

ANTIOXIDANT VITAMINS AND NITRIC OXIDE STATUS IN DRUG DEPENDANTS

BY

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ABSTRACT

The drug dependants are at risk of malnutrition particularly of different vitamins including A, C and E, vitamins. The malnutrition in these patients may be a consequence of alterations in the contribution, the absorption or in the metabolism of these nutrients, or for an increase their request. The present study was conducted on 150 drug dependants aged 12-58 years with the essential inclusion criteria i.e positive history and laboratory detection of reported substance abuse and major exclusion criteria as chronic disease (hepatic, renal, and gastrointestinal). From every drug dependant a history was taken and detection of substance abuse by enzyme immunoassay method (EMIT) and thin layer chromatography was done. Also measurement of antioxidants status of β -carotene, α -tocopherol and vitamin C by using calorimetric method while plasma level of the metabolic end products of nitric oxide (nitrite and nitrate) using Greiss reaction. The results of the present study showed that, the mean age of the studied drug dependants was 24.19 ± 7.84 with ranged between 12 and 57 years. They addicted to consumption of drug of abuse, specifically cannabis, morphine, barbiturates and benzodiazepines. In this study, the proportion of the low social participants was high (66.6%) and the proportion of the high educational level participants was "3.3%". Moreover, the majority of the individuals were below 30 years, which reflect that consumption of drugs abuse affected fundamentally the young adult sector. In our locality, substances abuse mainly in males and revealed marked affection of them. The majority of the drug dependants were abuser of opiates "tramadol", benzodiazepines "Apetryl", Cannabis "bango" and barbiturates "comidal". Multiplicity of abusing substances by the same person was common. The affection of number of abused substances is marked in the plasma nitric oxide level "direct relationship". The plasma nitric oxide level is directly related while β -carotene, vitamin C and α -tocopherol is inversely related with duration of substances abuses.

***Key Words:** Addiction - Tramadol - Nitric Oxide - Apetryl - Bango - Comidal - Antioxidants - Duration of Addiction - Number of abused substances.*

INTRODUCTION

Drug abusers are prone to malnutrition for several reasons e.g. reduced intake of food calories owing to the anorexic effect of addictive stimulants; decreased income for food purchases owing to under employment or diversion of funds for drug (Himmelgreen, et al.). Also drug abusers are prone to malnutrition due to ignorance of or indifference to basic principles of healthful nutrition; and direct adverse effects of drugs on nutrient absorption and /or metabolism (Gloria et al., 1997).

Drug abuse is often associated with immunological insufficiency with susceptibility to chronic debilitating diseases. These changes can lead to increased events rates of morbidity and mortality (Farahat, 2002). Drug dependance may lead to cerebrovascular strokes that may lead to sudden death..

Nitric oxide is a common gaseous free radical. It is synthesized in endothelial cells that line blood vessels and has a wide range of function that are vital for maintaining a health cardiovascular system. Reduced nitric oxide bioavailability is implicated in the initiation and progression of many cardiovascular diseases (Gangalli, 1998; Megson and Webb, 2002).

Dietary vitamins (C, E and Carotenoids) constitute key chain breaking antiox-

idants. Biologically plausible mechanisms such as a potential of these antioxidants to scavenge oxidants free radical and their ability to inhibit lipid peroxidation (Tsuchihashi et al., 1995). Although the latter mechanism remains controversial (Revean et al., 1993). In general these antioxidant vitamins have been implicated in preventing or slowing down atherosclerotic process with a potential role in prevention of ischaemic coronary and cerebrovascular strokes and death. Plasma ascorbic acid concentration is related to risk of death from ischaemic stroke after adjustment for age, sex and established cardiovascular risk factors (Nyss, et al., 1997). However Gale et al., (1998) can not confirm the association between vitamin C concentration and mortality from coronary heart diseases. On the other hand, Smit and Crespo (2001) examined the dietary intakes and nutritional status of Marijuana users and they revealed that serum carotenoids levels were lower among marijuana users.

So the aim of the work was to determine plasma vitamin C, E and carotenoids concentrations. At the same time nitrite/nitrate "the stable end products of nitric oxide metabolism" was estimated in drug dependants.

SUBJECTS AND METHODS

1- Subjects:

The present study was conducted on

150 patients referred to the Toxicology Unit of Mansoura Emergency Hospital and proved to be chronic drug dependants. using psychoactive drugs and substances such as "opiates, barbiturates, benzodiazepine, cannabis, alcohol". All patients were males except only two females. They were of different ages, levels of education and social states. The diagnosis of psychoactive drugs and substances was based on history of intake and positive clinical signs and symptoms. Moreover, all were subjected to urine analysis for psychoactive drugs and substances. Exclusion criteria were chronic terminal disease such as hepatic, renal, or infections. The studied cases were divided into 3 groups according to the number of the abused substances detected by TLC : group (a) one abused substance, group (b) two abused substances, group (c) three or more abused substances. Cases were divided into 3 groups according to the duration of the abused substances: subgroup (a) less than three years, subgroup (b) from three to five years and subgroup (c) more than five years.

At the same time 30 healthy volunteers who never used these drugs even therapeutically for at least one month were selected as a control group.

II- Methods:

All patients included in this study were subjected to the followings: history taking,

physical examination, laboratory investigations (Substance abuse detection, routine laboratory tests, and the objected oxidants and antioxidants measurements).

A- Methods for detection of abused substances:

1- Sampling:

From each patient with positive history of substance abuse 100 ml urine were obtained "at the time of arrival and again before receiving any treatment". Catheter was used if the patient was comatose or unable to void urine. Each sample was collected in a clean, dry, labeled container without preservation.

2-Preliminary tests:

One ml of different urine samples were analyzed for the presence of opiates, barbiturates, benzodiazepines, cannabis, alcohol, tricycles antidepressants and amphetamines by Syva, Solaris SLN 1067 Version 3.00 L. using Emit® d.a.u. Assay on the same day.

3- Chromatographic confirmation test:

Thin layer chromatography (T.L.C) was used to confirm positive results obtained by Emit system and detect drugs that could not be detected by Emit. Confirmation of the presence of morphine and tramadol were detected by using the method of Meadway et al., (1998). While, Delta 9 THC-11-oic acid (the metabolite of Cannabis), benzodiazepine and barbitura-

tes were detected by using the method of George and Braithwaite, (1995).

B- For detection of oxidants and anti-oxidants plasma levels:

Measurements of plasma levels of vitamin C, α -tocopherol, β -carotenoids and nitric oxide metabolites were determined.

1- Sampling:

Ten ml blood samples were collected from every subject "patient and controls". Of them three ml blood samples were collected into plain tube and non haemolysed sera were separated by centrifugation and used for assay of liver and kidney functions and total cholesterol levels.

The remaining blood were collected into tube containing EDTA "1mg/ml of blood" and aprotinin "500 KIU/ml of blood" and mixed gently. The non haemolysed plasma were separated by centrifugation. These samples were preserved in aliquots at -70°C till being used for determination of vitamin C, α -tocopherol, β carotene and nitric oxide metabolites.

2- Determination of vitamin C "ascorbic acid" (Jacob, 1990) :

Ascorbic acid in plasma was oxidized by Cu^{+2} to form dehydroascorbic acid, which reacted with acidic 2, 4 dinitrophenylhydrazine to form a red bis-hydrazone, which measured at 520 nm.

3- Determination of α -tocopherol (Baker and Frank, 1968) :

The method is based on an oxidation-reduction reaction. Following specific elution techniques, fraction were subjected commonly to the emmeric-Engel procedure, in which tocopherol was oxidized to tocopherolyl quinone by FeCl_3 and Fe^{2+} in the resultant FeCl_2 forms a complex with α, α' -dipyridyl to produced a red colour.

4- Determination of β - carotenoids (Varley et al., 1980) :

Proteins are precipitated with ethanol and the vitamin A and carotenes extracted into light petroleum. The light petroleum was evaporated of and the residue was taken up in chloroform. Carr-Price reagent was added and the amount of blue colour produced is read. Since carotenes can also give some colour, a correction for this has to be made in order to obtain the amount of colour due to the vitamin A present.

5- Determination of nitric oxide metabolites (Moshage, 1995) :

This assay determines total nitric oxide based on the enzymatic conversion of nitrate to nitrite. The reaction was followed by colorimetric detection of nitrite as an azo dye product of the Griess Reaction. The Griess Reaction is based on the two-step diazotization reaction in which acidified NO_2 produces a nitrosating agent, which reacts with sulfanic acid to produce

the diazonium ion. This ion is then coupled to N-(1-naphthyl) ethylenediamine to form chromophoric azo-derivative, which absorbs light at 540 nm.

Statistical analysis:

Statistical Package Social Science (SPSS), version 11 was used. Normality of data was detected by Kolmogorov-Smirnov test. Data was expressed as mean \pm SD. Being parametric. A probability value (p) less than 0.05 considered to be significant.

RESULTS

As shown in Table (1) the mean age \pm SD of the studied drug dependant group was 24.19 ± 7.84 . 22.7% of them were <20 year old, 59.3 % were in the age range 20-30 years and 18% were >30year old. While for control group, the mean \pm SD of the age was 24.8 ± 4.64 years. Ten percent of them were <20 year old, while in 76.7 %, the age ranged 20-30 years and 4% were >30 year old. As regard sex, 98.7% of drug dependant group were males and 1.3% were females. On the other hand, all control group were males. Most of drug dependants (78.9 %) lived at urban areas and 70.7% of were of low social state. Also most of them were of a low educational level (68.7%), 28% were in a moderate educational level and 3.3% were at a high education level.

Table (2) shows history recoding of the abused substances and laboratory detection of the abused substances by thin layer chromatography. All patients gave positive history of drug abuse "150 patients". The commonest detected substance by history recording was cannabis "114 patients out of 150; 76%", Opiates were detected positive in 34 patient "22.3%", 98 patients "65.3%" were positive history for Benzodiazepine and Barbiturates were detected positively in 38 patients "25.3%". All patients gave positive results by TLC "150 patients". The commonest substance detected by thin layer chromatography was cannabis "115 patients out of 150; 76.6%", Opiates were detected in 109 patient "72.6%", 79 patients "52.6%" were positive for Benzodiazepine and Barbiturates were only detected in 6 patients "4%".

As regard the duration of the abused substances, 51.2% had a duration of the abuse substance < 3 years, 19.4% had a duration of substance abuse 3-5 years and 29.4% of the studied cases gave a history of more than 5 years of the substance abuse. 24.7% cases were positive to one abused substance, 45.3% cases were positive to two abused substances, 29.3% cases were positive to three abused substances and one (0.7%) case gave positivity to four substances abused (Table3).

Table (4), shows the relation between body mass index, the number of abused

substances and the duration of abuse in the drug dependant group. There was a non-significant difference in the mean BMI with duration or number of abused substance "P= 0.280 and P=0.637" respectively.

As shown in Table (5) the plasma nitric oxide metabolites "NOx" levels ranged between a minimum of 24.6 μ mol/L and a maximum of 99 μ mol/L with a mean \pm SD of 59.04 \pm 18.89 μ mol/L. The plasma β - carotene levels ranged between a minimum of 11.0 μ g/dL and a maximum of 91 μ g/dL with a mean \pm SD of 43.49 \pm 23.33 μ g/dL. The plasma vitamin C levels ranged between a minimum of 0.22 mg/dL and a maximum of 0.99 mg/dL with a mean \pm SD of 0.61 \pm 0.18 mg/dL. The plasma α -tocopherol levels ranged between a minimum of 0.29 mg/L and a maximum of 17.68 mg/L with a mean \pm SD of 8.65 \pm 3.94 mg/L. While for the control group, the plasma nitric oxide metabolites "NOx" levels ranged between a minimum of 10.3 μ mol/L and a maximum of 46.5 μ mol/L with a mean \pm SD of 30.62 \pm 9.46 μ mol/L. The plasma α - carotene levels ranged between a minimum of 19.0 μ g/dL and a maximum of 91 μ g/dL with a mean \pm SD of 62.73 \pm 22.44 μ g/dL. The plasma vitamin C levels ranged between a minimum of 0.83 mg/dL and a maximum of 1.34 mg/dL with a mean \pm SD of 1.09 \pm 0.14 mg/dL. The plasma α -tocopherol level ranged between a minimum of 1.05 mg/L

and a maximum of 18.63 mg/L with a mean \pm SD of 13.38 \pm 4.03 mg/L. There were significant higher level of the plasma nitric oxide metabolites "NOx" in drug dependant group than control group "P < 0.001" and significant lower plasma β - carotene, vitamin C and α -tocopherol mean values in the drug dependant group than control group "P < 0.001"

Table (6), shows the relation between plasma NOx, β - carotene, vitamin C and α -tocopherol levels with number of abused substances. As regard the plasma NOx level, there was a significant higher mean levels by abusing different number of the substances "P=0.005". There was a significant increase of the mean plasma NOx level with increasing the number of the abused substances. However no significance difference was found between plasma nitric oxide metabolites level in group "b" when compared with group "c" "P=0.995". Overall, there was no-significant difference in between the mean plasma β -carotene levels, vitamin C, α -tocopherol in the three studied groups having different number of abused substances "P=0.382, 0.587, 0.820 respectively.

Table (7) shows that there was a non-significant increase in the mean plasma nitric oxide metabolites level with prolongation of duration of the substance abuse "P=0.546". Also there was non-significant decrease in the mean plasma β - carotene

levels with increase of the duration of the substance abuse "P=0.301". Longer duration of abuse "b & c" subgroup had a non-significant lower plasma α carotene levels compared to shorter duration of abuse subgroup "a". On the other hand there was a significant difference of the plasma vitamin C levels of the three studied subgroups with different duration of drug abuse "P=0.02". However, there was no significant difference in between the mean plasma vitamin C level in the group "b" when compared with subgroup "c" "P=0.946". Drug dependants with longer duration of substance abuse "b & c" subgroup had a significant lower plasma vitamin C level compared to drug dependants, with shorter duration of substance abuse subgroup a "P=0.198 & P=0.634".

There was a significant decrease in the mean plasma α -tocopherol level with increase of the duration of drug abuse in the drug dependants "P=0.03". Drug dependants with longer duration of substance abuse "subgroup b" had a significant lower values when compared with those of shorter duration of the substance abuse subgroup "a" "P=0.034". However there was a non significant lower value when compared "c" subgroup with "a & b" subgroups "P=0.198 & P=0.634" respectively.

DISCUSSION

It is widely accepted that drug addic-

tion is a social worldwide health problem (UNDCP, 1997). It affects every sphere of human life. Young adults' lives are damaged (Islam et al., 2001); teenagers experimentation with drugs, and use of illicit drugs has soared with the 'baby-boom' generation (Califano, 1998).

Although research on drug abuse is too much in the Western world, there are few reports regarding drug abuse effects on antioxidant status. Drug addiction impairs nutritional status and immunity (Varela et al., 1997a, b). In spite of the fatal consequences, the objective research on the illicit drug use has received relative little attention in Egypt.

In general fruit and vegetables intake in drug addicts is lower than general population (Himmelgreen et al., 1998; Varela et al., 1997b). Therefore, drug addicts have micronutrient deficiencies, including antioxidant vitamins. In addition to their antioxidant functions, they play an important role in immunity (Duggan et al., 1996; Brown et al., 1997; Chandra, 1997 and Lykkesfeldt et al., 1997).

NO is an endothelium derived factor that reduces the tone of vascular smooth muscle, and plays an important role in the physiological equilibrium in human. Therefore, the metabolic and functional states of NO are closely related to human health (Zhong and Sun, 1997;

Zhou et al ., 1997a , 1997b , 1997c , 1998 , 1999 , 2000). On the other hand, as NO is a very active free radical, an excess NO in the human body can induce physiological or pathological aggravation of oxidative stress, destroying the dynamic balance between oxidation and antioxidation (Zhou et al. 1997a 1997b; 1997c, 1998; 1999; 2000; and Zhong and Sun , 1997).

Vitamin C, α -tocopherol (vitamin E) and β -carotene (vitamin A precursor) are important antioxidants in human body, playing an important role in catching and eliminating excess free radicals such as $[O\cdot_2$, hydroxyl free radical (OH \cdot) , hydrogen peroxide free radical (HO \cdot_2) , singlet oxygen ($1O_2$) ,or hydrogen peroxide (H_2O_2)] in the human body. Antioxidants prevent the physiological or pathological aggravation of free radical chain reactions. These protecting biological membranes of cells against injuries by oxidation, peroxidation and lipoperoxidation. Moreover, vitamin C, α -tocopherol and β -carotene can promote synthesis and stabilization of immunoglobulins in the human body and obstruct formation of carcinogens such as nitrosamine and others (Zhou et al . 1998, 1999,2000). Marked decrease of antioxidant levels and antioxidant activities can cause pathological metabolic disorders and aggravation of a series of free radical chain reactions. Thus seriously damaging DNA, proteins, enzymes, biological membranes and immu-

nologic functions (Zhou et al., 2000).

The present study analyzed the plasma nitric oxide metabolites status, vitamin C, β -carotene and α -tocopherol levels in drug dependants cases and control subjects in an attemptness to assess the influence of illicit drugs on the nitric oxide and antioxidant vitamins status of the drug dependants.

The present study realized in a group of 150 subjects of them 148 males and two females. Their ages ranged between 12 and 57 years with a mean of 24.19 ± 7.84 . They were addicted to the consumption of certain drugs of abuse, specifically cannabis, morphine, barbiturate and benzodiazepine, who were transported or visited the toxicology unit of Emergency Hospital-Mansoura University. The majority of the individuals in this study were below 30 years, which reflected that the consumption of drugs of abuse is affecting fundamentally to the young sector. In this respect some authors found that the users of marijuana and other drugs were mainly use in the late adolescence and twenty years old (Johnston et al., 1994).

The present study, revealed that most of cases of drug dependence were masculine. Similar results were also reported in Egypt, by Abu El-Enine (2004), and In Bangladeshi, by Islam et al. (2001). This finding may be due to religious and moral

ethics in Islamic countries. As regard the social state of the studied drug dependants, it had been found that the proportion of participants with low social state was highest "68.7%". These findings revealed marked affection of the addiction on the social and educational state.

In this respect, Smit and Crespo, (2001) studied the socio-demographic characters, dietary intake and nutritional status of USA marijuana users. They found, the proportion of participants with high social state was highest in the non-current marijuana users "28%" and lowest in the current heavy marijuana users "8%". Similarly, the proportion of the participants with high educational level was highest in the non-current users "47%" and lowest in the heavy users "33%".

As regard body mass index, table(4) showed a mean BMI $<20\text{Kg/m}^2$ in the drug dependants were 27.3%. Similar data was presented by Smit and Crespo (2001), who observed that the mean BMI was lower in heavy marijuana users "more than 11 days per month using marijuana" than non current marijuana users. This difference remained after adjusting for age, gender and education.

Also in the present study, there was no significant difference between the body mass index and duration or number of

substance abuse "P=0.637, P=280". This may revealed neither the duration nor the number of abused substances affecting the body mass index. Similar results were reported by Smit and Crespo, (2001). They found that the mean BMI had no significant difference between different frequency of abused marijuana.

In the present study, the majority of cases "75.3%" gave positive results for more than one substance by thin layer chromatography. This declared the problem of substance abuse in Dakahlia due to multiplicity of abusing substances by the same person. In accordance with the present results are those reported by Islam et al. (2001) in Bangladesh who found that 39.5 % of drug dependants take one to two abused substances and 60.5% of drug dependants take three or more of abused substances.

On the other aspect Zhou et al., (2002) measured the oxidants antioxidants status in 114 heroine abusers only with no toxicological laboratory evidence. In developed countries the economic level is high that allows the drug dependants to buy the drug by any price. But in developing countries the economic level is low. So any available cheap psychoactive substances, producing effect or nearby it may be taken. Also, the addict may take more than one type of different drugs to produce synergism of their actions.

In the current study, the commonest detected substance by thin layer chromatography was cannabis "115" patients out of 150; followed by opiates 109 patients out of 150. While benzodiazepines were detected in 79 patients and barbiturates were found in only 6 patients. However, there was a wide discrepancy between the positive results by history recording "22.6%" and thin layer detection for opiate abuse "72.6%". This may revealed that most of patients tried to deny the addiction by opiate, being the worst and the last drug of addiction. Also this finding may be explained, on the wide scale of wrong believe that drug dependants to tramadol increase the sexual power and prolong the ejaculation time.

There are much free radicals, such as NO, O., .OH in Bango are inhaled and entered the blood when the abusers were abusing Bango, or result from the metabolism of other drug as opiates, benzodiazepines or barbiturates (Zhou et al., 1994 a, 1994b, 1995). These free radicals inactivated antioxidants. Moreover the NO may combine with O.- 2 to produce the superoxide nitroso free radicals "ONOO-" which has strong oxidative abilities. The free radicals attacked DNA, proteins, enzymes, biological membranes and various biochemical components in the cells, resulting in damaging cell function (Zhou et al., 1995, 1997a, b, c, d). In the present study there was a significant higher con-

centration of nitric oxide metabolites in the drug dependant group than those in control group. Zhou et al., (2002) in 114 chinese heroin abusers receiving abstinence treatment found significant higher nitric oxide levels in the heroin abusers than in healthy volunteers.

However, it is difficult for drug dependants to acquire sufficient amount of β -carotene, vitamin C and α -tocopherol from dietary sources because the drug dependants present recieved slightly balanced diet with preference to the meals rich in carbohydrates and poor in vitamins and minerals (Watson and Mohs, 1990; Varela et al., 1997-a ; Johnston et al., 1994). Therefore , the plasma nitric oxide metabolite levels in the drug dependants was significantly increased than the respective value of the control group. At the same time , the plasma levels of β -carotene vitamin C and α -tocopherol were significantly decreased in the drug dependants than control. These finding may be due to they had to use a great quantity of antioxidants in the bodies to catch and clean these excess free radicals (Jiang and Wan ,1992 ; Smit et al ., 1996 ; Zhou et al . , 1994a, 1994b, 1995). Furthermore, much of the antioxidative vitamins such as β -carotene, vitamin C and α -tocopherol are obtained from dietary sources (Zhou et al., 1997b, 1999, 2000). As increase the number of abused substances, there was a highly significant increase in plasma nitric

oxide level (Table 6). This may be due to abused substances which produce more free radicals that inactivated antioxidants by combining with hydrosulphide group "2SH", and the NO combined with O₂ to produce the superoxide nitroso free radicals "ONOO-" which has strong oxidative abilities. In the same aspect, Zhou et al., (2002) determined nitric oxide level in heroin abuser. They found that by increasing the amount of daily intake of heroin "0.1 gm/day, 1gm/day and 2gm /day " there was a highly significant increase in plasma nitric oxide level.

As regard the effect of duration of the abused substances, table (7) showed an inverse relationship between β - carotene, vitamin C and α - tocopherol levels and the duration of substances abuse. There was a decrease in the plasma β - carotene, vitamin C and α - tocopherol levels with prolongation of the duration of abuse. However, the decrease was statistically significant only with vitamin C and α - tocopherol levels. Accordingly the abused substances dependency produc-

es nutritional deficiency (Varela et al., 1997-b), and the use of multiple abused substances for long duration may result a greater deficiency of these vitamins. Also Islam et al., (2001) measured plasma β - carotene, vitamin C and α - tocopherol levels in drug dependants and found a negative correlation between the number of abused substances and duration of abuse with the levels of plasma β - carotene, vitamin C and α - tocopherol levels.

So in this study, the most important factors affecting an oxidant "nitric oxide", antioxidants " β - carotene, vitamin C and α - tocopherol" levels inside the body is the duration of substances abuse. By increasing the period of dependency the victims may be more exposed to free radical which consumed the antioxidants in their body. In view of these findings the drug dependants should acquire sufficient quantity of antioxidants such as vitamins A, C and E to abate the injuries by oxidant-antioxidant disturbance.

Table (1): The demographic characters of the studied drug dependant and control groups.

Parameter	Studied groups	Drug dependant group	Control Group
		Number of cases = 150	Number of cases = 30
Age: Means \pm SD		24.19 \pm 7.84	24.8 \pm 4.64
Sex: Male Female		148 2	30 —
Residence: Rural Urban		32 118	2 28
Social State: Low Moderate High		106 39 5	5 20 5
Educational Level: Low Moderate High		103 42 5	5 3 22

Low educational level: Not end the primary stage.

Moderate educational level: End the preparatory or secondary stages .

High educational level: End the university study.

Low social level: social score "0-7".

Moderate social level: score: "8-13".

High social level: social score: "above 13".

Table (2): Drug abuse detection and identification by history recording and TLC detection in the studied drug dependant group.

Parameters	Number of the cases	Percentage
Detection of substance abuse by history recoding: Positive history for any drug abuse.	150	100%
Positive history for specific drug abuse: Cannabis abuse Opiate abuse Benzodiazepine abuse Barbiturate abuse	114 34 98 38	76% 22.6% 65.3% 25.3%
Detection of substance abuse by T.L.C: Positive for any drug abuse.	150	100%
Positive TLC for specific drug abuse: Cannabis Opiate Benzodiazepine Barbiturate	115 109 79 6	76.6% 72.6% 52.6% 4%

Any person may give more than one positive abused drug.

Table (3): The duration and incidence of different abused substances in the studied drug dependant groups.

Parameter	Number of cases	Percentage
<u>Duration of the intake of the abused substance "s</u>		
< 3 Years	77	51.2%
3 - 5 Years	29	19.4%
> 5 Years	44	29.4%
<u>Number of abuse by T.L.C.:</u>		
One abused substance	37	24.7 %
Two abused substances	68	45.3 %
Three abused substances	44	29.3 %
Four abused substances	1	0.7%

Table (4): The relation between body mass index and duration to number of abused substance.

Parameter	BMI "kg/m ² "	Body mass index "Kg/m ² "	Significance test
<u>1- Number of abused substance</u>			
One abused substance		22.44 ± 3.43	<i>F= 0.453</i>
Two abused substances		22.46 ± 3.31	<i>P= 0.637</i>
Three abused substances		21.90 ± 3.26	
<u>2- Duration of substance abuse</u>			
<3 years		22.60 ± 3.30	<i>F= 1.282</i>
3-5 years		21.47 ± 3.35	<i>P= 0.280</i>
>5 years		22.29 ± 3.26	

Table (5): Plasma nitric oxide metabolites "NOx", β -carotene, vitamin C and α -tocopherol in both drug dependant and control groups.

Studied group Parameters	Drug dependant group n. = "150"	Control group n. = "30"	Significance Test "ANOVA test"
<u>NOX</u> (μ mol/L) <i>Range</i> <i>Mean \pm SD</i>	24.6 - 99.0 59.04 \pm 18.69	10.3 - 46.5 30.62 \pm 9.46	 <i>P = 0.001*</i>
<u>β- carotene</u> (μ g / dl) <i>Range</i> <i>Mean \pm SD</i>	11.0 - 91.0 43.49 \pm 23.33	19.0 - 91.0 62.73 \pm 22.44	 <i>P = 0.001*</i>
<u>Vitamin C</u> (mg/dl) <i>Range</i> <i>Mean \pm SD</i>	0.22 - 0.99 0.61 \pm 0.18	0.83 - 1.84 1.09 \pm 0.14	 <i>P = 0.001*</i>
<u>α-tocopherol</u> (mg/L) <i>Range</i> <i>Mean \pm SD</i>	0.29 - 17.68 8.65 \pm 3.94	1.05 - 18.63 13.38 \pm 4.03	 <i>P = 0.001*</i>

• Significant at $P \leq 0.05$.

Table (6) : The relation between plasma total nitrates, β carotene, vitamin C and α -tocopherol levels and number of abused substances.

Parameter	Number of abused substances	One abused substance n. = 37 Group "a"	Two abused substances n. = 68 Group "b"	Three abused substances n. = 45 Group "c"	Significance test "ANOVA test"
<u>NOx⁻</u> (μ mol/L) Range Mean \pm SD		24.60 – 81.5 50.40 \pm 14.51	25.00 – 99.0 61.73 \pm 18.49	25.0 – 98.0 62.06 \pm 20.06	<u>Between gps:</u> $P = 0.005^*$ <i>gp" a" vs gp" b":</i> $P = 0.006^*$ <i>gp" a" vs gp" c":</i> $P = 0.011^*$ <i>gp" b" vs gp" c":</i> $P = 0.995$
<u>β- carotene</u> (μ g / dl) Range Mean \pm SD		11.0 – 91.0 38.97 \pm 23.04	13.0 – 91.0 45.52 \pm 23.64	11.0 – 91.0 44.13 \pm 23.12	<u>Between gps:</u> $P = 0.382$ <i>gp" a" vs gp" b":</i> $P = 0.354$ <i>gp" a" vs gp" c":</i> $P = 0.579$ <i>gp" b" vs gp" c":</i> $P = 0.984$
<u>Vitamin C (mg/dl)</u> Range Mean \pm SD		0.32 – 0.99 0.63 \pm 0.19	0.22 – 0.95 0.61 \pm 0.18	0.32 – 0.92 0.59 \pm 0.16	<u>Between gps:</u> $P = 0.587$ <i>gp" a" vs gp" b":</i> $P = 0.906$ <i>gp" a" vs gp" c":</i> $P = 0.570$ <i>gp" b" vs gp" c":</i> $P = 0.754$
<u>α tocopherol</u> (mg/L) Range Mean \pm SD		2.29 – 17.60 8.99 \pm 3.94	2.62 – 17.37 8.56 \pm 3.99	2.81 – 17.68 8.48 \pm 3.88	<u>Between gps:</u> $P = 0.820$ <i>gp" a" vs gp" b":</i> $P = 0.854$ <i>gp" a" vs gp" c":</i> $P = 0.827$ <i>gp" b" vs gp" c":</i> $P = 0.994$

n = number
vs = versus.
Significant at $P \leq 0.05$.

Table (7): The relation between plasma "total nitrates, β -carotene, vitamin C, α -tocopherol" levels and duration of intake of substance abuse.

Duration of abuse Parameter	< 3 ys n. = 77 Subgroup "a"	3 – 5 ys n. = 29 Subgroup "b"	> 5 ys n. = 44 Subgroup "c"	Significance test "ANOVA test"
<u>NOx⁻</u> (μ mol/L) Range Mean \pm SD	25.0 – 99.0 57.41 \pm 18.13	24.6 – 97.5 60.41 \pm 18.22	25.0 – 90.0 60.98 \pm 20.09	<i>Between gps: P = 0.546</i> <i>subgp "a" vs subgp "b": P = 0.742</i> <i>subgp "a" vs subgp "c": P = 0.570</i> <i>subgp "b" vs subgp "c": P = 0.991</i>
<u>β- carotene</u> (μ g / dl) Range Mean \pm SD	11.0 – 91.0 45.53 \pm 22.57	13.0 – 91.0 45.03 \pm 24.59	11.0 – 91.0 38.91 \pm 23.73	<i>Between gps: P = 0.301</i> <i>subgp "a" vs subgp "b": P = 0.995</i> <i>subgp "a" vs subgp "c": P = 0.289</i> <i>subgp "b" vs subgp "c": P = 0.515</i>
<u>Vitamin C</u> (mg/dl) Range Mean \pm SD	0.32 – 0.99 0.65 \pm 0.17	0.34 – 0.93 0.56 \pm 0.17	0.22 – 0.92 0.57 \pm 0.18	<i>Between gps: P = 0.020*</i> <i>subgp "a" vs subgp "b": P = 0.053</i> <i>subgp "a" vs subgp "c": P = 0.06</i> <i>subgp "b" vs subgp "c": P = 0.946</i>
<u>α-tocopherol</u> (mg/L) Range Mean \pm SD	2.62 – 17.68 9.42 \pm 3.89	2.93 – 17.6 7.32 \pm 3.60	2.29 – 16.5 8.16 \pm 3.98	<i>Between gps: P = 0.030*</i> <i>subgp "a" vs subgp "b": P = 0.034</i> <i>subgp "a" vs subgp "c": P = 0.198</i> <i>subgp "b" vs subgp "c": P = 0.634</i>

* Significant at $P \leq 0.05$.

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مستوى الفيتامينات المضادة للأكسدة والمعدل الحيوى لأكسيد النيتريك فى المرضى المدمنين

المشركون فى البحث

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من المعروف إن مرضى الإدمان معرضون دائماً لخلل فى الجهاز المناعى ومن ثم تعرضهم إلى أمراض مزمنة فتاكه مما يرفع معدل العجز والوفاة بهم. إتضح أيضاً أن المرضى المدمنين معرضون لسوء التغذية وذلك لأسباب عديدة منها إستخدام مواد غذائية قليلة السعرات الحرارية مضافاً إليه أن غالبية الأدوية التى يتعودون عليها تفقد شهيتهم للطعام. كما أن عقاقير الإدمان تستهلك جزءاً كبيراً من دخلهم فى الحصول عليها مع الوضع فى الاعتبار أن غالبية هذه الطبقة يعملون فى وظائف متدنية تعطيهم دخلاً ضعيفاً، ولما كان من أهمية لمضادات الأكسدة ماسبق فكان الهدف من هذا البحث هو تقييم مستوى الفيتامينات المضادة للأكسدة وهى "حامض الإسكوريك، الكاروتينويد والفاثوكوفيرول" فى دم مجموعة من المرضى المدمنين وكذا مستوى نواتج أيض أكسيد النتريك.

وقد أجريت هذه الدراسة على ١٥٠ مريضاً من مرضى الإدمان من الذين يحولون إلى وحدة السموم بمستشفى الطوارئ كانوا من الريف أو الحضر، بعد إثبات أنهم مصابون بالإدمان عن طريق إيجابية التاريخ المرضى لكل حالة على حدة وكذا إيجابية التحاليل المعملية.

وقد أظهرت هذه الدراسة النتائج الآتية أن معظم المرضى المدمنين من صغار السن التى تنقص أعمارهم عن ٣٠ سنة وأن الذكور على الأخص هم الأكثر عرضة للإدمان. أن أكثر ما يتعاطاه المرضى المدمنين هو نبات البانجو ثم عقار الترامادول ثم عقار الأبتيرل، أن مشكلة الإدمان فى المدمن بحد ذاته هى مشكلة شديدة التعقيد حيث وجد أن ٧٥,٣٪ من المرضى المدمنين يتعاطون أكثر من عقار واحد فى ذات الوقت، يعانى المرضى المدمنين من إرتفاع فى مستوى نواتج أيض أكسيد النيتريك وانخفاض فى مستوى الفيتامينات المضادة للأكسدة "حامض الاسكوريك، الكاروتينويد والفاثوكوفيرول" عنه فى الأشخاص الأصحاء. يصاحب زيادة عدد الأنواع من المواد المخدرة وطول فترة إستخدامها زيادة فى مستوى نواتج أيض أكسيد النيتريك ونقص فى مستوى الفيتامينات المضادة للأكسدة "حامض الاسكوريك، الكاروتينويد والفاثوكوفيرول".

وعليه فمن هذه الدراسة نوصى بالآتى، عمل دراسة أشمل وأوسع على عدد أكبر من المدمنين وعلى مستويات أخرى من المؤكسدات ومضادات الأكسدة لتحديد أعمق لحجم المشكلة، تكاتف جميع برامج التوعية بجميع الجهات ضد الإدمان وتوجيه معظم جهودها إلى صغار السن من الشباب وبالأخص الذكور منهم فى المدارس، الجامعات، أماكن العمل، الأندية، وغيرها للتوعية عن خطورة الإدمان ونهاياته المظلمة، حث

الجهات الحكومية المختصة بوزارة الصحة لإدخال عقار الترامادول وعقار الأبيترييل فى جدول أول مخدرات وعدم صرفها من الصيدلانيات أو أماكن صرفها إلا بوصفه طبية موثقة. ينصح الأطباء المعالجين لحالات الإدمان بإعطاء الفيتامينات المضادة للأكسدة "حامض الاسكوربيك، الكاروتينويد والقاتوكوفيرول" لمرضاهم من المدمنين وذلك لتعويض النقص الحاد لهذه الفيتامينات وخصوصاً فى المراحل الأولى لسحب عقار الإدمان من أجسادهم، وأخيراً وهو الأهم الحث إلى العودة إلى تعاليم ديننا الحنيف "الإسلام" والتحلّى بأخلاق نبينا محمد "صلى الله عليه وسلم" أو الأديان السماوية الأخرى حيث أنها الطريق الوحيد والأفضل للبعد عن نيران المخدرات وشبح الإدمان.

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