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Effect of Chronic Exposure to Trace Anaesthetic Gases on Plasma Homocysteine levels in Operating Room Personnel

Adam Amararapu[1], Nagaraj Gajagouni[2], Manasa Surampalli[3]

[1]Associate Professor, [2]Assistant Professor, [3]Post Graduate, Dept. of Anesthesia, MNR Medical College and Hospital, Sangareddy District, Telangana 502285, India.

Abstract

Introduction: A growing body of evidence indicates that Homocysteine acutely rises as a side effect of exposure to Nitrous oxide during surgery in adults. Under normal conditions, Homocysteine is remethylated back to Methionine by the enzyme Methionine synthase which requires the reduced form of Vitamin B12 as a coenzyme and 5-Methyltetrahydrofolate as the methyl donor. Exposure to N_2O inhealthcare workers is associated with alterations of Vitamin B12 metabolic status. *Aim:* To find the Effect of Chronic Exposure to Trace Anaesthetic Gases on Plasma Homocysteine levels in Operating Room Personnel. Objective of my study is to find plasma Homocysteine levels in operating room personnel compared to non exposed. *Materials and Methods:* This study is conducted on 60 personnel. A total of 30 subjects exposed to waste Anaesthetic gases for a minimum of 5 years in unscavenged operation theatres and also 30 controls who were not exposed to Anaesthetic gases were selected at random to compare. From all the cases and controls detailed information pertaining to various epidemiological parameters and evaluated the level of serum Homocysteine by using ADVIA Centaur and ADVIA Centaur XP systems. *Results:* Mean Homocysteine value in over all analysis OT exposed group is 13.285 µmol/L and in controls is 10.545 µmol/L which are not equal. The p-Value of 0.00135 is "statistically significant", there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure. *Conclusion:* Subjects in the exposed group are distributed in the Homocysteine values of >12 µmol/L while the subjects in the control group are distributed within the Homocysteine value of <12 µmol/L. Statistical analysis showed significant difference in Homocysteine levels between OT exposed and non exposed groups. So we conclude that long term exposure to trace Anaesthetic gases like Nitrous oxide can lead to elevated Homocysteine levels in health care workers.

Keywords: Homocysteine levels; 5-Methyltetrahydrofolate; Nitrous oxide.

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Introduction

Nitrous Oxide was first Synthesized by Joseph Priestly in 1722. Its Psychotropic effects were first appreciated by Humphrey Davy. The first clear association of N_2O and hematologic disease was reported by Lassen et al. in the Lancet in 1956. They studied it prospectively and found that Granulocytopenia developed on the fourth day (with 50% N_2O). A Bonemarrow biopsy was consistent with Pernicious anaemia with Megaloblastic changes. In 1978, Sahenk reported a case of polyneuropathy from recreational Nitrous oxide use and Layzer reported on dentists who

Corresponding Author: Nagaraj Gajagouni, Assistant Professor, Dept. of Anesthesia, MNR Medical College and Hospital, Sangareddy District, Fasalwadi, Telangana 502285, India.

E-mail: nagaraj.gajagouni@gmail.com

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developed polyneuropathy and it was linked to the deficiency of Vitamin B12. A growing body of evidence indicates that Homocysteine acutely rises as a side effect of exposure to Nitrous oxide during surgery in adults [1]. Homocysteine is an intermediary metabolite in the metabolism of the sulfur-containing amino acids. It is produced by de-methylation of Methionine and is a substrate for synthesis of Cystathionine and then Cysteine. Under normal conditions, Homocysteine is remethylated back to Methionine by the enzyme Methionine synthase which requires the reduced form of Vitamin B12 as a coenzyme and 5-Methyltetrahydrofolate as the methyl donor.

Nitrous oxide irreversibly oxidizes the Cobalt atom of Vitamin B12, inactivating it which is a co-factor for Methionine synthase. Whether this acute effect translates into clinical outcomes of relevance has been the research objective of two recent prospective randomized control trials in adults1-3. In these trials, Nitrous oxide induced acute Hyperhomocysteinemia (>13.4 µmol/L) was associated with increased risk of Myocardial ischemia, and other major post-surgical complications1. Exposure to N_2O inhealthcare workers is associated with alterations of Vitamin B12 metabolic status, theextent of which depends on the level of exposure [4,5]. Some of these studies havedemonstrated a relationship between N_2O exposure and altered Vitamin B12 metabolismand plasma Homocysteine levels. Here, we evaluated the level of serum Homocysteinein personnel exposed to ot atmosphere in Gandhi hospital Secunderabad, and compared with non OT healthy controls by using ADVIA Centaur and ADVIACentaur XP systems.

Materials and Methods

Blood samples are collected according to National Committee for Clinical Laboratory Standards. 5 ml of blood collected in EDTA vaccutainers from an antecubital vein after 6-8 hours of fasting and should not have a high protein meal 6-8 hours before collection from all the subjects who gave their consent to participate in the study after explaining to them the purpose of study. Samples are centrifuged and red blood cells are separated. Speciemens are capped tightly and refrigerated at 2-8^{0}C until testing.

A total of 30 subjects exposed to waste Anaesthetic gases for a minimum of 5 years who routinely provide full-time assistance during operations on a day-to-day basis in operation theatres, who gave their consent to participate in the study are registered to study various epidemiological parameters and to screen for the plasma Homocysteine levels. Obtained the permission from institutional Ethical committee.

Inclusion Criteria

OT Personnel, who are exposed to Anaesthetic gases for >5 years in operation theatres. Also 30 controls who are not exposed to Anaesthetic gases are selected at random to compare with the data generated on the subjects exposed to these gases.

Exclusion Criteria

Age < 20 years and > 65 years, Recent use of vitamins, Pregnancy, Bleeding tendencies, Systemic diseases like liver and renal failure, Clinical signs and symptoms of cobalamine or folate deficiency . Medications known to effect plasma Homocysteine.

From all the cases and controls detailed information pertaining to various epidemiological parameters such as age, sex, history of exposure, other comorbidities are collected using a specific proforma.

Homocysteine testingdone by ADVIA Centaur XP assays use Acridinium ester (AE) as the chemiluminescent label, because AE does not require the addition of a catalyst or substrate. It is easy to automate direct Chemiluminescence using AE and provides many benefits, such as long reagent shelf life, fast reaction time, and assay sensitivity. The ADVIA Centaur XP assays use the dimethyl form of AE because its stability allows long reagent shelf life.

Statistical Analysis

The results are expressed as frequencies or mean values (SD). Differences in demographic characteristics between groups were analysed. Since we are studying the effectiveness of a single variable (Homocysteine Value) on two control groups (With Gas Exposure and Without Gas Exposure) a One-Way ANOVA with a Confidence Interval of 95% (Alpha = 0.05) is used between the subjects. To identify whether our null hypothesis (H0) that the means of the groups are equal or the alternative hypothesis (H1) that the means are not equal we shall look at the results. A p-value of 0.05 or less rejects the null hypothesis that is; the statistical assumptions used imply that only 5% of the time would the supposed statistical process produce a finding this extreme if the null hypothesis were true.

Results

The sample considered for the study included 60 subjects of which 30 subjects were in the exposed group who are exposed to waste Anaesthetic gases in unscavenged OT and 30 subjects were in the control group.

Table 1: Demographic distribution of the exposed group as well as control group

Demogrphic details	Exposed Group: With Gas Exposure	Control Group: Without Gas Exposure	p-Value
Age(in years)	41.9	42.8	0.68966
Males	7(23%)	23(77%)	0.78
Females	8(27%)	22(73%)	
BMI	24.497(6.629)	24.702(7.359)	0.7651
Average duration of exposure in years	14.5 0	0 0	1.95

All the subjects were aged between 28 to 58 years in both the exposed group and control group with a mean age of 41.9 years and 42.8 years respectively. The statistical analysis with a confidence interval of 95% resulted in a p-Value of 0.68 which is considered to be "statistically not significant" as it is greater than the ideal value of 0.05 (A p-value of 0.05 or less rejects the null hypothesis). In terms of the sex distribution of the sample, 23% (7) of the subjects were male and 77% (23) were female in the exposed group and 27% (8) of the subjects were male and 73% (22) were female in the control group. A balanced sample was selected to ensure that there were no statistical differences in the Homocysteine levels based on the sex (Table 1).

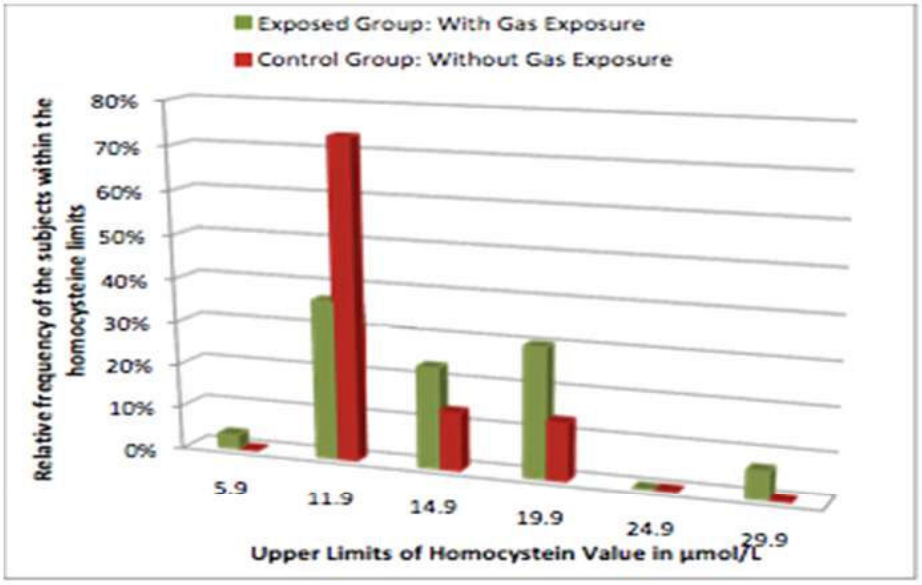
BMI Value resulted in a p Value of 0.76 which is considered to be "statistically not significant". Hence the BMI values of both the groups is equivalent.

To compare the difference between the Homocysteine values in the exposed and control groups, the subjects in the exposed group were exposed to > 5 years of Anaesthetic gas. The mean duration of exposure in OT exposed group is 14.5 years and is observed to be zero in the control group as it is not exposed to any gases. The statistical analysis resulted in a very low p-Value of 1.95E-13 which is considered to be "statistically highly significant". Hence we conclude that there is a difference in the duration of exposure which resulted in a statistical difference in the Homocysteine levels.

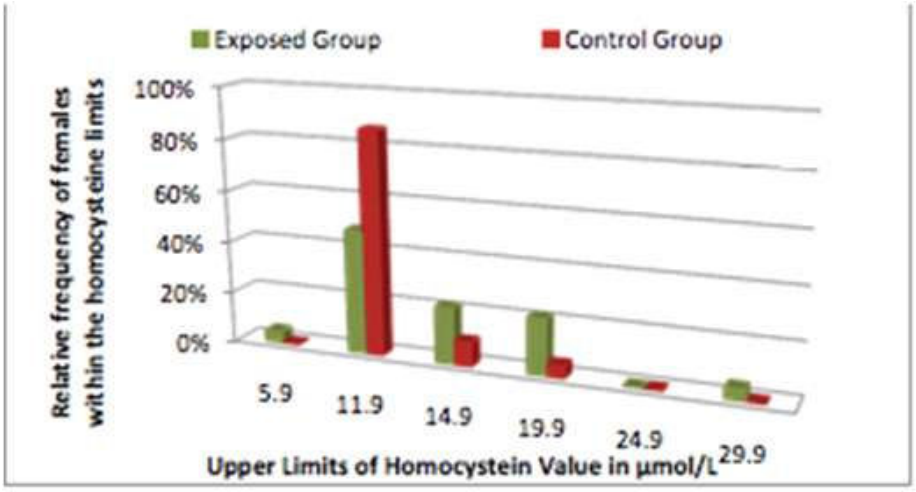
The graph 1 we can observe that the maximum number of subjects in the control group are distributed within the ideal Homocysteine value of < 12 µmol/L while the subjects in the exposed group are distributed in the Homocysteine values of > 12 µmol/L as well (Graph 1).

From the graph 2 we can observe that the number of females in the control group are distributed within the ideal Homocysteine value of < 12 µmol/L while the females in the exposed group are distributed in the Homocysteine values of > 12 µmol/L as well (Graph 2).

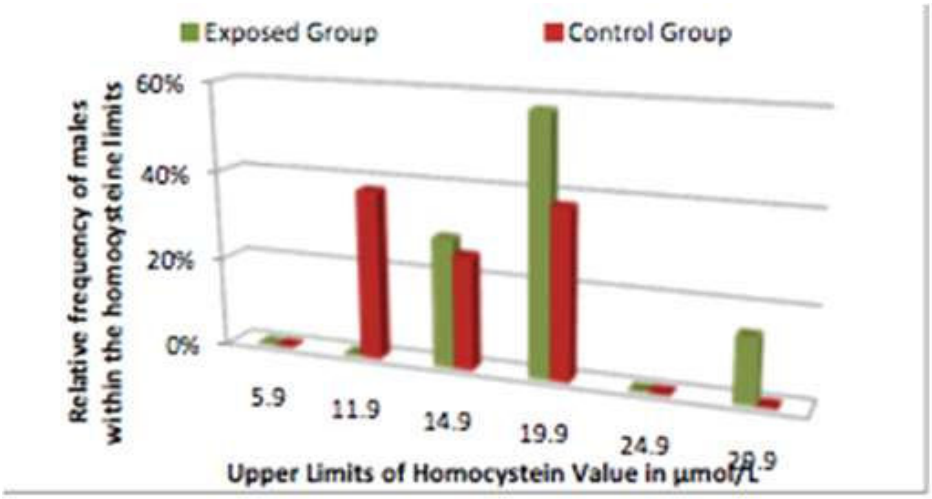
From the graph 3 we can observe that the number of males in the exposed group are distributed within



Graph 1: Distribution of Homocysteine values in the subjects



Graph 2: Distribution of Homocysteine values in female subjects



Graph 3: Distribution of Homocysteine values in male subjects

Table 2: Female and male observation of the mean values of homocysteine

Female Analysis	Homocysteine value (in umol/L)	Age in years	Duration of exposure in years	BMI
Mean values of Exposed Group	12.02956	39.260	12.6956	24.53957
Mean values of Control Group	9.510454545	40.090	0	24.09227
p Value	0.028131938	0.68656	5.46E-11	0.574845
Male analysis				
Mean values of Exposed Group	17.40714286	50.57143	20.42857143	24.35714
Mean values Control Group	13.39125	50.25	0	26.37875
p Value	0.050269817	0.946344	9.94E-05	
Over analysis				
Mean values of Exposed Group	13.28433333	41.9	14.5	24.497
Mean values of Control Group	10.54533333	42.8	0	24.702
p Value	0.01353611	0.6897	1.95E-13	0.7651

the Homocysteine value of >12 µmol/L (Graph 3).

Mean Homocysteine value in females OT exposed group is 12.029 µmol/L and in controls is 9.51 µmol/L. The p-Value of 0.0281 is "statistically significant" ($p < 0.05$) and hence concluding that there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure (Table 2).

Mean Homocysteine value in males OT exposed group is 17.408 µmol/L and in controls is 13.392 µmol/L which are not equal. The p-Value of 0.00502 is "statistically significant" and hence we conclude that there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure.

Mean homocysteine value inover all analysis OT exposed group is 13.285 µmol/L and in controls is 10.545 µmol/L which are not equal. The P-Value of 0.00135 is "statistically significant", and hence concluding that there is a difference in the Homocysteine levels between the two groups which is because of an effect of the Anaesthetic gas exposure.

Discussion

There are many trails indicating that exposure to Nitrous oxide during surgery in adults causes raise in Homocysteine levels during post operative period 1-3. The first clear association of N2O and hematologic disease was reported by Lassen et al in the Lancet in 1956. They found that Granulocytopenia was developed on the fourth day (with 50% N_2O) and Bonemarrow biopsy was consistent with Pernicious anaemia with Megaloblastic changes. Homocysteine is produced by demethylation of Methionine [3]. Under normal conditions, Homocysteine is remethylated to Methionine by the enzyme Methionine synthase and this requires the reduced form of vitamin B12 as a coenzyme and 5-methyltetrahydrofolate as the methyl donor 36. Nitrous oxide irreversibly oxidizes the Cobalt atom of vitamin B12. This leads to inactivation of vitamin B12, which is a co-factor for Methionine synthase. Whether this acute effect has relevant clinical outcome, has been the research objective of two recent prospective trials in adults [1,2]. In these studies, there is Nitrous oxide induced acute Hyperhomocysteinemia (>13.4 µmol/L) and this was associated with increased risk of major post-surgical complications. Paul S. Myles, Chan MT et al. [4] study showed there is significant increase in postoperative Homocysteine in N_2O exposed group. There was also decrease in flow-mediated dilatation in N_2O exposed group. Endothelial function in patients undergoing noncardiac surgery was significantly impaired. N_2O exposure could be a risk factor for postoperative cardiovascular morbidity [1]. Badner NH et al. [1] study found a significant increase in Homocysteine levels with N_2O administration in patients undergoing Carotid endarterectomy and these patients were associated with increased postoperative myocardial ischemia. There is an assosciation between exposure to N_2O and alteration of vitamin B12 metabolic status in healthcare workers and the extent of alteration depends on the level of exposure. Some of these studies have demonstrated a relationship between N_2O exposure and altered vitamin B12 metabolism and plasma Homocysteine levels.

The aim of our study is to find the effect of chronic exposure to trace anaesthetic gases on plasma Homocysteine levels in operating room personnel.

Subjects

Our study design included 30 subjects who are exposed to gases and 30 controls who are not exposed. In the present study subjects in the 2 groups did not vary much with respect to age, sex and BMI. In terms of sex distribution of the sample, 23% (7) of the subjects were male and 77% (23) were female in the exposed group and 27% (8) of the subjects were male and 73% (22) were female in the control group. In our study a balanced sample was selected to ensure that there was no statistical difference in Homocysteine levels based on the sex. Comparing the current study with that of W. Krajewski, M. Kucharska, et al. study which included only females (95) in study group and only females (90) in control group [5].

In the present study all the subjects were aged between 28 to 58 years in both the exposed group and control group with a mean age of 41.9 years and 42.8 years respectively. The similarity ensures that there is no statistical difference in the Homocysteine levels based on the age. W. Krajewski, M. Kucharska, et al. [5] study included subjects aged between 25 and 56 years. 5 Mean BMI Value in our study is 24.4 and 24.7 respectively in exposed group and control group. BMI values of both the groups is equivalent.

To compare the difference between the Homocysteine values in the exposed and control groups, the subjects were exposed to > 5 years

to Anaesthetic gases in one group. The subjects in exposed group are fulltime doctors and nurses working in OTs. The mean duration of exposure in OT exposed group is 14.5 years and it is zero in thecontrol group as it is not exposed to any Anaesthetic gases. There is a difference in theduration of exposure which resulted in a statistical difference in the Homocysteinelevels. Nitrous oxide reacts with the cobalamin corrin nucleus oxidizing the cobalt atom. So themolecule loses its power to form a carbon-cobalt bond with the methyl ligand [6]. Thus, Nitrous oxide prevents the formation of Methylcobalamin and inactivates circulating Methionine synthase. Nitrous oxide induced inactivation of Methylcobalamin isirreversible in animal and human tissues since only bacteria possess the enzymes torevert the oxidative damage to cobalamin. Therefore, recovery of Methionine synthaseactivity requires replenishment of cobalamin (I). Waclawik AJ et al. [7] described a case of Myeloneuropathy from Nitrous oxide abuse.

Following parenteral B12 administration, his neurological deficit resolved and B12 and MMA levels normalized, but Homocysteine level is elevated. After halting N_2O exposure patients Homocysteine level normalized [12] Because of interassay variability leading to method dependent normal ranges, tHcyconcentration of 12 µmol/litre reflecting 95th percentile value in the control group wastaken in this study as a cut-off value discriminating between elevated and normal tHcylevels.

In our study the mean value of Homocysteine is 13.285 µmol/L and 10.546 µmol/L in the exposed and control group respectively. The statistical analysis resulted in a P-Value of 0.0135 (confidence interval of 95%). This implies that the difference is statistically significant. In W. Krajewski, M. Kucharska et al. [5] study, subjects exposed to N2O presented with lower Vitamin B12 [372.8 (12.1) vs 436.8 (13.2) pmol litre, p = 0.001] and higher tHcy. [11.2 (0.5) vs 8.9 (0.5) mmol litre, p¼=0.006]. The changes in Vitamin B12 status were aggravated in subjects exposed to N_2O in concentrations substantially exceeding occupational exposure limit. Observations in present study are in accordance with the W. Krajewski et al. study [5]. The reason for increase in Homocysteine levels is, Nitrous oxide by oxidizing vitamin B12 and inactivating Methionine synthase. In patients exposed to Nitrous oxide there is inactivation of Vitamin B12 leading to increased circulating levels of Folates and Homocysteine.

Subjects in the exposed group are distributed in the Homocysteine values of >12 µmol/L while the subjects in the control group are distributed within the Homocysteine value of <12 µmol/L. Mean Homocysteine value in Females in OT exposed group is 12.029 µmol/L and in controls is 9.51 µmol/L, which are not equal. Mean Homocysteine value in Males in OT exposed group is 17.408 µmol/L and in controls is 13.392 µmol/L, which are not equal. There is a difference in the Homocysteine levels between the two groups. Chronic Hyperhomocysteinemia is concurrent with ischemic heart disease (coronary heart disease, myocardial infarction), and cerebrovascular disease, (fatal and hemorrhagic stroke) [8]. Whether this assosciation is due to pathogenic effect of Homocysteine (causational) or increased levels is an assosciated marker, remains controversial.

ENIGMA (Evaluation of Nitrous oxide In the Gas Mixture for Anesthesia) trial showed there is a pathophysiologic rationale for increased long-term cardiovascular morbidity and mortality in patients receiving Nitrous oxide. Post surgery Homocysteine concentrations were ≥13.5 µmol/L in these adults and these were also associated with an increased risk of major complications and cardiovascular events [9].

There is generation of reactive oxygen species like Superoxide anions (O^{2-}) and Hydrogen peroxide (H_2O_2), with high Homocyteine levels, since these originate from the auto-oxidation of Homocysteine. Reactive oxygen species promote loss of membrane function and increased membrane permeability (lipid peroxidation). Either the decreased production of Nitric oxide, or the increased formation of superoxide, or both may result in endothelial cell dysfunction. These observations are in accordance with the following Literature. W. Krajewski, M. Kucharska, et al. [5] study on Impaired vitamin B12 metabolic status in healthcare workers exposed to Nitrous oxide showed no significant differences in Haematological parameters and folic acid between both the groups. However, subjects exposed to N_2O presented with lower vitamin B12. The changes in vitamin B12 status was aggravated in subjects exposed to N_2O in concentrations exceeding occupational exposure limit. N_2O exposure level and vitamin B12 concentration showed significant negative correlation and N_2O exposure level and tHcy concentration showed a significant positive correlation. N_2O exposed subjects with various vitamin B12 concentrations have Abnormal tHcy concentrations.

Sharer et al. [10] studied the Effects of chronic

exposure to Nitrous oxide on Methionine synthase activity. A 24 hour exposure to concentrations of ≤ 860 parts per million (ppm) N_2O showed no change in Methionine synthase function in Sprague-Dawley rats. However, at anesthetic concentrations, Methionine synthase activity is inhibited rapidly in rats. In Koblin study on Inactivation of Methionine synthase by Nitrous oxide in mice demonstrated that N_2O (70%) inhibited Methionine synthase activity in Liver biopsies with a 50% reduction in activity predicted after approximately 1.5 hour. Consistent with this effect, the duration of N_2O exposure is correlated with increased Homocysteine levels. 5,10-Methylenetetrahydrofolate reductase (MTHFR), also plays an important role in the conversion of Homocysteine to Methionine by generating 5-methyltetrahydrofolate [11]. Waclawik AJ et al. [7] described a case of Myeloneuropathy from Nitrous oxide abuse. A Nitrous oxide abuse patient developed diffuse paresthesias and sensory loss and mildly reduced serum vitamin B12 concentration with high levels of Methylmalonic acid (MMA) and Homocysteine. There was no evidence of B12 malabsorption in this patient. Following parenteral B12 administration, his neurological deficit resolved and B12 and MMA levels normalized, but Homocysteine level is elevated. After halting N_2O exposure patients Homocysteine level normalized. This demonstrates the importance of serum Homocysteine level measurements in cases of suspected N_2O toxicity.

In Doran et al. [12] study on Toxicity after intermittent inhalation of Nitrous oxide for analgesia noted Nitrous oxide abusers present with altered mental status, paresthesias, ataxia, and weakness and spasticity of the legs. Tsung-Ta Chiang et al. [13] described a case of Recreational Nitrous Oxide Abuse Induced Vitamin B12 Deficiency. This patient presented with skin pigmentation over the dorsum of fingers, toes, and trunk, and Myeloneuropathy of the posterior and lateral columns. Low serum vitamin B12 level and an elevated serum Homocysteine level were present. Patients history revealed N_2O exposure. Only Symptoms improved significantly with vitamin B12 treatment. Methyl group from N5-methyltetrahydrofolate is transferred to Homocysteine by Methionine synthase producing Tetrahydrofolate and Methionine. In humans, inhibition of Methionine synthase results in the development of Megaloblastic anemia, and eventually Subacute combined degeneration of the spinal cord.

Repeated occupational exposure to N_2O may disturb vitamin B12 metabolic status. N_2O preferentially targets metabolically active cobalamin (I). So decreased levels of vitamin B12 were reported in N_2O abusers and sporadically during N2O anaesthesia. Several studies demonstrated that intraoperative exposure to N_2O is associated with postoperative increases in plasma tHcy [1-3]. In the present study, we extend these observations to operating theatre personnel under repeated occupational exposure to N_2O. Theoretically, in healthcare workers active under excessive occupational exposure to N_2O, disturbances of vitamin B12 metabolism were evident. They might be more susceptible to development of vitamin B12 deficiency symptoms under certain conditions such as dietary vitamin B12 restriction. Moreover, they are likely to develop Hyperhomocysteinaemia, and it is a well-recognized independent risk factor for Arterial and Venous thrombosis and Coronary heart disease. Our study was in contrast with following Literature. Gudrun Abascall et al. [14] studied whether routine blood test is of value, for evaluating effects among midwives working with Nitrous oxide for pain relief in delivery unit. The study was done to determine if work place ambient air Nitrous oxide exposure resultsin detectable Hyperhomocysteinemia or signs of Macrocytocis in midwives. One of 3 delivery units ambient air quality measures exceeded recommended ranges. There were no signs of routine blood test pathology in the personnel studied.

All the personnel in the present study are exposed continuously to trace gases in OTs unlike the midwives.

M Salo et al. [15] study on signs of vitamin B12 - Nitrous oxide interaction in operating theatre personnel showed no changes in the peripheral blood samples. Peripheral blood counts and films, serum vitamin B12 and plasma and erythrocyte folate concentrations were studied in eight anaesthetists and seven internists to find if the interaction is an occupational health hazard to operating theatre personnel chronically exposed to trace concentrations of Nitrous oxide. In addition, blood counts were studied in two retrospective materials of 118 operating theatre nurses working in scavenged operating theatres and in ten subjects working in unscavenged theatres. No definite signs of B12- nitrous oxide interaction could be observed in the peripheral blood samples from these persons. Number of subjects in the exposed group in the present study are 30 compared to the above study and even in this present study 12 out of 30 subjects in the exposed group showed elevated Homocysteine levels. Koblin et al. [11]. study on the of Effect of Nitrous oxide on Folate and vitamin B12 metabolism in patients did not find any changes in

formic acid and formimino glutamicacid urinary excretion after 3 hour of Nitrous oxide exposure during hip replacement inelderly patients. Formic acid and formimino glutamic acid urinary excretion are markers of Methionine synthase function. In younger patients undergoing longer surgery a minorincrease in these markers was found. Whether the elderly represent a vulnerable population to Nitrous oxide induced Methionine synthase inhibition needs further investigation. Care should be taken with folate or cobalamin deficient patients [60]. In 1990 another study by Waldman et al. [16]. on Hematologic effects of Nitrous oxide in surgical patients did not find hematologic abnormalities in orthopedic and neurosurgical patients exposed to Nitrous oxide, apart from a smaller perioperative increase in Leukocyte count [61].

Conclusion

Based on the present study, we conclude that there are Health Effects on OT personnel on Chronic Exposure to Trace Anaesthetic Gases. Our sample size was comparable in terms of age, sex, BMI. Subjects in the exposed group are distributed in the Homocysteine values of > 12 µmol/L while the subjects in the control group are distributed within the Homocysteine value of < 12 µmol/L. Statistical analysis showed significant difference in Homocysteine levels between OT exposed and non exposed groups. So we conclude that long term exposure to trace Anaesthetic gases like Nitrous oxide can lead to elevated Homocysteine levels in health care workers.

References

1. Badner NH, Drader K, Freeman D, Spence JD. The use of intraoperative nitrous oxide leads to postoperative elevations in plasma homocysteine. AnesthAnalg. 1998;87:711–3.
2. McNeely JK, Buczulinski B, Rosner DR: Severe neurological impairment in an infant after nitrous oxide anesthesia. Anesthesiology. 2000;93:1549–50.
3. Brosnan JT, Brosnan ME. The sulfur-containing amino acids: an overview. J Nutr 2006;136:1636S-1640.
4. Myles PS, Chan MT, Leslie K, Peyton P, Paech M, Forbes A. Effect of nitrous oxide on plasma homocysteine and folate in patients undergoing major surgery. Br .J Anaesth. 2008 Jun;100(6):780-6.
5. W. Krajewski, M. Kucharska, B. Pilacik, M. Fobker, J. Stetkiewicz, J.R. Noferand T. WronskaNofer: Impaired vitamin B12 metabolic status in healthcare workers occupationally exposed to nitrous oxide British Journal of Anaesthesia 2007;99(6):812–18.
6. Royston BD, Nunn JF, Weinbren HK, Royston D, Cormack RS. Rate of inactivation of human and rodent hepatic methionine synthase by nitrous oxide. Anesthesiology. 1988;68:213-6.
7. Waclawik AJ, Luzzio CC, Juhasz-Pocsine K, Hamilton V. Myeloneuropathy from nitrous oxide abuse: unusually high methylmalonic acid and homocysteine levels. WMJ. 2003;102(4):43-5.
8. Homocysteine Studies Collaboration. Homocysteine and risk of ischemic heart disease and stroke: a meta-analysis. JAMA. 2002 Oct 23-30;288(16):2015-22.
9. Leslie K, Myles PS, Chan MT, Forbes A, Paech MJ, Peyton P, Silbert BS, Williamson E. Nitrous oxide and long-term morbidity and mortality in the ENIGMA trial. AnesthAnalg. 2011 Feb;112(2):387-93.
10. Sharer NM, Nunn JF, Royston JP, Chanarin I. Effects of chronic exposure to nitrous oxide on methionine synthase activity. Br J Anaesth 1983; 55:693–701.
11. Koblin DD, Watson JE, Deady JE, Stokstad EL, Eger EI II. Inactivation of methionine synthetase by nitrous oxide in mice. Anesthesiology. 1981; 54:324–35.
12. Doran M, Rassam SS, Jones LM, Underhill S. Toxicity after intermittent inhalation of nitrous oxide for analgesia. BMJ. 2004; 328:1364–5.
13. Tsung-Ta Chiang, Chih-Tsung Hung, Wei-Ming Wang, Jiunn-Tay Lee, Fu-Chi Yang. Recreational Nitrous Oxide Abuse- Induced Vitamin B12 Deficiency in a Patient Presenting with Hyperpigmentation of the Skin. Case Rep Dermatol 2013;5:186–91.
14. Gudrun Abascall, Maud Johansson, JanJakobsson. Is routine blood test of value for evaluating health effects among midwives working with nitrous oxide for pain relief in delivery unit. 2011;3(3):162-65.
15. M Salo A Rajamäki J Nikoskelainen. Absence of signs of vitamin B12-nitrous oxide interaction in operating theatre personnel. ActaAnaesthesiologic aScandinavica. 1984 March;28(1):106-8.
16. Waldman FM, Koblin DD, Lampe GH, Wauk LZ, Eger EI II: Hematologic effects of nitrous oxide in surgical patients. AnesthAnalg. 1990;71:618–24.