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Heroin Abuse and Nitric Oxide, Oxidation, Peroxidation, Lipoperoxidation

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To further reveal the risks of heroin abuse to human body, and to determine the injuries of oxidation, peroxidation and lipoperoxidation induced by nitric oxide and other free radicals to heroin abusers, we determined and compared plasma values of lipoperoxides (LPO), nitric oxide (NO), vitamin C (VC), vitamin E (VE), β-carotene (β-CAR) and erythrocyte values of LPO, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) in 114 heroin abusers and 100 healthy volunteers. Using linear regression and correlation as well as stepwise regression and correlation, we also analyzed the effect of the abusing duration, and daily abusing quantity on the above-mentioned biochemical parameters in the heroin abusers. The results showed that, compared with the healthy volunteer groups, the average plasma values of LPO, and NO, and the average erythrocyte value of LPO in the heroin abuser group were significantly increased ($P < 0.0001$), and the average plasma values of VC, VE, and β-CAR and the average erythrocyte values of SOD, CAT, and GSH-Px were significantly decreased ($P < 0.0001$). Analysis of linear regression and correlation showed that with prolonged heroin abusing and with increased daily quantity in the heroin abusers, the plasma values of LPO, and NO, and the erythrocyte value of LPO were gradually increased ($P < 0.001$), whereas the plasma values of VC, VE, and β-CAR and the erythrocyte values of SOD, CAT, and GSH-Px were gradually decreased ($P < 0.001$). Analysis of stepwise regression and correlation indicated that the plasma values of NO, VC and VE were closely correlated with the abusing duration and daily abusing quantity. These results indicate that the balance between oxidation and antioxidation in the heroin abusers was seriously disturbed, and the injuries induced by nitric oxide and other free radicals, through oxidation, peroxidation and lipoperoxidation to the bodies of heroin abusers exacerbated. It is therefore necessary that in abstaining from heroin dependence, the heroin abusers should acquire sufficient quantities of antioxidants such as VC, VE and β-CAR.

INTRODUCTION

It is well known that heroin abuse is now one of the most serious and hazardous social and medical issues in the world and in China (Knight *et al.*, 1988; Jiang and Wan, 1992; Smit *et al.*, 1996; Zhou *et al.*, 1994a, 1994b, 1995). It has been pointed out that the level of urinary

Abbreviation: β-CAR: β-carotene, CAT: catalase, FR: free radical, GSH-Px: glutathione peroxidase, LPO: lipoperoxides, NO: nitric oxide, SOD: superoxide dismutase, VC: vitamin C, VE: vitamin E.

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lipoperoxides in the heroin abusers was significantly higher than that in healthy volunteers, and the level of urinary lipoperoxides was proportional to the duration and quantity of heroin abuse (Knight *et al*., 1988; Zhou *et al*., 1994a, 1994b, 1995). However, there are no reports on changes of levels of nitric oxide, antioxidants, antioxidases, or lipoperoxides in heroin abusers, not any reports on the correlation of the values of nitric oxide, antioxidants, antioxidases and lipoperoxides with the duration and quantity of heroin abusing. In order to evaluate the metabolic state of nitric oxide in heroin abusers, and to further reveal the risks of heroin abuse to the human body, we determined and compared the plasma levels of lipoperoxides (LPO), nitric oxide (NO), vitamin C (VC), vitamin E (VE) and β-carotene (β-CAR) as well as erythrocyte level of LPO and erythrocyte activities of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px) in 114 heroin abusers and 100 healthy volunteers. Additionally, we used linear regression and correlation, stepwise regression and correlation to analyze the relationship between the duration, daily heroin abusing quantity and the above mentioned values in the heroin abusers.

SUBJECTS AND METHODS

Subjects

Heroin abusers. The subjects were chosen, according as the inclusion and exclusion criteria, from hundreds of heroin abusers receiving abstinence treatment in our station. They were free from serious malnutrition, intravenous injection of heroin, HIV virus infection, hepatitis C virus infection and sexually transmitted diseases. A total of 114 heroin abusers were randomly sampled through the random numbers table. Their mean (± S) heroin abusing duration was 2.3(± 1.6) with a range of 0.5 ~ 5 years. Their mean daily heroin abusing quantity was 1.5 (± 0.9) with a range of (0.1 ~ 3.0) gram. These heroin abusers were divided into 3 groups according to the abusing duration and the daily abusing quantity.

Healthy volunteers. 100 healthy volunteers without heroin abuse history were randomly sampled through the random numbers table.

The demographic data of the heroin abusers and the healthy volunteers are presented in Table 1.

These heroin abusers and healthy volunteers had neither marked abnormality in the routine examination of blood, urine, feces, ECG or X-rays, nor obvious medical history about heart, brain, lung, liver, kidney or other organs. They were not exposed to radiation or toxic chemicals. Within the prior month, they did not take any antioxidant supplements such as vitamin C, vitamin E, ginkgo leaf agents, tea-polyphenol or other similar substances before they were enrolled in the study.

Methods

The methods used in the determination of various biochemical parameters are outlined below. Additional details and references have been provided (Zhou, *et al*., 2000). Fasting venous blood samples were collected in the morning from all the subjects and heparin sodium was added as anticoagulant. The separated plasma and erythrocytes were stored at 4℃ immediately. The colorimetry of thiobarbituric acid reaction products was used to determine the plasma LPO level. And the LPO concentration was expressed as μmol/L. The coloration of α-naphthylamine was used in determining the NO concentration in plasma and it was expressed as nmol/L. The ferrocene coloration was used and the concentrations of VC, and VE in plasma and they were expressed as μmol/L. The β-CAR in plasma was extracted

with a mixture of ethyl alcohol and petroleum ether, and was assayed with colorimetry. The β-CAR concentration was expressed as μmol/L. The colorimetry of thiobarbituric acid reaction products was used to determine the erythrocyte LPO level, and the LPO concentration was expressed as nmol/g· Hb. The colorimetry of inhibiting pyrogallol auto-oxidation was used to determine the erythrocyte SOD activity which was indicated as U/g·Hb. The colorimetry of hydrogen peroxide and acetic acid-potassium bichromate was used to determine the CAT activity, which was indicated as K/g·Hb. The improved Hafeman's colorimetry was used in determining the GSH-Px activity, which was indicated as U/g·Hb.

TABLE 1

The Demographic Data of the Heroin Abusers and the Healthy Volunteers

Group	*n*	Male	Female	Age($\bar{x} \pm s$)
Heroin Abusers	114	61	53	21 ~ 36(27.8 ± 4.5)
Heroin Abusing Duration (year)				
0.5 ~	35	18	17	21 ~ 31(26.7 ± 4.1)
1.0 ~	36	17	19	23 ~ 32(28.4 ± 5.3)
3.0 ~	43	26	17	25 ~ 36(28.2 ± 4.2)
Daily Heroin Abusing Quantity (gram)				
0.1 ~	35	20	15	21 ~ 34(27.1 ± 4.2)
1.0 ~	34	16	18	22 ~ 36(28.0 ± 5.0)
2.0 ~	45	25	20	26 ~ 36(28.2 ± 4.4)
Healthy Volunteers	100	50	50	20 ~ 35(27.2 ± 4.3)
		$X^2 = 2.6770$		$F = 0.7813$
		$P = 0.9132$		$P = 0.8351$

Major analytical reagents such as VC, VE, β-CAR, SOD, CAT, α-naphthylamine, 1,2,3-trihydroxybenzene, 1,1,3,3-tetraethoxypropane and 2-thiobarbituric acid were purchased from Sigma Chemical Company, USA; the other analytical-grade reagents were produced in China. The fresh four-distilled-water was prepared with quartz glass distilling apparatus. The main analytical instruments were 721-spectrophotometer, and UV-754-spectrophotometer.

Statistical Analysis

All data were analyzed with SPSS/8.0, Statistica/5.0 statistic software using a Compaq Pentium Ⅲ/600 computer. Statistical testing methods included the *t* test, analysis of variance (ANOV), rank test, chi square test (χ^2 test), linear regression and correlation analysis, stepwise regression and correlation analysis, and confidence interval (CI) of 95% . In the statistical analysis, the level of significance of hypothesis testing (α) $\leqslant 0.05$, and the power of test > 0.75.

RESULTS

The average plasma values of LPO, and NO, and the average erythrocyte value of LPO in the heroin abuser group were significantly higher than those in the volunteer group. The average plasma values of VC, VE, and β-CAR and the average erythrocyte values of SOD, CAT, and GSH-Px in the heroin abuser group were significantly lower than those in the volunteer group. The average values in the two groups and the corresponding confidence interval are shown in Table 2.

TABLE 2

Comparison of the Parameters ($\bar{x} \pm s$) in the Heroin Abusers (HA) With the Healthy Volunteers (HV)

Group	*n*	Plasma				
		LPO	NO	VC	VE	β-CAR
HA	114	14.4 ± 1.6	562 ± 146	33.5 ± 13.9	18.0 ± 4.3	1.28 ± 0.33
		(14.1 ~ 14.7)	(535 ~ 589)	(30.9 ~ 36.1)	(17.2 ~ 18.8)	(1.06 ~ 1.44)
HV	100	11.2 ± 1.7	357 ± 132	56.2 ± 15.3	26.1 ± 5.4	1.74 ± 0.41
		(10.9 ~ 11.5)	(331 ~ 383)	(53.2 ~ 59.2)	(25.0 ~ 27.2)	(1.66 ~ 1.82)
t^a		14.1769	10.7152	11.3709	12.2025	9.0858
P		< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Group	*n*	Erythrocyte				
		LPO	SOD	CAT	GSH-Px	
HA	14	41.6 ± 8.8	1732 ± 239	227 ± 47	21.4 ± 4.9	
		(40.0 ~ 43.2)	(1688 ~ 1776)	(218 ~ 236)	(20.5 ~ 22.3)	
HV	100	29.2 ± 6.9	1983 ± 213	321 ± 56	27.3 ± 5.6	
		(27.8 ~ 30.6)	(1941 ~ 2025)	(310 ~ 332)	(26.2 ~ 28.4)	
t^a		11.3565	8.0622	13.3480	8.2203	
P		< 0.0001	< 0.0001	< 0.0001	< 0.0001	

Note. [a]*t*-test, HA: Heroin Abusers, HV: Healthy Volunteers. The figures in parentheses are confidence limits

With prolonged heroin abusing, the average plasma values of LPO, and NO, and the average erythrocyte value of LPO in the heroin abuser group significantly increased. The average plasma values of VC, VE, and β-CAR, and the average erythrocyte values of SOD, CAT, and GSH-Px in the heroin abuser group significantly decreased. The average values in the four groups and the corresponding confidence interval are shown in Table 3.

Analysis of the linear regression and correlation of the plasma values of LPO, NO, VC, and VE, β-CAR, and the erythrocyte values of LPO, SOD, CAT, and GSH-Px with the abusing duration of the heroin abusers.

The results showed that with prolonged abusing the plasma values of LPO, and NO, and erythrocyte value of LPO in the heroin abusers gradually increased. Their linear correlative coefficients (r) were respectively 0.3240, 0.4688 and 0.4611, ($P < 0.001$), repre-

senting a significant linear positive correlation. Additionally, with prolonged abusing in the heroin abusers, the plasma values of VC, VE, β-CAR and erythrocyte values of SOD, CAT, GSH-Px in the heroin abusers gradually decreased. Their linear correlative coefficients (r) were respectively -0.6748, -0.3775, -0.4942, -0.4540, -0.3145 and -0.4253, ($P < 0.001$), representing a significant linear negative correlation.

TABLE 3

Comparison of the Parameters ($\bar{x} \pm s$) in the Different Heroin Abusing Duration Groups With the Healthy Volunteers(HV)

Group	n	Plasma				
		LPO	NO	VC	VE	β-CAR
0.5 year ~	35	$12.0 \pm 1.4^{*}$	$418 \pm 129^{*}$	$43.9 \pm 15.1^{+++}$	$22.8 \pm 4.6^{**}$	$1.47 \pm 0.36^{**}$
		(11.5 ~ 12.5)	(374 ~ 462)	(38.7 ~ 49.1)	(21.2 ~ 24.4)	(1.35 ~ 1.59)
1.0 year ~	36	$13.8 \pm 1.5^{***}$	$442 \pm 141^{**}$	$37.4 \pm 13.8^{+++}$	$19.3 \pm 4.3^{***}$	$1.25 \pm 0.33^{***}$
		(13.3 ~ 14.3)	(394 ~ 490)	(32.7 ~ 42.1)	(17.8 ~ 20.8)	(1.14 ~ 1.36)
3.0 years ~	43	$16.9 \pm 1.8^{***}$	$780 \pm 164^{***}$	$21.8 \pm 13.0^{+++}$	$13.0 \pm 4.1^{***}$	$1.15 \pm 0.31^{***}$
		(16.3 ~ 17.5)	(729 ~ 831)	(17.8 ~ 25.8)	(11.7 ~ 14.3)	(1.05 ~ 1.25)
HV	100	11.2 ± 1.7	357 ± 132	56.2 ± 15.3	26.1 ± 5.4	1.74 ± 0.41
		(10.9 ~ 11.5)	(331 ~ 383)	(53.2 ~ 59.2)	(25.0 ~ 27.2)	(1.66 ~ 1.82)

Group	n	Erythrocyte			
		LPO	SOD	CAT	GSH-Px
0.5 year ~	35	$32.9 \pm 8.3^{*}$	$1879 \pm \pm 249^{*}$	$293 \pm 51^{*}$	$24.2 \pm 5.2^{**}$
		(30.0 ~ 35.8)	(1793 ~ 1965)	(275 ~ 311)	(22.4 ~ 26.0)
1.0 year ~	36	$39.8 \pm 8.9^{***}$	$1838 \pm 237^{**}$	$241 \pm 48^{***}$	$22.1 \pm 4.9^{***}$
		(36.8 ~ 42.8)	(1758 ~ 1918)	(225 ~ 257)	(20.4 ~ 23.8)
3.0 years ~	43	$50.2 \pm 9.1^{***}$	$1524 \pm 234^{***}$	$162 \pm 43^{***}$	$18.5 \pm 4.6^{***}$
		(47.4 ~ 53.0)	(1452 ~ 1596)	(149 ~ 175)	(17.1 ~ 19.9)
HV	100	29.2 ± 6.9	1983 ± 213	321 ± 56	27.3 ± 5.6
		(27.8 ~ 30.6)	(1941 ~ 2025)	(310 ~ 332)	(26.2 ~ 28.4)

Note. ANOVA, vs HV group: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$; Rank test, vs HV group: $^{+++}P < 0.001$. 0.5 year ~, 1.0 year ~ and 3.0 years ~ are respectively stated for the different heroin abusing durations of the heroin abusers. Figures in parentheses are confidence limits.

Analysis of stepwise regression and correlation of the above values with the abusing duration in 114 heroin akusers.

Supposing the heroin abusing duration (year) of each heroin abuser to be y, and the above values to be x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8 *and* x_9 respectively, analysis of the stepwise regression and correlation showed that the closest correlation was between the abusing duration and plasma values of NO, VC and VE.

With an increase in the daily abusing quantity, the average plasma values of LPO, and NO, and the average erythrocyte value of LPO in the heroin abuser group significantly in-

creased. The average plasma values of VC, VE, and β-CAR, and the average erythrocyte values of SOD, CAT, GSH-Px significantly decreased. The above average values in the four groups and the corresponding confidence interval are shown in Table 4.

The analysis of the linear regression and correlation of the plasma values of LPO, NO, VC, VE, and β-CAR, and the erythrocyte values of LPO, SOD, CAT, and GSH-Px with the daily heroin abusing quantity.

TABLE 4

Comparison of the Parameters ($\bar{x} \pm s$) in the Different Daily Heroin Abusing Quantity Groups With the Healthy Volunteers (HV)

Group	n	Plasma				
		LPO	NO	VC	VE	β-CAR
0.1 g~	35	$12.1 \pm 1.3^{*}$	$422 \pm 132^{*}$	$48.3 \pm 15.4^{+}$	$21.6 \pm 4.5^{**}$	$1.51 \pm 0.39^{++}$
		(11.6 ~ 12.5)	(371 ~ 473)	(43.0 ~ 53.6)	(20.0 ~ 23.1)	(1.38 ~ 1.64)
1.0 g~	34	$13.2 \pm 1.6^{***}$	$450 \pm 147^{**}$	$35.1 \pm 13.7^{+++}$	$19.4 \pm 4.1^{***}$	$1.23 \pm 0.32^{+++}$
		(12.6 ~ 13.8)	(399 ~ 501)	(30.3 ~ 39.9)	(18.0 ~ 20.8)	(1.12 ~ 1.34)
2.0 g~	45	$17.1 \pm 1.8^{***}$	$756 \pm 156^{***}$	$20.8 \pm 12.9^{+++}$	$14.1 \pm 4.3^{***}$	$1.14 \pm 0.29^{+++}$
		(16.6 ~ 17.6)	(709 ~ 803)	(16.9 ~ 24.7)	(12.8 ~ 15.4)	(1.05 ~ 1.23)
HV	100	11.2 ± 1.7	357 ± 132	56.2 ± 15.3	26.1 ± 5.4	1.74 ± 0.41
		(10.9 ~ 11.5)	(331 ~ 383)	(53.2 ~ 59.2)	(25.0 ~ 27.2)	(1.66 ~ 1.82)

Group	n	Erythrocyte			
		LPO	SOD	CAT	GSH-Px
0.1 g~	35	$32.8 \pm 7.5^{+}$	$1870 \pm 246^{*}$	$292 \pm 53^{*}$	$24.7 \pm 5.4^{*}$
		(30.2 ~ 35.4)	(1786 ~ 1954)	(274 ~ 310)	(22.8 ~ 26.6)
1.0 g~	34	$37.7 \pm 9.6^{+++}$	$1835 \pm 232^{**}$	$240 \pm 49^{***}$	$22.4 \pm 4.8^{***}$
		(34.3 ~ 41.0)	(1754 ~ 1916)	(223 ~ 257)	(20.7 ~ 24.1)
2.0 g~	45	$51.4 \pm 9.2^{+++}$	$1547 \pm 239^{***}$	$167 \pm 41^{***}$	$18.1 \pm 4.6^{***}$
		(48.6 ~ 54.2)	(1475 ~ 1619)	(155 ~ 179)	(16.7 ~ 19.5)
HV	100	29.2 ± 6.9	1983 ± 213	321 ± 56	27.3 ± 5.6
		(27.8 ~ 30.6)	(1941 ~ 2025)	(310 ~ 332)	(26.2 ~ 28.4)

Note. ANOV, vs HV group: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$; Rank test, vs HV group: $^{+++}P < 0.001$. 0.1 g ~, 1.0 g ~ and 3.0 g ~ are respectively stated for the different daily heroin abusing quantity of the heroin abusers. Figures in parentheses are confidence limits

The results showed that, with higher daily abusing quantity the plasma values of LPO, and NO, and erythrocyte value of LPO in the heroin abusers increased. Their linear correlative coefficients (r) were respectively 0.4237, 0.5501 and 0.5027, ($P < 0.0001$), representing significant linear positive correlations. Additionally, with higher daily abusing quantity, the plasma values of VC, VE, and β-CAR and erythrocyte values of SOD, CAT, and GSH-Px decreased. Their linear correlative coefficients (r) were respectively −0.4340, −0.3796, −0.5050, −0.4481, −0.4182 and −0.4921, ($P < 0.0001$), rep-

resenting significant linear negative correlations.

Analysis of stepwise regression and correlation of the above values with the daily heroin abusing quantity in 114 heroin abusers.

Supposing the daily heroin abusing quantity (gram) of each heroin abuser to be y, and the above values to be x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8 *and* x_9 respectively, analysis of the stepwise regression and correlation, the result showed the closest correlation was between the daily abusing quantity and plasma values of NO, VC and VE.

DISCUSSION

NO is a neurotransmitter and endothelium-derived factor that reduces the tone of vascular smooth muscle, and plays an important role in the physiological equilibrium in humans. Therefore, the metabolic and functional states of NO are closely related to human health (Zhong and Sun, 1997; Zhou *et al.*, 1997a, 1997b, 1997c, 1998b, 1999c, 2000). 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 (Zhong and Sun, 1997; Zhou *et al.*, 1997a, 1997b, 1997c, 1998b, 1999c, 2000). VC, VE, β-CAR, SOD, CAT, and GSH-Px are the most important antioxidants and antioxidases in the human body, playing an important role in catching and eliminating excess superoxide anion FR ($O_2^{\cdot-}$), hydxoyl FR ($\cdot OH$), hydrogen peroxide FR ($HO_2^{\cdot}$), singlet oxygen ($^1O_2$), hydrogen peroxide (H_2O_2) and other free radicals (FRs) in the human body, obstructing and preventing the physiological or pathological aggravation of a series of FR chain reactions, protecting biological membranes of cells against injuries of oxidation, peroxidation and lipoperoxidation.

On the other hand, VC, VE and β-CAR can promote synthesis and stabilization of immunoglobulins in the human body and obstruct formation of carcinogens such as nitrosamine and others (Fang and Li, 1989; Chen and Zhou, 1991; Pan and Shi, 1988; Zhou *et al.*, 1997a, 1997b, 1997c, 1998b, 1999c, 2000). Marked decrease of antioxidant levels and antioxidase activities can cause pathological metabolic disorders and aggravation of a series of FR chain reactions, thus seriously damaging DNA, proteins, enzymes, biological membranes and immunologic functions (Fang and Li, 1989; Chen and Zhou, 1991; Pan and Shi, 1998; Zhou *et al.*, 1997a, 1997b, 1997c, 1998b, 1999c, 2000). LPO and its metabolic products such as malondialdehyde and conjugated diene are important poisonous residual products that can damage the biological membranes through lipoperoxidation. Therefore, marked increase of LPO levels can attack DNA, proteins, enzymes and biological membranes, so as to lead to a series of lipoperoxidation injuries in the human body and induce a variety of diseases (Fang and Li, 1989; Chen and Zhou, 1991; Chan, 1996; Pan and Shi, 1998; Zhou *et al.*, 1990, 1994a, 1994b, 1995, 1997d, 1998c, 2000).

The findings in this study showed that in the heroin abusers there were serious disorders of NO metabolism and grave unbalance between oxidation and antioxidation as well as pathological aggravation of oxidation, peroxidation and lipoperoxidation. The explanations may be as follows: there was much FRs, such as NO, NO_2, $O_2^{\cdot-}$, $\cdot OH$, in the heroin gas phase, which was inhaled and entered the blood when the abusers were abusing heroin. (Knight *et al.*, 1988; Zhou *et al.*, 1994a, 1994b, 1995). These FRs inactivated antioxidants and antioxidases by combining with hydrosulfide group (-SH), and the NO combined with $O_2^{\cdot-}$ to produce the superoxide nitroso FR ($ONOO^-$) which has strong oxidative abilities. These FRs attacked DNA, proteins, enzymes, biological membranes and various biochemical com-

ponents in the cells, resulting in serious disorder of balance between oxidation and antioxidation, and damaging cell functions (Zhou *et al.*, 1994a, 1994b, 1995, 1997a, 1997b, 1997c, 1997d, 1998b, 1998c, 1999b, 2000). Therefore, the plasma NO level in the heroin abusers significantly increased. At the same time, the plasma levels of VC, VE, β-CAR and the erythrocyte activities of SOD, CAT, and GSH-Px significantly decreased in the heroin abusers because they had to use a great quantity of antioxidants and antioxidases in the bodies to catch and clean these excess FRs (Knight *et al.*, 1988; Jiang and Wan, 1992; Smit *et al.*, 1996; Zhou *et al.*, 1994a, 1994b, 1995). Furthermore, much of the anti-oxidative vitamins such as VC, VE and β-CAR are obtained from dietary sources because they cannot be synthesized in the body (Zhou *et al.*, 1997b, 1999a). However, it is difficult for heroin abusers to acquire sufficient VC, VE and β-CAR from dietary sources because they had poor appetites or other nutritional problems. As a result, their plasma levels of VC, VE and β-CAR were significantly decreased (Zhou *et al.*, 1997b, 1999a, 2000). Again, NO_2 is a very active catalyst in lipoperoxidation, and aggravates lipoperoxidation of polyunsaturated fatty acids (PUFAs) (Zhou *et al.*, 1992, 1997a, 1998b, 1999c, 2000). Excess FRs also can directly attack PUFAs, leading to lipoperoxidation of a large number of PUFAs with subsequent formation of LPO, which damages cell functions (Zhou *et al.*, 1992, 1997a, 1998b, 1999c, 2000).

In conclusion, we found that long-term heroin abusing and daily abusing of large quantities caused the values of plasma LPO, and NO and erythrocyte LPO to gradually increase, and the values of plasma VC, VE, and β-CAR and erythrocyte SOD, CAT and GSH-Px to gradually decrease. These findings suggest that the longer a person abused heroin and the more a person abused heroin daily, the more severe the pathological oxidative stress and the damages induced by oxidation, peroxidation and lipoperoxidation, and the greater the risks of developing diseases including acquired immuno deficiency syndrome (AIDS) and death. These findings further support those reported by (Knight *et al.*, 1988; Jiang and Wan, 1992; Smit *et al.*, 1996; Zhou *et al.*, 1994a, 1994b, 1995). Furthermore, in view of the harmful effects heroin and the deficiency of antioxidant vitamins among the abusers, we suggest that in abstaining from heroin dependence, the heroin abusers should acquire sufficient quantity of antioxidants such as VC, VE and β-CAR so as to abate the injuries to their bodies. (Amstrong, et al., 1984; Fang and Li, 1989; Ginberg and Fietrich, 1989; Chen and Zhou, 1991; Chan, 1996; Zhou, et al., 1997a, 1998a, 1999a, 2000)

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