

The role of some antioxidants in treatment of adult bronchial asthma

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Abstract

This study has been performed to evaluate the role of antioxidants in the treatment of bronchial asthma in adult patients. The specific objectives of this study are to evaluate the therapeutic effect of antioxidants in the treatment of bronchial asthma in adult patients and whether the proper supplementation of antioxidants decreases the exacerbation of asthmatic attack. This study was conducted during the period from February through December 2008. Eighty asthmatic patients were included in this study. The patients were classified into 2 groups; first group was treated with vitamin E (tablet of 400 units per day) for 2 months duration, and those include 40 patients (24 males and 16 females), they have been subdivided according to the severity into mild asthma (28 patients) and moderate asthma (12 patients), while the other group of patients was treated with vitamin E (tablet of 400 units per day) and selenium (tablet 100 µg two times daily after meal) for 2 months, and those include 40 patients (27 males and 13 females), and they have been subdivided according to the severity into mild asthma (29 patients) and moderate asthma (11 patients). The results revealed a significant increase in peak expiratory flow rate (560.25 liter/min) after treatment with vitamin E, than before treatment with vitamin E (524.5 liter/min), while a highly significant decrease in serum malondialdehyde was recorded after treatment with vitamin E (2.98 nmol/ml) than before treatment with vitamin E (3.85 nmol/ml). There was significant increase in peak expiratory flow rate after treatment with vitamin E and selenium (567.25 liter/min) than before treatment (558.0 liter/min), serum malondialdehyde shows a highly significant decrease after treatment with vitamin E and selenium (1.60 nmol/ml) than before treatment (3.67 nmol/ml). The results also reveals a clinical improvement in those patients who received vitamin E and selenium, because vitamin E and selenium are a better antioxidant than vitamin E alone, and this proved by a lower serum malondialdehyde level in patients who had been received vitamin E and selenium.

دور بعض مضادات الأكسدة في علاج الربو القصبي لدى البالغين
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المستخلص

لقد أجريت هذه الدراسة لتقييم دور مضادات الأكسدة في علاج الربو القصبي لدى المرضى البالغين. إن الهدف الدقيق لهذه الدراسة هو لتقييم التأثير العلاجي لمضادات الأكسدة في علاج الربو القصبي لدى المرضى البالغين وكذلك عن دور تحسين تناول مضادات الأكسدة مع الغذاء لتقليل حدوث نوبات الربو. أن هذه الدراسة قد أجريت

للفترة من شباط ولغاية كانون الأول 2008م. تضمنت هذه الدراسة ثمانون مريضا مصابا بالربو القصبي. لقد قسم المرضى إلى مجموعتين, تضم المجموعة الأولى 40 مريضا (24 ذكرا و16 أنثى) عولجوا بإعطائهم فيتامين إي (حبة واحدة يوميا تحتوي على 400 وحدة) ولمدة شهرين ولقد قسمت هذه المجموعة وحسب شدة الربو القصبي إلى مجموعة الربو القصبي البسيط (28 مريضا) والربو القصبي المتوسط الشدة (12 مريضا). في حين ضمت المجموعة الثانية 40 مريضا مصابا بالربو القصبي (27 ذكرا و 13 أنثى) والذين عولجوا بإعطائهم فيتامين إي (حبة واحدة يوميا تحتوي على 400 وحدة) وسليينيوم (حبة تحتوي على 100 مايكرو غرام مرتين في اليوم) ولمدة شهرين أيضا وهذه المجموعة أيضا قسمت إلى مجموعتين وحسب شدة المرض, مجموعة الربو القصبي البسيط (29 مريضا) والربو القصبي المتوسط الشدة (11 مريضا). لقد دلت النتائج على وجود زيادة ملحوظة في معدل سرعة تدفق الزفير (560,25 لتر/ دقيقة) بعد العلاج باستخدام فيتامين إي بالمقارنة قبل استخدام فيتامين إي (524,5 لتر/دقيقة), في حين وجود انخفاض ملحوظ في مستوى المالونداالديهيد في مصل الدم بعد استخدام فيتامين إي في المجموعة الأولى (2.98 نانومول/مللتر) بالمقارنة قبل استخدام فيتامين إي (3,85 نانومول/مللتر). في حين توجد زيادة ملحوظة في معدل سرعة تدفق الزفير لدى المجموعة الثانية, حيث كان بعد استخدام فيتامين إي وسليينيوم (567,25 لتر/دقيقة) بالمقارنة قبل استخدام فيتامين إي وسليينيوم (558 لتر/دقيقة). أما بالنسبة لمستوى المالونداالديهيد في مصل الدم في المجموعة الثانية حيث كان انخفاض ملحوظ (1.6 نانومول/مللتر) بعد استخدام فيتامين إي وسليينيوم بالمقارنة قبل الاستخدام (3.67 نانومول/مللتر). لقد دلت هذه النتائج على التحسن السريري للمرضى المصابين بالربو القصبي باستخدام فيتامين إي وسليينيوم لأنهما معا لهما تأثيرا مضادا للأكسدة أكثر من فيتامين إي لوحده وهذا واضحا من مستوى المالونداالديهيد في مصل الدم.

Introduction

Oxidative stress describes the damage that occurs when reactive oxygen species (ROS) overwhelm the antioxidant defenses of the host. Oxidative stress may play an important role in the pathophysiology of asthma, and may be a final common pathway leading to tissue damage. (1-3)

Antioxidants such as vitamin E act to protect the cells against the effects of free radicals, which are potentially damaging by-products of energy metabolism, free radicals can damage cells and may contribute to the development of cardiovascular disease and cancer. (4, 5) Selenium is an essential mineral found in trace amounts in the human body. It works as an antioxidant. The principal dietary forms of selenium are selenoaminoacids; selenomethionine is derived from plants and selenocysteine from animal sources, inorganic forms of selenium are often supplied as supplements and in experimental diets. (6)

Malondialdehyde is an aldehyde considered to be the terminal

compound and the most important marker for monitoring lipid peroxidation and oxidative damage induced by ROS which is strongly associated with the development of serious disease, it is also considered as a thiobarbituric reactive substance (7,8) This study aims to evaluate the role of antioxidants in the management of adult bronchial asthma.

Patients and Methods

This study was conducted in Tikrit Teaching hospital during the period from the 1st of February 2007 till December 2008. Eighty adult patients of both gender, age group between 18 - 45 years, presented with signs and symptoms of asthma, and they had been checked for their age, height, body weight, and the severity of asthma. Severe asthma, those who were on steroid therapy, those who were smokers, and those who were escaped were excluded from this study. The patients were classified into 2 groups; those who received vitamin E only; they received vitamin E tablet

400 mg one tablet daily after meal for 2 months and those who received vitamin E and selenium, they received vitamin E tablet 400 units one tablet daily and selenium tablet 100 µg two times daily after meal for 2 months. Three milliliters of venous blood sample were aspirated for the measurement of blood hemoglobin,

WBC, differential count, ESR, and serum MDA before starting treatment and 2 months later. Those who have been received vitamin E alone considered being control group; those were 40 adult patients with mild and moderate asthma. The same methods and instruments used for all stages, for patients and Control.

Table (2-1): Demographic characteristics of patients and controls

Group	Total No.	Male	Female	Mild asthma	Moderate asthma
Those on vitamin E	40	24	16	28	12
Those on vitamin E + Selenium	40	27	13	29	11

Determination of blood hemoglobin concentration was performed by the cyanmethemoglobin method,⁽¹⁶⁾ determination of erythrocyte sedimentation rate by Westergren method,⁽¹⁶⁾ determination of white blood cell count with eosinophil count.⁽¹⁶⁾ Malondialdehyde level was analyzed in the sera of both groups by the Uchiyama and Mihara method.⁽⁹⁾ This method is based on the formation of a pink colored compound, which emits maximum absorbance at 535 nm upon the reaction of thiobarbituric acid with MDA. Statistical analysis was performed using the statistical package SPSS versions 12.0. Comparison of continuous variables was applied using student t-

test and person correlation test. Data were expressed as mean and standard deviation number (percentage) and a p-value < 0.05 is considered significant.

Results

Table (3.1) shows the effect of vitamin E on asthmatic patients. There is non significant increase in hemoglobin. On the other hand, ESR, WBC and eosinophil count exhibited a non-significant decrease. While PEFr exhibited significant increase after treatment with vitamin E (P < 0.05). Serum MDA shows a very high significant decrease was recorded in asthmatic patients on vitamin E (P < 0.01).

Table (3.1): Effect of treatment with vitamin E on the measured parameters.

Parameters	Before treatment				After treatment with Vit. E				P-value
	Mean	± SD	Min.	Max.	Mean	± SD	Min.	Max.	
Hb	13.38	1.34	11.7	19	13.68	0.81	12.5	15.5	0.14 (NS)
E.S.R.	12.90	5.06	5	23	12.68	4.96	5	24	0.75 (NS)
WBC	5983.75	907.26	4100	8000	5775	685.38	4000	6300	0.18 (NS)
Eosinophil	2.30	1.18	1	5	2.15	0.77	1	4	0.47 (NS)
PEFR	524.5	74.11	410	630	560.25	75.16	450	670	0.035*
MDA	3.85	0.26	3.47	4.29	2.98	0.29	2.49	3.52	<0.01*

NS = not significant using paired Z-test except for MDA paired t-test was used.

For the asthmatic patients on vitamin E and selenium, a non-significant increase was recorded in Hb, while a non-significant decrease in ESR, WBC, and eosinophil was recorded. In

contrast, they exhibiting significant increase in PEFR ($P < 0.05$), and a highly significant decrease in serum MDA was reported at a P of less than 0.01 (table 3.3).

Table (3.3): Effect of treatment with vitamin E and selenium on the measured parameters.

Parameters	Before treatment				After treatment with Vit. E & Se				P-value
	Mean	± SD	Min.	Max.	Mean	± SD	Min.	Max.	
Hb	13.49	0.68	12.5	15	13.54	0.69	12.5	15	0.70 (NS)
E.S.R.	12.10	5.94	4	28	11.83	5.84	3	28	0.84 (NS)
WBC	5562.5	1044.08	4000	8000	5375.0	973.96	4000	7800	0.11 (NS)
Eosinophil	2.48	1.25	1	5	2.155	0.85	1	4	0.12 (NS)
PEFR	558.0	62.77	430	690	576.25	64.05	450	680	0.034*
MDA	3.67	0.40	2.95	4.21	1.60	0.37	1.08	2.08	<0.01*

NS = not significant using paired Z-test except for MDA paired t-test was used.

Patients on vitamin E shows a non-significant negative correlation between PEFR and hemoglobin in asthmatic patients (fig 3.1; $r = -0.041$). On the other hand, a positive significant correlation was recorded

with ESR with correlation coefficient of 0.235 (fig. 3.2). Fig. (3.3) shows a positive non-significant weak correlation between PEFR and WBC ($r = 0.043$), while the eosinophil count exhibited a non-significant negative weak correlation (fig. 3.4; $r = -0.019$).

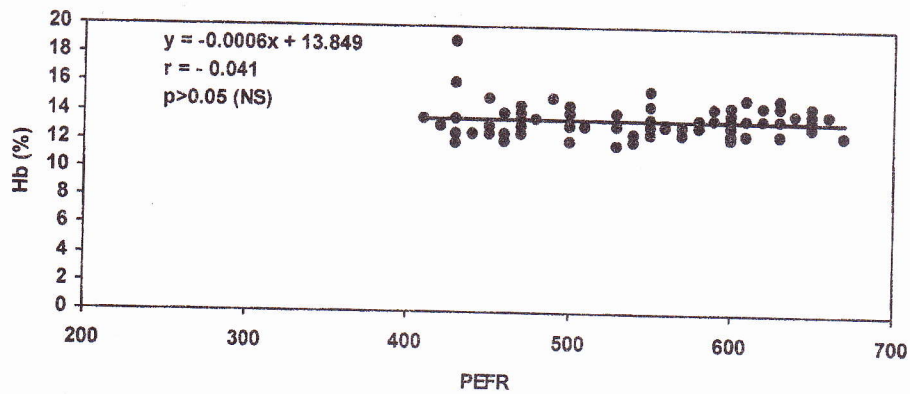


Figure (3.1): Relationship between PEFR (L/min) and Hb (g/dl) in asthmatic patients on vitamin E (NS = not significant).

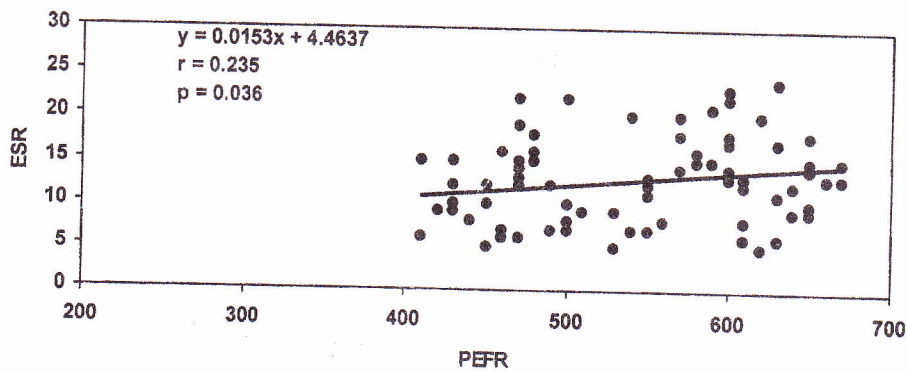


Figure (3.2): Relationship between PEFR (L/min) and ESR (mm/h) in asthmatic patients on vitamin E.

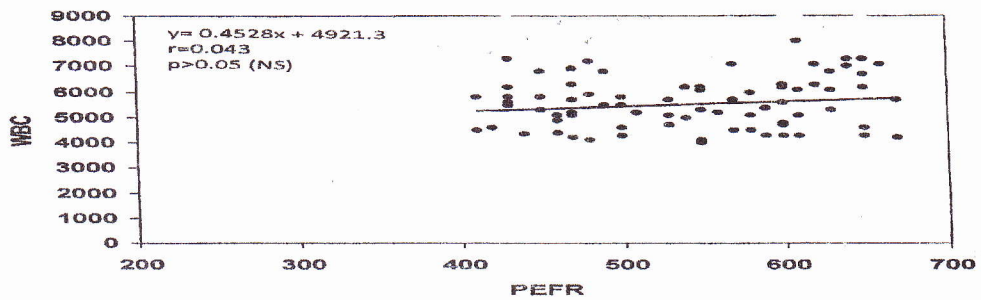


Figure (3.3): Relationship between PEFR (L/min) and WBC (cells/mm³) count in asthmatic patients on vitamin E (NS = not significant).

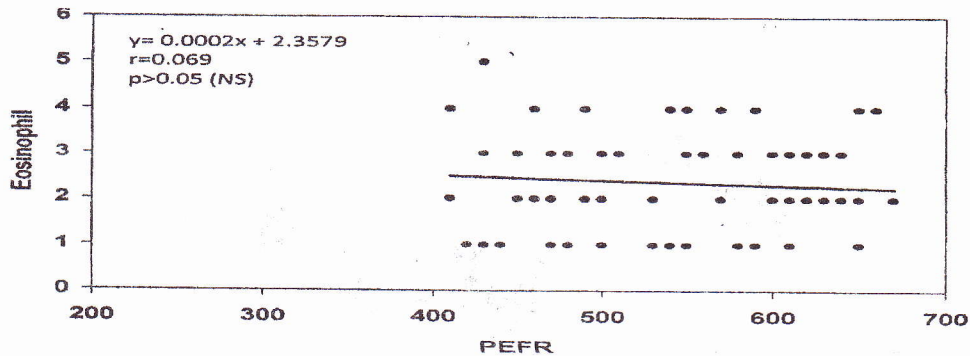


Figure (3.4): Relationship between PEFR (L/min) and eosinophil count (cells/mm³) in asthmatic patients on vitamin E.

The results for the asthmatic patients on vitamin E and selenium shows a non-significant positive correlation between PEFR and each of Hb, ESR, WBC, and eosinophil count with

correlations of ($r = 0.141$, $r = 0.147$, $r = 0.179$, $r = 0.011$) respectively, as it is evident from figures 3.5 to 3.8.

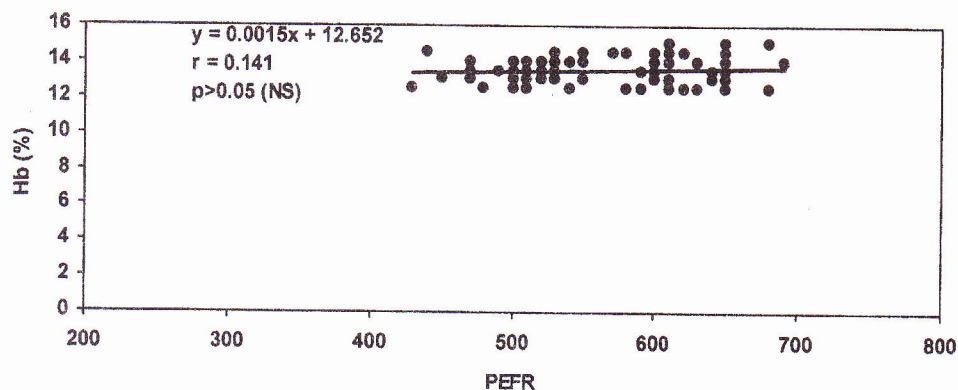


Figure (3.5): Relationship between PEFR (L/min) and Hb (g/dl) in asthmatic patients on vitamin E and selenium (NS = not significant).

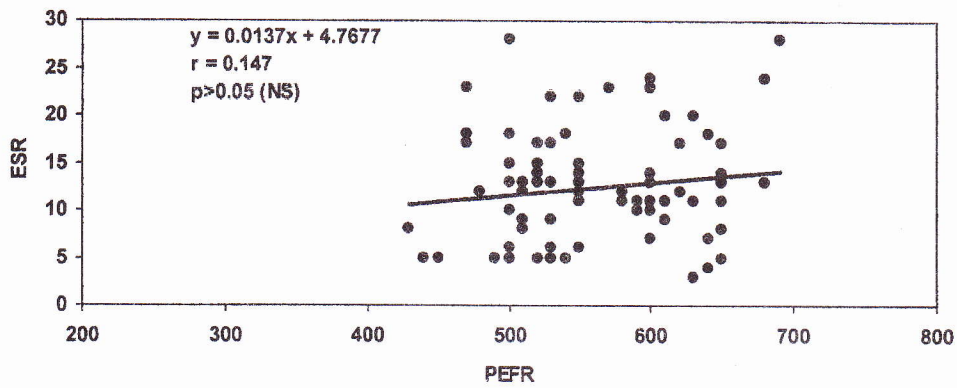


Figure (3.6): Relationship between PEFR (L/min) and ESR (mm/h) in asthmatic patients on vitamin E and selenium.

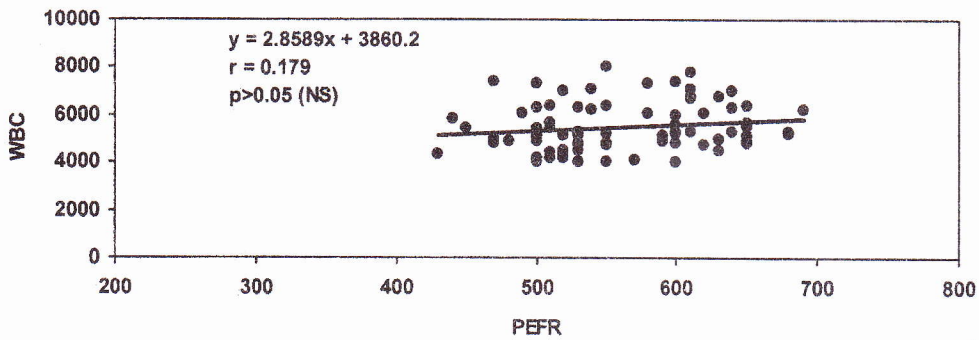


Figure (3.7): Relationship between PEFR (L/min) and WBC count (cells/mm³) in asthmatic patients on vitamin E and selenium (NS = not significant).

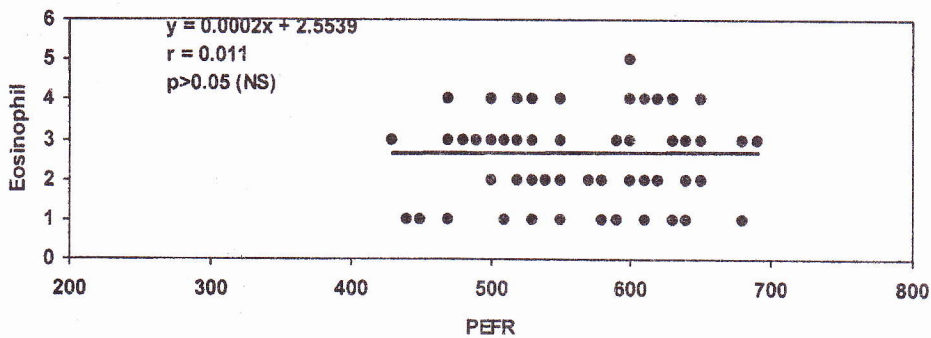


Figure (3.8): Relationship between PEFR (L/min) and eosinophil count (cells/mm³) in asthmatic patients on vitamin E and selenium.

Table (3, 5) shows the effect of selenium and vitamin E therapy on the measured parameters in asthmatic patients. The results show non-significant difference between patients

on vitamin E therapy and vitamin E and selenium therapy in Hb, ESR, and eosinophil count. However, WBC count and serum MDA exhibited a significant decrease.

Table (3.5): Comparison of treatment with vitamin E and vitamin E and selenium on the measured parameters.

Parameters	Mean \pm SD		P-value
	Vit. E	Vit. E + Se	
Hb	13.68 \pm 0.81	13.54 \pm 0.69	0.47 (NS)
E.S.R.	12.68 \pm 4.96	11.83 \pm 5.84	0.75 (NS)
WBC	5775.0 \pm 1001.2	5357.0 \pm 974.0.3	0.047*
Eosinophil	2.15 \pm 0.93	2.155 \pm 0.85	0.52 (NS)
PEFR	560.25 \pm 75.2	576.25 \pm 64.1	0.63 (NS)
MDA	2.98 \pm 0.29	1.60 \pm 0.37	< 0.01*

Discussion

In this study concerning the effect of vitamin E administration on the studied parameters, peak expiratory flow rate revealed a significant increase at a P value of less than 0.05, and this is due to the fact that vitamin E, as an antioxidant may improve lung function and, decrease inflammatory response, and this is in agreement with the study done by Holger.⁽¹⁰⁾ There was highly significant decrease in serum level of MDA in asthmatic patients on vitamin E therapy ($P < 0.001$) and this because that the MDA consider being most sensitive and a final stage of peroxidation, and it is considered as a marker of pro-oxidant level. There was a non significant increase in Hb after treatment with vitamin E, while the non-significant decrease in ESR, WBC, and eosinophil count could be attributed to a weak anti-inflammatory effect of vitamin E. Concerning the effect of administration of both vitamin E and selenium it was found that peak expiratory flow rate exhibited significant increase ($P < 0.05$). and this because that both selenium and vitamin E improves lung function, due to their

combined antioxidant effect, selenium plays a vital role in the body, so selenium can alleviate asthma, which is associated with high level of inflammation and oxidative stress.⁽¹¹⁾ Fogarty *et al.*⁽¹²⁾ found that selenium is a dietary mineral that plays a vital role in activating glutathione which improves the antioxidant effect of the mineral. Kadrobova. *et al.*⁽¹³⁾ reported that low selenium levels were observed in patients with asthma when compared to a group of patients without asthma, while Doelman and Bast⁽¹⁴⁾ noted that vitamin E and selenium play a role in decreasing the bronchoconstriction, reactive oxygen species are partly responsible for the observed pulmonary tissue damage, the reactive oxygen species induce bronchoconstriction elevate mucous secretion, and cause microvascular leakage which lead to edema formation. The improvement in PEFR indicates that antioxidants have a beneficial effect on asthma. In this study there was a highly significant decrease in serum level of MDA ($P < 0.01$) of those asthmatic patients treated with vitamin E and selenium

and because MDA is considered to be most sensitive indicator of oxidative stress, and it is the end product of lipid peroxidation, this finding indicate that vitamin E and selenium may play an important role in reducing oxidative stress. A non-significant increase was recorded in Hb, after treatment with vitamin E and selenium, and this may be due to the fact that vitamin E and selenium induce blood cell regulation and growth. The decrease in ESR, WBC, and eosinophil count after treatment with vitamin E and selenium may be attributed to that selenium and vitamin E is essential for maintaining an effective immune system, and the reduction of the inflammatory response. Table (3.5) shows the difference of the effect of treatment between vitamin E and vitamin E and selenium; WBC count and MDA exhibited a significant decrease, and this could be attributed to the additive anti-inflammatory effect of combination of two antioxidants (vitamin E and selenium) more than the effect of vitamin E alone.

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