Safety and Utility of a Novel Nitrous Oxide Delivery System in Cosmetic Surgery: A National Survey of Physician Practices

In recent years, cosmetic dermatologic surgery has witnessed tremendous growth. This is likely associated with expanding indications, improved technology, increased accessibility, and society's greater acceptance of cosmetic treatments, including men and millennials.[1,2] Although procedures can be effective, many are associated with periprocedural discomfort. Several modalities have been used to help alleviate this, including topical and local anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), benzodiazepines, and opioids. Inhaled nitrous oxide has received attention due to its rapid onset, short half-life, low side-effect profile, and ease of clinical integration. Since 1980, the field of dermatologic surgery has pioneered work on nitrous oxide,[3] which can reduce or even eliminate the need for systemic pain medication.[4] After final inhalation, its neurologic effects generally diminish within 5 to 7 minutes. Because of the increase in in-office cosmetic procedures, nitrous oxide may offer a practical solution. To shed more light on the use of nitrous oxide, we surveyed cosmetic physician practices to examine their experiences and perspectives on its safety and utility.

An online survey was distributed to physician practices who specialized in dermatology, plastic surgery, and aesthetics and who had a novel nitrous oxide delivery system (Pro-Nox, CAREstream America, Lake Mary, FL). The survey was sent in January to February 2021. The survey included demographic data as well as experiences and perspectives. Top-box scoring was used to evaluate questions using a Likert scale.

A total of 204 respondents completed the survey. Respondents had a mean of 14.3 years (R: 0–40 years) working in cosmetic surgery and 2.6 years (R: 1–15 years) using this nitrous oxide delivery system. On average, respondents performed 11 to 20 (23.5%), 31 to 40 (22.6%), >50 (19.6%), 21 to 30 (12.8%), 1 to 10 (10.3%), and 41 to 50 (10.3%) cosmetic treatments per week. For cosmetic treatments involving this nitrous oxide delivery system, there was an average of 1 to 3 (42.7%), 4 to 6 (27.9%), 7 to 9 (12.3%), 10 to 12 (8.8%), 0 (3.9%), 13 to 15 (3.4%), and >15 (1.0%) per week.

Of all respondents, 64.2% combined this nitrous oxide delivery system with other medications to increase patient comfort. These included an NSAID (47.1%), a benzodiazepine (22.1%), an opioid (12.8%), and a midazolam/ketamine/ondansetron melt (3.4%). The top 10 procedures performed using this nitrous oxide delivery system were radiofrequency microneedling (61.3%), ablative resurfacing laser (51.5%), nonablative resurfacing laser (45.1%), ultrasound device (32.8%), cosmetic injectable (29.4%), surgical procedure (27.0%), platelet-rich plasma (23.5%), other radiofrequency devices (18.1%), facilitation of local or tumescent anesthesia (16.2%), and microneedling (13.2%).

Respondents generally believed this nitrous oxide delivery system to be safe for patients (Figure 1). Of all respondents, 7.8% experienced any adverse event, which included headache, dizziness, and nausea and vomiting. Overall, 3 respondents (1.5%) reported that they may have experienced a patient who lost consciousness, and a single respondent (0.5%) had referred a patient to the hospital for headache and sense of doom caused by excessive inhalation. Most respondents (84.8%) have patients actively breathe this nitrous oxide delivery system during laser and other energy-based procedures on the head, neck, and chest areas, and no one has experienced a flammable situation.

Overall, 99.0% believed this nitrous oxide delivery system to be effective at making cosmetic procedures more comfortable, and 100.0% believed it to be easy to use. The majority were satisfied with their use (98.5%) and believed that their patients were also satisfied (99.0%).

This novel nitrous oxide delivery system has been widely used to provide patient analgesia during cosmetic procedures. It is cleared by the US FDA as an analgesic device that can deliver inhaled nitrous oxide 50%/oxygen 50%. Given this fixed blend, there is a low risk for losing consciousness. Although our data demonstrate that 3 respondents may have experienced loss of consciousness, descriptions of the events included "over inhalation" and "very brief and reversed quickly once [it was] stopped." More information is required to determine whether these events were true loss of consciousness or simply oversedation. Based on our data, a conservative estimate for the total number of cosmetic treatments performed with this nitrous oxide delivery system is 140,556, which would make the incident rate 0.002% for these 3 cases. The system only delivers nitrous oxide on demand through a one-way valve during inhalation, so patients must actively work to inhale the mixture. This reduces many of the risks attributed to continuous systems.

Supplemental databases were also reviewed to determine safety. Internal safety data from CAREstream America was assessed, and there were no reports of any significant adverse events from over 3,000 users over a 3-year period. There were no formal incident reports filed to the FDA. In addition, a retrospective database review was performed at an urban cosmetic dermatology clinic (Laser and Skin Surgery Center of New York, New York, NY) over a 2-year period. The billing database was queried for patients who used this nitrous oxide delivery system. Within a 2-year period, 263 patients were found, and there were no significant adverse events. This is an underestimate of the true number who used this system because it is not entered separately into the billing database for many patients. In practice, we have found this nitrous oxide delivery system to be an

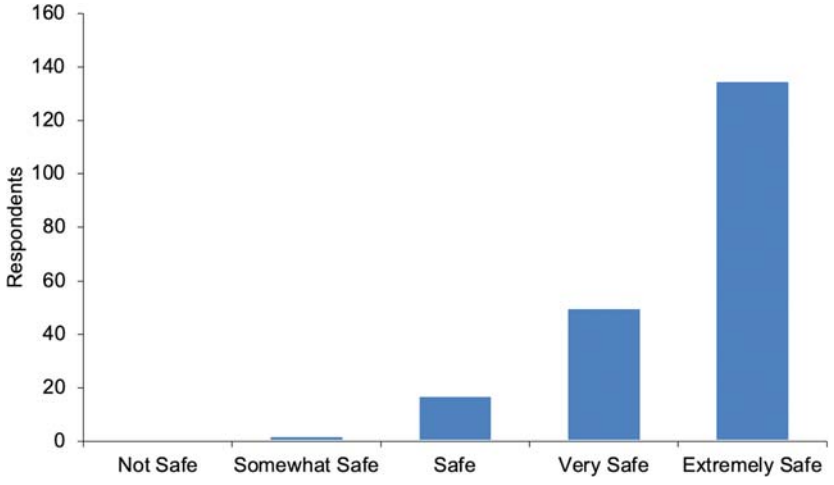

Figure 1. Perceived safety of a novel nitrous oxide delivery system by respondents.

effective analgesic, especially as an adjunctive modality, for several cosmetic treatments.

Owing to the COVID-19 pandemic, additional safety measures have been implemented to ensure patient safety, comfort, and confidence in clinical settings.[5] This nitrous oxide delivery system incorporates an antiviral filter, which can reduce the risk of exhalation of viral particles into the room. This filter has been independently verified to have 99.99% filtration efficiency. This can offer additional comfort when using this device in our current practice environment.

Although surveys provide lower-level evidence compared with prospective studies, our data still demonstrate an overall safety record in combination with 2 separate database reviews. This novel nitrous oxide delivery system is an FDA-cleared device that can safely, reliably, and predictably provide analgesia. It seems that this technology is a practical adjunctive agent that can provide pain control during procedures that are common in cosmetic surgery, including cosmetic injectables, surgical procedures, and treatments with lasers and energy-based devices.

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