THE ROLE OF TWO ENZYMES (LDH AND PHI) AND A TUMOUR MARKER (CEA) IN THE PROGNOSTIC EVALUTION OF HEAD AND NECK MALIGNANCY

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ABSTRACT : *A study of 30 patients with biopsy proven carcinoma of head and neck were taken and serum levels of CEA, LDH and PHI was estimated before treatment and 3 months post treatment. 30 patients were taken as controls for comparison. Pre- and post-treatment levels were statistically compared and the role of surgery, radiotherapy and chemotherapy compared. Variation with metastasis and with smoking was also evaluated.*

INTRODUCTION

Many tumour markers and enzymes have been used earlier to aid in diagnosis of various malignancies. CEA (Carcinoembryonic antigen) is one of the class of oncofetal antigen which has been utilized usefully as diagnostic marker of malignancy and particularly specific for large gut malignancies. Similarly LDH (lactate dehydrogenase) and PHI (phosphohexose isomerase) had been found to be elevated in certain malignancies. As single enzyme may exhibit similar changes in some malignant and non-malignant conditions, a combination of different tumour marker and enzymes is more significant. Thus CEA, LDH and PHI were compared as prognostic factors in our study taking 30 patients of various head and neck malignancies and comparing with 30 controls.

Aims and Objectives

1) Estimations of levels of LDH. PHI and CEA in 30 cases of head and neck malignancies.
2) Estimation of levels of LDH, PHI and CEA in same patients 3 months after treatment.
3) Comparison of levels of LDH, PHI and CEA before and after treatment.
4) Estimation of levels of LDH, PHI and CEA levels in control group of 30 healthy persons and comparison with levels in group of cancer patient.

MATERIALS AND METHODS

The study was carried out in Department of ENT and Biochemistry in Dayanand Medical College and Hospital. 30 diagnosed cases of head and neck malignancy were taken as study patients and 30 healthy persons (without malignancy) as controls. 5ml of blood was drawn from a peripheral vein and estimation of CEA, LDH and PHI was done. These were repeated 3 months after treatment.

Biochemical estimation - Serum was separated.

- CEA was estimated with kit from Boehringer Mannheim Ltd. Using ELISA/1-Step Sandwitch assay using streptovidin technology.

LDH was estimated using Enzokit from Ranbaxy Diagnostics. PHI was estimated manually using Seliwanoff reaction for ketose sugars based on conversion of glucose-6-phosphate to fructose-6-phosphate.

OBSERVATIONS

In the study group there were 70% males and 30% females. The mean age in study group was 47.2 yrs and in control group 43 yrs.

Forty percent of patients had carcinoma of larynx followed by 20% that of hypopharynx, 10% of oesophagus, 13.3% oropharynx, 13.3% oral cavity and 3.3% maxillary sinus.

Majority of patients (93.3%) had squamous cell carcinoma, 3.3% had haemangiopericytoma and 3.3% adenocarcinoma.

The Serum levels of LDH, CEA and PHI was significantly raised in study group as compared to controls and the levels were comparable for CEA and PHI. These levels were raised irrespective of the size of the tumour.

When comparing the histological typing, the levels of all

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Table - I :
Sex Incidence

Group	Sex	Patients	Percentage
Control	Male	19	63.3%
	Female	11	36.7%
Study	Male	21	70%
	Female	9	30%

Table - II :
Age Distribution

Group	Mean Age	Sex	Mean Age
Control	43 yrs	Male	43.2 yrs
		Female	42.6 yrs
Study	47.2 yrs	Male	48.6 yrs
		Female	43.8 yrs

Table - III :
Regional Distribution

Type	Total	Percentage	Male	Female
Larynx	12	40%	10(83.3%)	2(16.7%)
Hypopharynx	6	20%	4(66.7%)	2(33.3%)
Oesophagus	3	10%	0(0%)	3(100%)
Oral Cavity	4	13.3%	3(75%)	1(25%)
Oropharynx	4	13.3%	3(75%)	1(25%)
Max.sinus	1	3.3%	1(100%)	0(0%)

three parameters were highest in adenocarcinoma followed by haemangiopericytoma as compared to squamous cell carcinoma. However, statistical analysis could not be made in adenocarcinoma and haemangiopericytoma as there was only one case each.

There were significantly higher values of LDH in metastatic cancers compared to non-metastatic group. However, there was no significant difference in CEA and PHI.

All parameters were elevated irrespective of the character of tumour i.e. ulcerative, proliferative and infiltrative.

LDH, CEA and PHI were significantly elevated in poorly differentiated tumours as compared to moderately differentiated tumours. The well differentiated tumous

Table -IV :
Histological typing

Histological typing	No.	Percentage
Squamous cell carcinoma	28	93.3%
Haemangiopericytoma	1	3.3%
Adenocarcinoma	1	3.3%

Table - V :
Mean serum level

	LDH(IU/L) Mean±S. D.	CEA(ng/ml) Mean±S. D.	PHI(Bodansky unit /dL) Mean±S. D.
Control	145.06±59.09	3.69±0.95	81.63±7.24
Study	295.0±197.67	9.45±2.60	103.53±12.7
t value	2.29	6.67	8.10
p value	<0.05	<0.01	<0.01

could not be subjected to statistical analysis as there was only one case with well differentiated tumour.
In our study except LDH in stage I tumours, all parameters were significantly raised when compared with control group. LDH and CEA were further raised in the higher stages. However, PHI was not raised in accordance with higher stages.

In this study there was statistically significant decrease in all parameters 3 months post-treatment. However, difference was comparable for CEA and PHI and decrease more than in case of LDH. The results of radiotherapy and surgery were comparable. CEA and PHI decreased significantly post radiotherapy and LDH and CEA fell significantly following surgery. Chemotherapy could not be compared as there was only one case for chemotherapy.

The levels of LDH, CEA and PHI were significantly higher in smoker controls compared to non-smoker controls. However, there was no significant difference between smoker and non-smoker subjects.

DISCUSSION

In our study 93.3% of patients had squamous cell carcinoma. similar results were shown by various workers like Schwartz et al. (1962a), Mali et al (1985).

Table VI :
Serum levels in various regions

	No.	LDH (IU/L) Mean±S.D.	CEA(ng/ml) Mean±S.D.	PHI (Bodansky Unit/dL) Mean±S.D.
Control	30	145.06±59.09	3.69±0.95	81.63±7.24
Larynx	12	252.17±129.43*	7.17±2.17*	103.5±14.04**
Hypopharynx	6	467±281.67*	8.45±2.85**	106±8.66**
Oesophagus	3	216.67±99.76*	5.96±3.36*	91.33±14.70*
Oral Cavity	4	156.5±32.75*	8.2±2.95**	108.5±4.97**
Oropharynx	4	280.5±119.57*	6.5±0.93*	107.5±4.09**
Max. Sinus	1	624	10.0	110

*P < 0.05] compared to control
**P < 0.01]

Table - VII :
Serum levels and histological typing

	No.	LDH (IU/L) Mean±S.D.	CEA(ng/ml) Mean±S.D.	PHI (Bodansky Unit/dL) Mean±S.D.
Squamous cell carcinoma	28	276.4±190.65	7.48±2.63	104±12.35
Adenocarcinoma	1	624	10.0	110
Haemangiopericytoma	1	486	6.0	104

Table- VIII
Variation with metastasis

	No.	LDH (IU/L) Mean±S.D.	CEA(ng/ml) Mean±S.D.	PHI (Bodansky Unit/dL) Mean±S.D.
Non-metastatic	18	220.55±121.37	6.57±2.48	101.44±10.86
Metastatic	12	406.67±234.09	8.77±2.19	109.16±12.33
't' value		2.75	1.72	1.22
'p' value		<0.05	N. S.	N. S.

LDH, CEA and PHI were found to be elevated in study group compared to the control group. Similar results were obtained by Yadav et al. (1991) and Khan et al. (1984) on their study on LDH in head and neck malignancies. Also Silvermann et al. (1978) and Meeker (1973) found high CEA levels in head and neck cancer. Similar higher PHI levels were shown by Bhatia et al. (1979) and Vaid et al. (1974). Higher values of LDH, CEA and PHI were seen in adenocarcinoma as compared to squamous cell carcinoma. This is in accordance with the study by Bhatia et al. (1979) on PHI and by Yadav et al. (1994) on LDH and Meeker et al. (1973) on CEA.

In our study only LDH was significantly raised in metastatic cancer compared to non-metastatic groups. Similar results were shown by Khan et al. (1984) on his study on LDH and by Silverman et al. (1978) on his study on CEA.

Table - IX
Variation with character of tumour

	No.	LDH (IU/L) Mean±S.D.	CEA(ng/ml) Mean±S.D.	PHI (Bodansky Units)/dL Mean±S.D.
Control	30	145.06±59.09	3.69±0.95	81.63±7.24
Ulcerative	15	357.06±236.84**	8.3±2.54**	108.73±12.09*
Proliferative	11	198.90±112.86*	6.58±2.28*	99.36±9.69*
Infiltrative	4	326.5±82.56**	6.62±2.63	100.50±10.7*

*O< 0.05]
**P , 0.01] Compared to control

Table - X
Variation with differentiation

	No.	LDH (IU/L) Mean±S.D.	CEA(ng/ml) Mean±S.D.	PHI (Bodansky Units) Mean±S.D.
Well diff.	1	210	5.0	102
Mod. diff.	20	214.3±102.05	6.69±2.52	102.25±10.20
Poorly diff.	9	483.78±237.03	9.4±1.66	108.77±14.74
t value*	1	4.04	2.84	1.33
P value *		<0.01	<0.01	>0.05

* t & P value are between Mod. and poorly differentiated type.

Table - XI
Variation with staging

	No.	LDH (IU/L) Mean±S.D.	CEA(ng/ml) Mean±S.D.	PHI (Bodansky Units)/dL) Mean±S.D.
Control	30	145.06±59.09	369±0.95	81.63±7.24
I	4	163.5±39.65	592±1.06*	104.0±4.53*
II	6	245.33±145.11*	6.68±3.34*	93.0±13.34
III	14	249.14±123.76**	7.28±2.00**	107.43±13.03*
IV	6	539.33±242.72**	9.52±2.59**	106.17±5.79*

* P < 0.05] ** P<0.01]

There was significant decrease in CEA, LDH and PHI three months post-treatment. Similar results were shown by Silverman et al (1978) in their study on CEA and by Yadav et al. (1994) in their study on LDH and by Bhatia et al. (1979) in their study on PHI.

SUMMARY AND CONCLUSIONS

1) 70% of patients were males and 30% females
2) Mean age was 47.2 yrs in the subjects
3) 40% of patients had carcinoma larynx, 20% had that of hypopharynx, 10% of oesophagus, 13.33% of oral cavity, 13.3% of oropharynx and 3.3% of maxillary sinus.
4) 93.3% of patients had squamous cell carcinoma.
5) All three parameters LDH, CEA and PHI were significantly raised in study group compared to controls. CEA and PHI were comparable.

Table - XII :
Variation before and after treatment

	LDH(IU/L) Mean±S. D.	CEA(ng/ml) Mean±S. D.	PHI(Bodansky units)/dL Mean±S. D.
Control	145.06±59.03	3.69±0.95	±81.63±7.24
Pre-treatment	295.0±197.67	7.45±2.60	103.53±12.7
Post Treatment	206.83±133.20	4.08±0.89	82.0±7.14
t value	2.03	6.70	7.97
p value	<0.05	<0.01	<0.01

Table - XIIIa :
Variation with Mode of Treatment

Treatment Modality	No.	LDH IU/L		CEA ng/ml		PHI Bodansky/dL	
		Pre	Post	Pre	Post	Pre	Post
Radiotherapy	24	306.58±211.67	217.29±129.94	7.67±2.74	4.23±0.93	102.42±10.89	83.29±6.82
Surgery	5	201.2±5.36	104.6±14.82	6.44±1.99	3.2±0.4	111.4±15.3	76.4±5.82
Chemotherapy	1	486	472	6.0	4.5	104	89

Table - XIIIb :
Statistical analysis

		LDH (t,p)	CEA(t,p)	PHI(t.p)
Radiotherapy	t	1.71	5.67	7.48
	p	>0.05(N.S.)	<0.01	<0.01
Surgery	t	3.57	3.20	1.15
	p	<0.01	<0.05	>0.05(N.S)

Table - XIV :

	No.	LDH (IU/L)	CEA(ng/ml)	PHI (Bodansky Units/dL)
Non smoker controls	23	128.52±51.19	3.50±0.73	79.52±4.05
Smoker controls	7	199.42±49.97	4.5±1.25	88.85±10.17
't' value		3.12	2.55	3.45
'P'value		<0.05	<0.05	<0.05
Smoker subjects	16	380.87±221.88	7.79±2.64	104.56±12.76
Non-smoker subjects	14	196.87±96.95	7.05±2.50	104±11.03
't' value		0.46	0.76	0.12
'p' value		>0.05 (NS)	>0.05(NS)	>0.05(NS)

NS- Non-significant

6) All three parameters were raised irrespective of the site and the character of the tumour.
7) Only LDH was significantly raised in metastatic group compared to metastatic group.
8) LDH and CEA were higher in poorly differentiated tumour compared to moderately differentiated tumour.
9) There was no significant rise in values according to clinical staging of malignancy.
10) 3 months post treatment serum levels of CEA, LDH and PHI were significantly lower than preoperative values. However, they were comparable in case of CEA and PHI.
11) There was statistically significant fall in CEA and PHI after radiotherapy and fall in CEA and LDH levels after surgery. The levels did not significantly decrease following chemotherapy.
12) Smokers had significantly higher serum levels of all three parameters in smoker controls compared to non-smokers. However, there was no significant difference between smoker and non-smoker subjects.

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