SERUM COPPER LEVEL DIAGNOSTIC AND PROGNOSTIC VALUE IN FEMALE GENITAL MALIGNANCY

By

KUMKUM RANI SRIVASTAVA, ROCHISMATI PANDEY,
ANIL AGARWAL AND URMILA GUPTA

SUMMARY

The present study has been done to evaluate the significance of serum copper levels in cases of malignancies of female genital tract. It shows that with the advancement of malignancy serum copper level rises significantly and with successful treatment the level tends to decrease to normal levels. Increase in serum copper level during follow-up period indicates the recurrence of disease.

Introduction

The present study is an attempt, to estimate the serum copper level in various malignancies of female genital tract and probable role in prognosis of disease.

Material and Methods

One hundred cases were studied at Nehru Hospital, Gorakhpur from September 1984 to August 1985. Out of which 30 were healthy control, 20 patients suffering from benign diseases of female genital tract which served as comparison and 50 patients were those who were suffering from malignant lesions of female genital tract.

A detailed history was taken and thorough clinical and systemic examination was made to confirm the clinical staging of malignancy. Routine and special investigations were done in all cases. The clinical, histopathological and serological (serum copper level) findings were correlated.

The clinical staging of malignancy was done according to F.I.G.O. classification.

The patients, in the study, received the treatment in one of the following form viz. Surgery, Chemotherapy and combined therapy (includes surgery followed by chemotherapy or radiotherapy). Serum copper levels were estimated before treatment, during treatment and after treatment i.e. either at the time of discharge or a month after the treatment.

Serum copper level was estimated by Diethyl dithiocarbamate method (Eden and Green, 1940; Ventura and King, 1951).

Observations

The maximum cases of malignancy were between the age group of 41 to 50 years (42%) and in women having 6 or more children (32%). None of the uniparous case was having malignant lesions.

From: Department of Obstetrics and Gynaecology, B.R.D. Medical College, Gorakhpur.
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Table I shows the serum copper level of control, benign diseases and various malignant lesions of female genital tract, the mean serum copper level in control group was 109.86 ± 17.23 microgram/100 ml and 134.7 ± 59 microgram/100 ml in benign diseases. Mean serum copper level were certainly on higher side in malignant conditions of female genital tract.

As shown in Table II, the serum copper level was found to be higher in cases of advanced malignancy of cervix ,stage III and IV) as compared to the early malignancy group (stage I and II). In other words serum copper level was proportional to the extent of tissue involvement and in most of the cases some fall in serum copper level was found appropriate therapy except few cases of terminal stages whose serum copper level instead of declining kept on rising even after therapy (Table III).

All cases except choriocarcinoma of uterus showed favourable response with the treatment and resulted into lowering of serum copper level from pre-treatment levels. Both the cases of choriocarcinoma of uterus, did not show any improvement with the treatment, rather the serum copper level was elevated and ultimately both cases expired.

Discussion

Biological markers are being utilised for the diagnosis and to assess the host response to the treatment in a variety of malignant diseases and it serves as an important aid for effectively monitoring cancer therapy. The present study shows a definite role of serum copper level in the diagnosis and prognosis of female genital malignancies.

TABLE I

Serum Copper Level, Controls Benign Lesions and Malignant Lesions

S. No.	Groups	No. of cases	Serum copper level in microgram/100 ml				
			Range	Mean	± S.D.	t	P
1.	Control healthy female	30	80.6–136.2	109.86	17.23	—	—
2.	Benign lesion	20	83.5–375.8	134.7	59.00	13.6	<.01
3.	Malignant conditions	50					
	— Carcinoma cervix	23	163.4–552.8	288.2	109.29	76.4	<.01
	— Carcinoma body of uterus	10	200.4–456.0	372.3	88.01	91.4	<.01
	— Choriocarcinoma of uterus	2	445.8–501.0	473.4	N/A	—	—
	— Carcinoma of ovary	13	217.1–350.0	289.9	43.91	78.3	<.01
	— Carcinoma of vulva	2	125.2–187.5	156.3	N/A	—	—

S.D. = Standard Deviation. t = Calculated 't' statistics for malignant disease and control comparison.
P = Significance. N/A = Not applicable.

TABLE II

Effect of Treatment in Serum Copper Levels in Different Stages of Carcinoma of Cervix

Clinical stage of disease	No. of cases	Cases not came for follow-up	Serum copper level in microgram/100 ml			
			Before treatment		After treatment	
			Range	Mean	Range	Mean
Stage I	2	2	163.4–174.0	168.7	—	—
Stage II	7	4	476.2–241.0	200.6	156.2–238.0	197.3
Stage III	10	3	248.2–358.6	307.4	242.8–301.8	278.9
Stage IV	4	1	368.0–522.8	452.7	348.0–532.0	430.6

TABLE III

Relationship of Serum Copper Level in Various Phases of Treatment With Histological Pattern of Malignancy of Uterus

S. No.	Histological pattern	No. of cases	%age	Mean serum copper level in microgram/100 m'					
				Before treatment		During treatment		After treatment	
				Range	Mean	Range	Mean	Range	Mean
1.	Well differentiated adenocarcinoma of Endometrium	6	50.00	200.4-417	329.8	121.4-395	296.3	118-345	232.4
2.	Moderately differentiated adenocarcinoma and Endometrium	4	33.33	412.0-456	437.5	368.0-446	393.6	196-428.3	288.9
3.	Poorly differentiated adenocarcinoma of Endometrium	—	—	—	—	—	—	—	—
4.	Choriocarcinoma of body uterus	2	16.66	445.8-501	473.4	430.0-560	495.0	Both expired	

Fifty cases between 9 to 65 years of age suffering from female genital malignancies were studied. Maximum patients belongs to age group of 41 to 50 years followed by subjects of preceding decade. None of the patient was found between age group of 11 to 20. Maximum number of cases were suffering from carcinoma cervix 23 cases (46%), followed by carcinoma ovary 13 casaes (26%), malignancies of uterus 12 cases (24%) and only 2 (4%) patients suffering from carcinoma of vulva.

In present study, serum copper level in control group was ranging from 80.6 to 136.2 microgram/100 ml with a mean of 109.86 ± 17.23 microgram/100 ml. These findings are very much similar to those reported by Valle, 1952 (110 ± 13 microgram %), Wintrobe *et al* 1953 (109 ± 17 microgram %), Sood *et al* 1977 (72.3 to 135.8 microgram %) and Keshawa Rao *et al* 1977 (85 to 150 microgram %).

Slightly higher readings were observed by Briter *et al* 1978 (115 ± 17 microgram %) and lower by Johnson *et al* 1959 (99 ± 15 microgram %). The mean serum copper level of benign diseases in 134.7 ± 59 microgram/100 ml which is lower from malignant diseases but it is certainly higher than the control cases.

The serum copper level of premalignant conditions had a higher pretreatment serum copper level, though these are considered to be benign diseases in present study. After therapy their serum copper returned to normal.

The pre-treatment serum copper levels in all the cases of malignancy were found to be above normal except in 1 case of early stage 1 adenocarcinoma of vulva, in whom serum copper level was normal before therapy but after treatment it was unaltered. The highest value of 522 microgram % of serum coppper was found in an advanced case of carcinoma of cervix.

Present study suggests that serum copper reflects the state of active disease, remission response towards treatment and possibility of recurrence of the disease. The same conclusion has also been made in the past by Pagliand E and Gangrandi, 1960; Jehsen *et al* 1964; Hrgovcie *et al* 1968; Mortazavi *et al* 1972; Tessmer *et al* 1973; Keshva Rao *et al* 1979 and Swami *et al* 1983.

The elevation of serum copper level was also found to be directly associated with histological grading of the disease (as shown in Table III). Moderately differentiated carcinoma of endometrium had a comparatively higher serum copper level than well differentiated carcinoma of endometrium. Choriocarcinoma of uterus had much higher serum copper level. With the treatment also, the fall in serum copper level was observed much in well differentiated group than in moderately differentiated group. Both the cases of choriocarcinoma of uterus did not show any improvement with therapy and also serum copper level kept on rising during treatment in post operative phase. But their condition deteriorated and ultimately expired.

Fall of serum copper level had been noticed during and after treatment and in some cases it had returned to normal also. Perhaps the fall in serum copper level after successful surgical treatment was due to reduced escape of copper into circulation from the tumour mass which was removed surgically. The return of serum copper level to normal as a result of chemotherapy can also be explained by reduction of the tumour mass from treatment and therapy minimising the

release of copper from tumour into the circulation.

Similar explanation will also stand for the cases, who were treated by combined therapy.

Conclusion

Serum copper level although not specific but is a sensitive, accurate and potentially valuable bio-chemical index for evaluating the disease process in various malignancies of female genital tract prognosis in patients suffering from such a malady.

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