

ORIGINAL ARTICLE

Cerebrospinal Fluid Lactic Dehydrogenase Activity in Children with Acute Lymphoblastic Leukemia Treated for Cranial Prophylaxis

by

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Abstract

Total lactic dehydrogenase (TLDH) activity in cerebrospinal fluid (CSF) has been prospectively studied in order to determine whether it could be a biochemical marker for brain damage due to cranial prophylaxis in children with acute lymphoblastic leukemia (ALL). TLDH activity has been measured in 15 patients before prophylaxis, in 15 patients after the prophylaxis which consisted of cranial radiotherapy (2400 rads) and intrathecal methotrexate (0.5 mg/kg-dose, 5 doses), in 8 patients after radiotherapy alone (2400 rads) and in 9 patients after intrathecal methotrexate (0.5 mg/kg-dose, 5 doses) alone. TLDH activity in CSF of combined prophylaxis group has been found to be higher than the ones before study ($p < 0.05$). There were insignificant elevations of TLDH activity in the other two groups ($p > 0.05$; $p > 0.05$). This result indicated combined cranial prophylaxis seemed to be more toxic than the other prophylaxis regimens when they were used alone.

Introduction

It has been known that there is an increase of TLDH activity in the various systemic (Hicsonmez et al., 1986) and neurological (Goldberg and Weiner, 1981; Hall et al., 1980; Hallock et al., 1978) diseases. There are many reports about the complications due to central nervous system prophylaxis in children with ALL

(Eiser, 1978; Gangji et al., 1980; Laddy and Gilman, 1973; Mott et al., 1972; Wells et al., 1983). In this prospective study, we have tried to determine whether TLDH activity in CSF of children with ALL could be a biochemical marker for brain damage sourced from central nervous system prophylaxis.

Materials and methods

This study has been done in 32 children with ALL in remission (F/M:14/18) whose ages ranged from 2 to 16 years (mean 7.2) at Hacettepe Children's Hospital in Ankara, Turkey. TLDH activity has been determined in four groups :

1. The first group consisted of 15 children in whom TLDH activity was measured after combined prophylaxis (2400 rads radiotherapy and 0.5 mg/kg-dose methotrexate being 5 doses).
2. Second group consisted of 9 patients in whom TLDH activity was measured after only 2400 rads cranial radiotherapy

was given.

3. Third group consisted of 8 patients in whom TLDH activity was measured after only intrathecal methotrexate was given a dose of 0.5 mg/kg, being total 5 doses.
4. Control group consisted of all 15 patients in the first group in whom TLDH activity was measured before combined prophylaxis. All measurements were done in CSF and the method used here might be found elsewhere (Tietz, 1976).

Results

1. TLDH activity in the first group has been found to be between 24-1168 units/ml with a mean of 214.3 ± 322.9 units/ml.
2. TLDH activity in the second group has been found to be between 12-200 units/ml with a mean of 61.4 ± 54.4 units/ml.
3. TLDH activity in the third group has

been found to be between 11-100 units/ml with a mean of 27.67 ± 29.75 units/ml.

4. TLDH activity in the control group has been found to be between 12-56 units/ml with a mean of 30.8 ± 12.08 units/ml.

Discussion

TLDH activity has been investigated not only in serum, tissue and blastic cells, but also in CSF. During the neonatal period, it has been shown that TLDH activity in

term newborn babies with perinatal asphyxia was three-fold higher than the values of normal babies (Lending et al., 1959). It has also been emphasized that high TLDH

activity in CSF has poorer prognosis in newborn babies with perinatal asphyxia (Hall et al., 1980). Increase of TLDH activity in CSF has been observed in patients with primary and metastatic brain cancers (Nelson et al., 1975; Wroblewski et al., 1958). The TLDH activity of CSF has been used as a marker for central nervous system involvement in patients with lymphoma (Wroblewski et al., 1958).

Cranial radiotherapy and intrathecal methotrexate are given to children with ALL during remission in order to prevent central nervous system relapses. It is believed that this prophylaxis makes survival longer in children with ALL. However, there sometimes happens damage to brain due to cranial prophylaxis (Goldberg et al., 1982). There is clear evidence that increase of TLDH activity in CSF of cases with brain damage due to various causes are sourced directly from brain tissue (Wilcock et al., 1973).

In the presents study, a significant increase of TLDH activity in CSF of patients treated with combined prophylaxis has been determined at the end of the study

when compared to preprophylaxis values ($p < 0.05$). This finding might be interpreted to be a biochemical marker for damage of brain tissue.

Since there was no significant increase in the groups in which cranial radiotherapy or intrathecal methotrexate were given alone ($p > 0.05$; $p > 0.05$), the method consisting of combined prophylaxis can be assumed to have more toxic effects on central nervous system than do others. The reports in the literature (Kollmannskof, 1979; Pedersen and Clausen, 1981) indicating that there were more abnormal CAT scanning findings in patients treated with combined method than in the ones in whom only intrathecal methotrexate was given are supporting our finding. The significant increase of TLDH activity in CSF of combined prophylaxis group, when compared to other two regimens, indicates that there should be more damage to brain. In order to make precise conclusion, however, long-term follow-up studies comparing complications in these groups should be performed.

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