CORRELATION OF SERUM RETINOL AND ITS RELATION WITH LIPID PROFILE IN INDIAN CANCER PATIENTS

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ABSTRACT

The present study was undertaken to investigate the relation of retinol with lipid profile of patients with cancers of breast, stomach, oesophagus, colon, gallbladder, pancreas, lung and cervix. Serum retinol was assayed in 120 patients and 40 healthy normal control by reverse phase HPLC using CLC –ODS C-18 columns and retinyl acetate as an internal standard.

Significant decrease in serum cholesterol and LDL was observed in patients with cancers of esophagus, colon, stomach, pancreas and gallbladder respectively.

Retinol was reduced in all forms of cancers but pronounced decrease was observed in oesophagus, gallbladder, pancreas, stomach and colon. Serum Retinol in all patients was directly correlated with total cholesterol and LDL. These findings suggest that therapeutic modalities of this vitamin could be planned for these patients, as vitamin A is known to act as an antioxidant for prevention of certain cancers.

KEY WORDS

Retinol, lipid profile, cancer patients, antioxidant

INTRODUCTION

Vitamin A (retinol) has long been recognized, as an indispensable nutrient factor required for maintenance of vision as well as promotion of general growth and differentiation. (1) Vitamin A and its metabolite retinoic acid affect multiple processes in the body such as, cellular proliferation induction of cell differentiation, tissue remodeling and tissue integrity. (2-3) Retinoic acid has also been reported to regulate transcription of variety of genes. (3). Epidemiological and case control studies have indicated that individuals with lower intake of this vitamin are at higher risk of developing certain cancers (4-7). These studies also implicate retinol and other carotenoids as protective agents against cancers. (6) Carotenoids are important antioxidants and may protect against carcinogenesis because of their antioxidant function .eg β carotene and lycopene or because of their provitamin A activity (8). By counteracting oxidative processes that could

damage macromolecules such as proteins and DNA that could interfere with the normal functioning of the cells, carotenoids may contribute to the prevention of cancer and other degenerative disease(9).

Naturally occurring antioxidants such as vitamin A, E, β carotene and vitamin C can inhibit the oxidative modification of low density lipoproteins. As vitamin A is fat soluble, it is transported in LDL particles and in the circulating levels in the body and is correlated with serum cholesterol (10).

Schatzkin *et al* (11) have reported good association between low cholesterol and cancers of mouth, oesophagus pancreas and cervix (12-15), some of which are also common in India.

Deficiency of vitamin A is widespread in Indian population.(16-17) Also the nutrient status of our population significantly differs from others particularly the western population that offers most of the data available in the literature. Due to these facts the present study was carried out to determine vitamin A status and its relationship with lipid profile in the patients seen at Lucknow having cancers of breast, oesophagus, gallbladder, colon, pancreas, lung, cervix and stomach.

MATERIALS AND METHODS

The study included 160 individuals consisting of:

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- 1) Apparently, normal healthy controls (n=40) There were 25 males and 15 females age ranging between 20-45 years (mean age 35)
- 2) One hundred and twenty cancer patients 15 each, of breast, oesophagus, stomach, colon, pancreas, lung, gallbladder and cervix were selected for the study. There were 40 males and 80 females. The patients were clinically diagnosed at our Institute. The patients selected for the study were not consuming drugs at the time of sampling.

Blood samples required for various laboratory procedures were collected from the patients and healthy controls after overnight fasting. Standard biochemical procedures using Bayer's reagents were used for assaying serum cholesterol, triglyceride and HDL on Technicon autoanalyzer RA-1000 and RA-500. VLDL and LDL values were calculated according to Friedwald *et al* (18)

HPLC Analysis of Vitamin A (Retinol)

Retinol was assayed in the serum of patients and normal healthy controls by HPLC (Shimadzu LC-9A) as described earlier. (19) Briefly, chromatography was carried out on a 6mm X 15 cm CLC-ODS reverse phase column (Shimpack, Shimadzu Japan) using a 4mm X1cm CLC-OCS-4 guard column. Inert all trans retinyl acetate (Sigma) was used as an internal standard. All chemicals used were of HPLC grade. The results have been expressed as mean $\pm$ SE. Student 't' test was used to compare means, and correlation coefficients were determined by linear regression analysis (20). Differences in mean values between groups of patients with that of control was considered statistically significant at the level $p < 0.05$.

RESULTS

Vitamin A status in cancer: The mean serum retinol level in normal healthy controls was 7.05 ± 0.62 ug/dl. The vitamin levels decreased in all cancer patients (Fig 1). However, the decrease was nominal in breast,

FIGURE 1

lung and cervix but substantial in pancreas, oesophagus, colon and stomach cancer patients.

Lipid profile: Although total cholesterol and LDL decreased in all forms of cancer significant changes were observed in oesophagus, colon, stomach, pancreas and gall bladder cancer (Table 1). The HDL levels reflected minimal changes and were within the normal range. However, the concentration of

triglyceride was two fold higher in cancer patients as compared to control individuals.

Relationship of Vitamin A with lipid profile: In order to study the relation between vitamin A and lipid profile, correlation coefficient (r) were calculated. A significant correlation was observed between vitamin A levels with both cholesterol and LDL ($r > 0.68$ at $p < 0.05$; Table 2).

Table 1 : Lipid profile in cancer patients

Sl.No	Subject	Total CHOL(mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL(mg/dl)	TRIGLY(mg/dl)
1.	Controls (n=40)	197.75±8.81	52.06±2.29	120.06±7.93	26.74±2.42	114.33±7.82
2.	Lung	174.20±10.58	44.26±2.98	102.64±10.11	34.83±2.37	175.80±12.74 *
3.	Breast	170.14±9.43	42.26±2.49	85.20±13.26	42.03±5.73	230.60±23.49 *
4.	Cervix	164.73±10.62	40.73±3.49	90.58±10.46	37.18±4.63	211.40±36.93 *
5.	Gall Bladder	144.92±10.46 *	37.73±2.72	63.96±9.06 *	46.84±2.66	255.26±22.60 *
6.	Pancreas	138.25±11.77 *	45.33±2.20	61.85±7.72 *	45.53±4.22	227.66±21.14 *
7.	Stomach	136.53±8.80 *	37.80±2.49	54.43±7.11 *	40.44±3.13	202.20±15.66 *
8.	Colon	129.92±18.26 *	38.60±2.55	63.53±5.99 *	34.12±2.78	185.66±13.88 *
9.	Oesophagus	128.26±5.71 *	39.26±4.13	54.70±6.59 *	41.86±4.81	289.46±20.05 *

* p< .001

Values are Mean ±SE (n=15)

Table 2 : Correlation Coefficient (r) between Serum Vitamin A Levels and Lipid Profile in Cancer Patients

SL.NO	PARAMETERS	(r) VALUE
1.	Total Cholesterol	0.93*
2.	HDL	0.64
3.	LDL	0.87*
4.	VLDL	-0.37
5.	Triglyceride	-0.31

* : Significant correlation coefficient at p< 0.05 (>0.68)

DISCUSSION

Cancer represents one of the major contemporary public health problems and is responsible for adult deaths. The cause of most common cancers is a combination of genetic, environmental and behavioral factors. Cancer is greatly influenced by diet and is closely linked with dietary factors. There are variety of ways in which effect of diet are exerted, such as changes in lipid profiles and antioxidant metabolism (21)

Association of low serum cholesterol with various cancers is well known (2,6) Fat soluble vitamin E, A and other carotenoids are transported in LDL particles

(6-8) Low cholesterol levels, therefore, could mean low levels of these vitamins as observed in our studies. (Table1, Fig.1) shows cancer patients of stomach, colon, pancreas and esophagus with significant changes in cholesterol and vitamin A levels. It may be therefore, that the observed relationship between low serum cholesterol and cancer could be in fact, due to low levels of circulating vitamin A and not due to any direct effect of serum cholesterol. As evident from Fig 1 the most affected cancers were of upper and lower digestive tract. Lower levels of vitamin A in patients with cancers of stomach, oesophagus, colon and pancreas also suggest LDL oxidation resulting in low levels of LDL and high triglyceride levels. In western countries, cholesterol values are about 20% higher than in Asian population (14) It is also established that low cholesterol levels <160mg/dl are associated with risk of cancer, respiratory and liver diseases.

Vitamin A deficiency in cancer is well established (21). Some of the effect is mediated by its role as antioxidant (21-22). Retinol, β-carotene and lycopene as well as other carotenoids have antioxidant properties. The antioxidant capability however, is variable depending on the in-vitro system used. The antioxidant activity of these compounds can shift into pro-oxidant effect, depending on oxygen tension or carotenoid concentration. Mixtures of carotenoids alone or in association with other antioxidants can increase their activity against lipid peroxidation (22) In recent years; retinoids have been shown to modify gene expression through the mediation of intracellular binding proteins and nuclear receptors. (3)

In conclusion, low levels of vitamin A in cancer patients result from reduced cholesterol and LDL. This in turn leads to cascade of events resulting in tumor genesis.

ACKNOWLEDGEMENTS

The HPLC equipment provided by JICA (Japanese Agency for International Development) is greatly acknowledged. The technical help rendered by Mr Selavraj is appreciated.

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