The Dangers of Nitrous Oxide Administration in Patients with Cyanocobalamin (B₁₂) Deficiency: A Systematic Review

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Abstract

Background: This review was conducted to investigate the association between nitrous oxide and cyanocobalamin (B₁₂) deficiency, and the dangers of administering nitrous oxide to patients who may have unrecognized vitamin B₁₂ deficiency.


Results: The search assessed 219 reports. Fifty-two were included in the final analysis, including 11 case reports. The included studies were primarily concerned with raising awareness of the apparently increasing use and subsequently increasing harms of N.0. in patients with B₁₂ deficiency. There was limited reference to regulation of nitrous oxide exposure in the published studies, no suggestions for harm reduction strategies. In general, there is a lack of awareness of N.O.-related harms in cyanocobalamin deficient patients.

Discussion: There is a positive relationship between extended administration of nitrous oxide and severe depletion of vitamin B₁₂ in patients with cyanocobalamin deficiency. Such depletion could result in neurological disorders, peripheral paresthesia, even dysfunction of organ systems. Health Professionals should be aware of the toxic effects of N.O. and thoroughly evaluate each patient’s medical history prior to its administration.

Introduction

Nitrous Oxide (N.O.) use is very prevalent in dentistry and medicine alike, as the benefits of its use for mild sedation have been documented in the literature of both fields. Adverse effects of N.O. administration on certain populations have also been noted, but to a much greater extent in the medical literature. Due to its frequent use in dentistry in providing anxiolysis, analgesia, and aiding in behavioral management, it is imperative that dental professionals are well-informed about the dangers of N.O. use in particular populations of patients. One such population that continues to grow are those with Cobalamin (Vitamin B₁₂) deficiencies.

Methods

Systematic search: • Developed strategy to review literature regarding correlation between nitrous oxide administration and cyanocobalamin deficiency, adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Selection Criteria: • Inclusion: Studies that specifically address N.O. dangers, cyanocobalamin deficiency, and N.O. administration in patients with cyanocobalamin deficiency. • Exclusion: Duplicate records. Reports minimally relevant to the dental field and/or related to N.O. addiction.

Preliminary Results: For articles excluded within the full systematic review, the most common reason for exclusion was not specifically addressing cobalamin deficiency in patients and nitrous oxide together. Of full text articles meeting the established inclusion criteria (24.7%), the majority indicate that patients with vitamin B₁₂ deficiency are exceedingly sensitive to neurologic deterioration following nitrous oxide anesthesia. In children, cobalamin deficiency is a rare cause of developmental delay, but it is treatable and preventable. The use of nitrous oxide in a child with even mild developmental delay may be contraindicated if unrecognized, the neurologic deterioration becomes irreversible and may result in death.

Results

A review of the literature reveals the need for further research into the effects of nitrous oxide on patients with cobalamin deficiency. The results of this review suggest that there is a need for increased awareness among healthcare professionals regarding the potential dangers of nitrous oxide administration in patients with cobalamin deficiency. The findings of this review have important implications for the practice of medicine and dentistry, as well as for public health policy. The results of this review also have important implications for the practice of medicine and dentistry, as well as for public health policy. The results of this review also have important implications for the practice of medicine and dentistry, as well as for public health policy.

Discussion

Conclusions

• Patients who present with vitamin B₁₂ deficiency, and then are exposed to extended periods of nitrous oxide, can become severely depleted of vitamin B₁₂, which could result in neurological disorders, peripheral paresthesia, even dysfunction of organ systems.

• Dental professionals need to ask questions about diet, supplement use, OTC medication use, etc. for patient safety and liability if considering using N.O. for sedation.

• If pts have increased MCV prior to anesthesia, reconsider using N.O. If pts have unexplained anemia, reconsider using N.O.

• A good patient history is very important

• Health professionals should be aware of the toxic effects of Nitrous Oxide and be able to identify potential cyanocobalamin deficiency in patients pre-operatively.

Selected References

• Camille Desprairies, Apolline Imbard, Bérengère Koehl, Mathie Lorrot, Jean Gaschignard, Julie Sommet, Samia Pickard, Laurent Holvoet, Albert Faye, Malika Benkerrou, Jean-François Benoist, Manuel Schiff, “Nitrous oxide and vitamin B12 in sickle cell disease: Not a laughing situation,” Molecular Genetics and Metabolism Reports, 2020.


• Download .nbib Format: digimon.0909


• Admir Hadzic, Krzysztof Glab, Kevin V. Sanborn, Daniel M. Thys; Severe Neurologic Deficit after Nitrous Oxide Anesthesia. Anesthesiology 1995; 83:863–866.

Identification of new studies via databases and registers

Records identified from: Database (n = 219)
- PubMed (n = 219)
- Science Direct (n = 862)
- Jama Internal Medicine (n = 7)
- ASA Publications (n = 19)
- Semantic Scholar (n = 859)
- The American Journal of Clinical Nutrition (n = 26)
- The BMJ (n = 3,310)
Total (n = 5,302)

Records removed before screening: Duplicate records (n = 2,572)
- Records marked as ineligible by automation tools (n = 0)
- Records removed for other reasons (n = 0)

Records screened (n = 2,730)
- Reports sought for retrieval (n = 229)
- Reports assessed for eligibility (n = 219)

Records excluded (n = 2,531)
- Reports not retrieved (n = 10)
- Reports excluded: Patients w/o vitamin B12 deficiency (n = 53)
- Non-related to dental field (n = 44)
- Nitrous-oxide addiction (n = 68)

New studies included in review (n = 54)