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Evaluation of Some Antioxidants and Oxidative Stress Tests in Iraqi Lung Cancer Patients

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Abstract:

Vitamin K-dependent protein (VKDP) contributes to the development of lung cancer. The purpose of this research was to better understanding of the role of blood matrix Gla protein (MGP), VKDPs, Malondialdehyde (MDA), Superoxide dismutase (SOD) and Vitamin K (Vit K) in Iraqi patients with lung cancer before and after the first cycle of chemotherapy. Blood samples were collected from Al amal National Hospital for cancer treatment from October 2021 to May 2022, and a total of 80 samples were collected, divided into two groups (40 patient before taking a chemotherapy and 40 patients after taking chemotherapy), ranging in age from 20 to 45 years old. The results showed that although there were highly statistically significant differences in MDA, VKDPS, SOD, and Vit K, there was no difference in MGP serum levels between the two groups (P = 0.05). The current study found a significant positive correlation between MGP and VK1 values.Correlations before and after treatment. Based on the results obtained, no role for the blood matrix protein Gla was observed in patients after and before treatment. Therefore, it cannot be considered a sign of patients' response to treatment. In addition, it was observed that lung cancer patients had lower levels of SOD enzyme, which indicates the effect of treatment on the disease, in which knowing the extent to which the body is responding or not responding to treatment.

Keywords: Blood matrix Gla protein (MGP), Chemotherapy, Lung cancer, Malondialdehyde (MDA), Superoxide dismutase (SOD), Vitamin K (vit. K).

Introduction:

Deaths related to lung cancer account for about 18 % of all deaths in the world, affecting people of each man and women. Small cell carcinoma (SCLC) accounts for 13 % of all instances of lung cancer and non -small cell carcinoma is two main categories (NSCLC, accounting for 83 % of all cases) [1-2].

It is known that one of the lipid peroxidation products that exist in human plasma is called MDA and has biological characteristics that may be related to cancer. Lipid peroxide and it's by -products are related to many diseases, including cancer and may damage enzymes and other major molecules, including Deoxyribonucleic acid (DNA) [3].

At present, 17 known vitamin K dependent proteins are found in bones, blood vessels and heart [4]. During the condensation process, factors II, VII, IX, and X have been widely recognized in VKDP. The coagulation factor mentioned earlier leads to the carboxylation process of the liver experience, resulting in VKDP active. The periphery, blood vessels have also experienced this process. In order to make VKDP run normally, γ-glutamate carboxylase is needed. The enzyme is internal and external of the brain and is dependent on vitamin K [5]. In recent years, research on the importance of VKDPS in lung cancer has increased. The current research is particularly focused on the role of MGP in tumor progress [6].

Blood matrix Gla protein (MGP) is a calcium restricting grid protein that secretes and includes many posts (carboxyl glutamic acid residues) modified by Vit.K dependent carboxyl. In vitro, MGP associates its GLA residue with calcium and hydroxyapatite to act as a key regulator/inhibitor for mineralization [7]. Tumor aggressiveness and a poor prognosis have been linked to high circulating levels of MGP. Additionally, it was found that patients with lung metastases from osteosarcoma had high serum levels of MGP at the time of diagnosis. By modifying endothelium adhesion, the tumor cell's capacity for extravasation, and by manipulating metalloproteinase activities, MGP's action of promoting metastatic spread can be explained [8].

Vitamin K is unequivocally known for its part in blood coagulating. Much examination is occurring as of now checking out at the vitamin K family and its expected anticancer impact. Nutrient K2 may securely smother development and intrusion of human hepatocellular carcinoma by means of protein kinase an enactment and result in moderate concealment of growth repeat. It has likewise been displayed to bring about development concealment in a portion subordinate way in cellular breakdown in the lung's cells in vitro [9]. The purpose of the study was to measure levels of vitamin K-dependent protein (VKDP), which contributes to lung cancer development, and to measure antioxidants and oxidative stress in patients.

Materials and Methods:

Eighty samples in total, separated into two groups (40 before chemotherapy and 40 after chemotherapy), with ages ranging from 20 to 45 years, were collected from patients attending Alamal National Hospital for cancer management throughout the study period from October 2021 to May 2022. Patients' blood was drawn in five milliliter amounts. Following that, serum was isolated and utilized to evaluate further biochemical characteristics. Enzyme-linked immunosorbent assay was used to evaluate the following substances from blood samples: MDA, VKDPS, MGP, SOD, and Vit K (MyBioSource, USA, Cat Nos. MBS2540407, MBS164319, MBS700351, MBS9718960, and MBS746981) (ELISA), The same techniques were used to identify the parameters in the second blood sample, which was taken about three weeks following the first chemotherapy treatment.

Statistical Analysis:

The significance of the results and correlation were evaluated using SPSS Version 20 t _ test. P values≤ 0.05 were considered statistically significant. Data are expressed as mean ± standard error.

Results and Discussion:

According to the biochemical parameter MDA, VKDP, SOD and VIT K comparison, the statistical differences are significant (P <0.001), but there is no difference between the two groups in MGP (P 0.05) as indicated in Table 1.

Table 1. The features of the clinical parameters of lung cancer group.

Variable	Sample No.80	Mean	S.E	P Value
MDA (mmol/L)	Pre-Treatment	2.60	0.23	**0.0001
	Post-Treatment	0.34	0.03	
VKDPS (ng/mL)	Pre-Treatment	235.71	12.16	**0.0001
	Post-Treatment	86.17	3.378	
MGP (pg/mL)	Pre-Treatment	4505.71	432.19	0.08
	Post-Treatment	4366.31	475.17	
SOD (ng/mL)	Pre-Treatment	44.08	3.78	**0.0001
	Post-Treatment	25.80	0.55	
Vit K (pg/ml)	Pre-Treatment	651.43	69.80	*0.011
	Post-Treatment	629.82	37.70	

- **MDA: Malondialdehyde, VKDPs: Vitamin K-dependent Protein S, MGP: Matrix Gla protein, SOD: Superoxide dismutase, Vit K: Vitamin K.**

As shown in Table 2 and Fig. 1(A, B), as far as the correlation between treatment and processing, the significant positive correlation between MGP and VK1 values.

Table 2. The correlation between group variables (r- values).

Parameter	MGP- Pre-Treatment		MGP- Post-Treatment	
Vit K	r	P	r	P
	0.471	P<0.05	0.477	
			P<0.05	

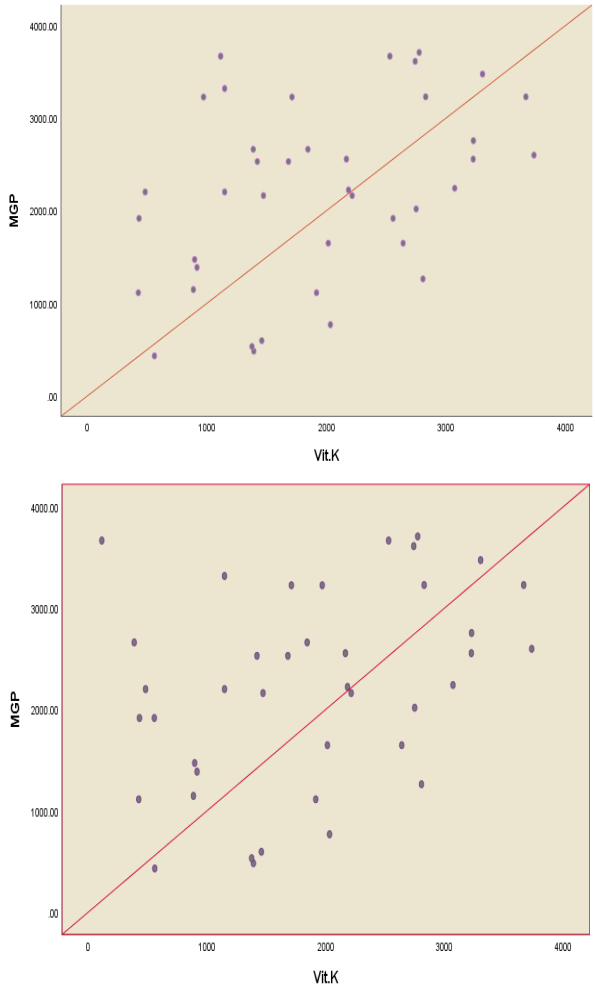

Figure 1. (A). pretreatment correlation between MGP and Vit. K, (B). post treatment correlation between MGP and Vit. K.

Adenocarcinoma is the most prevalent kind lung cancer in our study and occurs in 50% of patients. Most patients are non -smokers or smokers, which are related to this. Despite great progress, the treatment of adenocarcinoma has caused the survival rate of most patients to increase [10-11]. MGP expression is related to the recent cell differentiation of cancer and tumor progress [12].

This study also shows that MGP improves the resistance of cancer to chemotherapy by enhancing the interaction between the base cancer cells and extracellular matrix components. In addition, each chemotherapy drug has been related to the enhancement expression of MGP [12-13].

Only before therapy, in our investigation, did MGP serum values and VK1 values show a significant correlation. Additionally, after treatment in our trial, MGP dropped barely. The current study found that patients had no vitamin K deficiency after the first chemotherapy cycle, which is consistent with the study by Crintea et al. [14], as MGP is a marker of extrahepatic vitamin K deficiency. The production of free radicals is related to the subsequent lipid peroxidation may be related to lung disease. Considering that the level of MDA in our study of lung cancer patients is significantly higher, which is consistent with research by Domej et al. [15]. The information about SOD expression and activity in tumor cells is unclear. According to research by Skórska et al., and our work, compared with tumor -free lung tissue, SOD has been found to be elevated in lung cancer cells [16].

Based on the main pathological tissue types, lung cancers are divided into two main groups: small cell carcinomas (13% of cases) and non-small cell carcinomas (83% of cases). Non-small cell lung cancer is divided into adenocarcinoma and its variants, squamous cell carcinoma, large cell lung carcinoma, as well as salivary gland tumors and carcinomas. Adenocarcinoma is the most common type of non-small cell carcinoma and is the most common subtype of lung cancer in non-smokers, which originates in the bronchial mucosal glands. Antioxidants are formidable substances, mostly derived from plants, which until now were considered beneficial agents capable of treating many oxidative-reducing injuries[17].

Conclusions:

To sum up what has been found, antioxidant agents such as the enzyme SOD may protect lung cancer patients from the damages of oxidative stress. As oxidative stress, oxidizing fractions have detrimental effects on both the development of cancer and the aggravation of the patient's pathology.

In conclusion, for diagnosis, classification, and treatment, lung cancer requires a multidisciplinary approach due to its complexity and heterogeneity. The main direction for effective cancer treatment in the future is the identification of cancer serum markers, targeted therapy, and the potential to use antioxidants as a treatment to limit the spread of the disease. There is a significant correlation between pre-treatment values of MGP and vitamin K1 levels among VKDPs. In addition to the decreased levels of SOD enzyme after treatment, which indicate the effect of treatment on antioxidants and oxidative stress, therefore the change in superoxide dismutase levels can be considered as the best biomarker for the diagnosis and treatment of lung cancer.

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Authors' declaration:

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are mine ours. Besides, the Figures and images, which are not mine ours, have been given the permission for re-publication attached with the manuscript.
- Authors sign on ethical consideration's approval
- Ethical Clearance: The project was approved by the local ethical committee in University of Baghdad.

Authors' Contribution Statement:

Israa F. Ascar, Fayhaa M. Khaleel and Areej Sh. Hameed: contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript and Dr. Musaab contributed to diagnosing the disease and making adjustments requested by the assessor. All authors discussed the results and commented on the manuscript.

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تقييم بعض مضادات الأكسدة واختبارات الإجهاد التأكسدي في مرضى سرطان الرئة العراقيين

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الخلاصة :

يساهم البروتين المعتمد على فيتامين ك (VKDP) في تطور سرطان الرئة. كان الغرض من هذا البحث هو فهم دور مصفوفة الدم Gla protein (MGP) و VKDPs و مالون ثنائي الالديهايد (MDA) و انزيم سوبراوكسيد دسميوتيز (SOD) ,فيتامين ك (vit. K) في المرضى العراقيين المصابين بسرطان الرئة قبل وبعد الدورة الأولى من العلاج الكيميائي. جمعت عينات الدم من مستشفى الأمل الوطني لعلاج السرطان من أكتوبر 2021 إلى مايو 2022 ، وجمعت ما مجموعه 80 عينة ، مقسمة إلى مجموعتين (40 مريض قبل العلاج الكيميائي و 40 مريضا بعد العلاج الكيميائي) ، تتراوح أعمارهم بين 20 إلى 45 سنة. أظهرت النتائج أنه بالرغم من وجود فروق ذات دلالة إحصائية عالية في MDA، VKDPS، SOD ، وفيتامين K ، لم يكن هناك فرق في مستويات مصل MGP بين المجموعتين (P = 0.05). وجدت الدراسة الحالية علاقة إيجابية ذات دلالة إحصائية بين قيم MGP و.VK1 . الارتباطات قبل العلاج وبعده. بناءً على النتائج التي تم الحصول عليها ، لم يلاحظ أي دور لبروتين مصفوفة الدم Gla في المرضى بعد العلاج وقبله. لذلك ، لا يمكن اعتباره علامة على استجابة المرضى للعلاج. كما لوحظ أن مرضى سرطان الرئة لديهم مستويات أقل من إنزيم SOD ، مما يشير إلى تأثير العلاج على المرض ، حيث يمكن أن تساهم هذه الآثار في تحسين البقاء على قيد الحياة بين المستجيبين.

الكلمات المفتاحية: بروتين ماتريكس جلا (MGP) ، العلاج الكيميائ ، سرطان الرئة، مالون ثنائي الالديهايد ، (MDA) انزيم سوبراوكسيد دسميوتيز (SOD) ،فيتامين ك (vit. K) .