Role of Serum Lactate Dehydrogenase in Isolated Head Injury

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Abstract

Keywords

- surgery
- diagnostic tests
- head injury
- survival after head injury
- prognostic test

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 (LDH). In our study, we included 100 patients with isolated head injury arriving at trauma center, PGIMS Rohtak within 24 hours of injury, studied levels of serum LDH on days 1, 3, and 7 of injury, and concluded that levels have diagnostic as well as prognostic significance.

Introduction

Head injury is the major cause of both morbidity and mortality, which includes > 10 million cases annually. Traumatic brain injury is a neurosurgical emergency, and life can be saved by timely intervention. Thus, for predicting prognosis, an early prediction of survival and functional outcome appears to be important, and it allows for informed counseling of relatives and helps the treating physician decide aggressiveness of treatment. Cases of head injury can be divided into primary and secondary brain injury. The secondary insult (secondary damage, delayed nonmechanical damage) represents consecutive pathologic processes initiated at the moment of injury with delayed clinical presentation. Cerebral ischemia and intracranial hypertension refer to secondary insults, and in treatment terms, these types of injury are sensitive to therapeutic interventions. Therefore, it will lead to different outcome if any intervention is done.

An ideal marker is one that is quickly and simply measured in the serum. Serum is preferred over cerebrospinal fluid (CSF) because it is more readily available than CSF. Above all, however, ideal markers of brain damage should be both highly brain specific and sensitive. Lactate dehydrogenase (LDH) catalyzes oxidation of lactate to pyruvate and is widespread in many body tissues. LDH has five isoenzymes with different electrophoretic properties. In patients with trauma and

head injury, 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. Elevated serum LDH as a marker for diagnosis and assessment of severity of head injuries has gained interest in recent years, and we are more focusing on assessing the degree of brain damage by estimating serum LDH. 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.¹ Patients with different types of brain injury may have similar clinical pictures. 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.

Materials and Methods

In our study, total 100 patients were screened for inclusion and exclusion criteria. Patients arriving in emergency and trauma center were included in study after their written informed consent about participation in the study was obtained. They were explained that study is for academic purpose only and that it would not alter their treatment. Inclusion criteria included patients of age group 16 to 60 years,

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having isolated head injury with Glasgow coma scale (GCS) < 15, arriving at department within 24 hours of trauma, and willing to participate in study. Patients who were excluded were with GCS = 15 and other associated injury. No control groups were included in the study, and level of LDH estimated was compared with subgroups and repeat value on days 3 and 7. A detailed history of patients was taken from their attendants, if possible, and mode of trauma, history of loss of consciousness, posttraumatic amnesia, scalp bleed, and ENT (ear-nose-throat) bleed followed by detailed head-to-toe general physical examination of patients was conducted with special emphasis on systemic signs of blood loss and intracranial hypertension, vomiting, blood pressure, and pulse rate.

Patients' GCS was calculated and classified on the basis of GCS and pupillary reaction into three categories: mild (GCS 13–15), moderate (GCS 8–13), and severe (GCS < 8).

For LDH estimation, we used calorimetric assay² for quantification of serum LDH activity. Blood samples were centrifuged to separate the serum. Serum LDH was analyzed. Patients displaying the danger signs were sent for computed tomographic (CT) imaging of the head once the vitals were stabilized. Patients were classified on the basis of CT finding into seven groups: hemorrhagic contusion (HC), subdural hemorrhage (SDH), pneumocranium (PC), extradural hemorrhage (EDH), subarachnoid hemorrhage (SAH), depressed fracture (DF), and diffuse axonal injury (DAI). Patients' GCS was noted after 12 hours. If patients' GCS fell or tracheostomy was required, they were tracheostomized after proper consent and documentation. Repeat level of serum LDH was analyzed on days 3 and 7 of trauma.

Outcome of patients will be divided on the basis of clinical examination into four groups: dead, severely disabled, moderately disabled, and good. The level of serum LDH was compared in all the four groups with radiologic and clinical correlation. The collected records and data were analyzed

statistically by using chi-square test, paired *t* test, and repeated measure ANOVA (analysis of variance) test.

Observation and Results

In our study, patients' mean age was 34.375 years with range of 16 to 60 years. Most patients of trauma were of young age group, and male patients (*n* = 89) outnumbered female patients (*n* = 11).

In our study, we divided total head injuries into mild, moderate, and severe on the basis of GCS score. In case of mild head injury, it was raised on day 1 and then started decreasing, whereas in case of moderate head injury, the levels were less on day 1 and then started decreasing with mean value of 483.08 on day 1, 448.4 on day 3, and 428.68 on day 7 (►Table 1). Therefore, we conclude from these data that level of rise in serum LDH was significant (*p* < 0.01) in patients with severe head injury (GCS 3–8), it and can differentiate severe cases from mild and moderate, but it was poor in differentiating mild and moderate head injury.

We further divided patients on the basis of CT finding into seven groups: HC, SDH, PC, EDH, SAH, DF, and DAI. Levels of serum LDH were estimated in each group for days 1, 3, and 7, and their values were tabulated (►Table 2). We compared the data using repeated measure ANOVA test and concluded that serum LDH has significant diagnostic role in head injury.

Other factors that suggest severity of head injury include duration of loss of consciousness, posttraumatic amnesia, and GCS. Out of 100 patients, loss of consciousness was found in all patients with head injury; however, its duration had significant correlation with outcome. We divided duration into four categories as shown in ►Table 3: < 1, 1 to 12, 12 to 24, and > 24 hours. We found that most patients with duration < 12 hours had mild head injury and good outcome. As per

Table 1 Severity of head injury

Severity of head injury	GCS range	No. of patients	Serum LDH day 1	Serum LDH day 3	Serum LDH day 7
Mild	13–15	32	504.75 ± 152.36	443.18 ± 125.7	408.38 ± 120.9
Moderate	9–12	46	483.08 ± 143.93	448.4 ± 95.09	428.68 ± 84.75
Severe	3–8	22	631.81 ± 215.4	575.75 ± 190.42	476.25 ± 107.2

Abbreviation: LDH, lactate dehydrogenase.

Table 2 Diagnostic significance of serum LDH

Injury	No. of patients	Day 1	Day 3	Day 7	<i>p</i> -Value
HC	41	560.17	497.43	475.93	< 0.001
SDH	26	540.5	512.9	446.54	< 0.001
PC	11	396	358.36	332.7	< 0.001
EDH	8	553	470	463	< 0.001
SAH	7	571.28	415.74	403.42	< 0.001
DF	5	396	408	349.2	< 0.01
DAI	2	743	706	520	< 0.01

Abbreviations: DAI, diffuse axonal injury; DF, depressed fracture; EDH, extradural hemorrhage; GCS, Glasgow coma scale; HC, hemorrhagic contusion; LDH, lactate dehydrogenase; PC, pneumocranium; SAH, subarachnoid hemorrhage; SDH, subdural hemorrhage.

► **Table 3**, the level of serum LDH was 450 in patients with duration of loss of consciousness < 1 hour. Further, there was decrease in the level on day 3 that further decreased on day 7. Patients with duration of 1 to 12 hours had mean serum LDH 519 on day 1, 526 on day 3, and decrease to 469 on day 7. Patients with duration between 12 and 24 hours had mean serum LDH of 548 on day 1 and then decreased to 452 and 426 on days 3 and 7, respectively. However, patients with duration > 24 hours had highest mean value of serum LDH, that is. 689.23 on day 1, 598.94 on day 3, and 442 on day 7. In our study, the level of rise in serum LDH was in direct relation to duration of consciousness indicating prognostic significance.

► **Table 4** summarizes that patients with LDH in range of 474.53 ± 135.48 have good outcome. On serially monitoring its value, we can further comment on survival of patients. It was mildly raised in case of patients with good survival indicating less brain insult. Whereas in case of dead and severely disabled, it was significantly raised throughout the study indicating poor prognosis, the level > 600 indicates the close monitoring of patients or early intervention focusing toward severe brain injury.

Discussion

In our study, we included 100 cases arriving at trauma center and emergency department of Pt. B.D. Sharma PGIMS Rohtak and concluded that there was significant rise in level of serum LDH in case of patients with severe head injury. We concluded from the data and found that the rise in the level of serum LDH is in direct proportion to severity of head injury. It was found that patients having mild head injury have borderline or mild rise in level of serum LDH whereas those with severe head injury have significant rise in serum LDH level. Rao et al³ concluded that there is corresponding increase in LDH activity with the increase in duration of unconsciousness and posttraumatic amnesia, and that estimation of serum LDH can be used effectively to predict the extent of

brain damage. Lindlom and aberg⁴ drew similar conclusion. Jain et al⁵ found that mean level of serum LDH was higher, with duration of unconsciousness and posttraumatic amnesia exceeding > 1 day. We used repeated measure ANOVA test to check relation between loss of consciousness and rise in serum LDH and found $p < 0.001$ suggesting significance of data. Thus, we can say serum LDH is raised significantly in case of duration of loss of consciousness > 24 hours.

Lindlom and Aberg⁴ found that level of serum LDH is increased in head injury and rise to peak at 7 days in case of extracerebral hematoma. They also found that there is less degree of rise in serum LDH level in nontraumatic brain injury. Level of rise in LDH was in direct proportion to severity of injury, and it was found that prognostic significance was less certain, but raised level was seen in most cases with severe head injury. However, in our study, there is statistically significant prognostic role of serum LDH with $p < 0.001$. Rabow et al and Hausdorfer et al studied effect of serum LDH on a series of patients in relation to serial LDH isoenzyme up to 1 month of injury⁶ and found that there is significant level of rise in serum LDH in head injury indicating its diagnostic and prognostic significance. Similarly, in our study there is prognostic significance of LDH is statistically significant ($p < 0.001$), and results are similar to this study. Thomas and Rowan⁷ studied on 92 surgical patients with damaged brain and used LDH1 and LDH2 to assess severity of brain injury. Because we are ruling out extracerebral injury and serum LDH is more easily available than LDH1, we go for total serum LDH and conclude that raised serum LDH indicates degree of parenchymal damage in head injury. Jain et al⁵ studied the diagnosis and assessment of severity of head injury and found that serum LDH was raised in patients with parenchymal brain injury and was raised more in patients died of head injury, thus indicating prognostic role and having similar results with our study. They even concluded that the patients with loss of consciousness and posttraumatic amnesia > 1 day have significantly higher LDH. Our study has similar outcomes with

Table 3 LDH and its relation with duration of loss of consciousness

Duration of unconsciousness (h)	No. of patients	Mean LDH on day 1	Mean LDH on day 3	Mean LDH on day 7	p-Value
< 1	53	451.81	420	399.01	< 0.001
1–12	14	519	526	469	< 0.001
12–24	12	548	452	426	< 0.001
> 24	21	689.23	598.94	442	< 0.001

Abbreviation: LDH, lactate dehydrogenase.

Table 4 Serum LDH correlation with outcome

Outcome	Day 1	Day 3	Day 7	p-Value
Good	474.53 ± 135.48	430.32 ± 95.91	400.58 ± 76.65	< 0.001
Moderately disabled	547.06 ± 132.23	498.25 ± 98.28	506.18 ± 101.28	< 0.001
Severely disabled	585.88 ± 52.14	590.44 ± 92.89	563.77 ± 101.28	< 0.001
Dead	852.5 ± 210.20	855 ± 141.50	–	< 0.01

Abbreviation: LDH, lactate dehydrogenase.

this study group, showing diagnostic and prognostic significance of serum LDH in head injury. Sohlepur et al⁸ studied the level of rise in serum LDH in head injury and found that there is marked elevation in serum LDH in head injury. More specifically their study was able to differentiate between the patients who will die or not because of head injury. In view of close correlation between duration of unconsciousness and serum LDH, estimation of serum LDH can be used effectively to predict the severity of brain damage.

Conclusion

The level of serum LDH was significantly raised in case of severe head injury with GCS < 8 and was 631.81 on day 1, 575.75 on day 3, and 476.25 on day 7, whereas in case of mild and moderate head injury, the value was far away from severe head injury. Therefore, serum LDH can easily differentiate patients with severe head injury from those with mild to moderate head injury. On basis of CT finding, the level was maximum in DAI patients with mean value 743 on day 1, and it was raised throughout the study with mean value of 520 on day 7. In case of SAH and IC bleed, the level was second highest with mean value of 571.28 on day 1 that decreased to 403 on day 7. In case of HC, levels were increased with mean value of 560.17 on day 1, which decreased to 475.93 on day 7. EDH and SDH have comparable values indicating extra-cerebral hematoma with LDH on day 1 in EDH 553, 470 on day 3, and 463 on day 7. SDH value measures slightly lower than EDH counting value of 540 on day 1, 512.9 on day 3, and 446.54 on day 7. PC and DF of the brain have slightly low rise in serum LDH, and both have the same mean value on day 1, that is, 396, and it decreased to 358.36 on day 3 and 332.7 on day 7 in PC, whereas in DF, there was rise of 408 in level of serum LDH on day 3 and then decrease to 348 on day 7. We find that data are statistically significant, and that there is relation of rise in serum LDH with head injury.

Level of rise in serum LDH is related to duration of unconsciousness in direct proportionless raised if duration < 1 hour

and two to three times raised with duration exceeding 24 hours. Estimation of serum LDH can be used effectively to predict the extent of brain damage. It was found that high mean serum LDH level was raised on day 1 in good survival (474.53 ± 135.48) and then decreased to borderline value till day 7. In moderately disabled, the level (547.06 ± 132.23) was much higher on day 1 but was on decreasing trend till day 7. It was consistently raised in severely disabled (585.88 ± 52.14) and dead groups (852.5 ± 210.20). Therefore, from LDH value we can differentiate the patients between good survival, moderately disabled, severely disabled, and those who can die. Thus, it has important prognostic role.

We conclude that serum LDH has important diagnostic role as it can predict the severity of injury with some precision and has greater prognostic role. It can tell which patients are going to die and which ones are not. Patients with high value of serum LDH throughout this study required close monitoring and timely intervention.

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