Changes in Oxidative Stress Parameters as Response to Supplementation With Vitamin E and Omega-3 Fatty Acids in Male Workers Exposed to High Level Noise

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Abstract

Background: The present study aimed to assess the effects of the supplementation consumption of vitamin E and Omega 3 fatty acid on the oxidative stress parameters among workers exposed to high levels of noise in an automobile parts manufacturing plant. Moreover, the effects of the exposure to noise on SOD, total oxidative stress (TAC) and MDA will be investigated.

Methods: The participants were deployed into 4 groups (vitamin E (100 mg), Omega 3 fatty acids (180 mg EPA and 120 mg DHA), vitamin E+ Omega 3 and Placebo), as per the double-blind block randomization method. The oxidative stress parameters of the participants were analyzed before and after three month consumption of supplements via enzyme-linked immunosorbent assay method. The level of workers' exposure to noise, was measured according to ISO 9612.

Results: Before intervention, mean MDA, SOD and TAC were 27.52 (7.46) nmol/ml, 58.84 (10.44) U/ml and 2.57 (0.67) mM respectively. After intervention, mean MDA, SOD and TAC were 24.57 (7.58) nmol/ml, 63.46 (11.02) U/ml and 2.70 (0.84) mM respectively. The use of supplement Omega 3 fatty acids had a significant decremental effect on MDA levels. The use of vitamin E alongside Omega 3 fatty acids had a significant incremental effect on SOD activity.

Conclusion: Noise exposure had a decremental effect on TAC and SOD as well as an incremental effect on MDA, but this was only statistically significant for TAC. It appears that the simultaneous use of vitamin E and Omega 3 fatty acids for three months had a positive effect on the anti-oxidant performance of workers exposed to noise.

Introduction

Employees in occupational environments are at risk of various hazardous physical and chemical agents which, depending on the nature of the stress and exposure conditions, can have detrimental effects on the health of those exposed [1]. These environmental stressors can disrupt the balance of Reactive Oxygen Species (ROS) inside the body causing oxidative stress [2]. Oxidative stress is the prognosis of oxidative damage and occurs when the body is unable to outnumber the free radicals by producing enough anti-oxidants to neutralize them [3]. Increased oxidative stress is involved in the onset of disorders and is the results of either high levels of ROSs or the weakening of the capacity to neutralize them, which in turn can lead to tissue damage [3]. Environmental stressors are known to affect the endocrine system and the functioning mechanism of hormones [4]. Research has shown that the damaging effects of the endocrine glands are due to oxidative stress caused by exposure to environmental agents [5].

Noise is recognized as an environmental stressor and is of interest in occupational environments due to its adverse auditory and non-auditory effects [6]. The biological and physiological effect mechanism of noise is still not fully understood, but research has shown that oxidative stress, vascular issues and mechanical damage can be caused by exposure to noise. The role of oxidative stress in the onset of disorders associated with noise has been confirmed in numerous studies [7]. Literature review suggests that chronic or acute exposure to noise can cause excessive amounts of free radicals with the subsequent oxidative stress resulting in irreversible effect to the auditory system. This can also result in neurological disorders, endocrine disorders and cardiovascular issues as well [8].

Oxidative stress increases the production of free radicals in the body. Free radicals, are atoms or molecules that are extremely reactive due to having free outer electrons and can cause a lot of harm to macro molecules in the body including DNA, proteins, fats and hydrocarbons. ROSs are free radicals which are created through various metabolic processes such as aerobic respiration in mitochondria. They play a central role in tissue damage caused by metabolic stress. Oxidative stress is also involved in the pathogenesis and progression of various disorders. During oxidative stress, many macro molecules are damages in the body including the oxidation of lipids, oxidation of DNA, oxidation of proteins, inactivation of certain enzymes and disruptions in the functioning of various membranes [9, 10]. The anti-oxidant response within the body is either enzymatic or non-enzymatic in dealing with free radicals. Enzymatic responses include superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase. Non-enzymatic responses include vitamin C, vitamin E, melatonin, coenzyme q10, pyruvic acid, hypo taurine and thiol antioxidant [11]. Omega 3 fatty acids are known to have anti-coagulant properties and can improve anti-oxidant performance by raising catalase levels in the peroxisome and cytoplasm. The effect mechanism of Omega 3 fatty acids in the removal of ROSs has already been established [12]. There are two major groups of Omega 3 fatty acids, Docosahexaenoic acids (DHA) and Eicosapentaenoic acids (EPA). Omega 3 fatty acids function as anti-inflammatory agents by distancing the arachidonic acid metabolism from PGF2α and increasing PGE1 levels which are less inflammatory [13]. It has been demonstrated that Vitamin E can reduce oxidative stress and inflammation by reducing the expression and release of pre-inflammatory Cytokine, reducing Monocytes adhesion to the Endothelium, reduction of plasma C-reactive protein (CRP), reduction of plasma MDA and increasing the ROS neutralizing function of red blood cells [14]. Furthermore, antioxidants with different chemical properties may reinforce each other in the anti-oxidant network and improve internal anti-oxidant defense by including anti-oxidant enzymes [15].

The present study aimed to assess the effects of the supplementation consumption of vitamin E and Omega 3 fatty acid on the oxidative stress parameters among workers exposed to high levels of noise in an automobile parts manufacturing plant. Moreover, the effects of the exposure to noise on SOD, total oxidative stress (TAC) and MDA will be investigated. MDA is the final product of lipid peroxidation and is often used to describe oxidative stress. SOD is an enzyme that is responsible for converting anion superoxidase radicals ($O2^{\bullet-}$) to hydrogen peroxide and molecular oxygen and is important in controlling cellular ROS levels. TAC is related to a group of compounds (enzymatic systems such as SOD, small molecules such as vitamin E and proteins such as Albumin) [16].Literature review shows very few field studies that have been conducted on effects of exposure to high

levels of noise on oxidative stress parameters among workers. Almost no study can be found that have evaluated the effects of vitamin E and Omega 3 fatty acid supplement use on oxidative stress parameters in workers exposed to high level noise in the field.

Materials And Methods

The present study was conducted on workers of an automobile parts manufacturing plant. After calculating sample size, considering entry criteria [17, 18] and filling consent form, a number of consenting participants were enrolled into the clinical trial. As per the formula for calculating sample adequacy, a group sample size of 23 was determined, with the total number of participants being 92 (23×4). Using the double-blind block randomized method, the participants were divided into 4 groups. Group 1 was given vitamin E (100 mg) plus a placebo of Omega 3 fatty acids. Group 2 was given Omega 3 fatty acids (180 mg EPA and 120mg DHA) plus a placebo of vitamin E. Group 3 was given vitamin E as well as Omega 3 fatty acids. Group 4 received placebos (containing light liquid paraffin) of both vitamin E and Omega 3 fatty acids. Serum levels of oxidative stress including SOD, TAC and MDA were analyzed again before cand after 3-months of supplement use. Of the 92 participants, only 80 remained until the end of the study with reasons mostly having to do with changing of job, sickness (Covid-19) and an unwillingness to continue.

The vitamin E and Omega 3 fatty acids and their placebo were obtained from the Daana Pharma Co. (Tabriz. Iran) and Karen Pharma and Food Supplement Co. (Tehran. Iran), respectively. This clinical trial was registered and approved by the Iranian Registry of Clinical Trials (IRCT) with the registration number ID: IRCT20210207050290N1.

Noise Measurement

In order to measure individual exposure to occupational noise, a calibrated noise dosimeter (TES – 1354; Taiwan) was used. Since the exposure pattern of the participants had a similar alternation, short-term dosimetry was employed. This is done by measuring exposure during two separate sampling periods which includes one hour of sampling during the work shift (10 hours daily) and another one during the rest period (2 hours daily). The microphone of the dosimeter is attached to the collar about 10 to 30 cm away from the participant's ear [19]. The dose equivalent levels were measured according to Eq. 1, while 12-hour (usual shift duration) equivalent levels were calculated using Eq. 2 [20].

Dose equivalent level = TLV + 10log (exposure duration ×daily shift/100 × noise dose) (Eq. 1)

$$leq_{12h} = 10\log\left[\frac{1}{12}\sum_{i=1}^{n} 10^{lp_i/10} \times t_i\right] \quad \text{(Eq. 2)}$$

where, daily shift is equal to 10 hours of work and 2 hours of rest, exposure duration is 1 hour and hreshold Limit Value (TLV) is 85 dBA for 8 work-hours (considering 3 dBA rule). Additionally, Lpi is the measured equivalent level (it has been calculated from dose equivalent level) and t_i is the relevant exposure duration. The TLV of exposure to noise based on 12-hour equivalent continuous sound pressure level) equals 83 dBA [21]. It must be noted that the nature of the noise was combined (continues, impact) and all workers were using hearing protection (Uvex Earmuffs 3V, Germany; -31dBA reduction).

Nutritional supplementation

Before any intervention, the participants were instructed to balance their daily life in terms of their physical activity, diet, work situation and prepare themselves for the study (run-in period). A daily-intake form was given to the participants along with the supplements so they can more easily track and remember their supplement regiment. As was mentioned, the participants were designated into 4 groups via the double-blind block randomized method. The placebos used were identical to their supplement counterpart with similar containers except they contained light paraffin oil instead. As per the double-blind criteria, a third party was responsible for coding and providing the containers to the researchers. Participants were instructed to maintain their regular diet and exercise routines throughout the intervention and refrain from changing any dosage without informing the researchers. Participants were informed via various methods regarding dosage, consumption, when to stop consumption, potential side effects, cautionary advice and storing conditions both before and during intervention. During the study, researchers stayed in contact with the participants at least once every two weeks to further ensure protocols are followed. It must be stated that neither the participants nor the researchers were aware of the contents of each dose until the end of the study.

In order to estimate nutrient intake among participants, a 3-day food intake report was drafted using a software program called Nutritionist v.4 (Tinuviel Software, Warrington, UK). The reports made both before and after the intervention were pooled and entered into the Microsoft Excel software suite. As was mentioned, the effects of supplement use on reproductive indices will be evaluated. For this, the participant's food intake is monitored using self-report both before and after the intervention and any significant change is detected. The paired sample t-test is used in this case and mean differences for minor and major nutrients are calculated both before and after the intervention. No significant changes in food intake were observed among the participants ($P > 0.05$). Each participant's physical activity is estimated by instructing them to complete the International Physical Activity Questionnaire (IPAQ) before and after intervention [22].

Oxidative Stress Measurements

The levels of SOD, MDA and TAC were measured as the target oxidative stress parameters. For this, a laboratory professionals took blood samples (10 cc) from 7 to 9 in the morning from each participant who were required to abstain from eating for 8 to 10 hours beforehand. The blood samples were

placed in an ice box and transferred to the lab where they were kept at -20°C until analysis. The target parameters were measured using an ELISA reader (StatDax 2100, Awareness CO., USA) in a bio-chemistry lab according to the guidelines of the ELISA kits (Kiazist CO., Iran) [23].

All stages in the preparation of work solution, standard samples and unknown samples (serum) were performed according to the catalogue provided by the manufacturer of the TAC measurement kit (Kiazist CO., Iran) [24]. In this test, Cupric (Cu + 2) is converted to Cuprous (Cu + 1) in the presence of anti-oxidants and produces color due to the existence of Chromogen. This color has adsorption at the 450nm range and can be read. Adsorption has a direct correlation with the amount of anti-oxidants. The dynamic measurement range[1] of this method is 40–400 nmol/ml and its Trolox Equivalent sensitivity is 20 nmol/ml [24]. For SOD monitoring, all stages in the preparation of work solution, standard samples and unknown samples (serum) were performed according to the catalogue provided by the manufacturer of the SOD activity measurement kit (Kiazist CO., Iran) and per the colorimetry method (wavelength = 570nm) [25]. MDA was monitored in the same way [26]. In this test, MDA is combined with Thiobarbituric acid to form a TBA-MDA complex which is adsorbent at 532nm. The dynamic measurement range of this method is 20–100 uM with a sensitivity of 10 uM [26].

Statistical Analysis

The SPSS v.22 (Chicago Il, US) software suite was used for statistical data analysis. Descriptive statistics including mean, percentage, minimum, maximum and standard deviation were used to show blood analysis before and after the use of supplements. The Shapiro test was applied to determine whether the data follows a normal distribution. Median difference between pre and post intervention values of variables was assessed by Wilcoxon Signed Ranks Test. Median of variables between different studied groups were compared using Kruskal-Wallis test or Chi-squared test. The effect size of the dietary supplements on the target parameters as well as the predictive model for the effect mechanism were estimated using univariate analysis of variance (ANOVA). A significance level of 0.05 was considered for the present study.

[1]The maximum and minimum concentrations of the target analyte that the method is able to determine accurately. The dynamic range extends from the lowest point on a standard curve up to the highest.

Results

Table 1 contains descriptive-analytic statistics regarding the participants' demographic properties based on the supplement group. The Shapiro test shows that demographic data had a mostly non-normal distribution except for the Body Mass Index (MBI) ($P < 0.05$). The participants had a mean age and employment duration of 33.57 (5.19) and 8.30 (5.59) years respectively. Among the various participants, 61% worked in the grinding hall while 64% of them had either a high school diploma or had a higher education. BMI was normal in 43% of the participants while 37% had a waist-hip ratio (WHR) that was in the normal range. As for exercise, 55% had regular exercise and 69% of the participants were not former or current smokers.

The participants were separated in various exposure groups based on the amount of their exposure to noise. The cut-off point for this was the 33rd and 66th percentiles. Table 2 presents descriptive analytic statistics regarding the level of exposure for both the exposure groups and the supplement groups. As per the Shapiro test, exposure data distribution was non-normal ($P < 0.05$). Mean exposure to noise was higher than Threshold Limit Value (83 dBA for 12 hours of work) in all three exposure groups. The differences between exposure levels and TLVs were statistically significant ($P = 0.001$). Results indicate that differences in exposure to noise among the supplement groups were statistically significant when considering overall exposure ($P = 0.002$) but not significant when considering exposure categorized level ($P = 0.053$).

Table 3 presents descriptive-analytic statistics regarding the participants' oxidative stress parameters before and after intervention. Statistically significant difference in MDA levels before intervention and after intervention were not found in any of the supplement groups (except for the Vitamin E group). However, difference in MDA levels was statistically significant between the supplement groups after intervention ($P = 0.045$). Overall, after intervention, mean serum MDA was lower in the supplement groups. The highest MDA levels observed before intervention was in the Omega 3 group while this was true for the Placebo group after intervention. The difference in SOD levels before and after intervention was not significant in any of the supplement groups (except in the Vitamin E + Omega 3 group). Differences in SOD levels between the supplement groups was statistically significant after intervention ($P = 0.018$). Overall, mean SOD levels were higher among the supplement groups after intervention. Lowest SOD level after intervention was observed in the Placebo group. The difference in TAC levels before and after intervention was not statistically significant in any of the supplement group. The difference in TAC levels between the participants after intervention was also not significant. Overall, mean serum TAC levels were higher among the supplement groups after intervention. The lowest TAC levels after intervention were observed in the Placebo group.

Table 4 shows the results of the univariate analysis of variance which was used to model the effect of supplement use, noise exposure and demographic effect on oxidative stress parameters. In order to determine the effect of each variable and its role within the regression model, the standard regression coefficient (Beta/B) is consequential. A variable with a higher Beta has a more impactful role in determining the dependent variable (oxidative stress). As per Table 4, the use of ω-3 fatty acids can have a significant decremental effect on MDA levels, with a 20-fold increase in the probability of reduced MDA levels compared to the placebo group. The use of Vitamin E + ω-3 had a decremental effect on MDA but this was not statistically significant. Supplement use had increased SOD activity in all supplement groups, though this was only significant in the case of Vitamin E + ω − 3, with a 27-fold increase in the probability of higher SOD levels compared with the placebo. Supplement use had an incremental effect on TAC levels in all supplement groups but this was not statistically significant. The highest effect on TAC was observed in the Vitamin E + ω − 3 group, with a 1.5-fold increase in the probability of higher TAC levels compared to the placebo. Exposure to noise had a significant effect on TAC only ($P = 0.001$),

with a single unit increase in noise level corresponding to a mean TAC reduction of 0.05 units. Noise had a decremental effect on SOD levels and an incremental effect on MDA levels. None of the demographic variables had a statistically significant effect on oxidative stress parameters.

Discussion

Before intervention, mean MDA, SOD and TAC were 27.52 (7.46) nmol/ml, 58.84 (10.44) U/ml and 2.57 (0.67) mM respectively. After intervention, mean MDA, SOD and TAC were 24.57 (7.58) nmol/ml, 63.46 (11.02) U/ml and 2.70 (0.84) mM respectively. Since there is no commonly acknowledged normal range for oxidative stress parameters, the levels observed among the control groups are usually considered as the basis for comparison. It must be noted that due to budget limitations, regulations of the manufacturing plant and moral considerations regarding sampling, it was not possible to include employees from office environments as controls (no noise exposure), which raises the issue of exposure levels.

In a previous study by the authors, potential biomarkers involved in exposure to crystalline silica were investigated in an insulation manufacturing company. In that study, mean serum MDA was 8.26 (4.65) nmol/ml in the control group (office employees) [23], while this was significantly higher at 22.48 nmol/ml among the participants of the present study. Joshaghani and Shafe'i conducted a study in order to determine if serum superoxide dismutase levels and red blood cells have any relationship with serum homocysteine among patient with myocardial infarction. They report mean serum SOD among the control group (selected among healthy candidates) to be 8.44 (6.24) U/ml [27] while this was significantly higher at 61.28 U/ml among the participants of the present study. Prohan et al. conducted a study aimed at determining dietary and serum TAC levels and its relationship with depression among men. Mean TAC levels in their control group was 1.92 (0.34) mM [28] which is higher than that measured among the participants of the presents study at 1.64 nmol/ml.

The Effects of Noise Exposure on Stress Oxidative Parameters

Oxidant and anti-oxidant levels may differ depending on exposure duration, type of exposure and its intensity. But in general, increased oxidative stress during exposure is usually accompanied by a steady rise in anti-oxidant mechanisms [16]. The results of the partial correlation test (while controlling for demographic variables) showed no significant correlation between exposure to noise and oxidative stress parameters, except for SOD activity which was statistically significant (R=-0.242, P = 0.042). A weak inverse relationship was observed between exposure levels and TAC and SOD activity, while MDA levels had a weak but direct relationship with exposure levels. As per the univariate analysis of variance, exposure to noise had a significant relationship with TAC only (P = 0.001), with a single unit increase in noise levels resulting in a 0.05 unit decrease in TAC. Noise exposure had a decremental effect on SOD activity and an incremental effect on MDA levels.

Elsayed & Gorbunov (2003). state that the oxidative stress caused by exposure to high levels of noise can reduce TAC which is followed by lipid peroxidation [29]. Haghighat et al. showed that acute exposure to noise causes increases in 8-hydroxy2, deoxy guanosine and MDA as well as decreases in Glutathione (GSH), catalase (CAT) and SOD activity [30]. Hosseinabadi et al. report that exposure to noise among workers occupied in the food industry increased the number of free radicals released while also increasing MDA levels depending on the increase in noise exposure. Their results show that MDA was higher in the exposure group at 19.96 (2.55) nmol/ml compared to the control group at 18.04 (2.41) nmol/ml with the difference being statistically significant (P > 0.001) ([31]. Additionally, SOD activity was higher in the exposure group at 15.68 (2.01) U/ml compared to the control group at 13.57 (1.81) U/ml, but this difference was not statistically significant. According to their regression model, among the demographic and noise variables, noise level was the most important predictor of MDA levels (B = 0.48, P = 0.033), SOD activity (B=-0.34, P = 0.068) and TAC (B = 0.11, P = 0.001). Mean MDA levels and SOD activity among the participants of the present study were higher than that reported by Bagheri et al. in their study. Also, the effect of noise on oxidative stress parameters was only significant in the case of TAC, with the effect of noise on MDA being incremental while its effect on SOD and TAC was decremental. The reason for the differences between these two studies may be due the fact that the participants of the present study were simultaneously exposed to various physical and chemical stressors at varying intensities.

Yildirim et al. also report that MDA levels among textile workers exposed to 105 dBA noise was 2.17 (1.09) nmol/ml compared to the control group at 1.37 (0.50) nmol/ml, with the difference being statistically significant [32]. Demirel et al. (2019) investigated the effects of noise on oxidative stress parameters in rats. Their results showed that MDA levels and Glutathione were significantly higher after the experiment. This suggests that the effects of noise exposure are not limited to the auditory system and may affect the whole body leading to oxidative stress [33]. The inverse relationship between level of exposure to noise and SOD as well as TAC mean that with increased exposure, anti-oxidant capacity is reduced since these two parameters determine the anti-oxidant defense system of the body. Under normal conditions, the formation of free radicals is usually the result of cellular processes such as the mitochondrial respiratory chain and is controlled by the enzymatic and non-enzymatic defense mechanism of the body. When the body is exposed to an oxidative agent, the formation of free radicals in the body is increased which stimulates the anti-oxidant defense system of the body. In order to control the chain reactions of these free radicals, anti-oxidants step in with various mechanisms and combat the free radicals. By giving a hydrogen atom to the free radicals, the anti-oxidant itself is used up and the oxidative chain reactions are mitigated and oxidative damage to tissue is prevented.

Prolonged exposure to high intensity stressors can lead to uncontrolled lipid peroxidation beyond the capacity of the immune system. This reduces enzymatic activity due to its sensitivity to damage from the oxidative system which can result in reduced TAC. The increased oxidative stress observed in the present study may be due to various issues such as increases in general oxidations, reduction in the creation of anti-oxidants, the inability of the cell to recover from oxidative damage as well as damage caused to the cell from ROSs [34].

Keep in mind that during exposure to oxidative agents, the anti-oxidant defense system attempts to maintain the balance between oxidants and anti-oxidants. Initially, the anti-oxidant situation in the body changes and when the anti-oxidant system is unable to maintain redox, damage to macro molecules and the onset of lipid peroxidation occurs. Evaluating oxidative parameters in the present study reveals that among the various exposure groups, the amount of exposure was so high as to stimulate an anti-oxidant response within the body. There are a number of studies that have evaluated oxidative stress parameters as well as enzymatic activity such as glutathione peroxidase, superoxide dismutase and catalase in response to exposure to physical agents (such as noise). However, most studies in this regard look at oxidative stress in response to exposure to chemical agents or various disorders such as diabetes, Alzheimer's disease, high blood pressure, cardiovascular disorders and cognitive function among human subjects as well as laboratory scale studies on animals. Evaluation of these studies is outside the scope and aim of the present paper and thus, there were limitations regarding the comparison and discussion of results obtained regarding changes in TAC. Still, in various disorders and under physiologically stressful situation, research suggests changes in TAC which are usually decremental. Keshvari et al. looked at oxidative stress biomarkers in workers of a ceramics manufacturing plant. Their results show a significant reduction in TAC and total serum thiol groups among workers compared to the control group [35].

The Effects of Nutritional supplementation on Stress Oxidative Parameters

Regarding supplement use and its effect on oxidative stress parameters, results show that the difference in MDA levels before and after intervention was only significant in the Vitamin E group and was not significant in any other supplement group. After intervention, mean serum MDA levels had gone down in all supplement groups. Differences in mean serum SOD levels before and after intervention was only significant in the Vitamin E + Omega 3 supplement group and was not significant in any other supplement group. After intervention, mean serum SOD levels had gone up in all supplement groups. The differences in TAC before and after intervention was not significant in any of the supplement groups but overall, serum TAC had increased after intervention among the participants.

Based on univariate analysis of variance, the use of ω − 3 can have a significant decremental effect on MDA levels. The use of Vitamin E + ω − 3 on MDA levels was decremental but not statistically significant. Supplement use had an incremental effect on SOD levels in all supplement groups but this was only significant in the Vitamin E + ω − 3 group. Supplement use in all groups had an incremental effect on TAC with the largest effect being observed in the Vitamin E + ω − 3 group but none were statistically significant. Similar to the presents study, a significant reduction in MDA levels after daily ω − 3 supplement use among those suffering from Atherosclerosis [36]) and Hemodialysis [37] have been observed. Fazlian et al. showed in their systematic meta-analysis review that the use of ω − 3 fatty acids can cause a significant reduction in MDA levels [38].

One of the important targets of oxidative stress is lipid profiles. Oxidation of lipid profiles leads to increased production of MDA as a secondary by-product. The positive effects of ω-3 consumption on MDA levels may be due to its effect on improved lipid profiles and reduced lipid peroxidation. Lipid peroxidation is mediated by free radical compounds and thus the reduction in MDA production resulting from ω-3 use may be due to its anti-inflammatory properties [39]. There are a number of studies that agree with the finding of the present study regarding the positive effects of ω-3 and vitamin E supplement use on the anti-oxidant system. Rahmani et al. (2017) have shown that a 12-week ω-3 and vitamin E supplement regiment in woman suffering from polycystic ovary syndrome resulted in a significant increase in plasma TAC (+ 89.4 ± 108.9 vs. +5.9 ± 116.2 mmol/L, P = 0.003) as well as a significant decrease in MDA levels compared with the placebo (-0.3 ± 0.4 vs. -0.008 ± 0.6 µmol/L, P = 0.01) [40]. Liu et al. (2015) investigated the effects of Omega 3, Omega 6 and vitamin E consumption on the anti-oxidant performance of wild boars [41]. Their results show that using 400mg/kg of vitamin E (compared to 200mg/kg) increased SOD and TAC anti-oxidant parameters while reducing MDA levels. Lie et al. state that using ω-3 and ω-6 at a ratio of 6/6 as well as 400mg/kg of vitamin E can improve anti-oxidant performance (38). Similarly, another study conducted on pregnant women shows that a 6-week consumption of vitamin E (400 units) and Omega 3 (1000mg) resulted in a significant increase in plasma TAC (224.9 mmol/L vs. 136.1 mmol/L) as well as a significant reduction in MDA (0.9 µmol/L vs 6.4 mmol/L) compared to the placebo [41].

Vitamin E is soluble in fat and can be found in various foods such as wheat, meat, plant-based oils, eggs and leafy vegetables. Vitamin E is also useful in curing many disorders. In humans and mice, vitamin E is converted to alpha-Tocopherol metabolite. Vitamin E (Tocopherol) plays a protective role in preventing free radicals from destroying the cell membrane [42]. The benefits of Omega 3 fatty acids in preventing cardiovascular disorders are also clear. Evidence has been mounting in recent years regarding the positive effects of using Omega 3 fatty acids including studies on animals. However, these studies are not conclusive and further investigation is required. It is important to maintain a suitable daily intake of fatty acids since these acids (such as DHA and EPA) are not naturally created in the human body. Omega 3 fatty acid supplements are widely available, safe and cheap which makes them a highly valuable solution [43].

It is not easy to arrive at a definitive conclusion in the present study regarding the effects of exposure to high level noise on oxidative stress parameters as well as the role of supplementation in improving anti-oxidant performance. This is mainly because even though the calculated sample size and the requirements for entry were all determined with confounding factors in mind, it is not feasible to control all factors that may be influential in this regard. This is usually the case when it comes to human trials and field studies. This does not mean that the testing of theories in field studies is not without its merit as these studies are better at reflecting real world conditions [44]. Overall, there are some limiting factors that make it hard to make conclusions about the effects of exposure to high level noise on oxidative stress parameters as well as the role of supplement use which include:

- The lack of suitable control groups from office environments with no noise exposure due to budget constraints.
- Natural daily variations in oxidative stress parameters.
- Limitations in repeating self-monitoring due to budget constraints, strict role of the industry and ethical issues.

- Inability to biologically monitor the supplements used due to budget constraints.
- Various influential factors such as harmful chemical agents (polycyclic aromatic hydrocarbons or heavy metals), physical agents (electromagnetic fields, vibration and heat stress) as well as psychological stressors and background disorders.
- Limitations and sample drop caused by the Covid-19 pandemic.
- Lack of historical records regarding oxidative stress parameters of the participants at the beginning of their employment.
- The inability to homogenize the participants in terms of demographic characteristics such as age, employment duration and BMI.
- The inability to remove participants who are smokers or those who use recreational drugs due to a lack of suitable replacements and the resulting sample size.

Conclusion

The presents study was conducted with the aim of determining the role of vitamin E and Omega 3 fatty acid supplement use in improving anti-oxidant performance. Furthermore, the effects of high-level noise exposure on oxidative stress parameters was evaluated. The use of supplement Omega 3 fatty acids had a significant decremental effect on MDA levels. The use of vitamin E alongside Omega 3 fatty acids had a significant incremental effect on SOD activity. Noise exposure had a decremental effect on TAC and SOD as well as an incremental effect on MDA, but this was only statistically significant for TAC. It appears that the simultaneous use of vitamin E and Omega 3 fatty acids for three months had a positive effect on the anti-oxidant performance of workers exposed to noise. A follow-up study is highly suggested considering the limitation of the presents study noted above. This follow-up study should focus on workers exposed to noise and should monitor stress oxidative parameters from the beginning of their employment as well as having a better sample size and a more suitable control group. The present study still has its merits despite the limitation noted above since it is hard to find field studies where, not only the effects of noise exposure on oxidative stress parameters are evaluated, but the role of supplementation in improving anti-oxidant performance is also considered, while the amount of occupational exposure is taken into account as well.

Abbreviation List

ANOVA	Analysis of Variance
BMI	Body mass index
CAT	Catalase
CRP	C-reactive protein
DHA	Docosahexaenoic Acid
DNA	Deoxyribonucleic acid
EPA	Eicosatetraenoic Acid
GSH	Glutathione
IPAQ	International Physical Activity Questionnaires
ISO	International Organization for Standardization
MDA	Malondialdehyde
PGE1	Prostaglandin E1
PGF2α	Prostaglandin F2alpha
ROS	Reactive Oxygen Species
SOD	Superoxide dismutase
TAC	Total Antioxidant Capacity
TLV	Threshold Limit Values
WHR	Waist-Hip Ratio

Declarations

Ethics approval and consent to participate

Ethical approval for this study was obtained from School of Public Health & Allied Medical Sciences- Tehran University of Medical Science (IR.TUMS.SPH.REC.1398.297) and School of Public Health & Neuroscience Research Center, Shahid Beheshti University of Medical Sciences (IR.SBMU.PHNS.REC.1399.157). All participants filled consent form and were participated voluntarily in the study.

Consent for publication

Not applicable.

Availability of data and materials

Not available.

Competing interests

The authors have no competing interests to declare.

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Authors' contributions

HM carried out experiments and analyzed data. FG and SFD supervised the research, contributed to the study design, managed and planned the project and drafted and provided critical revision of the article. MAR contributed to the environmental assessment. MCH supervised on nutrition intervention and NM supervised on serum analysis. All authors reviewed and provided final approval of the version to publish.

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Tables

Table 1. Demographic characteristics of participants

Table 2. Exposure levels of participants to noise

Table 4. Results of univariate analysis of variance

Variable	MDA		SOD		TAC	
	P-value	B	P-value	B	P-value	B
Supplementation Group	0.031	-20.561	0.052	25.106	0.317	1.056
	0.147	-14.029	0.951	0.850	0.416	0.938
	0.680	-3.012	0.007	27.763	0.059	1.577
Noise exposure	0.938	0.010	0.387	-0.156	0.001	-0.051
Age	0.069	0.330	0.552	-0.145	0.153	-0.003
Employment Duration	0.631	0.092	0.205	-0.033	0.130	-0.033
BMI	0.243	0.261	0.073	-0.550	0.552	-0.015
Smoking	0.136	12.797	0.784	-3.166	0.952	-0.057
Physical Activity	0.092	-18.484	0.583	5.246	0.868	0.132
BMI= Body Mass Index MDA= Malondialdehyde SOD= Superoxide dismutase TAC= Total antioxidant capacity						

Due to technical limitations, table 3 docx is only available as a download in the Supplemental Files section.

Supplementary Files

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- Table3.docx

Parameter		Statistical measure (N = 80)			Supplementation Group				P-value*
		Mean (SD)	Median (IQR)	Max-Min	Vitamin E (N=22)	Omega-3 (N=21)	E+ Omega-3 (N=19)	Placebo (N=18)	
					Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)		33.57(5.91)	32.50(11.75)	46.25-22.00	(6.27) 34.27	31.85(6.33)	35.52(5.53)	32.66(4.99)	0.144
Employment duration (years)		8.30(5.59)	6.50(7.75)	19.2-02.00	10.31(5.96)	6.33(4.79)	10.63(5.93)	5.66(3.72)	0.005
Manufacturing Section	Aluminum	17(22)			9(52.9)	0(0)	4(23.5)	4(23.5)	0.004
	Cast iron	14(17)			3(21.4)	2(14.3)	7(50)	2(14.3)	
	Grinding	49(61)			10(20.4)	19(38.8)	8(16.3)	12(24.5)	
Education (%) N	Illiterate	2(2)			0(0)	0(0)	1(50)	1(50)	0.838
	Primary school	7(9)			2(28.6)	1(14.3)	2(28.6)	2(28.6)	
	Junior high school	20(25)			5(25)	6(30)	3(15)	6(30)	
	High Diplomaschool	44(55)			13(29.5)	12(27.3)	13(29.5)	6(13.6)	
	Associate Degree	4(5)			1(25)	1(25)	0(0)	2(50)	
	Bachelor's degree	3(4)			1(33.3)	1(33.3)	0(0)	1(33.3)	
BMI (kg/m^2)		25.06(4.49)	24.79(6.23)	16-.33 33.90	27.98(3.48)	23.88(4.65)	25.93(4.32)	21.95(3.13)	**0.001
N (%)	Underweight (<18.5)	6(7)			0(0)	2(33.3)	1(16.7)	3(50)	0.009
	Normal (18.5-24.9)	34(43)			3(8.8)	10(29.4)	9(26.5)	12(35.3)	
	Overweight (25-29.9)	27(34)			13(48.1)	6(22.2)	5(18.5)	3(11.1)	
	Obese (>30)	13(16)			6(46.2)	3(23.1)	4(30.8)	0(0)	
WHR		0.93(0.21)	0.93(0.12)	0-.10 1.95	0.96(0.06)	0.89(0.06)	0.97(0.43)	0.89(0.05)	0.002
N (%)	Healthy (≤0.9)	30(37)			3(10)	10(33.3)	5(16.7)	12(40)	0.003
	Unhealthy (>0.9)	50(63)			19(38)	11(22)	14(28)	6(12)	
Smoker- N (%)	Yes	25(31)			7(28)	8(32)	6(24)	4(16)	0.594
	No	55(69)			15(27)	13(24)	13(24)	14(25)	
Regular exercise N(%)	Yes	44(55)			13(29.5)	15(34.1)	7(15.9)	9(20.5)	0.161
	No	36(45)			9(25)	6(16.7)	12(33.3)	9(25)	
Physical activity (IPAQ score)	Walking	-			-	-	-	-	-
	Moderate	-			-	-	-	-	
	Vigorous	80 (100)			22 (100)	21 (100)	19 (100)	18 (100)	

* Differences of variables between different manufacturing units (Kruskal-Wallis Test / Chi-squared Test)

** Mean differences of BMI between different manufacturing units (One-way analysis of variance (ANOVA))

SD= Standard Deviation IQR=Interquartile Range BMI= Body Mass Index WHR=Waist to Hip Ratio IPAQ = International Physical Activity Questionnaire

Categorized Values of Noise	Total (N=80)				Supplementation Group								P-value*
	N	Mean (SD)	Median (IQR)	Min-Max	Vitamin E (N=22)		Omega-3 fatty acids (N=21)		E+ Omega-3 (N=19)		Placebo (N=18)		
					N (%)	Mean (SD)	N (%)	Mean (SD)	N (%)	Mean (SD)	N (%)	Mean (SD)	
-	-	7(7.37) 93.1	0(12.86) 94.4	78-.14 104.68	-	0(7.19) 92.3	-	8(6.15) 97.5	-	(6.49) 90.05	-	7(7.63) 94.9	0.002
<90 .44	26	8(3.63) 84.8	09(6.24) 86.	78-.14 90.01	(42.3) 11	7(2.97) 85.2	2(7.7)	6(7.53) 84.8	(34.6) 9	(2.81) 84.34	(15.4) 4	9(5.99) 83.1	0.056
97.74-90.44	28	5(2.48) 94.1	04(5.39) 94.	90-.60 97.74	(21.4) 6	7(2.22) 95.5	(28.6) 8	2(2.35) 95.2	(21.4) 6	(0.89) 92.26	(28.6) 8	5(2.82) 94.8	
>97.74	26	6(4.16) 101.7	05(3.13) 101.	97-.78 104.68	(19.2) 5	4(1.50) 101.6	(42.3) 11	1(2.33) 102.7	(15.4) 4	(1.23) 99.60	(23.1) 6	3(1.62) 102.3	

* Differences of variables between different studied groups (Kruskal-Wallis Test / Chi-squared Test)

SD= Standard Deviation IQR=Interquartile Range