Nitrous Oxide as a Cause of Myelopathy in Younger Patients: A Case Series, Management Strategies and Review of Literature

Thomas Noh MD; Osman Gamaleldin MD; Hebah Hefzy MD; Mokbel K. Chedid MD, FACS
Department of Neurosurgery and Neurology, Henry Ford Hospital
Detroit, MI

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Introduction

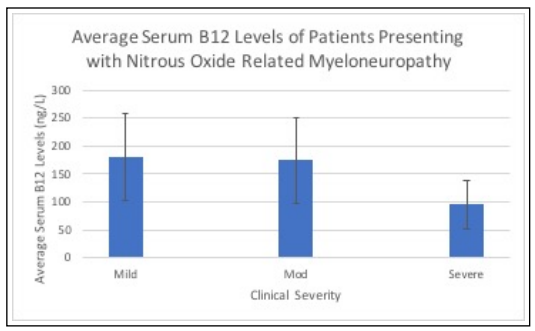
As the recreational use of nitrous oxide in the public has increased, there have been increasing case reports of nitrous oxide related myeloneuropathies. Although myelopathy is a common finding in severe cervical spinal stenosis, it should raise flags in younger patients. We report the clinical and radiological manifestations in 6 cases with nitrous oxide related subacute combined degeneration of the spinal cord from a single large tertiary medical center and offer a review of the literature.

Methods

Our case series included 6 patients seen from 2014 to 2018 and followed over 3-60 months that were identified as having nitrous oxide related myelopathy. Chart review was conducted to describe the history and physical findings of each patient. A thorough literature search was performed using MEDLINE and EMBASE using the search terms "nitrous oxide", "subacute combined degeneration", "case report", and "myelopathy." In total, 34 publications met the inclusion criteria, with 58 patients included in our analysis.

Results

- The majority of cases occurred after prolonged NO use, however, close to half of our pooled cases (23/49, 47%) presented after an NO-related anesthetic event
-Some of these patients were discovered to have some underlying B12 depleting pathology such as pernicious anemia, however not everyone was tested
-The average age of patients overall was 37 years. There was a predominance of males (63%) compared to females (37%). The average age of an anesthetic-related patient was 50 while the average age of patients who abused NO was 25 years
-We noticed a clinical pattern that all patients reported sensory symptoms and so we graded those with only sensory symptoms and subjective weakness as having mild symptoms (10/49, 20%). Many patients were noted to have additional symptoms indicating involvement outside the dorsal columns such as observer-graded weakness and urinary symptoms. We categorized these patients into a "moderate" symptom group (32/49, 65%). Some patients were found to have all of the above with diffuse spinal cord involvement and cognitive effects which we categorized as "severe" (6/49, 12%)
-A trend between the severity of neurologic impairment and serum levels of B12 was noted (Graph 1), although this was not statistically significant
-The average B12 levels on presentation of all anesthesia cases (109, 95% CI: 22-196) also tended to be lower than cases related to abuse (222, 95% CI: 133-311), although again not statistically significant



Discussion

-NO induced myelopathy always involves the cervical dorsal columns from both a clinical and radiographic standpoint. Patients often complain of feeling subjectively weaker in their lower extremities. Urinary/fecal symptoms and sexual dysfunction are also not uncommon, however, these also usually improve. Since the corticospinal and sympathetic tracts are more anterior and lateral to the posterior columns, it would stand to reason from an anatomical standpoint that there is involvement in these systems when the disease is severe.
-There are many established reports of nitrous oxide anesthesia-related subacute combined degeneration. The majority of these cases unmask underlying cobalamin deficiencies as pernicious anemia, vegetarian diets, or malabsorption. Patients abusing nitrous oxide, however, are typically younger and have no predisposition- which was reflected in our series and in the review of pooled cases.
-NO related myelopathy has been reported after anesthetic events and abuse by healthcare professionals. More recently, however, recreational use has skyrocketed with up to half of young adults in the UK admitting to use
-Diagnostic workup should includes CBC, B12, MMA, homocysteine levels, parietal cell and intrinsic factor antibodies. Imaging and neurodiagnostic includes MRI of the likely involved spine levels, nerve conduction studies/EMG and, rarely, visual evoked potentials (VEP). B12 levels are usually low but can be normal or only mildly decreased in some cases
-Treatment Recommendations: Abstinence from NO, B12 replacement either in the form of intramuscular or subcutaneous injections or via oral replacement. If oral therapy is pursued, strict compliance should be advised. B12 and MMA levels should be followed up in clinic.
-There is very limited evidence from one case report published nearly 30 year ago suggesting a beneficial effect for methionine in patients not responding to abstinence and B12 supplementation

Conclusions

Although myelopathy is a common finding in patients with severe cervical spinal stenosis, further consideration should be given to younger patients. Patients with nitrous oxide related myelopathy tend to have worse symptoms when vitamin B12 levels are less than 100 ng/L and have improved recovery

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Learning Objectives

1) Suspect other pathology when younger patients present with signs of myelopathy

2) Measuring B12 levels may correlate with severity of disease

3) Treat B12 deficiency with IM injections