VITAMIN ‘A’ IN CANCER

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SUMMARY

Fifty biopsy proven cancer cases were studied after excluding liver and kidney disorders for changes in lipid metabolism with special reference to fasting retinol and B-carotene. Significant changes in serum B-carotene and vitamin A were observed between controls and different groups of male and female cases, in adenocarcinoma changes were quite marked. Serum retinol was 25.37 ug/dl and b-carotene was 37.96 ug/dl as compared with control 39.9 ug/dl and 54.3 ug/dl respectively.

INTRODUCTION

In 1920, it was discovered that deficiency of vitamin A leads to metaplastic changes in the epithelia of respiratory, gastrointestinal and genitourinary tracts and hyperkeratosis of the skin. These metaplasia are considered to be the first step in transformation process from normal to neoplastic tissue. Vitamin A cannot be synthesized in body and must therefore be taken with food.

A major physiological role of Vitamin A is to control cell differentiation. Since loss of cell differentiation is a basic feature of cancer, there is ample reason to suspect that vitamin A may be related to cancer incidence. Although the majority of the studies that have examined the relation between carotene intake cancer have found a protective effect of carotene, this observation has not been entirely consistent. A protective effect against lung cancer is currently the most strongly supported relation.1,2,34

Retinol levels of subjects in whom cancer subsequently developed were measured in serum samples that had been collected and frozen before diagnosis were compared with retinol levels of subjects without cancer. Over all cancer rates were found to be highest amongst persons with the lowest levels of serum retinol.5,6

Objective: To elucidate facts about altered vitamin A metabolism in cancer patients and explain the current hypothesis concerning its low concentrations in different types of malignancies.
MATERIAL AND METHODS

The present study included 50 pretreatment biopsy diagnosed cases of different types of malignancies admitted in JPMC, Karachi. Patients were classified into the following groups:

1. Epithelial tumors 38
   a. Carcinoma 28
   b. Adenocarcinoma 10
2. Non epithelial tumors 12
   a. Sarcoma 5
   b. Leukemia 6
c. Astrocytoma 1

Only those patients and controls were included whose following tests were within normal limits. Liver Function Test, serum glucose, serum creatinine and prothrombin time. The determinations carried out after an overnight fast were serum retinol and serum carotene.

RESULTS

Highly significant changes in serum B-carotene and vitamin A were observed between controls and different groups of male and female cases, in adenocarcinoma changes were quite marked.

Retinol levels decreased significantly in non-epithelial and highly significant in epithelial cancers. (Table 1). Individual tumors such as bladder, colon, tongue and cheek showed significant decreases where as changes in case of lung and maxilla were marked. In cases of larynx, esophagus, and leukemia serum retinol levels decreases were highly significant. Significant changes in B-carotene levels were observed in bladder and marked changes in leukemia, larynx and cheek and highly significant in lung, larynx and maxilla. (Table 2) Serum retinol was 25.37 ug/dl and b-carotene was 37.96 ug/dl as compared with control 39.9 ug/dl and 54.3 ug/dl respectively.

Mean age of the control group was 49.4 years and that of the patients was 48.73 years. No significant difference was observed between average age of control and cases.. (table -1). Serum AST was significantly raised in individual groups of studied cases but the level was within normal limits. Serum ALT was not significantly changed in cases as compared to controls. Similarly GGT levels in serum was also within normal limits in controls as well as in cases, no significant changes observed. ALP levels in serum of patients with epithelial carcinoma was significantly raised (P<0.05) as com-
COMPARISON BETWEEN CONTROLS AND DIFFERENT GROUPS OF MALE AND FEMALE CASES

The values are expressed as mean ± s.e.m. Number of cases are given in parenthesis.

<table>
<thead>
<tr>
<th>Groups</th>
<th>B-CAR (ug/dl)</th>
</tr>
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<tbody>
<tr>
<td>Controls (15)</td>
<td>54.30 ± 2.64</td>
</tr>
<tr>
<td>Epithelial Tumours</td>
<td></td>
</tr>
<tr>
<td>LUNG (6)</td>
<td>32.7 ± 4.78***</td>
</tr>
<tr>
<td>BLADDER (5)</td>
<td>33.42 ± 6.21*</td>
</tr>
<tr>
<td>LARYNX (4)</td>
<td>39.22 ± 3.52***</td>
</tr>
<tr>
<td>OESOPHAGUS (4)</td>
<td>43.4 ± 5.36</td>
</tr>
<tr>
<td>TONGUE &amp; CHEEK (6)</td>
<td>38.66 ± 3.15**</td>
</tr>
<tr>
<td>BREAST (4)</td>
<td>45.77 ± 4.35</td>
</tr>
<tr>
<td>COLON (2)</td>
<td>35.3 ± 16.9</td>
</tr>
<tr>
<td>Non Epithelial Tumours</td>
<td></td>
</tr>
<tr>
<td>MAXILLA (3)</td>
<td>37.7 ± 1.72***</td>
</tr>
<tr>
<td>LEUKAEMIA (4)</td>
<td>37 ± 4.71**</td>
</tr>
</tbody>
</table>

* P<0.05 values are significant as compared to Control Subjects.
** P<0.01 values are markedly significant as compared to Control Subjects.
*** P<0.001 values are highly significant as compared to Control Subjects.

TABLE 2

pared to controls. ALP was also high in patients with adenocarcinoma. Non-epithelial tumors showed no significant change, however, the levels were increased.

DISCUSSION

Vitamin A, a polyisoprenoid compound exists as long chain fatty acid ester of retinol in animals and as B-carotene in vegetables.7 Protein synthesis by membrane bound polyribosomes of intestinal mucosa is depressed under conditions of vitamin A deficiency.8 Retinoic acid not only stimulates differentiation of pluripotent embryonal cell lines but also induces differentiation of so-called nullipotent embryonal cell lines.9 It also enhances binding of epidermal growth factor (EGF) to various fibroblastic and embryonic cell lines and increases the EGF receptor sites.10

Inhibition of tumour development by retinol is possibly mediated by cRBP (cellular retinol binding protein) and cRABP (cellular Retinoic acid binding protein), which are significantly higher in tumor tissues of epidermoid cancer of oral cavity,11 breast, lung, cervix, endometrium and ovary.12 In human tumour cloning system, the retinoid analogue can occasionally decrease the number of tumor colony forming units (T-CFU)13 Melanoma14 Neuroblastoma cells.15 In MCF-7 mammary cancer cells in culture, Retinoic acid revealed maximum activity in inhibiting cell proliferation and thymidine synthesis suggesting suppression of DNA synthesis as primary cause of restriction of cell growth by retinoids.16 Polyoma virus replication inhibition was mediated by a newly synthesized protein induced by vitamin A, which blocked expression of viral T-antigen,17 it also inhibits collagenases thereby localizing tumor cells within a capsule.18

Low risk of gastric19 and lung20 cancer was associated with ingesting uncooked vegetables. Significantly low serum vitamin A levels were observed in patients with esophageal21 stomach,22 prostate,23 and colorectal cancers24.

Topical application of Trans-retinoic acid has been reported to achieve regressions in most patients with precancerous actinic keratosis or basal cell carcinomas.25,26 Prolonged use of vitamin A in pharmacological dosage causes important side effects, which have greatly limited its clinical development, these include fatigue, irritability, anorexia, nausea, headaches, hair loss, pains and hepatomegaly. Many synthetic retinoids have been investigated with a view to overcoming the side effects and have been used in dermatology and oncology.

Retinoids are most effective when administered shortly after the carcinogenic insult. However, even when retinoid treatment is delayed, the compounds are still effective cancer chemopreventive agents for the mammary gland and urinary bladder.27
REFERENCES


