

## Nitrous Oxide Analgesia for Labor

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Nitrous oxide – this option has not traditionally been used in the United States (US) for labor and delivery, but is becoming more common. It may help reduce anxiety, but does not eliminate pain. Intrapartum analgesia is commonly used for labor pain with multiple modalities available, including systemic opioids, inhaled gas, and neuraxial analgesia. Nitrous oxide, commonly known as “laughing gas,” is a tasteless and odorless gas used as a labor analgesic by some hospitals. It reduces anxiety and increases a feeling of well-being so that pain is easier to deal with. It does not numb pain. The pain felt during childbirth is different for every woman. Some women choose natural childbirth, or giving birth without medicine for pain. If all goes well, it can be a great experience. For some women, the techniques learned in childbirth classes are enough to relieve their pain. Other women may choose to use pain medicine during childbirth.

The purpose of this document is discuss the association between intrapartum nitrous oxide use and adverse short-term neonatal outcomes. Intrapartum analgesia is commonly used for labor pain with multiple modalities available, including systemic opioids, inhaled gas and neuraxial analgesia. The null hypothesis is that there would be no significant difference in neonatal outcomes based on nitrous oxide exposure.

### Overview

Nitrous oxide (N<sub>2</sub>O) is a colorless gas stored as a liquid, Breathing nitrous oxide can cause dizziness, unconsciousness, and even death. Long-term exposure can lead to infertility. Contact with liquid can cause severe frostbite. The level of exposure depends on the dose, duration, and type of work being done. Nitrous Oxide is used in many industries. It can come from anesthetic equipment, surgical patients, and storage cylinders. Some examples of workers at risk of nitrous oxide exposure include the following:

- Medical personnel who work in surgical rooms in hospitals, surgery centers, or medical offices;
- Dental workers where nitrous oxide gas is used as an anesthetic;
- Recovery room personnel who are exposed to outgassing patients who emit fumes after surgery;
- Workers in laboratories and facilities where compressed gas cylinders are moved and stored;
- Service workers who clean and maintain surgical rooms before and after surgery.

The National Institute for Occupational Safety and Health (NIOSH) recommends the employer use the Hierarchy of Controls to prevent workers exposure.<sup>1</sup> Over the years there have been significant improvements in the control of anesthetic gas pollution in healthcare facilities. These have been accompanied through the use and improved design of scavenging systems, installation

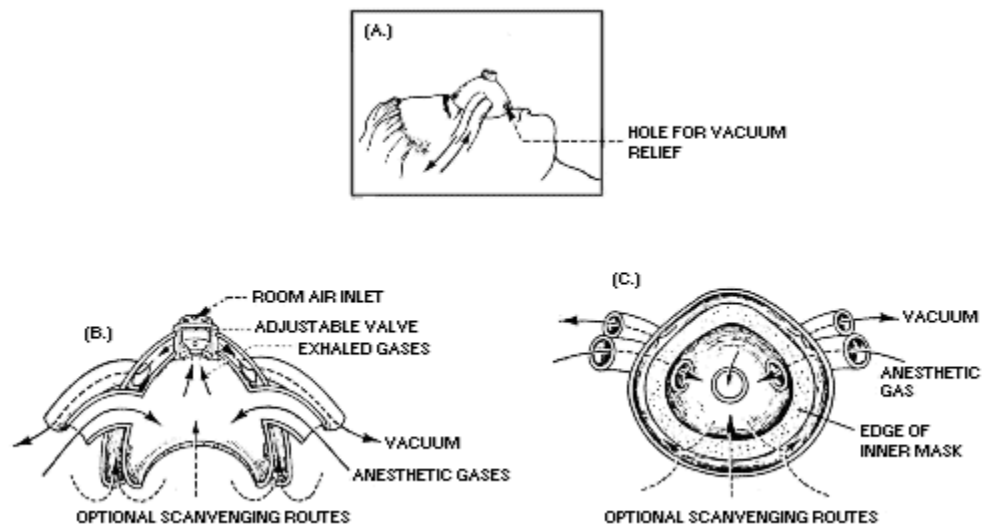
and more effective general ventilation systems, and increased attention to equipment maintenance and leak detection as well as to careful anesthetic practices. However, occupational exposure to waste gases still occurs.

## Work Safety Practices

Work practices, as distinct from engineering controls, involve the way in which a task is performed. Occupational Safety and Health Administration (OSHA) has found that approximate work practices can be a vital aid in reducing exposures to operating room personnel to waste anesthetic agents.<sup>2</sup> In contrast, improper anesthetizing techniques can contribute to increased waste gas levels. These techniques can include an improperly selected and careless filling of vaporizers and spillage of liquid anesthetic agents.

Face mask, which is used for administration of inhaled anesthetics, should be available in a variety of sizes to fit each patient properly. The mask should be pliable and provide as effective a seal as possible against leakage into the surrounding air.

**A common nasal mask**, shown below in figure 1, consists of an inner and a slightly larger outer mask component. The inner mask has two hoses connected that supply anesthetic gas to the patient. A relief valve is attached to the inner mask to release excess nitrous oxide into the outer mask. The outer mask has two smaller hoses connected to a vacuum system to capture waste gases from the patient and excess supplied to the patient by the analgesia machine. The nasal mask should fit over the patient's nose snugly as possible without impairing the vision or dexterity of the healthcare provider.



**Figure 1.** Circle breathing system connected to a closed reservoir scavenging interface.

Gases exhaled orally are not captured by the nasal mask, a flow rate of approximately 45 L/min has been recommended as the optimum rate to prevent significant nitrous oxide leakage into the room air.<sup>3</sup> A newer type of mask is a frequent choice – a single patient use nasal hood. This mask

does not require sterilization after patient use because it is used only by one patient and it is disposable.

## **Nitrous Oxide Intrapartum Use for Analgesia: Background**

Although historically used for pediatric analgesia and dental care, inhaled nitrous oxide has been found to be an effective intrapartum analgesic and is increasingly used during labor in the United States (U.S.).<sup>4</sup> Nitrous oxide is known to rapidly cross the placenta.<sup>5</sup> Despite its increasingly common use, it remains unclear whether there are associated short-term adverse neonatal effects after maternal intrapartum exposure.<sup>6</sup>

Nitrous oxide has a rapid onset and a short half-life, and its toxicity seems to be proportional to duration and dosage of exposure.<sup>7</sup> It is known that nitrous oxide displaces oxygen from the lungs, but studies have not demonstrated newborn hypoxia or newborn respiratory depression with maternal use of nitrous oxide.<sup>8</sup> Still, theoretical concerns about “diffusion hypoxia” exist, in which rapid diffusion of nitrous oxide from maternal blood into lungs can cause relative oxygen desaturation, which could in turn alter fetal perfusion.

### **How is nitrous oxide given?**

It is mixed with oxygen and inhaled through a mask. Patient should hold mask herself and decide when to inhale. It works best when patient begins inhaling 30 seconds before the start of a contraction. Nitrous oxide inhalation gas, usually, is administered as 50% nitrous oxide and 50% oxygen by self-administration through a face mask after informed consent has been obtained, by the primary care team.

## **Side Effects and Safety of Nitrous Oxide Analgesia**

Nitrous oxide is fairly safe for the patient and her baby. Patients may feel dizzy or nauseous while inhaling nitrous oxide, but these sensations go away within a few minutes. Nitrous oxide is also known to alter cobalamin (Vitamin B12) metabolism and lead to inhibition of methionine synthesis, and essential amino acid involved in multiple metabolic pathways including hepatic gluconeogenesis, which assists with glucose regulation.<sup>9</sup> Consequently, there is biological plausibility that there could be negative short-term effects on the newborn with maternal nitrous oxide use.

## **Discussion**

In this single-center retrospective cohort study, inhaled nitrous oxide for intrapartum maternal analgesia was not associated with an increased risk of short-term neonatal adverse effects.<sup>10</sup> Some studies have found lower rates of intrapartum cesarean delivery among patients who used nitrous oxide at any time during their labor course, compared with patients who used other form of analgesia, though their rates of cesarean delivery were higher than in this analysis (13% and 15%) respectively.<sup>11</sup> This may be because nitrous oxide is a newer mode of labor analgesia in the US, and patients with prior labor experience may be less likely to choose a new modality.

Previous studies have reported low Apgar scores and NICU admission after nitrous oxide use but have not directly compared neonatal outcomes among recipients of nitrous oxide compared with recipients of no analgesia.

Although prior research suggests that neonates with hyperbilirubinemia may have elevated levels of nitric oxide (chemically: NO) resulting from phototherapy treatment postnatally. Nitrous oxide (chemically N<sub>2</sub>O) is not known to directly affect neonatal bilirubin metabolism. Neonatal bilirubin metabolism is influenced by many factors, including prematurity, hemolysis, and genetic disorders.<sup>12</sup> The association between maternal nitrous oxide use intrapartum and neonatal hyperbilirubinemia should be explored in future research.

Nitrous oxide rapidly enters alveoli when inhaled, but it is also eliminated quickly by the lungs, and therefore, is not thought to accumulate in the pregnant patient or fetus or neonate. These pharmacokinetics make it unlikely that nitrous oxide would have long-term effects on the neonate.<sup>13</sup> However, given previously described effects of nitrous oxide on multiple organ systems, studies that investigate long-term neonatal adverse outcomes of nitrous oxide exposure should be considered.

The US Food and Drug Administration (FDA) first approved a delivery system for nitrous oxide analgesia in 2012.<sup>11</sup> Most of the institutions in US are adapting to nitrous oxide as an option for labor analgesia, with widespread buy-in from the labor teams. The less invasive nature of nitrous oxide compared with neuraxial analgesia, along with support from healthcare professionals likely led to high proportion of nitrous oxide recipients, and is an acceptable and desired analgesic option for many individuals.

## **Effects on Lactation and Breastmilk**

Because the serum half-life of nitrous oxide in the mother is short and the drug is not expected to be absorbed by the infant, no waiting period or discarding of milk is required.<sup>14</sup> The serum half-life of nitrous-oxide is less than 3 minutes, so extensive passage into milk is unlikely. Some evidence indicates that primiparous mothers who use inhaled nitrous oxide during labor for analgesia have better breastfeeding success than mothers who do not. If used as part of general anesthesia, breastfeeding can be resumed as soon as the mother is recovered sufficiently from anesthesia to nurse the baby. When a combination of anesthetic agents is used for a procedure, follow the recommendations for the most problematic medication used during the procedure.

## **Summary**

Nitrous oxide may potentially affect patient's breathing, decrease awareness and cause nausea, vomiting, and dizziness. More research is needed to determine how effective nitrous oxide is, potential complications it could cause, in addition to any possible long-term side effects for patient and her baby. Overall, experience with nitrous oxide for intrapartum analgesia is positive and can be safely used in low-risk patients. Intrapartum exposure to nitrous oxide, compared with no analgesia, in most the studies is associated with lower likelihood of NICU admission, a higher likelihood of neonatal hyperbilirubinemia, and no differences in other short-term neonatal outcomes. These findings add to available data informing neonatal safety of maternal nitrous

oxide use and may be used to inform clinical counseling for patients who are considering use of intrapartum nitrous oxide.

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