SERUM LEVEL OF VITAMIN C IN MALIGNANCY

Dr. Al. Naama L. M (PhD) Professor*; Dr. Abdul. Barry J. A(PhD) Professor *;
Dr. Al. Manaseer Z.A(M.Sc) Assistant Lecturer *; Dr. Al Khayat H (MBCHB,FRCS) consultant of surgery **

ABSTRACT

The present paper reports selected results of 184 surgical patients in Basrah. They were 82 males and 102 females. Their ages ranged between 22-84 years. From those, 100 patients had different malignancies. 43% from the total number, of malignant tumors with gastrointestinal GIT cancer, while breast cancer and malignancy of urinary systems each represents 18%. And the other types of malignancy were 21%. The remaining 84 patients were suffering from surgical ailments other than malignancy. Their serum vitamin C were measured.
The results showed high significant reduction in serum Vitamin C in all type of malignancy , specifically in GIT (P< 0,00l)in respect to age mainly at the age less than 45 and between 45-65 years old, as well as sex and nutritional habit mainly among those consuming fruit and Vegetables less than 3 times per week. Therefore, we conclude that serum Vitamin C are measurable biochemical indices that can be used as predictors for following those patients during and after treatments.

Key words : Vitamin C, Different types of malignancy, Non – malignant patients

INTRODUCTION

Vitamin C is an essential micronutrient required for the normal metabolic function of the human body. It is not synthesized inside the body human and other primates, because of the lack of enzyme required for its synthesis via the glucouronic acid pathway[1]. Citrus fruits potatoes and green vegetable in general are good sources of vitamin, its absorption was in small intestine by means of specific energy dependent transport system[2].
Vitamin C is a vitamin which is required for collagen and creatine synthesis[3], also serve in tyrosine synthesis and catabolism, neurotransmitter and serotonin synthesis[3] and as an important antioxidant function in the body, which mean that it acts as a reducing agent in aqueous solution, reverses oxidation and reduces hydroxyl, hydro peroxyl, super oxide, alkoxyl and peroxyl radicals from attacking and damaging the cell membrane, DNA and cellular protein[4].
Two major properties of vitamin C appears to make it as an ideal antioxidant, the low reduction potential of both ascorbate and ascorbic radical and the stability and low reactivity of the ascorbic radical[5].
Clinical trials currently in progress are investigating the hypothesis that, vitamin E intake was associated with consumption of other synergistic antioxidant micronutrients, such as vitamin C and selenium and suggested that the cardio protective effect of vitamin E may be derived if it is administered with other cofactor nutrients[6].
Vitamin C is reported to inhibit tumor spared and micro metastasis by enhancing the collagen synthesis and basement membrane integrity as well as it role in hyaluronide inhibition[3].
Research showed that, increased vitamin C intake has protective effect on pulmonary fxn, protects against protein oxidation in eye and associated with decreased risk for certain cancors[7].
This study was under taken to determine serum vitamin C level indifferent type of

* Department of Biochemistry. College of Medicine, University of Basrah,
** Department of Surgery, Basrah General Hospital, Basrah.

malignant cases and non- malignant subjects to used it as a marker for following these patients during and after treatment.

MATERIAL & METHODS

Between October 2000 till May 2001, a total of 184 patients whom were admitted to the surgical ward of Al Basrah General and Teaching Hospitals in Basrah city were included. Their ages range from 22-84 years old. They were 100 patients with different types of malignancy and 84 patients with out malignancy but admitted for other surgical reasons.

The malignant patients (42 males and 58 females) were allocated in to 4 different groups according to their type of malignancy. The first group are those with GIT cancer, they were 43 patients (21 males and 3 females),while the second group are 18 females with breast cancer however the third one are 18 patients (13males and 5 females) those with urinary system of malignancy and the least group are21 patients with other types of malignancy.

Eighty four person participated in this study as a control group 40 males and 44 females, their age ranged from 21-85, allocated as non- malignant patients but admitted to the surgical ward for hernia, fissure, fistula and piles.

From each subject a full information was obtained using questionnaire that include name, age, sex, occupation, as well as the following question about the medical history for any previous and recent illness and their type of treatment, family history for any malignant condition, social history for smoking and drinking habits and dietary question about the type and frequency per week, include fruits mainly citrus fruit, vegetables intake of vitamin supplement including dose and duration.

Physical and radiological examination was done including U/S and X- ray especially for those suspected case with malignancy, as well as biopsy was taken for histopathological examination. Laboratory investigation for hemoglobin, fasting blood sugar, blood urea, general urine examination and estimation of sedimentation rate were obtained from their case sheet.

Blood samples were collected from each patient after an average fast of 12 hrs, and they were tested for vitamin C by reduction of colored dye 2,6 di hydro phenol indo phenol from a blue to colorless, and the amount of de colorization was determined photometrically[8].

Statistical analysis was expressed as mean ± SD, t- test and chi square test were used to determine the relative importance of various variable. The comparison between groups was performed with one way analysis of variance (ANOVA). P. value at <0.05 was regarded as significant, and 0.001 as highly significant.

RESULTS

The basic clinical characteristics of subjects participated in this prospective study regarding to age, sex, cigarette smoking, family history, type of malignancy and nutritional habit are presented in **Table1**.

Effect of age

The **Table 2** shows the results of measurement of vitamin C in malignant and non – malignant subjects according to the age. Statistical comparison between the mean of serum vitamin C of all the patients showed highly statistically significant decrease ($p<0.01$) in the level of serum vitamin C in the total types of malignarcy mainly with GIT cancer at the age group less than 45 and at other age group 45-65 years old for urinary system malignancy. No significant finding was observed in those patients at age group above 65 years old.

Effect of sex

The mean ± SD of serum vitamin C in malignant and non- malignant subjects was grouped according to the sex and presented in **Table 3**. There was significant decrease ($p<0.05$) in serum level of vitamin C for both sexes with GIT cancer as compared with non – malignant subject.

Effect of smoking

The effect of smoking on vitamin C levels is presented as mean ± SD in **Table 4**. There was highly significant decrease ($p<0.01$) in serum level of vitamin C in non – smoker malignant patients presenting with GIT cancer. No significant finding was also observed among smoker malignant patients ($p<0.01$).

Effect of family history

The results of vitamin of vitamin C in malignant and non – malignant subjects were grouped according to their family history, presented in **Table 5.** There was highly significant decrease ($p<0.01$) in serum level of vitamin C in those patients presenting with – ve family history, mainly GIT cancer. No significant finding was observed in serum vitamin C levels in those patients presenting with +ve family history ($p<0.05$).

Nutritional habit

Fruit intake:

The comparison between the mean of vitamin C in all subjects according to their frequency of fruit intake / week showed highly statistically significant decrease ($p<0.01$) in serum level of vitamin C, in those consuming fruits less than 3/ week. This was observed mainly in patients with GIT cancer as well as there was a significant decrease ($p<0.05$) for patients with urinary system and other types of malignancy with frequency of fruits intake less than 3/ week **Table 6**.

Vegetable intake

The mean ± SD of serum vitamin C levels in malignant and non- malignant subjects with respect to their frequency of vegetable intakes per week is presented in **Table 7**. The evaluation of serum vitamin C level among those consuming vegetable less than 3/ week showed significant decrease ($p<0.05$) in serum vitamin C level mainly in patients with GIT cancer.

DISCUSSION

For decades vitamin C has maintained a position along with vitamin E and calcium as one of three most popular single-ingredient dietary supplements. As scientists continue to examine the role of free radicals in disease initiation and promotion, research substantiates this potent aniti oxidant's ability to treat cancer.[9]

The results of study concluded that serum level of vitamin C was highly significant decrease $p<0.01$ in all types of malignancy specifically in GIT cancer. This reduction was also observed in respect to age, sex and nutritional habit and demonstrated mainly among those consuming fruit and vegetables less than 3/wk.The same finding was observed in other studies that confirmed an inverse association between the frequency of fruit and vegetable and the risk of GIT cancer.[7,10]

The other possible cause for this finding could be attributed to highly intake of body prepared food in which bad storage, cooking and drying will lead to loss the most of nutritive values of ingested fruit and vegetables[11] . All these findings explained the protective effect of vitamin C against GIT cancer.

Four different possibilities of mechanism of action of ascorbic acid in cancer prevention could be attributed either to its low molecular weight antioxidant that plays a major role in free radical scavenging and protection against lipid peroxidation[7], or to its role in re constituting the active forms of vitamin E and spares other important antioxidant like pro vitamin A[12]. While, the third mechanism was the functioning of vitamin C in the immune system which[15], either enhanced the natural killer cell activity by stimulation the enzyme protein kinase C, that is involved in the mechanism of induction of natural killer cell, activity[15], or through the effect of ascorbate on complement C19 activity[14], (which is the recognition protein of classical complement pathway a system of blood proteins that constitute an important part of host defense against pathogens). The effect of ascorbate on C19 concentration is consistent with the known role of ascorbic in hydroxy proline biosynthesis, and C19 is a hydroxyl proline – containing protein with structural similarities to collagen. The fourth possible mechanism of vitamin C

was the inhibiting tumor spread and micro metastasis by enhancing the collagen synthesis and basement membrane integrity as well as its role in hyalurcnide inhibition[7].

All these findings explained the protective effect of vitamin C against GIT cancer. The anti carcinogenic mechanism of vitamin C was related to it's inhibitory effect against formation of N- nitro so compound which is a potent gastric carcinogen[15,16]. In addition high does of vitamin C will inhibit the growth of Helicobacter pylori {H. Pylori} infection in – vitro and in- vivo. It is well known that gastric cancer is one of the sequel of chronic H. Pylori infection[17].

Further more there was significant reduction in serum vitamin C in urinary system malignancy with regard to age (particularly at 45-65 years old) and nutritional habit mainly in those consuming fruit less than 3/ wk. this is in consistent with other studies and clearly reveals the inhibitory effect of vitamin C against metabolism of carcinogens and thus reducing the risk of lung, stomach, colon, rectum and bladder cancer. This finding was mainly presented among persons with more frequent ingestion of vegetables and fruits, which are important source of vitamin C and other nutrlents.[10,18,19]

In addition, there was a significant decrease in serum level of vitamin C in other type of malignancy. This significant observation was related to the dietary habit, where there was significant decrease in serum level of vitamin C among those consuming fruit <3/wk. Other workers, who found that diets high in vegetables and fruits probably, decrease the risk of laryngeal cancer[19].

Finally the ability of vitamin C to detoxifying carcinogens and block damage to DNA as well as its beneficial effects on immune function which may enhance tumor surveillance by the immune system. May add another role for vitamin Crate in the prevention of cancer[20].

From this study we conclude that, serum vitamin C showed a highly significant decrease in all malignant tumors with respect to age, sex and nutritional habit. This significant observation was demonstrated mainly in GIT cancer and among those consuming fruit and vegetables less than 3 times per week.

Table 1. Clinical characteristics in malignant and non-malignant subjects

Variables		Malignant N=100	%	Non-malignant N=84	%
Age/year	< 45 45 – 65 > 65	26 53 21	26% 53% 21%	41 35 8	48% 41% 9%
Sex	Female Male	59 41	59% 41%	44 40	52% 47%
Smoking habit	+ve -ve	36 64	36% 64%	16 68	19% 80.9%
Family history	+ve -ve	18 82	18% 82%	5 79	5.9% 94%

Fruit intake/ week	**< 3** **3 – 5** **> 5**	**51** **28** **21**	**51%** **28%** **21%**	**21** **29** **34**	**25%** **34.5%** **40%**
Vegetable Intake /week	**< 3** **3 – 5** **> 5**	**28** **38** **34**	**28%** **38%** **34%**	**11** **11** **62**	**13%** **13%** **73.8%**
Type of malignancy	**GIT** **Breast** **Urinary system** **Other**	**43** **18** **18** **21**	**43%** **18%** **18%** **21%**		

Table2. Serum level of vitamin C according to the age in malignant and non-malignant subjects

		Type of malignancy				
Age	**Non-malignant**	***GIT***	**Breast**	**Urinary system**	**Other type**	**Total**
< 45	**1.08±0.08 (40)**	**0.5±0.4** (9)**	**0.7±0.4 (8)**	**0.7±0.26 (3)**	**0.9±0.6 (3)**	**0.68±0.46** (23)**
45 – 65	**0.92±0.09 (32)**	**0.68±0.4 (20)**	**1.02±0.48 (7)**	**0.53±0.35* (7)**	**0.7±0.26 (13)**	**0.7±0.4 (47)**
> 65	**0.83±0.2 (7)**	**0.59±0.3 (7)**	**0.4±0 (1)**	**1.06±0.7 (5)**	**0.65±0.2 (4)**	**0.73±0.5 (17)**
Total	**0.96±0.48 (79)**	**0.6±0.4 (36)**	**0.86±0.4 (16)**	**0.73±0.55 (15)**	**0.73±0.32 (20)**	**0.7±0.4** (87)**

Values were expressed as mean ± SD, (n)

Types malignant patients vs. non-malignant subjects P*<0.05, P<0.01**

All results were expressed as mg/dl.

Table3. Serum level of vitamin C according to sex in malignant and non- malignant subjects

		Type of malignancy				
Sex	**Non-malignant**	***GIT***	**Breast**	**Urinary system**	**Other type**	**Total**
Female	**0.98±0.49 (40)**	**0.65±0.38* (18)**	**0.86±0.45 (16)**	**0.41±0.3 (4)**	**0.7±0.28 (12)**	**0.7±0.39* (50)**
Male	**0.9±0.48 (39)**	**0.5±0.4* (18)**		**0.85±0.6 (11)**	**0.77±0.39 (8)**	**0.69±0.5 (37)**

Values were expressed as mean ± SD, (n)

Types malignant patients vs. non-malignant subjects P*<0.05

All results were expressed as mg/dl.

Table 4. Serum level of vitamin C according to smoking history in malignant and non-malignant subjects

		Type of malignancy				
Smoking habit	**Non-malignant**	***GIT***	**Breast**	**Urinary system**	**Other type**	**Total**
+ve	**0.82±0.4 (16)**	**0.6±0.5 (12)**	**1.6±0 (1)**	**0.72±0.6 (7)**	**0.8±0.4 (10)**	**0.76±0.5 (30)**
-ve	**1.02±0.5 (63)**	**0.6±0.4** (24)**	**0.8±0.4 (15)**	**0.64±0.55 (8)**	**0.65±0.2 (10)**	**0.68±0.39****

Values were expressed as mean ± SD, (n)

Types malignant patients vs. non-malignant subjects P<0.01**

All results were expressed as mg/dl.

Table 5. Serum level of vitamin C according to family history in malignant and non-malignant subjects

		Types of malignancy				
Family history	**Non-malignant**	***GIT***	**Breast**	**Urinary system**	**Other type**	**Total**
+ve	**0.96±0.62 (4)**	**0.87±0.6 (4)**	**0.78±0.4 (8)**	-	**0.97±0.5 (4)**	**0.85±0.47 (16)**
-ve	**0.98±0.62 (75)**	**0.58±0.4** (32)**	**0.9±0.5 (8)**	**0.73±0.5 (15)**	**0.66±0.2 (16)**	**0.67±0.43** (71)**

Values were expressed as mean ± SD, (n)

Types malignant patients vs. non-malignant subjects P<0.01**

All results were expressed as mg/dl.

Table 6. The effect of fruit intake per week on serum level of vitamin C in malignant and non-malignant subjects

		Types of malignancy				
Fruit intake/wk	**Non-malignant**	***GIT***	**Breast**	**Urinary system**	**Other type**	**Total**
< 3	**0.89±0.4 (21)**	**0.44±0.4*** (21)**	**0.62±0.17 (7)**	**0.48±0.3* (9)**	**0.5±0.13* (8)**	**0.48±0.23*** (45)**
3 – 5	**0.81±0.4 (29)**	**0.8±0.3 (11)**	**0.97±0.5 (8)**	**1.03±0.6 (3)**	**0.7±0.1 (3)**	**0.88±0.4 (25)**
> 5	**1.17±0.55 (29)**	**0.9±0.5 (4)**	**1.6±0 (1)**	**1.3±0.62 (3)**	**0.94±0.36 (9)**	**1.03±0.45 (17)**

Values were expressed as mean ± SD, (n)

Types malignant patients vs. non-malignant subjects P*<0.05, P*<0.001**

All results were expressed as mg/dl.

Table 7. The effect of vegetables intake per week on serum level of vitamin C in malignant and non-malignant subjects

		Types of malignant				
Vegetable intake/wk	**Non-malignant**	**GIT**	**Breast**	**Urinary system**	**Other type**	**Total**
< 3	**0.96±0.54 (11)**	**0.33±0.2* (10)**	**0.75±0.46 (7)**	**0.47±0.3 (4)**	**0.47±0.17 (4)**	**0.49±0.3* (25)**
3 – 5	**0.99±0.44 (11)**	**0.65±0.42 (16)**	**0.74±0.26 (7)**	**0.72±0.5 (7)**	**0.7±0.14 (2)**	**0.7±0.3 (32)**
> 5	**0.96±0.5 (57)**	**0.83±0.5 (10)**	**1.65±0.07 (2)**	**0.98±0.8 (4)**	**0.8±0.34 (14)**	**0.89±0.5 (30)**

Values were expressed as mean ± SD, (n)

Types malignant patients vs. non-malignant subjects P*<0.05

REFERENCES

1. Gut brie HA., Picciano MF., Human Nutrition. New York. Mosby year book, INC. 1995.21- 24.
2. Word low GM., Insel PM. Perspectives in nutrition. Philadelphia : Mosby, 1996.
3. Mayes PA. structure and function of the water soluble vitamins. In : Murray RK., Granner PK., Mayes PA. Harper's Biochemistry 24th ed., California. Appleton and Lange company. 1996; 599- 613.
4. Pryor WA. The antioxidant nutrients and disease prevention what do we know and what do we need to find out? Am .J. Clin. Nutr. 1991; 53: 391-393.
5. Car Ac., Frei B. Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. Am , J. Clin. Nutr. 1999; 69: 1070- 1086.
6. Meydani M., Martin A., Gong J., etal. B- carotene supplementation in creases antioxidant capacity of plasma in older women. Nutrition. 1994; 24: 2397- 2404.
7. Block G. Vitamin C and cancer prevention. The epidemiologic evidence. Am. J. Clin . Nutr. 1991, 53: 270- 272.
8. Toro G., Ackermann PG. Practical clinical chemistry.1st . ed. Boston: Little, Brown and Company, 1975; 634- 636.
9. Anderson R. Assessment of the roles of vitamin C, vitamin E and B carotene in the modulation of oxidant stress mediated by cigarette smoke- activated phagocyte Am J. Clin. Nutr 1991; 53: 358- 361.
10. Lee IM. Antioxidant vitamins in the prevention of cancer. Proc- Assoc. Am. Physicians. 1999; 111 (1): 10-15.
11. Anderson L. Dibble MV., Turkkipr., etal. Nutrition in health and diease.17th ed. Philadelphia :J. B. Lippincott Company, 1982.
12. Sealy WM., Gatlin DM. Dietary vitamin C and E interact to influence growth and tissue composition of Juvenile Hybrid Striped Bass (moron chrysops female symbol xm. Saxatitis male symbol) but have limited effects on Immune Responses. J. Nutr. 2002;132:748-755.
13. Houser G., Vojdani A. Enhancement of natural killer cell activity and T and B cell function by buffered vitamin C in patients exposed to toxic chemicals. The role of protein kinase – C. Immuno pharmacol. Immuno toxicol. 1997; 19 (3), 291- 312.

14. Haskell BE., Johnston CS., Complement component C19 activity and ascorbic acid nutritive in guinea pigs. Am. J . Clin. Nutr. 1991; 5416 suppl:1228- 1230.
15. Yang CS. Vitamin nutrition and gastro esophageal cancer . J. Nutr. 2000; 130 (25 supple) 338- 339.
16. Tannenbaum SR., Wishnok JS, Leaf CD. Inhibition of nitrosamine formation by ascorbic acid. Am .J. Clin Nutr 1991; 53:247- 250.
17. Zhang HM., Wakisaka N., Macda O., etal. Vitamin C inhibit the growth of a bacterial risk factor for Gastric Carcinoma. Helicobacter pylori. Cancer 1997; 80: 1896- 1903.
18. Choi MA, Kim BS, YuR. Serum anti oxidative vitamins levels and lipid peroxidation in gastric carcinoma patients. Cancer. Lett . 1999., 136 (1): 89-93.
19. Graham S., Mettle C., Marshal J, etal. Diet in epidemiology of cancer of larynx. Am. J. epidemiology, 1981; 113 (6) 675- 680.
20. Hughes DA. Effect of dietary antioxidants on the Immuno Function of middle aged adult., Proc. Nutr. Soc.1999; 58 (1): 79- 84.

مستوى فيتامين ج عند مرضى السرطان

أ.د. لمياء مصطفى النعمه*، أ.د. جمال احمد عبد الباري*، م م.د. زينب احمد المناصير*،
ألاستشاري د. هاشم صادق الخياط **.

الخلاصة:

نظمت الدراسة الحالية لقياس مستويات فيتامين ج لدى مرضى السرطان واختير لهذا الغرض ١٨٤ مريضا". منة منهم مصابين بأنواع مختلفة من السرطانات .شكلت نسبه ٤٣% مرضى مصابين بسرطان الجهاز الهظمي، بينما شكلت نسبة سرطان الثدي وسرطان المجاري البولية كل على حده ما يساوي ١٨%، اما مرضى المصابين بالسرطانات الاخرى فكانت نسبتهم ٢١% وقورنت النتائج مع ٨٤ مريضا" من غير المصابين بالسرطان كمجموعة ضابطة.

أظهرت نتائج الدراسة نقصا" معنويا" كبيرا" ($p<0.01$) بمستوى فيتامين ج عند جميع المرضى وللأنواع الاربعة المختلفة من السرطانات وخصوصا" عند مرضى سرطان الجهاز الهضمي ضمن اطار العمر (وخاصة" للفئة العمرية اقل من ٤٥ سنه وللذين تتراوح اعمارهم بين ٤٥-٦٥سنه، وكذلك الجنس والعادات الغذائية حيث ظهر ذلك مليا" للذين يتناولون الفواكه والخضروات وبمعدل اقل من ٣ مرات في الاسبوع).

ولهذا فقد توصلنا لخلاصه توجز بان قياس مستوى فيتامين ج يعتبر من العلامات البايوكيميائية المهمه لمتابعة هؤلاء المرضى خلال فترة المرض وبعد العلاج .

مفتاح الكلمات : فيتامين ج، انواع مختلفة من مرضى السرطان ،مرضى من غير المصابين بالسرطان.

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* فرع الكيمياء الحياتية، كلية الطب – جامعة البصرة .
** مستشفى البصرة العام ، قسم الجراحة- دائرة صحة البصرة.