



The Safety of using 50% nitrous oxide/50% oxygen mix for analgesia

The PRO-NOX™ Nitrous Oxide Delivery System delivers a blended mixture of 50% oxygen and 50% nitrous oxide to spontaneously breathing patients.

The effects from breathing this mixture are analgesia (decreasing the sensation of pain), anxiolysis (decreased sense of anxiety) and dissociation (where the patient recognizes the presence of pain, but feels detached from the pain and is not bothered by it). The 50/50 mixture comes from separate oxygen and nitrous oxide cylinders at the point of use by a blender, as is the case with the PRO-NOX™ system. In some areas, it can be delivered as a pre-mixed solution in a single compressed-gas cylinder (trade names include Linde's Entonox, and Air Liquide's ALnox and Equanox).

This inhaled analgesic has a long history of use, both within the hospital, and in alternative care settings (for home births, on-scene use by EMS, dentist offices). These uses outside of the hospital are all under the care of non-MD healthcare providers, including nurse-midwives, paramedics, and dentists.

The safety of nitrous oxide use with spontaneously breathing patients is due to several factors.

1. The properties of nitrous oxide.

While nitrous oxide is sometimes referred to as a weak anesthetic, this anesthetic action only becomes significant at concentrations much higher than delivered with the PRO-NOX™ system. Nitrous oxide has a MAC value (minimum alveolar concentration required to prevent movement in 50% of patients when a noxious stimulant such as an incision is applied) of 105. That means that even breathing 100% nitrous oxide (which is only theoretical, as you need oxygen as well), you will not be providing reliable anesthesia. At 50% concentration with oxygen, nitrous oxide does not induce anesthesia.

50% nitrous oxide does not inhibit the airway reflexes₁ or affect respiratory pattern.

The safety of 50% nitrous oxide is reflected in Rosen's review of its use in the labor and delivery setting.

Although nitrous oxide is certainly not a potent analgesic, studies suggest a beneficial effect for many parturient women. It is easy to administer and, despite some early reports of unconsciousness, particularly with 75% nitrous oxide, 50% nitrous oxide appears to have been safely used by very large numbers of women over many years. This technique potentially could be safely used by a wide variety of health caregivers (e.g., midwives, labor nurses, obstetricians, family physicians) without need for an anesthesiologist or nurse anesthetist. (Rosen 2002)₂

2. The rapid elimination of nitrous oxide through the lungs.

When the patient stops inhaling from the PRO-NOX™, the concentration of nitrous oxide within the blood and its effects on the patient are both markedly diminished within one minute, and clinical effect is entirely reversed within 5 minutes³.

3. Demand valve delivery with patient control of the mask or mouthpiece.

The PRO-NOX™ system incorporates a demand valve. The patient holds their own mask or mouthpiece in place and must maintain an active seal by pressing the mask to their face or with their lips around the mouthpiece. Only then will an active inspiratory effort trigger the demand valve allowing the patient to pull in the 50/50 mix. Respiration without the deliberate placement of the mask or mouthpiece does not result in further delivery of the mix, preventing unintended exposure.

4. The presence of oxygen.

Using oxygen as the second gas in a 50/50 mix provides reassurance that the patient will be well oxygenated regardless of minor changes in respiratory pattern due to pain or patient position during the procedure.

A recent German study looked at the use of nitrous oxide analgesia in the setting of aesthetic dermatology. Their conclusion was this:

The pronounced analgesia, the easy self-administration, the fast onset and complete recovery after a few minutes and the low ratio of side effects make the N₂O/O₂ inhalation to an ideal addendum in the management of larger painful procedures in dermatology as long as contraindications and safety precautions are respected.⁴

Self-administration of 50% nitrous oxide with 50% oxygen is well-studied, safe, and effective. Its value is summed up in this statement from the website of Air Liquide, producer of ALnox gas:

A 50% Nitrous Oxide and 50% Oxygen mixture is an analgesic drug. It delivers safe sedation (2) and analgesia for elective diagnostics and therapeutic procedures that can provoke significant anxiety or pain in adult or pediatric patients. It does not provide any anesthetic effect or respiratory drive depression. It does not cause loss of consciousness and the laryngeal closure reflex is maintained (3). It is very well tolerated (2) and with 50% Oxygen, the risk of hypoxemia is minimized. With rapid reversal, the effects disappear in 1 to 3 minutes (1).

(1) **Pons PT.** Nitrous oxide analgesia. *Emergency Medicine Clinics of North America* 1988;6:777-82.

(2) **Onody P.** et al. *Safety of inhalation of 50% Nitrous Oxide/Oxygen Premix.* *Drug Safety* 2006; 29(7):633- 40

(3) **Cleaton-Jones P.** The laryngeal-closure reflex and nitrous oxide-oxygen analgesia. *Anesthesiology* 1976; 45: 569-70.

1. Cleaton-Jones P. The laryngeal-closure reflex and nitrous oxide-oxygen analgesia. *Anesthesiology* 1976; 45: 569-70.

2. Rosen, MA. Nitrous oxide for relief of labor pain: A systematic review. *Am J Obstet Gynecol* 2002; 186: S110-26.

3. Position Statement: Nitrous Oxide for Labor Analgesia. American College of Nurse-Midwives, 2009

4. M. Drozner. [Nitrous oxide - oxygen analgesia in aesthetic dermatology]. *Hautarzt.* 2013 Jun;64(6):435-42. Translation accessed from Pubmed <http://www.ncbi.nlm.nih.gov/pubmed/23760542>

This paper is intended to inform practitioners about nitrous oxide use and related literature. It is not intended to replace legal or medical opinion. Every practitioner must decide whether the use of nitrous oxide within their practice is appropriate and/or within the regulatory guidelines to which they are subject.