

# Changes of serum transferrin and ceruloplasmin after radiation therapy in women with cervical or uterine carcinoma

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*Summary:* Serum transferrin and ceruloplasmin were measured in 27 healthy women as well as in 21 women who received fractionated radiation therapy (RT) after undergoing surgery for cervical or uterine carcinoma. Although no significant difference in the mean values of transferrin was found between the healthy women and the patients before the initiation of RT, a significantly lower concentration of transferrin after the end of RT ( $p < 0.001$ ) was observed in comparison to that of controls and of patients before RT. On the contrary, a significantly higher serum concentration of ceruloplasmin was found in patients before and after RT compared to that in healthy women ( $p < 0.001$ ). The observed increase of ceruloplasmin after RT was not found to be significantly different from the mean value before RT.

In conclusion serum transferrin is reduced by RT, while ceruloplasmin which is higher in patients before RT shows a tendency for increase following RT.

*Key words:* Transferrin; Ceruloplasmin; Cervical-uterine neoplasia.

## INTRODUCTION

Serum ceruloplasmin and transferrin, apart from their traditional role in iron metabolism, also behave as acute phase reacting proteins (<sup>1, 2</sup>).

The concentration of ceruloplasmin increased during inflammatory disease as well as in patients with malignant tumors (<sup>1</sup>).

The serum concentration of transferrin is also an indicator of malnutrition, and acts as a growth and mitogenic factor, while, in the presence of inflammation is reduced (<sup>2, 3</sup>).

It is well known that radiation therapy causes inflammatory reactions and temporary deterioration of the general condition of the patients with malignancy (<sup>4, 5</sup>).

The purpose of this study was to investigate the serum changes of ceruloplasmin and transferrin in women with uterine or cervical neoplasia, who received radiation therapy after surgical remission of the carcinoma.

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## MATERIALS AND METHODS

A total of 48 women was used for this study. Twenty-one women aged 35 to 75 years (median 55 years) had undergone surgery for uterine or cervical carcinoma before receiving fractionated irradiation of 28 to 60 Gy in relatively large body areas by a cobalt 60 unit or a 6 Mev linear accelerator. All patients were in good general condition with normal liver function and blood count.

The control group consisted of 27 healthy women between 30 to 70 years of age (median 49 years). Blood samples were taken from the control group, as well as from patients before and after the completion of radiation therapy, and serum concentration of ceruloplasmin and transferrin were measured.

Serum concentration of transferrin was determined by using the Turbitime system (Behring Turbi-Time System). The normal levels for transferrin range between 230-430 mg/100 ml. Serum concentration of ceruloplasmin was determined by using radial immunodiffusion kits from "Binding-site Institute of Research and Development Birmingham". The normal levels were  $280 \pm 50$  mg/l.

For the statistical analysis of the results, unpaired student's *t* test was used.

## RESULTS

Serum levels of transferrin in all subjects are illustrated in Figure 1. There was no significant difference in the mean value of transferrin between the control population ( $263.35 \pm 38.78$  mg/100 ml) and the patients before the initiation of radiotherapy ( $299.52 \pm 89.27$  mg/100 ml). A significant reduction of mean serum value of transferrin ( $231.23 \pm 40.46$  mg/100 ml) was found after the end of radiation therapy ( $p < 0.001$ ), from controls and from patients before RT.

The levels of ceruloplasmin in all subjects are illustrated in Figure 2. Although no statistically significant difference in mean value of ceruloplasmin was found between the patients before ( $374.28 \pm 16.37$  mg/l) and after the radiotherapy ( $425.27 \pm 155.27$  mg/l), the mean level of ceruloplasmin ( $253.22 \pm 64.5$  mg/l) was

significantly lower in healthy women ( $p < 0.001$ ) as compared to that of patients before and after RT.

## DISCUSSION

Neoplastic diseases can reduce the concentration of blood serum transferrin. This reduction seems to be related to the stage of cancer and there is evidence that patients with low levels of serum transferrin have poor prognosis (<sup>2, 3, 6</sup>).

According to our results, women operated for cervical or uterine cancer and re-

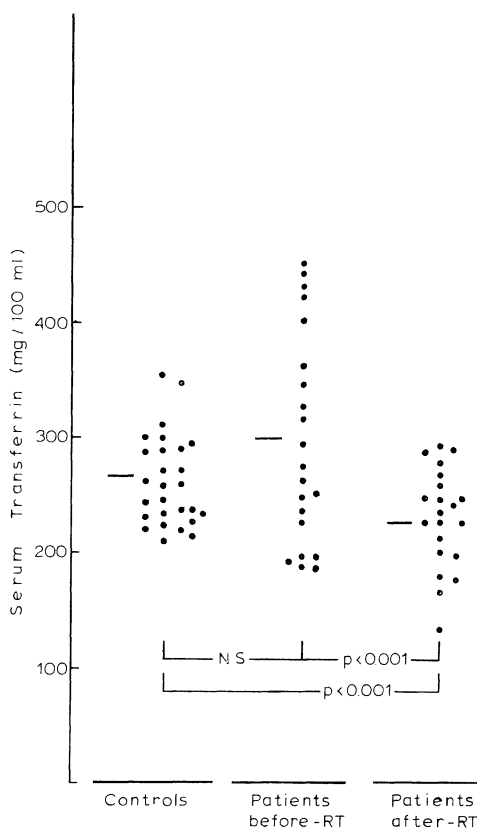


Fig. 1. — Serum transferrin values of controls and patients [before-after radiation therapy (RT)]. Mean value (—) and statistical significance are illustrated.

ceiving radiation therapy showed a significant reduction in serum transferrin after the end of the therapy.

The cause of the reduction of transferrin by radiation is not known exactly and some explanations could be suggested. Radiation therapy may not affect liver function, as it was excluded from the irradiation field, but may cause functional impairment as well as a reduction in the number of circulating lymphocytes which have the ability to compose transferrin (<sup>2, 7</sup>). Another explanation of low transferrin levels may be the result of systemic side-effects and local reactions due to radiation therapy. The systemic side-effects of radiation therapy are anorexia, vomiting and lassitude, whereas the local reactions are due to inflammatory damage of the tissues (<sup>4, 5</sup>). The inflammation of the tissues is usually accompanied by an increased number of macrophages which may cause degradation of the circulating transferrin (<sup>2, 8</sup>).

Our data also showed an increase of the mean serum value of ceruloplasmin before, and a further increase after radiotherapy in patients with malignant disease compared to that found in control subjects.

It is evidenced that a positive relationship between high levels of ceruloplasmin and the occurrence of cancer might exist. Some reports suggest that serum copper might increase before the diagnosis of cancer, whereas others have shown that ceruloplasmin levels are elevated in patients with advanced cancer (<sup>9</sup>). It has also been postulated that the increase of ceruloplasmin may have a protective effect against cancer because of its antioxidant properties.

According to our results the serum concentration of ceruloplasmin was high despite the remission of the disease by operation, and was increased further by radiation therapy.

Radiation causes inflammatory tissue damage, and anti-inflammatory drugs are usually used to attenuate it (<sup>1, 5, 9, 10</sup>). Because ceruloplasmin is an acute phase reacting protein, its increase during radiation therapy may be a response to inflammatory tissue damage caused by radiation.

Serum transferrin is essential for growth and differentiation of cells, while ceruloplasmin by its antioxidant effect may prove protective not only against cancer but also against the inflammation caused by radiation therapy (<sup>2, 10, 11</sup>). Thus measurement of transferrin concentration,

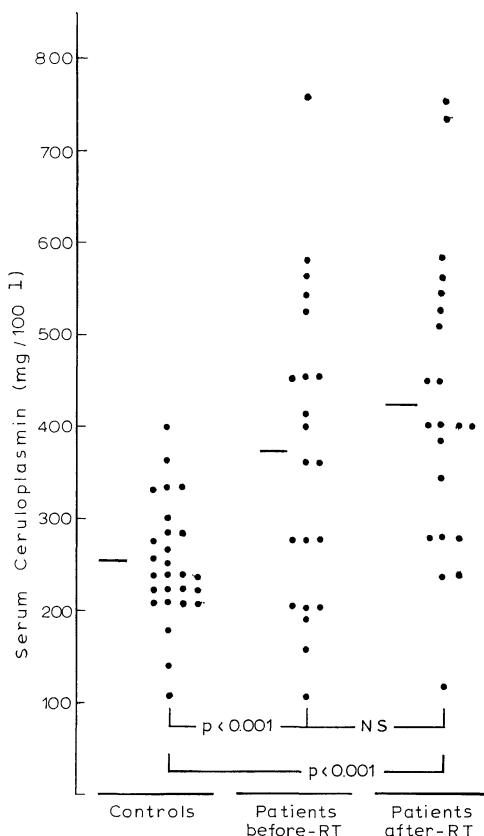


Fig. 2. — Serum ceruloplasmin values of controls and patients. [Before-after radiation therapy (RT)]. Mean value (—) and statistical significance are illustrated.

especially that of ceruloplasmin, may be an index of tissue protection against inflammatory damage due to radiation therapy.

However, further studies are needed to establish the relationship of serum concentration of transferrin and ceruloplasmin to radiation therapy and to the prognosis of the disease.

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