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Serum Lactate Dehydrogenase in Children with Sickle Cell Disease

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Summary

Adebonojo, Festus O. (1975). *Nigerian Journal of Paediatrics*, **2** (**2**), 38. **Serum Lactate Dehydrogenase in Children with Sickle cell disease.** Measurement of serum LDH is frequently employed diagnostically in disease states associated with tissue destructions of various types. Since children with sickle cell disease suffer from chronic red cell destruction and associated necrosis of other body organs, it is important to recognize that this enzyme is normally elevated in sera of patients with sickle cell and sickle-thalassaemia states during periods when they are free of intercurrent illnesses. In this study, both forward and backward reactions catalyzed by lactate dehydrogenase were measured using pyruvate and lactate as substrates respectively. Serum levels of LDH were twice as high in children with sickle cell disease as in those with sickle trait or normal haemoglobin. Children with Sickle-Thalassemia had levels which were intermediate but still significantly higher than those of sickle trait or normal haemoglobin. The role of haemolysis and the contribution made by hepatic-splenic necrosis in LDH elevation in sickle cell disease are discussed.

MANY investigations (Zimmerman and Weinstein, 1956; Zimmerman, West and Heller 1958; Heller, *et al.*, 1960 a and b; Gordon and Enari, 1959) have shown that the serum levels of lactate dehydrogenase (LDH) is moderately elevated in sickle cell disease and markedly elevated in megaloblastic anaemia. In most of the other types of anaemia, the serum levels of LDH are normal (Zimmerman, West and Heller, 1958).

While in megaloblastic anaemia, the very high serum LDH levels have been attributed to the release of the enzyme from the marrow megaloblasts rich in LDH (Stein, *et al.*, 1969), in sickle cell disease and sickle-thalassaemia, the elevation is probably due to the increased erythrocyte destruction in circulation since red cells are also known to have high levels of this enzyme (Blanchaer, Weiss and Bergsagel, 1951).

Since measurements of serum LDH activities are frequently undertaken in children and adults with acute tissue damages of various types, it is important to recognize the significance of a normally elevated serum LDH level in certain disease states, especially those like sickle cell disease in which crises may be associated with pains localized in some crucial locations such as in the hepatic and precordial areas. The problem may be compounded by acute tissue damage which in itself may produce elevations in serum LDH values.

In order to define the extent of the elevation of serum LDH and the relationship between the forward and backward reactions catalyzed by this complex enzyme, both pyruvate and lactate have been employed as substrates to measure the enzyme in the sera of normal children and children with sickle cell disease and sickle-thalassaemia.

Materials and Methods

The 29 children in this study, aged 11 months to 10 years, receive health care at the Rebound Health Centre which is located in a predominantly black community in South Philadelphia. The demographic and haematologic characteristics of the childhood population from which they derive have been previously reported (Adebonojo, 1973, 1974). Six children with sickle cell disease (SS haemoglobin electrophoretic profile), three with sickle-thalassaemia (S-Thal. profile), ten with sickle-trait (AS profile) and ten controls with normal haemoglobin electrophoretic profile (AA profile) were venipunctured at routine visits for well-child care. At the visits none had any evidence of intercurrent illnesses, nor did the children with sickle cell disease have any evidence of crisis, haemolytic or aplastic. The serum in each case was immediately separated from the red cells by centrifugation ensuring that no haemolysis or red cell contamination of the serum occurred. Within two hours of venipuncture, duplicate determinations of the activities of lactate dehydrogenase (E.C.1.1.1.27) in both directions of the enzyme reactions were done. In the forward reaction, pyruvate was employed as substrate using a modification of the technique of Wroblewski (1955). In the reverse reaction, lactate was used as substrate employing a modification of the technique of Wacker (1956). All assays were performed at 30°C in a Hitachi digital spectrophotometer 191 connected to a sequential automatic printer (Arthur Thomas & Co.). Activities were calculated and expressed as milli-units per millilitre of serum (mU/ml), where one milli-unit of enzyme was the amount of enzyme necessary to cause the consumption of one micromole of substrate per minute.

Results

The mean activities of serum LDH with pyruvate as substrate was approximately four times as high as the mean activities with lactate as substrate in nearly all measurements (Table).

TABLE

Serum values of LDH (with pyruvate and lactate as substrate) in the different groups of Children (milliunits/ml of serum).

	SS $N=6$	*S-Thal* $N=3$	*AS* $N=10$	*AA* $N=10$
LDH-Pyruvate substrate	676 ± 67	490 ± 61	352 ± 47	323 ± 49
LDH-Lactate substrate	153 ± 15	121 ± 9	88 ± 10	83 ± 13

With pyruvate as substrate, the mean activity of LDH in the sera of the six children with SS-profile was 676 mU/ml compared with 490 mU/ml for children with S-Thal profile, 352 mU/ml for children with AS profile and 323 mU/ml for children with AA profile. The difference in the measured activities of LDH in children with SS and S-Thal profiles on the one hand and the children with AS and AA profiles on the other was statistically significant ($p < 0.001$). There was no significant difference in the measured activity levels of sera of children with AA and AS profiles. The LDH activity levels in children with S-Thal profile was statistically significantly higher than the levels in children with AA and AS ($p < 0.05$)

With lactate as substrate, the activities of LDH in the sera of children with SS profile was 153 mU/ml, with S-Thal profile 121 mU/ml, with AS profile 88 mU/ml and with AA profile 83 mU/ml. The statistical differences in these assays were similar to those found when pyruvate was used as substrate.

Discussion

Serum LDH has been studied in 29 children aged 11 months to 10 years. Six children with sickle cell disease had twice the levels of serum LDH as the 20 children with either AA or AS profiles. The three children with sickle thalassaemia had intermediate levels of serum LDH. This agrees with findings previously reported by Heller, *et al.*, (1960) and by Zimmerman, *et al.*, (1958) in which patients with SS and SC profiles have elevated serum LDH, while patients with S-Thal had intermediate values and patients with AS profile had normal values. It also agrees with the usual observation that patients with S-Thal profile generally have intermediate haemoglobin values when compared with patients with SS and SC profiles on the one hand or patients with AA and AS profiles on the other. It should be noted that the haemoglobin values of children with AS profile is similar to those with AA profile (Adebonojo, 1974 Brown, *et al.*, 1972). Patients with SS, SC and S-Thal profile have varying degrees of increased haemolysis, which as was suggested by Heller, *et al.*, (1960 b) may be the primary basis for their elevated serum LDH activities. These authors also suggested that hepatic necrosis may contribute to the elevated serum LDH levels seen in patients with sickle cell disease. The contribution made by hepatic and splenic necrosis, frequent concomitants of sickle cell disease, to the elevation of serum LDH levels in these children awaits elucidation and it will probably require that detailed isozyme studies of this complex enzyme be done in children with sickle cell disease in order to better define the role of hepatic and splenic abnormalities in serum LDH elevation.

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