)
	• Increased intracranial pressure	
	• Vertigo, lightheadedness	
	• Drowsiness, dysphoria (rare)	

Table 2. Effects of Nitrous Oxide[4,5,10,11,14,19,28]

posure to N_2O. From an anesthetic standpoint, patients who receive N_2O for greater than 6 hours are at increased risk of complications secondary to exposure.[6]

Almost all anesthetic drugs have demonstrated neural breakdown in young animals.[15] Synaptogenesis occurs in the last 3 to 4 months of gestation and during the first 3 years after birth in humans but only the first 2 weeks after birth in rats. Exposing rodent newborn pups to high doses of virtually any systemic anesthetic can cause apoptotic damage leading to cell death.[16] The cause of neuronal damage is assumed to be mistimed neuroapoptosis, a type of natural cell death that is necessary for normal brain development. Nitrous oxide by itself does not cause apoptosis in neonatal rat brains at concentrations less than or equal to 75%, thus theoretically making it clinically insignificant in anesthesia.[7] In one study, repeated exposure to anesthesia before the age of 3 years in children was a significant independent risk factor for the later development of learning disabilities.[15]

• ***Loss of Consciousness.*** One of the greatest maternal risks of any inhaled anesthetic or analgesic is the loss of protective airway reflexes secondary to loss of consciousness, leading to aspiration of stomach contents.[11] In the early days of N_2O use in controlling labor pain, maternal loss of consciousness was reported when N_2O concentrations from 75% to 100% were used.[17] Rare instances of unconsciousness can occur with 50% N_2O/O_2 and usually occur when someone other than the laboring woman holds the mask on the woman's face.[17]

• ***Nausea and Vomiting.*** The most commonly reported adverse effects in labor are nausea and vomiting, with an incidence ranging from 5% to 36%.[8] Nausea and vomiting are considered common during the labor process, but research suggests it is increased among women using N_2O.[9] Findings from a large international randomized controlled trial showed that N_2O-based anesthetic plans had higher rates of postoperative nausea.[11] A tendency for motion sickness or preexisting nausea may be a clue that a particular patient is a poor candidate for inhaled N_2O treatment, and other options should be explored.

• ***Megaloblastic Anemia.*** In a patient with vitamin B_{12} deficiency, administration of N_2O further inhibits its methionine synthase production which can result in megaloblastic anemia.[18] Damage to the protective myelin sheath of neural axons can also occur, resulting in neurotoxic effects.[6,10] Vitamin B_{12} deficiency is seen in patients who adhere to strict vegan diets, suffer from malnourishment, or who have certain gastrointestinal absorption disorders such as Crohn disease. Fortunately, after adequate vitamin B_{12} replacement therapy, N_2O use is not contraindicated for this population.[19]

• ***Myocardial Risk.*** Certain studies associate N_2O with increased myocardial risk perioperatively[10] and implicate hyperhomocysteinemia as an independent risk factor for coronary vascular disease,[20] although this association as cause instead of consequence is considered questionable.[8,20] The use of N_2O at high concentrations (ie, greater than or equal to 70%) is shown to increase the incidence of postoperative hyperhomocysteinemia, related to inhibition of cobalamin.[21] Myles et al[8] evaluated morbidity and mortality 1 year postoperatively in noncardiac surgical patients at risk of perioperative cardiovascular events after perioperative exposure to 70% N_2O compared with a control group. The results indicate that the use of 70% N_2O does not increase the incidence of death, disability, or major cardiovascular complications, supporting the notion that N_2O is safe to use in patients at risk of cardiovascular events. Although N_2O is not associated with depression of the cardiovascular system,[22] it should be used with caution in hemodynamically unstable patients in labor.[9]

• ***Diffusion Hypoxia.*** Diffusion hypoxia is another potentially deleterious effect of N_2O administration. When N_2O is inhaled at high concentrations and then discontinued without immediate administration of high concentrations of inhaled oxygen, the elevated arterial partial pressure of N_2O rapidly transfers the agent into the alveoli displacing alveolar oxygen, which can lead

Contraindications	Discontinue when
• Patient refusal	• Patient no longer desires use
• Inability to self-administer	• Persistence of substantial adverse effects
• Hypoxia	• Any evidence of maternal or fetal compromise
• Recent inner ear surgery	
• SpO_2 < 95%	
• Hemodynamically unstable	
• Documented vitamin B_{12} deficiency	
• Opioids administered within 2 hours	
• Evidence of fetal compromise	
• Acute drug or alcohol intoxication	
• Decreased level of consciousness	
• Recent trauma, pneumothorax, increased intracranial pressure	
• Emphysema	
• Pulmonary hypertension	
• Bowel obstruction	
• Vitreoretinal surgery (< 30 days)	

Table 3. Contraindications to and Discontinuation of Nitrous Oxide[4,6,21]
Abbreviation: SpO_2, oxygen saturation measured by pulse oximetry.

to hypoxemia.[10] The influx of N_2O can also dilute alveolar carbon dioxide levels, decreasing carbon dioxide-mediated respiratory drive and impairing ventilation.[23] These effects are documented with the use of N_2O in concentrations higher than 70%,[9] and the published data do not suggest it is a significant factor in labor.[23] Oxygen desaturation seen during active labor is believed to result from hyperventilation followed by hypoventilation, in response to the pain of uterine contractions.[24]

• ***Hypoxic Drive.*** Another concerning side effect of N_2O is the effect on hypoxic drive. Use as a sole agent at subanesthetic concentrations, it does not depress ventilation; however, when combined with sedatives or opioids that cause respiratory depressant effects, a more pronounced respiratory depression may occur.[9] It causes a dose-dependent depression of the hypoxemic drive with as little as 0.1 MAC, producing a depression of up to 50%.[23] Nitrous oxide is routinely delivered concurrently with high concentrations of oxygen, further weakening the ventilatory response to hypoxia. As a result, it is recommended that the use of this gas should be avoided in patients with chronic obstructive pulmonary disease, because they may be reliant on the hypoxemic drive.[25] With proper supervision and judicious administration of sedatives and opiates, a laboring patient could easily be instructed to breathe more deeply if necessary, effectively attenuating the risk.

• ***Effects on the Fetus.*** Nitrous oxide readily crosses the placenta and after approximately 15 minutes of continuous inhalation, the maternal-fetal concentration ratio is about 0.8.[23] As respirations are initiated in the neonate, the agent is quickly eliminated, preventing respiratory and central nervous system depression.[9] The half-life of N_2O in the neonate directly after birth is reported to be less than 3 minutes,[10] with no evidence of any effect on fetal heart rate or uterine contractions.[11]

Su et al[27] compared outcomes in a study group of laboring patients receiving N_2O with those of a control group of patients who inhaled only oxygen during labor. The study group, who intermittently inhaled a mixture of 50% N_2O and 50% oxygen, were noted to have more efficient pain relief during labor, a lower rate of cesarean delivery, and a shorter active phase of labor vs the control group members who inhaled oxygen. No statistically significant differences were found between the 2 groups in terms of Apgar scores, postpartum bleeding, meconium-stained amniotic fluid, or umbilical blood gas analysis. A limitation of this study is that the population included only Chinese women, who may have a different perspective on labor pain than those from Western Hemisphere countries. Research on neonatal exposure to N_2O during the birthing process results in consistent conclusions that there are no negative effects on Apgar scores, neonatal neurobehavioral scores, or suckling behavior, regardless of the duration of administration to the mother.[27]

Occupational Exposure Risk

Occupational safety and risk related to N_2O exposure during use in labor is a valid concern for healthcare providers. Exposure to trace amounts of gas in the workplace is addressed by occupational exposure limits (OELs) for specific inhaled agents. In the United States, the Netherlands, and Ontario, Canada, the OEL for N_2O is limited to an 8-hour, time-weighted average concentration of 25 parts per million. In the United Kingdom, Italy, Sweden, Norway, Denmark, and Alberta, Canada, the

Plan	Action
Precautions	1. Determine no contraindications present
	2. Perform history and physical examination
	3. Obtain informed consent
	4. Use with caution if other sedating drugs are administered during use of nitrous oxide/oxygen
Preparation	1. Inform the woman of potential side effects of nausea, vomiting, and/or dizziness.
	2. Instruct on how to hold the mask or tube so it creates a seal; instruct on timing of inhalation
	3. Review with the woman and any labor support persons that only the woman can hold the mask
	a. Sedation from nitrogen is possible only if the woman continues to inhale the gas after she can no longer hold the mask tightly to her face or the tube tightly in her mouth. Nitrous oxide dissipates rapidly with exhalation, and the effects resolve very quickly.
	b. Self-administration gives the woman personal control of management of pain, and this control may potentiate the analgesic effect
Equipment	Administration device with adequate scavenging system
	50/50 nitrous oxide and oxygen (maximum concentration)
	No additional monitoring required (as this is classified by the ASA as anxiolysis/minimal sedation)
Technique	1. The woman holds the mask or tube in a manner that creates a seal
	2. She starts inhaling the gas 30 seconds before a contraction starts because the onset of action takes about 30 seconds; full analgesic effects occur in 50 seconds. It often takes 3 to 4 contractions to learn the best technique.
	3. The woman should exhale into the mask to facilitate scavenging
	4. She should stop breathing through the mask when the contraction terminates
	5. Use may be continued between contractions as needed for anxiolysis or discomfort

Table 4. Clinical Use of 50% Nitrous Oxide/50% Oxygen for Labor Analgesia[5,6,10,21,28]

OEL for N_2O allows for up to 100 parts per million. The lower limit seen in the United States was suggested in the 1970s by the National Institute for Occupational Safety and Health and was set at this specific point to ensure the utmost precaution for US healthcare workers.[26]

The occupational risk of N_2O exposure is due to methionine synthase inhibition and its potentially harmful effects on female fertility.[11] This enzymatic inhibition is dose and duration dependent,[8] whereas the exposure risk is dependent on the concentration of the agent and the efficacy of the scavenging system. Multiple studies examining dental hygienists and workplace exposure to N_2O find an association with infertility, preterm labor, and spontaneous abortions.[9] It should be noted that the exposure risk of the dental hygienists (ie, 70%-80%) is significantly higher than that associated with use in labor and occurs in closer proximity to the source.[28] Animal models indicate that N_2O does not cause fertility problems at 1,000 parts per million or lower,[10] suggesting that the OELs in place are safe and appropriate for healthcare workers.

Contraindications to Use

It is crucial for the healthcare provider to understand the risks and contraindications for the use of N_2O in order to safely deliver patient care (Table 3). General contraindications for N_2O administration include acute drug or alcohol intoxication, reduced level of consciousness, inability to hold the N_2O delivery device to one's face, recent trauma, pneumothorax, emphysema, pulmonary hypertension, increased intracranial pressure,[29] bowel obstruction, or vitreoretinal surgery within 30 days.[30] Women who have had recent ear surgery or who have conditions that predispose them to vitamin B_{12} deficiency should not use N_2O during labor, unless it has been determined that their vitamin B_{12} levels are within normal limits.[8] Patient selection for this type of labor analgesia is critical, and risks vs benefits should be clearly explained to the patient, as well as an explanation of alternative methods of pain control.

Administration of Inhaled Nitrous Oxide

The procedure for using 50% N_2O/O_2 is described in Table 4, with images of the N_2O portable delivery system shown in Figures 2 and 3. There are 2 methods for administration: intermittent or continuous inhalation. With intermittent inhalation, inhalation begins 30 seconds before the onset of a contraction, which maximizes the peak effect of N_2O/O_2 so the peak analgesic effect occurs during the peak of the uterine contraction. Continuous inhalation is easier to initiate but exposes the woman to N_2O between contractions. Exposure to N_2O between contractions could unmask dizziness or dysphoria, which are not as noticeable during the pain of contractions.

When a woman inhaling 50% N_2O/O_2 begins to become sedated, she is unable to appropriately hold the mask, and as the mask falls, she stops breathing the gas mixture. Because N_2O is eliminated from the blood through the lungs very rapidly, she recovers in a matter of minutes.

Figure 2. Portable Gas Blender (Nitronox)
Image courtesy of Parker Hannifin, Porter Instrument Division, Hatfield, Pennsylvania.

Foremost, the administration of inhaled N_2O requires the use of a device equipped with a proper scavenging system.[11] This minimizes exposure and risk to healthcare providers and others present. A scavenging system is the only specialized equipment required. This system is composed of 3 key components; positive pressure relief, negative pressure relief, and a reservoir.[31] Positive pressure relief protects the equipment and patient from dangers (eg, barotrauma) that are possible in events such as occlusion. If the flow of gas is excessive, the gas mixture is diverted into the reservoir, thus preventing release into the surrounding environment. In instances in which the reservoir becomes full, an audible noise is heard as the positive pressure relief valve vents excess gas into the surrounding environment, preventing dangers associated with excessive pressures while simultaneously notifying the provider of the need to decrease the rate of flow. In active systems, a negative pressure relief valve prevents the formation of a vacuum in instances where flow rate is too low (eg, sudden increase in patient minute ventilation). The reservoir plays an important role in these negative pressure circumstances by providing a reserve of gas mixture until flows can be increased.

The American Society of Anesthesiologists classifies the manner in which N_2O is administered for labor analgesia as anxiolysis/minimal sedation.[32] Specifically this refers to the use of N_2O alone at concentrations no greater than 50%. The result is that the parturient requires no additional monitoring device, such as pulse oximetry. If any additional treatment steps (eg, intravenous fentanyl) are used, pulse oximetry should be monitored.

Figure 3. Portable Gas Blender (Nitronox) in Use
Image courtesy of Parker Hannifin, Porter Instrument Division, Hatfield, Pennsylvania.

The most important administration guideline is that it must be self-administered (ie, parturient alone holds mask to her face). It is vital that the patient receive absolutely no assistance because it is the inability to hold the mask to one's face that limits intake, preventing overdose.[32] The healthcare provider simply instructs the patient to breathe through the mask deeply and slowly at the first sign of a contraction. If contractions are regular, it may be beneficial to begin inhalation 10 to 15 seconds before a contraction to compensate for the drug's onset time and thus provide fuller analgesic coverage.[4,30] Inhalation is often discontinued when the contraction terminates. The parturient can be told that inhaling the gas between contractions is acceptable as needed for relief of possible uterine discomfort or anxiety.[9,10]

Nitrous oxide is permissible to use throughout the entire labor process (stages 1-3) and may be of particular use in the final phase if there is difficulty removing the placenta or for repair of a perineal laceration. There are 3 main reasons to discontinue its use earlier: (1) patient no longer desires it, (2) persistent adverse side effects (ie, nausea, vomiting, vertigo), and (3) any evidence of maternal or fetal compromise (see Table 3). The parturient should be carefully monitored throughout administration and instructed to discontinue use if she experiences intolerable side effects.[30,33]

Discussion

The effects of inhaled N_2O are both analgesic and anxiolytic, an invaluable combination in the practice of obstetrics that is safe in all 3 phases of labor.[30] Pain management is an obvious factor in planning labor care; it sometimes overshadows consideration for anxiolytic management. Labor is surrounded with many things considered scary and unpleasant (eg, needles, epidurals, risks) by patients. Prompt and effective attention to

managing a patient's anxiety benefits all involved in the labor process.

Nitrous oxide is pharmacologically fast in onset and clearance, making it valuable in the treatment of breakthrough pain and anxiety. Many women describe that the analgesic and anxiolytic benefits are felt within 30 to 60 seconds of self-administration, and manifest as relief of or indifference to the unpleasant stimuli.[4,5,30,33] Clearance from both maternal and fetal tissue is extremely rapid as well, with complete elimination of residual effects taking less than 5 minutes.[9] If negative or unpleasant side effects are felt or if the mother decides for any reason to discontinue N_2O administration, that can be achieved promptly and completely, distinguishing it from other treatment options that require a higher degree of commitment as a plan (eg, continuous labor epidurals).

The pharmacologic profile of this agent is made more impressive by the things it does not do that many other treatment methods cannot claim. For instance, N_2O does not affect the rate of spontaneous vaginal births, a major criticism and risk of epidurals. Normal labor physiology is largely preserved; uterine function, endogenous oxytocin levels, and progression of labor are unaltered.[2] Furthermore, no studies have indicated an increase in neonatal resuscitation or alteration in Apgar scores. There is no decrease in the newborns' ability to bond with the mother or participate in breastfeeding immediately after birth.[28]

Patient satisfaction is and should remain a driving force in obstetrics. Providing as many reasonable analgesic options should be a priority in striving to best care for this patient population. In the United States, the most common means of analgesic management continues to be continuous labor epidurals and opiate administration, both intravenously and intramuscularly.[34] Providing additional options (ie, inhaled N_2O) help to improve the overall experience, particularly for women desiring less invasive and low-commitment interventions. Nitrogen oxide is an especially viable option for those seeking the most natural means possible but who ultimately require a brief reprieve from pain in the latter stages of labor. Women report that having N_2O as an option provides an increased sense of control throughout the entire process while significantly increasing satisfaction through the avoidance of invasive measures, such as peripheral intravenous catheter placement, Foley catheters, and cumbersome electronic fetal heart monitoring, that accompany alternative methods.[35] The parturient remains in control of all motor and sensory function throughout the process, further increasing her sense of situational control.[11] Furthermore, it requires minimal education for both patients and staff,[10] adding to its ease of use.

Nitrous oxide is simple, versatile, and effective in the treatment of mild to moderate pain while posing little to no increased risk of maternal or fetal complications. This inhalational agent is another option to be offered or at least considered in US obstetrics. As patient advocates, anesthesia providers have the responsibility to be knowledgeable about and to actively seek to offer and provide the best care possible in what is one of the most personal and special experiences in healthcare.

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