SERUM LACTIC DEHYDROGENASE LEVELS IN THE DIAGNOSIS AND TREATMENT OF OVARIAN CANCER

by

V. S. Singh,* M.Sc.,

R. Idnani,** M.S.,

Usha Sharma,*** M. S.

V. K. Pratap,**** M.D.,

R. K. Aran,***** M.B.B.S.

and

Yeshovardhana, M.Sc

About 50 years ago, Warburg and Minami (1923) and Cori and Cori (1925) demonstrated that malignant tissue has high glycolytic activity. This pointed to a major difference between normal and malignant tissues. Lactic dehydrogenase (LDH) is a major enzyme in glycolysis and reversibly catalyses pyruvate to lactate. With increased glycolytic activity one would expect a concomitant increase in LDH enzyme activity which may be reflected in certain tissue fluids. Meister (1950), studying tumour and normal tissues in the mouse and rat, concluded that tumours possess appreciable LDH activity. In studies of malignant and non-malignant human tissue, several investigators showed that LDH isoenzymes differ (Nissen and Bohn, 1965). Assay of the LDH enzyme in normal and malignant human tissue suggested an increase in total LDH activity in malignant tumours (Goldman *et al* 1964). Some investigators reported an elevation of serum LDH in patients with neoplastic disease (Hill and Levi, 1954). Hill (1957) could not confirm the presence of cancer by measurement of serum LDH. The purpose of the present study is to find out the significance of serum LDH levels in the diagnosis of carcinoma of the ovary and to assess its response to treatment.

Material and Method

Seventeen cases of primary carcinoma of the ovary admitted at S.V.P. Hospital, Medical College, Meerut were taken for this study. The histopathologic findings in 11 patients showed papillary adenocarcinoma of which 8 were poorly differentiated, 2 were moderately differentiated and 1 was well differentiated. Three cases were papillary mucinous cystadenocarcinoma, and remaining 3 showed papillary serous cystadenocarcinoma. A retrospective staging with the International Federation of Gynaecology and Obstetrics ovarian Cancer staging was undertaken, and 14 patients had stage III disease, 1 had stage IV disease, and 2 had stage I disease. None of the patient had taken any

* *Lecturer in Biochemistry.*
** *Lecturer in Obst. & Gynecology.*
*** *Reader in Obst. & Gynaecology.*
**** *Reader in Pathology.*
***** *Registrar in Medicine.*
L.L.R.M. Medical College, Meerut.
Accepted for publication on 6-4-76.

treatment before the study started. The serum lactic dehydrogenase (SLDH) (Wooten 1964), levels were measured in all the patients before and after the treatment. Ten had operation and 7 had chemotherapy, in different combination. 20 normal healthy women (control) were also included in present study.

Results

Normal range of SLDH determined in 20 healthy subjects is 85-155 I.U./litre with a mean of 110.3 ± 17.6 I.U./litre. All the patients (100%) with carcinoma of the ovary had a significant increase in SLDH ranging from 215 to 375 I.U./litre with a mean of 306.7 ± 23.3 I.U./litre which returned to normal range after the treatment.

TABLE I

Serum Lactic Dehydrogenase (SLDH) Levels in Patients with Carcinoma of the Ovary Before and After the Treatment

Group	No. of cases	Before treatment			After treatment		
		Range	Mean	S.D.	Range	Mean	S.D.
Control	20	85–155 I.U. /L.	110.3	17.6	—	—	—
Cancer Ovary	17	215–375 I.U. /L.	306.7	23.3	105–145	137.6	12.4
				p 0.01			

Discussion

All the patients with carcinoma of the ovary had a significant increase in SLDH ranging from 215 to 375 I.U./litre (mean 306.7 ± 23.3). These findings are in agreement with Awais (1973) who reported increased levels of SLDH in patients with carcinoma of the ovary before any treatment. Several investigators reported increased levels of SLDH in patients with lymphoma, granulocytic leukemia, carcinoma of the pancreas and gall bladder, metastases from carcinoma of the breast, and metastatic disease of the liver. Increase in the activity of this enzyme was also noted in cases of acute myocardial infarction, infectious mononucleosis, obstructive jaundice, and acute hepatitis (Denis and Prout, 1963; Hsieh and Blumenthal, 1956; Wroblewski and Gregory, 1961; Wroblewski 1961).

Keiser and Riggins (1966) studied LDH in the urine specimens of patients with malignant and non-malignant diseases of urinary tract and found increased LDH activity but could not confirm any specific diagnostic relationship. Whereas Asada and Galambos (1962) observed an increased level of SLDH in 5 cases of metastases of carcinoma of the ovary.

Market and Moller (1959) reported that the cells of some embryologic tissue differ from the adult cells in the complement of LDH isoenzymes. The same authors confirmed that the pattern of LDH isoenzymes in different species and tissues show specific changes during embryologic differentiation of the tissue. The ovary, being a multipotential and totipotential organ, may, during malignant activity, show an increased total activity which can be measured in the circulating plasma. If so, the serum LDH test may well be useful in carcinoma of the ovary. The present study appears to confirm this

hypothesis. In any woman who has a pelvic mass or a chief pelvic complaint and high SLDH, in the absence of carcinomatosis, leukemia, liver disease, uncontrolled diabetes mellitus, or myocardial infarction, carcinoma of the ovary should be suspected.

In our series we observed that after effective treatment of the carcinoma of the ovary, the SLDH levels decreased to the normal limits and continued to be normal as long as the carcinoma is controlled. When carcinomatous activity recurs, there was a concomitant rise of SLDH. Two patients with carcinoma of the ovary had an increased SLDH before treatment but after surgical treatment, SLDH returned to normal levels, but 7 months later they returned with evidence of recurrent disease with high SLDH which again returned to normal after chemotherapy.

Wieczorek (1971) studied the activity of SLDH before and after gamma radiation therapy in cases of carcinoma of the cervix and found SLDH well within normal limits before and after the treatment. Whether there is specificity between serum LDH and ovarian carcinoma remains to be confirmed, but evidence to this effect is presented in this retrospective study where we observed significantly raised levels of serum LDH in all the cases of ovarian cancer (100%).

Ovarian Cancer is insidious, and the incidence was reported to be 2.6% of the all gynaecologic admissions (Randall and Hall, 1952), and 8.1% in all gynaecologic cancers (Pearse and Behrman, 1954). It has a poor prognosis and cure rate is little better than 20%, much less than for carcinoma of the uterine corpus or cervix (Corscaden, 1953). Delay in diagnosis has been suggested as a major cause of the poor result. There is no available test for the detection of this growth in its early stages, and there is no known effective therapy. All of these make the control of the disease difficult and expensive. Progress towards an early diagnosis of carcinoma of the ovary is welcome development and will contribute to a more favourable outcome of the disease. The present study is retrospective, and, although, it shows that SLDH can be helpful in the diagnosis of carcinoma of the ovary, no decisive or unequivocal claim is being made. Further work is required to clarify the role of SLDH in the diagnosis of carcinoma of the ovary and its response to different modalities of treatment. Further prospective studies, which include the determination of different isoenzymes, may clarify this problem.

Summary

Serum lactic dehydrogenase levels were measured in 17 cases of primary carcinoma of the ovary to find out its significance in the diagnosis and treatment of ovarian cancer. Serum LDH was significantly raised in all the patients with carcinoma of the ovary (100%), before treatment and returned to normal limits after an effective treatment. The significance of estimation of serum LDH in ovarian cancer is discussed in light of its diagnostic and prognostic values.

References

1. Asada, M. and Galambos, J. T.: Amer. Jr. Dig. Dis. 7: 1001, 1962.
2. Awais, G. M.: Amer. J. Obst. & Gynec. 116: 1053, 1973.
3. Corscaden, J. A.: Gynaecologic cancer. ed-4, Baltimore, 1953, The William & Wilkins Com. p. 521.
4. Cori, C. F. and Cori, G. T.: J. Biol. Chem. 65: 397, 1925.
5. Denis, L. J. and Prout, G. R. Jr.: Invest. Urol. 1: 101, 1963.
6. Goldman, R. D., Kaplan, M. O. and Hall, T. C.: Cancer Research. 24: 389, 1964.

7. Hill, B. R. and Levi, C.: Cancer Research 14: 513, 1954.
8. Hill, M. H.: J. Natt. Cancer Inst. 18: 307, 1957.
9. Hsieh, K. M. and Blumenthal, H. T.: Proc. Soc. Expt. Biol. Med. 91: 626, 1956.
10. Kiser, W. S. and Riggins. R. S.: J. Urol. 96: 559, 1966.
11. Meister, A.: J. Natt. Cancer. Inst. 10: 1263, 1950.
12. Markert, C. L. and Moller, F.: Proc. Natl. Acad. Sciences. U.S. 45: 753, 1959.
13. Nissen, N. I. and Bohn, L.: Eur. J. Cancer. 1: 217, 1965.
14. Pearse, W. H. and Behrman, S. J.: Obst. & Gynec. 3: 32, 1954.
15. Randall, C. L. and Hall, D. W.: Amer. J. Obst. & Gynec. 63: 497, 1952.
16. Warburg, O. and Minami, S.: Klin. Wochenschr. 2: 776, 1923.
17. Wroblewski, R. and Gregory, K. F.: Ann. N.Y. Acad. Sci. 94: 912, 1961.
18. Wroblewski, F.: Med. Clin. North America. 45: 513, 1961.
19. Wieczorek, F.: Pol. Tyg. Lek. 26: 1572, 1971.
20. Wotton, I. D. P.: Micro Analysis in Medical Biochem. J. & A. Churchill Ltd. 4 Edit. p. 117, 1964.