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Stress in Modern Life

Noorjehan Begum*, Sandhya H.P.**

Modern life is full of hassles, deadlines, frustrations, and demands. For many people stress has become so commonplace that it has become a way of life. Stress is not always bad; acute stress can help an individual to perform under pressure and also motivates him to do his best, but chronic stress causes, both the mind and the body pay the price of it over a period of time[1].

Two kinds of stress have been identified: Eustress and Distress. Eustress is the positive and essentially valuable form of stress that will contribute to the well-being of an organism. When stress becomes unpleasant or harmful, it will result in discomfort and distress. According to caplan, stress is a "condition in which there is a marked discrepancy between the demands made on an organism and the organism's capability to respond" [2].

An individual can respond to stress in two ways: physiolgical and psychological.

Physiological Response

It involves the CRH-ACTH-cortisol axis which is central to the integrated responses to a variety of stress stimuli. It was the primitive signal of glucose (substrate) lack that has now expanded to the broader signal of stress or fright which then evokes a coordinated neural and endocrine response in order to maintain internal homeostasis. To meet the emergency situations during stress, there is an increased secretion of ACTH which is exclusively mediated through the hypothalamus via release of CRH. The paraventricular nuclei produce and secrete CRH into the median eminence, which is then transported via the portal hypophyseal vessels to the anterior pitutary; where it stimulates ACTH secretion[3]. An increased secretion of ACTH in turn causes an increased secretion of cortisol by the adrenal glands. Stress can override the diurnal variation in cortisol secretion as well as the suppressive effects of negative feedback. Several neurotransmitters mediate the stressful inputs that stimulate CRH(and ADH) release[4]; as several afferent nerve pathways from many parts of the brain converge on the paraventricular nuclei viz. Nerve fibers from the amygdaloid nuclei which mediate responses to emotional stresses, fear, anxiety, and apprehension cause marked increase in ACTH secretion via CRH release. Input from the suprachiasmatic nuclei provides the drive for the diurnal rhythm. Also in response to injury, the nociceptive pathways carry the pain impulses via the reticular formation to the hypothalamus to trigger increased ACTH secretion. The baroreceptors are also known to exert an inhibitory input via the nucleus of the tractus solitarius[3].

Both the adrenal medulla and adrenal cortex participate in the process of adaptation to stress. Their intimate anatomical juxtaposition shows the

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fundamental functional relationship between the sympathetic nervous system and the CRH-ACTH-cortisol axis. Stress is perceived by many areas of the brain, from the cortex down to the brainstem. Major stresses almost simultaneously activate CRH neurons, ADH neurons, adrenergic neurons in the hypothalamus; and the activation is mutually reinforcing. The release of CRH (and ADH) elevates plasma cortisol levels and adrenergic stimulation increases plasma catecholamine levels; together these hormones increase glucose production by inducing gluconeogenesis and glycogenolysis. An increased blood glucose levels so produced is then shifted towards the CNS and away from the peripheral tissues. Epinephrine also increases the supply of FFA to heart and the muscles and the cortisol facilitates this lipolysis. Both these hormones raise BP and cardiac output and enhance the supply of substrates to the tissues which are critical to the immediate defence of the organism. Vasopressin causes water retention by the kidneys.

Then it is the norepinephrine and the cortisol which mediate other adaptive responses to stress. Norepinephrine stimulates the pertinent brain centres and produces a general state of arousal, vigilance and an activation of defensively useful behavior along with appropriate aggresiveness in an individual during stress. At the same time there is inhibition of appetite, sexual activity, growth hormone and gonadotropin release, that are brought about by the cortisol input to other hypothalamic neurons. These changes are reinforced by excess of cortisol, which also produces suppression of growth and ovulation. Cortisol suppresses cell mediated immunity with greater effects on T and B lymphocytes[4].

Psychological Response

The psychological responses are coping mechanisms, which, depending on the emotional, physiological and genetic predisposition of an individual and the nature and intensity of the threat, can be divided into adaptive and reactive response.

One facet of adaptive response involves fight or flight response. Another facet of the adaptive response is the use of defense mechanisms at the time of crisis. In an attempt to overcome the pain and anxiety generated by stressful circumstances, the individual, very often unconsciously, resorts to one or more of the following psychological defenses: denial, amnesia or selective attention, withdrawal (e.g., escape), counter behaviour (e.g., aggression, prejudice), rituals, somatic complaints and altered state of consciousness. Depending on the personal and cultural attitudes and values, the choice of these or other defense responses may vary from person to person. Objectivity, problem-solving and decision-making processes are other facets of adaptive measures that are being used at the time of crisis. A certain amount of emotional discomfort and anxiety is normally experienced in any response to stressors.

Reactive responses are nonadaptive or distressful responses which consist of severe anxiety, fear, grief, despair, rage and depression. To a mild or moderate degree, these feelings may be experienced as part of adaptive responses in coping with stress, but are more likely to be dominant when the stress is extensive[2].

To conclude, individual stresses lead to specific patterns of response and different individuals may respond more or less strongly or in qualitatively different ways to the same stress; but usually low responders to one stress (eg: exercise) tend to be low responders for another stress (eg: psychological disturbance). Change in lifestyle such as healthy diet, regular exercise such as a brisk walk, and abstinence from habits like smoking, consumption of alchohol, beverages (tea, coffee), and drugs can reduce the detrimental effects of stress on physical and mental health. Yoga has

also proved to be benefecial in reducing stress as well as in the management of stress related disorders. Yoga has a been used for the rehabilitation of patients of post- traumatic- stress disorder well.

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Effects of Tobacco Chewing on Cardiovascular Autonomic Function Tests

Baljoshi*, Noorjehan Begum, Sandhya H.P.***, Tejaswini****, S.B. Kulkarni*******

Abstract

Cardiovascular autonomic function tests were conducted in twenty five male tobacco chewers and twenty five male non-tobacco chewers in the age group of 20-25 years. Resting heart rate showed a statistically significant increase (p value <0.05) in tobacco chewers. A significant increase (p value <0.01) in the incidence of resting tachycardia was also observed in tobacco chewers after Gutka chewing. Heart rate response to standing (Parasympathetic system test), (p value <0.01) and blood pressure response to sustained hand-grip (Sympathetic test), (p value <0.01) showed a statistically significant higher incidence of abnormality among tobacco chewers as compared to controls.

Keywords: Cardiovascular autonomic function tests; Tobacco chewing.

Introduction

Smokeless tobacco is re-emerging as a popular form of tobacco, particularly among male adolescents. Use of smokeless tobacco (chewing tobacco and snuff) indeed represents a health concern of growing magnitude for children and adolescents.[1] Nicotine is a major component of tobacco.[2] Use of smokeless tobacco results in levels of nicotine and cardiovascular effects throughout the day that are similar to those observed with daily cigarette smoking.[3] But smoking has been widely hypothesized to be associated with the dysfunction of the autonomic nervous system[4] and cardiac deaths in smokers are associated with cardiovascular autonomic dysfunction. Previous study[5] conducted in our laboratory showed that even smoking of short duration of one to five years is associated with significant increase in the cardiovascular autonomic dysfunction. However, effects of smokeless tobacco on cardio-vascular autonomic functions have not been studied so far. Therefore the present project was undertaken.

1. To study selective cardiovascular autonomic functions in tobacco chewers of duration one to five years.
2. To study the effects of chewing a packet of Gutka on the autonomic functions.

Materials and Methods

The present study was conducted on twenty five apparently healthy male tobacco chewers of age group 20 to 25 years, and equal number of healthy age and sex matched non tobacco chewer controls. Height, weight and surface area of tobacco chewers were matched with controls.

Duration of tobacco chewing was in the range of one to five years (mean duration three years) and the number of packets being chewed were in the range of two to ten packets per day. All subjects were non

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alcoholics and non smokers. No subject had any symptoms suggestive of autonomic dysfunction.

Tobacco chewing history was recorded in detail. On the day before the study Gutka chewers were instructed to abstain from Gutka chewing for at least 3 hours prior to the study of tests to avoid residual effects of their last Gutka chewing dose. Acute effects of Gutka on autonomic function tests were determined in Gutka chewers twenty minutes after chewing one packet of Gutka (4.6 gms). Study protocol was briefly explained to the subjects .Informed consent was obtained from them before taking part. This study was performed between 10.00 AM to 1.00 PM.

Five objective and reproducible Ewing tests were performed on all the subjects. Detailed instructions regarding the procedure employed for each test were given to the subjects. Autonomic function tests were performed by using the student physiograph (Bio-Devices).In our study, ECG coupler was used and heart rate was recorded on physiograph paper during various manoeuvres of cardio-vascular autonomic tests using limb II and paper speed 25 mm/sec. The different manoeuvres were demonstrated to the subjects, and they were trained to perform the tests. Actual recordings were made only after they were able to perform tests satisfactorily. The following cardiovascular autonomic function tests were performed. Results of tests were expressed as ratios and differences as suggested by Ewing and Clarke.[6]

1. Heart rate response to Valsalva manoeuvre (Valsalva ratio)
2. Heart–rate variation during deep breathing
3. Heart–rate response to standing (30:15 Ratio)
4. Blood pressure response to standing (Immediate)
5. Blood pressure response to sustained handgrip

(1), (2) and (3) tests reflect parasympathetic function and (4) and (5) tests reflect sympathetic function.

All these tests were conducted on twenty five male healthy controls (C), and tobacco chewers before Gutka chewing (T_1) and after 20 minutes of Gutka chewing (T_2). Resting heart rates and all the corresponding ratios and differences were calculated, the results were analysed by using student 't' test.

Results

There was no statically significant difference between the controls and tobacco chewers with respect to their age, height weight, body surface area.

A significant increase in resting heart rate, and heart rate response to standing was observed in tobacco chewers in comparison to controls before tobacco chewing.

A significant rise in resting heart rate, heart rate response to standing, and blood pressure response sustained hand grip was observed in tobacco chewers after 20 minutes of tobacco chewing in comparison with the controls.

There was a statically significant increase in resting heart rate, heart rate response to

Table 1: Physical Parameters

Parameters	Controls(n=25) (Mean± S.D)	Tobacco chewers(n=25) (Mean±S.D)
Age(Years)	21.4±1.68	21.88±1.59
Height(cms)	165.24±8.13	164.04±8.13
Weight (Kgs)	59.48±6.73	61.36±5.89
Body surface area(sq.mts)	1.65±0.13	1.66±0.1

Table 2: Comparision of autonomic function tests between controls and tobacco chewers before tobacco chewing

Variable	Group	Mean	SD	t-value	p-value	Significance
Resting heart rate(Beats/min)(n=25)	C	78.88	6.53	1.7705	0.0419 or <0.05	S
	T_1	77.08	9.89			
Valsalva Ratio(V.R.)(n=25)	C	1.40	0.15	0.1893	0.4254 or >0.05	NS
	T_1	1.41	0.26			
(Heart rate variation during deep breathing)E:1 ratio(n=25)	C	1.46	0.18	0.0064	0.4975 or >0.05	NS
	T_1	1.45	0.26			
30:15 ratio (Heart rate response to standing)(n=25)	C	1.08	0.08	3.6624	0.0064 or <0.01	S
	T_1	1.00	0.06			
Systolic fall in B.P(mm of Hg)(n=25)	C	6.44	1.63	0.6274	0.267 or >0.05	NS
	T_1	6.16	1.51			
Rise in diastolic B.P(mm of Hg)(n=25)	C	18.88	1.64	0.338	0.3685 or >0.05	NS
	T_1	18.72	2.57			

S - Significant, NS-Not significant,
C - Control, T_1 Tobacco chewers (Before Gutka chewing)

Table 3: Comparision of autonomic function tests between controls and tobacco chewers after tobacco chewing

Variable	Group	Mean	SD	t-value	p-value	Significance
Resting heart rate(Beats/min)(n=25)	C	78.88	6.53	6.6182	0.00 or <0.01	S
	T_2	91.04	12.06			
Valsalva ratio(V.R.)(n=25)	C	1.40	0.15	0.0845	0.4665 or >0.05	NS
	T_2	1.41	0.21			
(Heart rate variation during deep breathing)E:1 ratio(n=25)	C	1.46	0.18	1.4672	0.0745 or >0.05	NS
	T_2	1.37	0.20			
30:15 ratio (Heart rate response to standing)(n=25)	C	1.08	0.08	6.066	0.00002 or <0.01	S
	T_2	0.96	0.05			
Systolic fall in B.P(mm of Hg)(n=25)	C	6.44	1.63	0.0608	0.2729 or >0.05	NS
	T_2	6.72	1.62			
Rise in diastolic B.P(mm of Hg)(n=25)	C	18.88	1.64	8.9917	0.00 or <0.01	S
	T_2	25.12	3.05			

S - Significant, NS-Not significant,
C - Control, T_2 Tobacco chewers (After Gutka chewing)

Table 4: Comparision of autonomic function tests in tobacco chewers before tobacco chewing and after tobacco chewing

Variable	Group	Mean	SD	t-value	p-value	Significance
Resting heart rate(Beats/min)(n=25)	T_1	77.08	9.89	7.4709	0.00 or<0.01	S
	T_2	91.04	12.06			
Valsalva ratio(V.R.)(n=25)	T_1	1.41	0.27	0.176	0.4309 or >0.05	NS
	T_2	1.41	0.21			
(Heart rate variation during deep breathing)E:1 ratio(n=25)	T_1	1.45	0.03	1.5561	0.06664 or >0.05	NS
	T_2	1.37	0.20			
30:15 ratio (Heart rate response to standing)(n=25)	T_1	1.01	0.07	4.5107	0.0 or <0.01	S
	T_2	0.96	0.05			
Systolic fall in B.P(mm of Hg)(n=25)	T_1	6.16	1.51	2.2811	0.0159 or<0.05	S
	T_2	6.72	1.62			
Rise in diastolic B.P(mm of Hg)(n=25)	T_1	18.72	2.57	8.7949	0.0008 or<0.01	S
	T_2	25.12	3.05			

S - Significant,T_1 Tobacco chewers (Before Gutka chewing)
NS - Not significant, T_2 Tobacco chewers (After Gutka chewing)

standing, and blood pressure changes to sustained hand grip test in tobacco chewers after chewing tobacco, in comparison to the same parameters being recorded before tobacco chewing in them.

Discussion

Tests reflecting parasympathetic system damage

1. Resting heart rate

Resting heart rate showed a statistically significant increase, even before chewing tobacco (p value <0.05). some studies have shown greater prevalence of resting tachycardia in tobacco chewers.[7] Resting heart rate also statistically significant increase after chewing a pocket of Gutka (p value <0.01) Nicotine, on its turn has been reported to bring about these changes through sympathetic stimulation[8,9], release of epinephrine and norepinephrine[9] and the consequent vasoconstriction.[8,9]

2. Incidence of resting tachycardia

After chewing a packet of Gutka there was a significant increase of resting tachycardia (Heart rate more than 100 beats/ min).The major action of nicotine consists of a primary transient stimulation and a secondary more persistent depression of all sympathetic and parasympathetic ganglia.[10]

Therefore higher resting heart rate and higher incidence of resting tachycardia seen in Gutka chewers appears to be due to an increase in the catecholamine activity as well as decrease in the vagal tone.

3. Valsalva manoeuvre (Valsalva ratio)

Valsalva ratio did not show any significant abnormality in the experimental group as compared to the control group.

The absorption of nicotine from smokeless tobacco produces a similar level and temporal pattern of sympathetic nervous system activation as does cigarette smoking. Daily exposure of nicotine in smokeless tobacco use is in general similar to that of cigarette smokers.[3] Otfried N. Niedermaier *et al* (1993) observed that there is an augmented sympathetic activity during Valsalva manoeuvre after smoking a cigarette. Peak sympathetic nerve activity and systolic pressure overshoots during and after valsalva straining; also increased significantly in proportion to increase of plasma nicotine levels.[11].

Valsalva ratio depends upon both sympathetic and parasympathetic control on heart. Valsalva ratio does not appear to be very sensitive to tobacco chewing induced autonomic dysfunction.

4. Heart rate variation during deep breathing

Incidence of heart rate variation during deep breathing was not statistically significant among control group as well as in experimental group. Nadeau and James have shown that, although the direct perfusion of nicotine (10μg) to the sinoatrial node in the dog causes a cholinergically mediated brief slowing of the heart within the initial 10 seconds it also causes a non reaction of the heart to electrical stimulations of the cervical vagus for over 5 minutes.[12]

5. Heart rate response to standing: (30:15 ratio)

In the present study, 30;15 ratio showed a statistically significant higher incidence of abnormality among tobacco chewers as compared to controls.

Ewing and Campbell et al (1978)[13] showed that heart rate changes to immediate standing may also be detected with routine electrocardiography. As loss of a normal response is due to vagal damage,

this provides the basis for a simple test of autonomic function that has considerable advantages over those autonomic tests now in use. Measurements of the 30:15 ratio gives a simple numerical value that reflects the presence or absence of the relative bradycardia. Ewing *et al*[12] found abnormality of this test in all diabetics with autonomic neuropathy but none in control group.

Tests reflecting sympathetic system damage

Blood pressure response to standing shows statistically higher values in T_2 as compared to T_1 and in response to sustained hand-grip which showed statistically higher values in T_2 as compared to C and T_1.

Ewing and Clarke[6] (1986) have reported that the natural course of autonomic damage in diabetics is characterised by an early damage and a late damage. The present study shows both parasympathetic and sympathetic abnormalities with tobacco chewing of one to five years duration.

Conclusion

Chewing tobacco for a short duration of one to five years (mean duration three years) predisposes one for cardiovascular autonomic dysfunction. However, it is too premature to conclude the significance of this particular observation. Further studies may follow more light in this regard.

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Role of Neurotrophic and Nerve growth factors in Physiology, Pathology and Treatment of Diabetic Peripheral Neuropathy (DPN)

Kumar Senthil P.*, Adhikari Prabha, Jeganathan*****

Abstract

Neurotrophic factors were first reported in 1950s, and are widely acclaimed for their ability to provide effective therapy for untreatable neurodegenerative disorders.Diabetic peripheral neuropathy (DPN) is a common microvascular complication of diabetes mellitus (DM) and is acclaimed as a potentially untreatable neurodegenerative peripheral nerve disorder due to structural and functional changes in lower extremity nerves. Although existing evidence suggested alterations in nerve growth factor levels in experimental DPN, it is yet to be established whether observed growth factor deficiencies were due to decreased synthesis, or functional, e.g. an inability to bind to their receptor, and/or abnormalities in nerve transport and processing. Recombinant human nerve growth factor (rhNGF) was extensively studied and reported for its efficacy in animal studies of DPN.

Keywords: Neurotrophins; Neurotrophism; Nerve growth factors; Diabetic neuropathy.

Neurotrophic factors were first reported in 1950s, and are widely acclaimed for their ability to provide effective therapy for untreatable neurodegenerative disorders. The first neurotrophic factor to be discovered was Nerve growth factor (NGF), which was selectively trophic for small fiber sensory and sympathetic neurons.[1] The other factors were brain-derived neurotrophic factor, neurotrophin [NT]-3, and NT-4/5), and insulin-like growth factor (IGF)-I and IGF-II, and glial cell-derived neurotrophic factor.[2]

Neurotrophic factors have physiological effects on neurons such as inducing morphological differentiation, enhancing nerve regeneration, stimulating neurotransmitter expression, and otherwise altering the physiological characteristics of neurons.[3] Studying neurotrophic and other nerve growth factors is essential in a commonly "difficult-to-treat" neuropathic pain condition such as diabetic peripheral neuropathy (DPN).[4]

One contributing factor in DPN was an altered neurotrophism that resulted from changes in the synthesis and expression of neurotrophins, insulin-like growth factor, and various cytokine-like growth factors that could directly act upon distinct subpopulations of sensory and motor neurons.[5] Neurotrophins and other growth factors or inflammatory mediators influence neurons and axons in diabetic peripheral neuropathy (DPN) and these substances prevent loss of diabetic dorsal root ganglion (DRG) cells or enhance regeneration of diabetic nerves.[6]

"Pre-clinical studies in animal models of DPN have demonstrated the likely efficacy of factors such as NGF for small-fibre sensory neuropathy, BDNF, CNTF and IGF-I for motor neurone disease, and NT-3 for large-fibre neuropathy."[7] Tomlinson *et al*[8] found, "in rodent models of diabetes,

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there were expression deficits in nerve growth factor (NGF) and in mRNA for its high-affinity receptor, trkA, leading to decreased retrograde axonal transport of NGF and decreased support of NGF-dependent sensory neurons, with reduced expression of their neuropeptides, substance P and calcitonin gene-related peptide (CGRP)."

"Nerve regeneration or sprouting in diabetes may occur not only in the nerve trunk but also in the dermis and around dorsal root ganglion neurons, thereby being implicated in the generation of pain sensation."[9] Growth factors may be important in this disorder as listed by : (1) endogenous growth factors promote survival and health of neurons, (2) expression levels of growth factors are altered in diabetic neuropathy and peripheral neuron injury, and (3) growth factors induce neuronal regeneration in in vitro and in vivo models of diabetic injury".[10]

Neurotrophic factors can promote the survival or growth of different neuronal populations which was demonstrated by in-vitro evidence[11] through their paracrine and autocrine actions.[12] Studies with NGF, NT-3, IGF-I and IGF-II both in vitro and in animal models of neuropathies (including DPN) suggest that these factors ameliorate nerve degeneration.[13,14] Recombinant human nerve growth factor (rhNGF) was extensively studied and reported for its efficacy in animal studies of DPN.[15]

Although existing evidence suggested alterations in nerve growth factor levels in experimental DPN, it is yet to be established whether observed growth factor deficiencies were due to decreased synthesis, or functional, e.g. an inability to bind to their receptor, and/or abnormalities in nerve transport and processing.[16]

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Letter to Editor Vol.1 No.1, January - June 2013

Antioxidants and Insulin Sensitivity in Diabetes Mellitus

P.S. Nahar*, A.S. Udupa S.H. Shah***, M.J. Kshirsagar****, B.B. Ghongane******

Sir,

Diabetes mellitus (DM) is a chronic disease that places tremendous economic burden on patient as well as health care system. It is a disorder that simultaneously affects multiple organ systems and can lead to plethora of complications. Most of the current therapies (oral hypoglycemic drugs and insulin) are aimed at improving the insulin secretion or at decreasing the glucose production by the liver. However these therapies are not able to tackle the basic pathology of the disease i.e. insulin resistance. Another problem is that most of the oral hypoglycemic drugs lose their efficacy over prolonged treatment and have to be replaced by insulin. Antioxidants, by their unique mechanism of action, can be used to tackle this problem. So in the present study we studied the effect of antioxidant supplementation on insulin sensitivity.

Various clinical trials have been performed to assess the effects of antioxidants on insulin sensitivity. The roles of ω-3 fatty acids, α-lipoic acid (ALA), and vitamin E were investigated in various trials and it was proven that they improve insulin sensitivity.[1-3]

However, the above trials are limited by small sample size and none of the trials compared the effects of two or more antioxidants at the same time. Therefore, the present study was planned to assess the comparative effects of three different antioxidants on insulin sensitivity, reflected by parameter homeostatic model for assessment of insulin sensitivity (HOMA-IR). HOMA – IR is an indicator of insulin sensitivity. A decrease in HOMA – IR value is considered as an improvement in insulin sensitivity.

Our objectives were to assess the effects of antioxidants, *viz*., vitamin E, ω-3 fatty acids, and ALA, on endogenous insulin sensitivity in patients of type 2 DM.This study was a prospective, randomized, double-blind, placebo-controlled, single-center study with a sample size of 100 diagnosed DM patients.

The patients were randomized into four groups as follows:

- Group I (n = 25) ALA group
- Group II (n = 25) ω-3 fatty acid group
- Group III (n = 25) vitamin E group
- Group IV (n = 25) placebo group

All the groups were given the respective drug for 90 days.

There was a statistically significant decrease in HOMA – IR levels in Group I (alpha-lipoic acid) Group II (omega-3 fatty acids) and Group III (vitamin E) at visit 2 compared to visit 1. Group IV (Placebo)

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Table 1: Change in HOMA IR within the groups

Groups	Gr. I (α- lipoic Acid)	Gr. II (Omega-3 fatty acid)	Gr. III (Vitamin E)	Gr. IV (Placebo)
Visit 1	3.73 ± 0.65	3.76 ± 0.74	3.78 ± 0.77	3.99 ± 0.49
Visit 2	3.07± 0.20	3.11± 0.43	3.09 ± 0.30	3.66 ± 0.76
p value	0.05*	0.031*	0.045*	0.062

* $p < 0.05$

showed a decrease which was not statistically significant.

The present study was designed to evaluate the effect of supplementation of antioxidants – α-lipoic acid, ω-3 fatty acids, and vitamin E – in patients of type 2 DM who had documented insulin resistance. A significant improvement was observed in values of HOMA – IR among the three treatment groups at the end of 3 months, while no significant improvement was noted in the placebo group in comparison with respective baseline values.

It has been postulated that a variety of stimuli in diabetes such as hyperglycemia, elevated free fatty acids, cytokines and others are responsible for increase production of reactive oxygen species and oxidative stress. These increase oxidative causes increase phosphoryaltion of insulin receptor resulting in decrease insulin action (insulin resistance). Antioxidant decreases this insulin resistance by these neutralizing reactive oxygen species.

The results of this study demonstrate that the antioxidants – α-lipoic acid, ω--3 fatty acids, and vitamin E – may be used in patients with type 2 DM. Also, since the antioxidants differed in their effects on parameters of insulin sensitivity, combining these drugs might prove as an attractive option in patients with type 2 DM.[1-4]

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