

Effects of Nitrous oxide on Serum Vitamin B12 Levels in Healthcare Workers: An Institutional Based Study

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ABSTRACT

Background: Nitrous oxide is a gas that is odorless, colorless, and has a sweet taste at room temperature. Nitrous oxide has several uses, including in surgery and dentistry (referred to as "laughing gas"), in automotive racing, and in aerosol spray propellants. The present study was conducted for assessing effects of nitrous oxide on serum vitamin B12 levels in healthcare workers.

Material and methods: The study included a sample of 50 healthcare professionals, ranging in age from 24 to 55 years. The exposed group consisted of surgeons, anesthesiologists, and operating room nurses, all of whom provided full-time assistance during surgical operations on a daily basis. These professionals typically spent a minimum of five hours in the operating room, a setting characterized by the presence of nitrous oxide (N₂O) and volatile anesthetics such as isoflurane and sevoflurane. In contrast, the control group was composed of 25 nurses from various departments within the same hospitals, none of whom had experienced occupational exposure to N₂O or volatile anesthetics during their careers.

Results: In this study, the mean age of the exposed subjects was 44.25 ± 7.69 years, and the mean age of the controls was 45.11 ± 8.56 years. There were 5 males and 20 females in the exposed group and there were 8 males and 17 females in the control group. Among the exposed subjects, nausea/vomiting were observed in 4 subjects, dizziness was seen in 3 subjects,

tachycardia was faced by 7 subjects and euphoria was faced by 4 subjects. Mean vitamin B12 levels in the control subjects were 525.14 ± 6.5 pg/ml and the mean vitamin B12 levels among the exposed subjects were 499.67 ± 2.01 pg/ml.

Conclusion: This study concludes that more side effects are seen in individuals who are exposed to nitrous oxide. There were not significant differences in vitamin B12 levels in exposed groups.

Keywords: Nitrous Oxide, Vitamin B12, Side Effects, Deficiency.

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INTRODUCTION

Nitrous oxide is a gas that is odorless, colorless, and has a sweet taste at room temperature. Nitrous oxide has several uses, including in surgery and dentistry (referred to as "laughing gas"), in automotive racing, and in aerosol spray propellants. The aerosol spray propellants that typically use nitrous oxide are whipped cream canisters and cooking sprays. Unfortunately, these over-the-counter household items are a source of nitrous oxide that can be used for recreational use. The most popular is the use of industrial-grade canisters having the slang term "whippets." The nitrous oxide can be extracted by pushing the nozzle down slightly to the side and catching the released gas with a balloon. The contents of the balloon can then be directly

inhaled, giving an instant feeling of euphoria.¹⁻³ Vitamin B₁₂ (cyanocobalamin) is an integral component of two biochemical reactions in man: the conversion of L-methylmalonyl coenzyme A into succinyl coenzyme A and the formation of methionine by methylation of homocysteine. The transmethylation reaction is essential to DNA synthesis and to the maintenance of the myelin sheath by the methylation of myelin basic protein. Active vitamin B₁₂ contains cobalt in its reduced form (Co⁺). Nitrous oxide produces irreversible oxidation to the Co⁺⁺ and Co⁺⁺⁺ forms that renders vitamin B₁₂ inactive. Five cases (four from the literature and one new case) are presented in which patients unsuspected of having vitamin B12 deficiency developed subacute combined

degeneration of the spinal cord following nitrous oxide anesthesia. Patients with vitamin B₁₂ deficiency are exceedingly sensitive to neurologic deterioration following nitrous oxide anesthesia. If unrecognized, the neurologic deterioration becomes irreversible and may result in death.⁴⁻⁶ Hence; the present study was conducted for assessing effects of nitrous oxide on serum vitamin B12 levels in healthcare workers.

MATERIALS AND METHODS

The study included a sample of 50 healthcare professionals, ranging in age from 24 to 55 years. The exposed group consisted of surgeons, anesthesiologists, and operating room nurses, all of whom provided full-time assistance during surgical operations on a daily basis. These professionals typically spent a minimum of five hours in the operating room, a setting characterized by the presence of nitrous oxide (N₂O) and volatile anesthetics such as isoflurane and sevoflurane.

In contrast, the control group was composed of 25 nurses from various departments within the same hospitals, none of whom had experienced occupational exposure to N₂O or volatile anesthetics during their careers. The statistical analysis was conducted utilizing SPSS software.

RESULTS

In this study, the mean age of the exposed subjects was 44.25 ± 7.69 years and the mean age of the controls was 45.11 ± 8.56 years. There were 5 males and 20 females in the exposed group and there were 8 males and 17 females in the control group.

Among the exposed subjects, nausea/vomiting were observed in 4 subjects, dizziness was seen in 3 subjects, tachycardia was faced by 7 subjects and euphoria was faced by 4 subjects.

Mean vitamin B12 levels in the control subjects were 525.14±6.5 pg/ml and the mean vitamin B12 levels among the exposed subjects were 499.67±2.01 pg/ml.

Table 1: Distribution of the study group by age and gender.

Variable	Exposed (n=25)	Non-exposed (control) (n=25)
Age	44.25 ± 7.69	45.11 ± 8.56
Gender		
Males	05	08
Females	20	17

Table 2: Health effects in the exposed subjects.

Health effects	Exposed group (n=25)
Nausea/vomiting	04
Dizziness	03
Tachycardia	07
Euphoria	04
Total	18

Table 3: Effect of Nitrous Oxide on Vit B12 levels

Group	Mean Vit B12 levels (pg/ml)
Exposed group	499.67±2.01
Control group	525.14±6.5

DISCUSSION

Nitrous oxide has long enjoyed a reputation for being the safest general anaesthetic. This position was recently challenged when it was discovered that nitrous oxide oxidizes and inactivates vitamin B₁₂ in the form methylcobalamin, the bound cofactor of the methionine synthase, the enzyme responsible for recycling methionine. The serum methionine level is, in fact, reduced during nitrous oxide anaesthesia and there are extensive metabolic consequences.³

Methionine plays a crucial role in the synthesis of thymidine, one of the bases of deoxyribonucleic acid (DNA). This is almost certainly the cause of the megaloblastic anaemia and leucopaenia which follows prolonged administration, and it could well explain the foetotoxic effects of nitrous oxide. Methionine depletion is also

implicated in the neurological deficit which has been clearly shown to be a complication of chronic nitrous oxide abuse.⁷⁻¹⁰

In this study, the mean age of the exposed subjects was 44.25 ± 7.69 years and the mean age of the controls was 45.11 ± 8.56 years. There were 5 males and 20 females in the exposed group and there were 8 males and 17 females in the control group. Among the exposed subjects, nausea/vomiting were observed in 4 subjects, dizziness was seen in 3 subjects, tachycardia was faced by 7 subjects and euphoria was faced by 4 subjects. Mean vitamin B12 levels in the control subjects were 525.14±6.5 pg/ml and the mean vitamin B12 levels among the exposed subjects were 499.67±2.01 pg/ml. Hakimoglu S et al⁴ investigated the effects of nitrous oxide on plasma total homocysteine and vitamin B12 levels in patients with or without methyltetrahydrofolate reductase

(MTHFR) gene mutation. After obtaining the ethics committee approval and written informed consents of patients, 93 patients between 18-70 years of age scheduled for surgery anticipated to last 1-4 hours were enrolled in the study. Patients with contraindications for nitrous oxide use were excluded. Preoperatively, blood samples were obtained from all patients for the determination of MTHFR gene mutation. Anesthesia induction was achieved with 3 mg.kg⁻¹ of propofol and 1 µg.kg⁻¹ of fentanyl. Anesthesia maintenance was performed with sevoflurane and with a carrier gas composed of 40 % O₂ and 60 % N₂O. Venous blood samples were obtained after venous cannulation, and 24 hours after extubation for the analysis of plasma total homocysteine, vitamin B12 levels. Eighty-one patients were included in the study. Postoperative vitamin B12 levels were found to be significantly lower when compared with their preoperative levels ($p < 0.05$). It was found that MTHFR gene polymorphism had no significant effect on postoperative plasma total homocysteine and serum vitamin B12 levels ($p > 0.05$). Postoperative plasma total homocysteine levels were found to be significantly different between patients with operation times under and over 3 hours ($p = 0.028$). They concluded that MTHFR gene polymorphism had no significant effects on postoperative plasma total homocysteine levels. Massey TH et al⁵ reported case of a 36-year-old man who presented to hospital with a 5-week history of ascending limb paraesthesiae and balance difficulties. He had no medical or travel history of note but admitted habitual nitrous oxide (N₂O) inhalation. Neurological examination revealed a sensory ataxia with pseudoathetosis in the upper limbs and reduced vibration sensation to the hips bilaterally. Significant investigation results included a low serum vitamin B12 concentration, mild macrocytosis and raised serum homocysteine concentration. T2 MRI of the spinal cord demonstrated increased signal extending from C1 to T11 in keeping with a longitudinal myelitis. The patient was diagnosed with a myeloneuropathy secondary to vitamin B12 deficiency, resulting from heavy N₂O inhalation. He was treated with intramuscular vitamin B12 injections and received regular physiotherapy. At discharge, he was able to mobilise short distances with the aid of a zimmer frame and was independently mobile 8 weeks later.

CONCLUSION

This study concludes that more side effects are seen in individuals who are exposed to nitrous oxide. There were not significant differences in vitamin B12 levels in exposed groups.

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