Predictive Value of Serum Lactate Dehydrogenase in Head Injury
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Citation

Abstract
Background: Elevated serum lactate dehydrogenase (LD) as a marker for diagnosis and assessment of severity of head injuries has gained interest in recent years and some encouraging reports have appeared on assessing the degree of brain damage by estimating serum lactate dehydrogenase. Methods: Prospective observational study of 63 patients admitted at a trauma centre with head injuries in a 2½-month span with no extracerebral injury. Upon admission, vital parameters were recorded and blood samples were drawn for serum LDH on 5 consecutive days. The patients were further evaluated by radiological tests. Results: Serum LDH was raised in patients with parenchymal brain injuries. Serum LDH was raised significantly in patients with contusion injury, followed by patients with diffuse axonal injuries. Patients with extracerebral hemorrhage have higher serum LDH than patients of cerebral oedema. Serum LDH was highest in patients who died of head injury, suggesting that an increase in serum LDH activity indicated the degree of parenchymal brain damage. Serum LDH in children was found to be higher compared to that of adults in the same group of head injury (cerebral oedema); the reason remains to be investigated by further studies.

INTRODUCTION
Assessment of head injury and prediction of the extent and outcome are difficult in early stages. Multiple and complex factors operate in the brain in head injury. Patients with different types of brain injury may have similar clinical pictures. Clinical, biochemical and radiological studies have proved useful in estimating the prognosis of head injury patients. But sometimes the real extent of primary brain injury is marked by traumatic brain oedema and cerebral metabolic derangement. In recent years, some encouraging reports have appeared on assessing the degree of brain damage by estimating serum and cerebrospinal fluid enzymes such as lactate dehydrogenase. Our hypothesis was that parenchymal brain injury would lead to rise in serum lactate dehydrogenase and that the degree of rise would correlate with the severity of injury and we aimed to know how serum lactate dehydrogenase correlates with different types of head injury. Most head injuries were diagnosed clinicoradiologically using CT scan. At the time of admission, the Glasgow Coma Scale determines the severity of head injury and prognosis. Predictors of the outcome following head injuries are severity of the initial injuries, patient factors, timing of therapeutic intervention, quality of care, imaging studies (CT, MRI) and other clinical and biochemical variables like lactate dehydrogenase in CSF and serum.

Lactate dehydrogenase catalyzes oxidation of lactate to pyruvate and is widespread in many body tissues. LDH has five isozymes with different electrophoretic properties. In trauma and head injury patients, LDH is increased in serum due to injury to the brain tissue. There have been some studies showing relation between serum LDH level and brain injury. In this study, the significance of LDH in predicting the severity outcome of head injury and correlating the levels with different types of head injuries is studied.

MATERIALS AND METHODS
STUDY CENTRE
The study centre was the tertiary level trauma centre at King Georges Medical University (CSMMU), Lucknow, India. The hospital is a busy academic and state level trauma referral centre with almost 4000 annual admissions, resulting from a large number of trauma referrals alone.
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**Cohort Definition**
This study comprised patients presenting with head injury with parenchymal brain injury and with no extracerebral injury over a period extending from January 2009 to March 2009, with no age exclusion.

Data Collection
Proforma directed demographic profiles (age, sex, address, mode of injury, GCS) and clinicoradiological examination findings of all patients at admission were recorded and blood samples were drawn for laboratory evaluation which included serum lactate dehydrogenase (LDH).

Serum LDH activity was estimated from 63 patients admitted at the trauma centre during the course of 2½ months. Isolated head injury patients with no extracerebral injuries were selected and serum LDH was estimated at the time of admission and serially on 5 days. Serum LDH samples drawn were transported to the respective laboratory at the earliest.

Any patient revealing extracerebral injury, either at admission or at subsequent follow-up, was excluded from the study.

Head injury patients were classified in four groups 1. Contusion 2. Extracerebral hemorrhage 3. Diffuse axonal injury. 4. Cerebral edema.

Patients were classified as having brainstem injury when they had decerebrate rigidity, pupillary changes, and marked autonomic disturbances; where these clinical features manifested after a lucid interval and were associated with either intracranial hemorrhage or cerebral edema, they were regarded as being caused by secondary brainstem injury. However, if brainstem disturbances were evident immediately after injury and no obvious cerebral compression was detected, the case was classified as primary brainstem injury and diffuse axonal injury. Pathological diagnosis was confirmed by clinical examination, investigation, operative or necropsy findings. Outcome was reviewed and specified as (1) dead (2) severely disabled (3) moderately disabled and (4) good. In the contusion group, 17 patients out of 28 had good survival and were discharged, 2 patients underwent neurosurgical intervention and 9 patients died.

In the extracerebral hemorrhage group, 5 patients out of 10 underwent surgical intervention, 1 patient died and 4 patients had good survival. In the brainstem injury and diffuse axonal injury group there was no good survival; out of 3 patients, 1 patient died and 2 patients were moderately disabled.

In patients with cerebral oedema, 18 out of 18 patients had good survival, with no disability and casualty recorded.

A parallel study on 15 neurologically normal patients with no other injuries formed the basis of normal control values.

Precaution was taken to prevent hemolysis of blood samples drawn.

Statistical analysis of the recorded data was done; mean, standard deviation and standard error were calculated, comparisons between the groups were made and statistical significance was established by Student’s t-test.

The null hypothesis was that there are no differences between the means of the two samples;

the difference between means of samples was calculated as \((X_1- X_2)^2\);

the standard error of differences between two means was calculated as \(S_Ε\).

Figure 2

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t-value = \frac{X_1 - X_2}{S\sum} \]

degree of freedom was determined from the formula

\[df = (n_1 - 1) + (n_2 - 1), \text{ where } n_1 \text{ and } n_2 \text{ are the numbers of observations in each of the two series}\;.
and the calculated value of ‘t’ was compared with the table value at the particular degree of freedom to find the level of significance in two tests.

If the calculated value exceeds the value given under p in the table, it is said to be significant at this level and the null hypothesis is rejected.

RESULTS

In the control group, the mean serum total lactate dehydrogenase (LDH) activity was 141 IU/L with a standard deviation (σ) of 49.5 and a standard error of 6.3. The range of LDH in different groups of head injuries is shown in Table 1 with the standard error of mean LDH values. The mean LDH was higher when duration of unconsciousness was longer and post-traumatic amnesia exceeded more than 1 day.

In patients with contusion, a significant increase in the serum LDH level was found on the 1st day, which remained elevated on the 5th day. On the first day, the mean serum LDH (μ) was 458.1 IU/L, with a standard error of 58, t-value of 5.8, degree of freedom (df) of 37 and P<0.001. On the 5th day, the mean serum LDH remained elevated with a mean of 479 IU/L, standard error of 90, t-value of 3.93, degree of freedom (df) of 18 and P<0.001.

In patients with extracerebral hemorrhage, the mean serum LDH was significantly raised as compared to the normal control group, with a mean of 377 IU/L, standard error of 52.6, t-value of 4.5, degree of freedom of 18 and P<0.001.

In patients with pneumocephalus, on the 1st day the mean serum LDH was 378 IU/L, with a standard error of 90, t-value of 7.60, degree of freedom of 12 and P<0.05. On the 5th day, the mean serum LDH was 345 IU/L, with a standard error of 67.8, t-value of 4.1, degree of freedom of 10 and P<0.01.

In adult patients with cerebral oedema, the mean serum LDH was 249 IU/L, with a standard error of 1, t-value of 7.2, df of 11 and P<0.001. While children with cerebral oedema had a mean serum LDH of 460 IU/L, with a standard deviation of 67, t-value of 25 and P<0.001. The mean serum LDH was significantly higher in children compared to adults in the same group of head injury (cerebral oedema).

In patients with diffuse axonal injury, the mean serum LDH was 448.6, with a standard deviation of 113.07, t-value of 7.2, df of 11 and P<0.05.

In patients who died of head injury, the mean serum LDH was 582.7 IU/L, with a standard deviation of 129.6, t-value of 34, df of 18 and P<0.01, suggesting that serum LDH activity correlates with disease severity and can be an important prognostic tool, together with clinical radiological assessment, in predicting the outcome of head injuries.

DISCUSSION

Results of the study suggest that there is definite correlation between increase in serum LDH activity and severity of head injury. There is corresponding increase in LDH activity with the increase in duration of unconsciousness and post-traumatic amnesia. Estimation of serum LDH can be used effectively to predict the extent of brain damage. Serum lactate dehydrogenase was highest in patient who died of head injury. Out of the other groups of head injury, serum LDH was highest in the contusion group and remained elevated on the 5th day of admission; some of these patients died suggesting the need of close monitoring of the patients of contusion injury with markedly raised LDH level.

Serum LDH can play an important role in the management of such patients by predicting the outcome and need of close monitoring. High mean serum LDH was found in patients with poor outcome, and LDH was consistently raised throughout the period of study in the groups of the severely-disabled and of the dead. Thomas and Rowan (1976) correlated the serum isoenzymes LDH-1 with the type of brain damage and eventual outcome and concluded that LDH was raised after head injury. A similar conclusion was drawn by Lindlom and Aberg (1972). We concluded that serum LDH can itself give adequate information regarding the extent of brain injury.

Patients with extracerebral hemorrhage have relatively good outcome when compared to the contusion group, which was also revealed when the serum LDH was compared between...
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the two groups. Half of the patient underwent surgical intervention, 10% died and 40% had good survival.

Patients with diffuse axonal injury have poor outcome and their serum LDH levels were markedly raised, close to the contusion group. Patients in this group had very low GCS scores at the time of admission. Markedly raised levels of serum LDH in patient with low Glasgow Coma Scale scores and non-specific CT findings are helpful in predicting the progress and outcome of disease and also in planning further management.

Adults with cerebral oedema had marginally raised serum LDH activity and good survival. However, children with cerebral oedema showed significantly raised serum LdH activity compared to adults in the same group of head injury, but had good outcome. The reason remains to be investigated by further studies.

Serum LDH activity estimation with clinicoradiological evaluation can help in prediction of the outcome of head injury and also be helpful in decision-making on further management. Lactate dehydrogenase is a cytoplasm enzyme present in brain, is released into the blood when the brain is injured, and the rise of its serum level indicates the degree of brain damage. We conclude that measurement of serum LDH can be used effectively in the management of head injury by indicating the extent and type of brain damage at an early stage and in assessing the prognosis.

References

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