

Original Article

Serum Lactate Dehydrogenase Level in Patients with Head and Neck Malignancy Treated with Radiotherapy

Arun Chougule¹, Bhawani Kochar²

¹Senior Professor and Head, Department of Radiological Physics, SMS Medical College and Associated Group of Hospitals, Jaipur; ²Biochemist, Department of Biochemistry, SMS Medical College and Associated Group of Hospitals, Jaipur.

ABSTRACT

Introduction: Cancer is a leading cause of death worldwide. Early detection followed by properly planned treatment usually increases the life expectancy of the patient but unfortunately most of the common available diagnostic tools detect tumor when it is more than 5mm in size and hence the prognosis is poor. If micro nuclear level alterations due to malignancy are detected with sufficient sensitivity and specificity, it might prove to be an effective tool in management of cancer. Few of the serum enzymes play a pivotal role in this regard and lactate dehydrogenase (LDH) is an important biochemical tumor marker among them. The aim of the present study was to analyze the significance of LDH in head and neck malignancies treated with radiotherapy as a diagnostic and prognostic tool.

Methodology: Serum LDH levels were analyzed before, midway and at completion of radiotherapy and monthly follow up for six months in 90 biopsy proven head and neck cancer cases treated with radiotherapy.

Results: It was observed that in all the malignant cases the pretreatment enzyme level was much higher [293.6±36.9IU/L] than that of control group [168.5±27.27IU/L]. Further, it was observed that as the radiotherapy progresses, the serum LDH levels decreases and during follow-up in the patients with no apparent disease activity, the levels approached near to that of the control group. Serum LDH showed significant association with the disease activity.

Conclusion: Findings of the study indicates that serum LDH may be a prognostic tool in head and neck malignancies and the treatment strategies can be optimized accordingly.

INTRODUCTION

A number of serum enzymes have been used in clinical practice for the diagnosis of various malignancies of

different sites. The level of serum enzyme acts as an important biochemical tumor marker in the diagnosis of malignancy. Under the normal conditions, each tissue maintains a steady and consistent pattern which is significantly altered in malignancy because membrane constituents are shed into the surrounding milieu at an increased rate when cells replicate more rapidly. When cells are destroyed the enzymes and proteins present in the nucleus, cytoplasm and mitochondria are also released in the circulation. Therefore, alteration in a particular enzyme level in serum could be a good index of malignancy in its early and best manageable stage of the disease provided they turn to be sufficiently specific and sensitive. Among the serum enzymes which have received clinical attention in malignant patients is lactate dehydrogenase (LDH).

Lactate dehydrogenase, a glycolytic enzyme occurs in most body tissues. As early as in 1954, increased levels of LDH were detected in serum of melanoma patients¹ ever since, the value of LDH as a tumor marker for malignant melanoma has been discussed. The increase of serum LDH in patients with malignant lymphoma may be due to release from tumor cell.² Serum LDH activity is known to be of prognostic value in other hematological malignancies such as leukemia and malignant lymphoma.³⁻⁶ The significance of LDH in prognosis of head and neck malignancy patients has yet not been established. The present study was undertaken to determine the value of LDH activity and its relation with the histopathology in serum of patients with head and neck malignancy undergoing radiotherapy treatment.

METHODS

The present study was carried out with prior approval of institutional ethics committee on 90 patients with biopsy proven malignancies of head and neck who attended the Radiotherapy department for radiotherapy. Patients having metastasis were excluded from the study.

25 age matched normal healthy subjects of both sexes were selected as the control group. The control subjects included in this study were asymptomatic, free from any abnormality on routine examination, non smokers, not on antioxidant supplementation, not taking any drug, alcohol or chewing tobacco and were free from any disease. Patients were classified according to Union for International Cancer Control (UICC classification).⁷ All the patients were treated by External Beam Radiation Therapy (EBRT) using Cobalt-60 Teletherapy unit with a rectangular field. Blood samples were taken and serum lactate dehydrogenase (LDH) was estimated by enzymatic method⁸ in all patients before EBRT (BT), midway of EBRT (MT;30 Gy tumor dose), at completion of EBRT (CT;60-70 Gy tumor dose) and subsequently monthly follow up for six months. All values are expressed as mean values with standard deviation (SD). Observations were compared with Student's t test and p value <0.05 were considered to indicate statistical significance

RESULTS

In the present study, the mean serum LDH levels were found to be 168.5±27.27IU/L in control subjects. Further, the mean serum LDH in study group was 293.6±36.9IU/L at BT, which reduced to 236.1±31.8IU/L at CT and 164.6±20.4 IU/L at 6 months follow up (Table 1, Figure 1). The levels of LDH were found to be raised significantly in the study group patients at BT as compared to the control group (healthy volunteers). At 6 months follow up, the levels of serum LDH returned to the normal range however it was statistically non-significant. Further serum LDH levels were compared according to

the histopathological grade of the malignancy (Table 2). It was observed that the decrease in the level of serum LDH at 6 month follow up was more pronounced in poorly differentiated malignancies followed by moderately differentiated and well differentiated malignancies respectively as compared to before therapy.

DISCUSSION

Lactate dehydrogenase was first isolated in crystalline form from ox and pig by Straubin⁹ and has now been obtained in a pure state from a variety of human and animal tissues. Lactate dehydrogenase occurs in most body tissues such as heart, liver, skeletal muscle, erythrocytes and serum. Further, it is well known that serum LDH is a useful index of cell damage in many organs. Despite the ubiquitous distribution of LDH, its serum level has proved to be of considerably confirmatory value in the diagnosis of variety of health conditions.

Many patients with myelogenous leukemia, lymphoma, sarcoma and disseminated carcinoma have increased serum LDH. The untreated or therapeutically resistant patients maintain elevated serum LDH or manifest increasing serum LDH with progression of the cancer. In patients with tumor showing response to surgical, hormonal and / or ionizing radiation therapy, there is usually a decreasing activity of serum lactate dehydrogenase with a return towards the normal range as remission of the disease is attained. The fall of serum LDH towards or to the normal range may occur after treatment in spite of the presence of tumor and presumably the serum enzymes change is a reflection of the metabolic change in the tumor rather than presence of the tumor in the body.¹⁰

Table.1: Statistical analysis of serum LDH [IU/L] in head and neck malignancy

	Control	BT	MT	CT	1M	2M	3M	4M	5M	6M
Mean	168.5	293.1	255.6	236.1	210.6	196	185.2	176.3	170.6	164.6
SD	27.2	36.9	31.8	21.2	13.7	13.4	11.8	14.6	15.9	20.4
P		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	NS	NS	NS

Table 2: Comparison of serum LDH levels [IU/L] in head and neck malignancy according to histopathological grading

	Before Therapy			6 Month Follow Up		
	Well differentiated	Moderately differentiated	Poorly differentiated	Well differentiated	Moderately differentiated	Poorly differentiated
Mean	252.6	298.4	331.7	147.2	167.2	184.7
SD	24.9	21.4	39.7	16	17.8	8.8
p				<0.001	<0.001	<0.001
% (↑ / ↓)				71.6 ↓	78.4 ↓	79.5 ↓

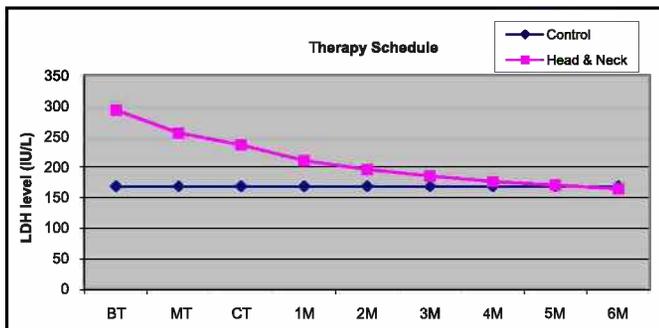


Figure 1: Comparative trend of serum LDH [IU/L] in head and neck malignancy.

In the present study, the mean serum LDH were found to be decreased significantly during EBRT as compared to BT, however, serum LDH was decreased non-significantly at the six months follow up as compared to the control group. This shows that high serum LDH were in normal level or controlled due to treatment. Our findings were similar to Chougule et al.¹¹ They reported that all the cancer patients had LDH activity above normal level of control before therapy and the pretreatment enzyme level in malignant cases showed positive association with the extent of the disease. In our study, according to the histopathologic grade of the tumor, at 6 months follow up the levels of the serum LDH were decreased by 71.6% in well differentiated tumors as compared to levels before therapy whereas in moderately differentiated tumors and in poorly differentiated tumors the levels decreased by 78.4% and 79.5% respectively as compared to levels before therapy. The decrease was statistically significant ($p < 0.001$) in all the three pathologic grading. This indicates that cancer with better differentiation of cells had low serum LDH activity while undifferentiated and anaplastic carcinoma had high serum LDH activity.

Narang¹² found the serum levels of LDH to be 306.58 ± 211.67 IU/L in pretreatment and 217.29 ± 129.94 IU/L in post treatment of head and neck malignancy patients. In well differentiated tumors the level was 210 IU/L, in moderately differentiated tumors the level was 214.3 ± 102.05 IU/L and in poorly differentiated tumors the level was 483.78 ± 237.03 IU/L. LDH levels were significantly elevated in poorly differentiated tumors as compared to moderately differentiated tumors. The results of the present study are strongly in agreement with the study of Singh¹³, who studied 50 patients of head and neck malignancy. Higher levels of serum LDH were observed in patients with malignancy of head and neck. Further, they assumed that serum LDH levels were also related to the histopathological stage of the malignancy, being higher in poorly differentiated tumor as compared to moderate and well differentiated malignancy.

Zhou¹⁴ studied the serum LDH levels in nasopharyngeal cancer patients undergoing radiotherapy and reported that the serum LDH levels were significantly elevated in malignant patients as compared to the control group. They observed that higher the stage of the disease, the increased levels are significant and the monitoring of LDH levels during treatment can be indicator of response to the radiotherapy treatment. Similar observations were reported by Xiang-bo et al.¹⁵ They have studied LDH levels in 400 patients of nasopharyngeal carcinoma undergoing neoadjuvant chemotherapy and concurrent chemo radiation. They reported a strong correlation of serum LDH level with the extent of disease and followed up the patients for five years and showed that the prognosis of the disease can be tracked with estimation of LDH levels. In another study Zhengbo Wei et al¹⁶ have reported study of 601 patients of nasopharyngeal carcinoma wherein they have measured the serum LDH levels before treatment, at the end of treatment and regular follow-up up to 5 years and observed that the pretreatment serum LDH values are very good predictor of disease progression and prognosis.

CONCLUSION

Determination of serum LDH concentration may have potential prognostic value in patients with head and neck malignancy. The findings of the present study suggests to adjust treatment strategies ahead of time, considering not only the histopathological stage but also the prognosis related serum enzyme. However, other clinical and laboratory studies must be used before reaching a final interpretation and studies with more number of cases are also needed to evaluate the importance to this subject.

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Corresponding Author:

Dr. Arun Chougule, Senior Professor and Head,
Department of Radiological Physics, SMS Medical
College and Associated Group of Hospitals, Jaipur,
Rajasthan, India.

email: arunchougule11@gmail.com