Nitrous Oxide for Labor Analgesia

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Disclosures

• Sandra Hoffman has no disclosures

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OBJECTIVES

- Discuss history of nitrous oxide use for birth
- Describe candidates for nitrous oxide, and contraindications for use
- Discuss safe implementation of nitrous oxide for labor, as well as some of the potential barriers

Nitrous Oxide: Some History

- Discovered in 1771

- Analgesic potential for labor pain-1881 Russian MD Klikovich developed a machine that delivered 80% nitrous - 20% oxygen

- Regular use for labor pain in 1934 with the creation of a device that allowed self administration

- 1961-Introduction of Entonox machine (50%/50% blend)

- As of 2014, only 19 hospitals and 14 birth centers were using or in the process of offering nitrous oxide to women in labor (Plenda 2014)
Nitrous Oxide at the Present

- Most utilized gaseous anesthetic worldwide
- #1 utilized modality for labor analgesia worldwide
- UK- 60% of laboring women utilize N20
- Australia- 50% utilization
- Norway- offered at 85% of birthing centers
- Finland- 48% utilization
- More common than regional anesthesia worldwide

(Rooks, 2007; STAKES 2006)

& in the United States...

- UCSF (over three decades)
- Vanderbilt (over three years)
- Only recently widely available in the Twin Cities (Birthing centers and hospitals)
- Growing consumer interest....

Why has it taken so long to catch on in the US?
Nitrous Oxide: Why so long to adopt?

• Rooks: $$

• 61% of women who have singleton vaginal births in the U.S. receive regional anesthesia for labor pain. Epidurals are the most effective pain mgt modality.

Nitrous Oxide

• All women do not need or want regional anesthesia. Those who do may be denied accessibility due to lack of or competing needs for the services of anesthesia professionals.

• This is especially true for women living in rural areas and delivering in institutions where anesthesia may not staff 24/7.

(Rooks, 2007)

Nitrous oxide may become increasingly in demand as the supply of anesthesiologists and nurse anesthetists to provide 24/7 access to labor epidurals and the need for some kind of relatively effective analgesia during labor (Rooks 2010)
Women want choices!

- *Great adjunct for natural childbirth* because it does not affect the fetus like narcotic analgesia
- Does not have the numbing effect of an epidural
- Has a calming effect which is helpful to relieve anxiety during labor
- Some women are not candidates for epidural

Nitrous Oxide: What is it??

- Commonly known as “laughing gas”
- Colorless, tasteless, non-flammable gas
- Liquid at room temperature
50% Nitrous Oxide/50% Oxygen used in labor is analgesia-not anesthesia!

- Analgesia or “minimal sedation” per American Society of Anesthesiologists (ASA)

- No special regulations or guidelines-”minimal risk”

Analgesia...NOT Anesthesia

- Patient awake and alert

- Protective laryngeal reflexes intact

- Self administration

- Effect titrated by frequency and intensity of inhalation
According to the ACNM Position Statement on Nitrous Oxide 2010... “Women should have access to a variety of approaches to promote comfort and reduce pain throughout labor”

Why Offer Nitrous Oxide in Labor?

“It is a fact that women in the United States have fewer options for childbirth pain management than women in Canada, Australia, and most of Western Europe.”

“Women in the United States need alternative ways to relieve labor pain.”

(Leeman et al., 2003; Marmor and Krol, 2002; Rooks, 2011)

Long history of safe use- over 50 years!
**Advantages**

- Rapid onset/offset
- Low cost
- Can be given at any point in labor
  - (never “too late”)
- Does not diminish contractions or slow labor
- No impact on the ability to push
- No known effect on fetal heart rate or newborn APGARs
- Allows for intact, but lessened, sensation of labor and birth
  - (which is desired by many women)
- Procedural analgesia option: repairs, manual removal, manual OP rotation, tamponade balloon placement

**Nitrous Oxide Advantages**

- Easy to set up quickly, and teach the patient how to use. Self administered

- Option for women who want minimal intervention, rapid onset of action

- May be able to postpone or avoid narcotics or epidural

- For normal, low risk, term patients- for those who cannot have an epidural...it’s another option!
Nitrous Oxide Mechanism of Action: How Does it Work?

- Exact mechanism is unknown

- Increases the release of endorphins, dopamine, prolactin, and various endogenous opioids within the spinal cord and brain while decreasing the release of cortisol (Rooks 2011)

- Anxiolysis-mediated by GABA (GABA plays the principal role in reducing neuronal excitability throughout the nervous system.)

- Basically… N20 affects the brain which modulates pain stimuli by way of descending spinal cord nerve pathways.

(Gabbe, Niebyl, & Simpson, 2006; Rosen, 2002)

Nitrous Oxide Mechanism of Action: How Does it Work?

- Nitrous oxide works by reducing the perception of pain and lowering anxiety levels.

- Resulting euphoria and dissociation may make pain more manageable.

- The ability to self administer nitrous oxide may help the woman feel more in control of pain (Zauderer 2016)
Physiology: How Does it Work?

- Enters body through inhalation, exits through exhalation
- Onset is <60 seconds
- Dose dependent for onset and effect
- Very weak accumulation in fat/tissues (metabolism is 0.004%)
- Elimination half-life is 5 minutes

(Gabbe, Niebyl, & Simpson, 2006; Rosen, 2002)

Excreted rapidly through the lungs...

Nitrous Oxide: How does it work?

- Less than 1% of nitrous oxide is metabolized or stored in the body- over 99% is exchanged through exhalation

- No effect on uterine activity or the progress of labor

- Sensory and motor functions are not altered

- Maternal respiratory depression is not a risk factor from nitrous oxide alone
Nitrous Oxide

Is it safe for the fetus or newborns?

• Potential neurotoxicity of anesthetic agents has been topic of interest in recent years
  • phenomenon called “apoptosis” seen ONLY in animal studies when exposed to extreme amount over long periods of time
• Also applies to sedatives, hypnotics, narcotics, and all anesthetic gases
• Nitrous oxide is one of a very long list of agents of interest in this regard

Fetal/Newborn Effects

• Nitrous oxide crosses the placenta resulting in approximately 80% of the concentration of the maternal serum blood level accumulating in the fetus within 15 minutes

• Nitrous oxide quickly leaves the body upon the first few respirations of the newborn. It does not cause respiratory depression

• Studies have not shown an effect on the fetal heart rate, breastfeeding, APGAR or behavioral assessment scores
What about use Preterm?

- Hemodynamic effect on maternal and fetal circulation: central vascular resistance in both were decreased by 30% with nitrous oxide inhalation

- Preterm fetuses are susceptible to ICH-use of nitrous oxide may increase the risk
  
  Polvi et al Obstet Gynecol Vol 87 No 6, June 1996

Nitrous Oxide

Challenges:

- Potential for
  - nausea (0-24%)
  - Dizziness (6-23%)
- Dysphoria may be unacceptable to some women
- Mobility:
  - patient is limited by length of tubing on machine
- Not for women who desire complete pain relief
Who may use Nitrous Oxide? (Allina)

- Can be used in any stage of labor, no time limit established in the literature

- Normal low risk patients >-37 weeks gest.

- Initial electronic fetal monitoring tracing reflects adequate oxygenation demonstrated by normal baseline rate, moderate variability, absence of recurrent variable or late decelerations, or prolonged decelerations. Intermittent auscultation or intermittent EFM may be used.

Use of Nitrous Oxide cont.

- If any concern for fetal status or category II EFM-continuous EFM should be done

- Minimal variability with recurrent variable or late decelerations that persists for >30 min despite intrauterine resuscitation efforts, any concern for fetal status, or Cat III EFM, discontinue nitrous oxide.

- Patient must be able to self administer nitrous oxide by holding her own mask without difficulty
Other Care Considerations

• No need for continuous pulse oximetry- baseline reading only, reapply if any concerns

• **2 hours** must pass after narcotic, benzodiazepine, or similar sedative medication before starting nitrous

• Epidural consent prior to nitrous use not needed, can be done just prior to the procedure.

Care Considerations

• No defined time limit for duration of use has been identified- provider order

• Nurse to remain with patient first 15 min, pt should be instructed to notify RN if she wants to get out of bed, must have someone in attendance if out of bed using nitrous

• Diffusion hypoxia- 100% oxygen by partial rebreather when discontinuing nitrous oxide for 5 min will prevent this
Contraindications for use

- Cannot be used in combination with other agents — e.g. IV opioids within last 2 hours, sedatives, epidural (considered conscious sedation)

- Acutely intoxicated, or on Methadone, Buprenorphine, Suboxone

Contraindications

- Documented B12 deficiency, pernicious anemia.

- Patients with pneumothorax, bowel obstruction, recent ear or eye surgery where there is potential for accumulation in a closed space.

- Cannot or unable to hold face mask

- Patients with impaired oxygenation (<95% on room air)

- Patients may not use nitrous oxide in tub or shower
Relative Contraindications (provider to assess suitability)

- Hx pneumothorax, acute asthma, emphysema, pulmonary hypertension, middle ear surgery or occlusion, current URI, COPD, cystic fibrosis, bowel obstruction, Crohn’s disease, graves disease, lupus erythematosus, increased intracranial pressure or intraocular surgery might not be candidates.

Use Caution.....

- The potential for nitrous oxide to accumulate in closed air spaces has been well documented.

- Use caution before using it in women with a previous history of pneumothorax, retinal surgery, and recent middle ear or sinus infection.

- Retinal surgery is a particular concern- Visual loss has been identified in patients who got nitrous oxide after eye surgery involving gas injection into the eye.

Starr and Baysinger, Anesthesiology.theclinics.com 2013
Equipment

• Portable tanks (N20 and O2) or may use wall O2

• Blender device mixes O2 and N20 to deliver a set 50:50% concentration

• Self administration by face mask with a demand valve-only get the nitrous by inhalation

• Patient exhales into the mask, scavenging system filters and diverts exhaled gas to wall suction. Not exhaled into room air

Implementation of a Nitrous Oxide Program

• Need buy-in from key stakeholders:
  - Anesthesia
  - OB Providers
  - Pediatric providers
  - All of the regulatory folks

• Staff and Provider Education: Toolkit (policy, consent, patient education, nitrous oxide articles, educational PowerPoints)

  Excellent Video: Society for Obstetric Anesthesia
  https://www.youtube.com/watch?v=l90bFv5Lg8g.

RN’s complete an online education and hands on competency
Implementation: What does Joint Commission say about Nitrous Oxide for Labor Analgesia?

- Self-administered Nitrous Oxide for an active laboring patient would be considered “Anxiolysis/Analgesia” – not moderate sedation.

- No H&P/H&P update required prior to initiation.

Before Nitrous is Used

- Provider assessment for suitability, H & P update (if required), order for use

- Informed consent documented

- Equipment check and proper set up

- Ensure no narcotics, sedatives, or benzodiazepines used prior to use
Order Example

- Continuous, 50% Nitrous Oxide/50% oxygen via Nitronox device.
- Intermittent or continuous self-administration for labor analgesia and anxiolysis.
- Assess vital signs within 30 minutes of initiation of nitrous oxide, and per labor orders/policy. Assess pain and RASS scores q 1 hour.
- Wait 2 hours to begin nitrous oxide if narcotics, benzodiazepines, or similar sedative medications have been given.
- No concurrent administration of narcotics with nitrous oxide.
- Wait 5 minutes after nitrous oxide administration to administer narcotics.
- Discontinue nitrous oxide if any concerns regarding maternal or fetal status, and initiate necessary resuscitation measures. (Contraindications to nitrous are patient with inability to hold their own facemask, patients who are intoxicated or have impaired consciousness, patients who have had intravenous opioids in the last 2 hours, those with pernicious anemia or documented B12 deficiency, anyone with oxygen saturations less than 95% on room air, or anyone taking methadone, buprenorphine, or suboxone.)

Patient/Family Education

- Proper use of mask—proper seal for inhalation and exhalation into the mask
- Patient must hold own mask—education is key!
- Call when getting up, someone in attendance when patient out of bed
- Educate re possible side effects (nausea, dizziness, dysphoria), report side effects
Patient/Family Education

- Intermittent vs continuous use
- Peak analgesic effect lags the start of it’s administration by 50 seconds, uterine contractions typically peak 30 seconds after they start
- Educate that may not provide complete pain relief
- Elimination quickly via lungs (elimination half life 5 min)

That’s a NO! If anyone else uses the mask - they will be escorted out and nitrous removed from the room
Nitrous Oxide (Allina)

Monitoring:

- RN in room for first 15 minutes to observe
  - thereafter, standard OB cares with intermittent external fetal monitoring
- **Studies show that women breathing nitrous oxide have higher O2 saturations than those breathing room air**
  - continuous pulse oximetry is not indicated
- Nitrous oxide mixture is 50% oxygen/50% Nitrous oxide
  - room air 21%
- Mild desaturations do occur during active labor in all women, regardless of pain relief method used

**Any concerns- call OB provider**

Patient/Staff Safety

- Biggest concern raised: apoptosis= programmed cellular death

  - Dose is critical determining factor for risk from exposure (occupational and pt use)

  - Apoptosis has only been demonstrated in animal studies when exposed to extreme amounts over long periods of time. (higher than amts typically used in general anesthesia)

  - FDA 2007: after investigating “we have no evidence that supports detrimental CNS effect in pediatric patients/staff exposed. They recommend no changes

Allina Health
Neurotoxic effects

• The effects on human fetuses or in children later in life who were exposed to nitrous oxide or other anesthetic agents in utero are unknown.

• Low concentrations and brief period to which a fetus would be exposed during labor (even a prolonged one) would be unlikely to result in a measurable effect even if such effects were later shown to be real.

(Starr and Baysinger, Anesthesiology.theclinics.com 2013)

Patient/Staff Safety: N2O effects on Cobalmin

• N2O oxidizes a physiologically active form of cobalmin (vit B12)- inactivating it

• Extremely high doses of N2O and/or long term exposure can cause bone marrow depression, macrocytic anemia, and neuropsychiatric disorders

• Effects reverse with time: Royston et al. research concluded that surgical (anesthetic doses) are at risk when receiving N2O >70% for >6 hrs.

• Conditions that reduce cobalmin (Crohns disease, celiac disease, gluten intolerance, pernicious anemia, strict vegan diet etc. increase risks of N2O exposure )

(Rooks 2011)
**Diffusion hypoxia???

- Defined as: Arterial O2 saturation below 90%.

- When N2O and oxygen is stopped, the amount of O2 available to the lungs is 21%.

- **N2O leaves the blood and enters alveoli faster than nitrogen can leave the alveoli to enter the blood** - this causes a rapid rise in the amount of N2O in the alveoli reducing the amount of oxygen even lower than 20% for normal blood absorption

- O2 sat drops can occur (less likely with 50/50 mix), it is usually not significant in healthy populations.

- Administering 100% O2 when d/c’ing nitrous can prevent any issues - follow your own hospital policy

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**Safety: N2O Monitoring/Exposure**

- NIOSH occupational exposure guidelines are <25 ppm/8 hrs (in Europe it’s <100 ppm)

- Periodic monitoring is done per institutional anesthetic gases policy

- No documented levels using Nitronox equipment have come close to 25 ppm
Need for Research

• *There is a general lack of US data on maternal and fetal outcomes, and a specific lack of data on:*  
  - sense of control/satisfaction with the childbirth experience  
  - effect on mother/baby interaction  
  - breastfeeding  
  - admission to special care  
  - infant outcomes at long term follow up  
  - costs

Nitrous Oxide

In Conclusion:

• Nitrous is a great option for many laboring women  
  – Many women will desire and appreciate

• Some will not tolerate it d/t side effects

• Nitrous can be a useful tool in helping patients who desire a less-medicated birth

• Nitrous can provide pain relief for bedside procedures requiring analgesia or anxiolysis
QUESTIONS?

References

thank you!

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