THE VALUE OF SERUM β-GLUCURONIDASE ESTIMATION IN ASSESSING THE RESPONSE TO THE THERAPY FOR PEMPHIGUS

G. SULOCHANA, * S. M. MANIVANNAN † AND L. PADMANABHAN ‡

Summary

Successive estimation of β-glucuronidase, a lysosomal acid hydrolase, was carried out in 20 cases of pemphigus, before and after administering corticosteroid, which is the drug of choice in the treatment of pemphigus. It is observed that there is significant decrease in this enzyme activity, when the lysosomal membrane stability is maintained by adequate dosage of corticosteroids. The value of successive estimation of β-glucuronidase is discussed and the enzyme activity is suggested as a biochemical marker in assessing the response to treatment as well as maintenance therapy with corticosteroid.

KEY WORDS : β-glucuronidase, pemphigus.

Introduction

Pemphigus vulgaris is a rare relapsing disease, manifesting as chronic vesiculo bullous eruptions on the skin and mucous membranes.

β-glucuronidase is one of the 24 lysosomal enzymes and its activity in human skin is seen largely in the epidermis Its concentration in epidermis is 16 times greater than that in the dermis[1]. It is established that β-glucuronidase is elevated in various types of cancer and other disease states[2,8]. It is found to be selectively released from leukocytes when these were incubated with insoluble immune complexes and also from leukocytes of patients with immune complex disease, when incubated with their own plasma[9]. The lysosomal acid hydrolases such as β-glucuronidase and acid phosphatase are found to be increased in the serum of patients with pemphigus, indicating damage to lysosomal membrane. Corticosteroid, one of the stabilizers of lysosomal membrane, is the drug of choice in the treatment of pemphigus. The present study was conducted to ascertain whether estimation of β-glucuronidase could be used as a biochemical marker to assess the dose of corticosteroid in the treatment of pemphigus as well as to regulate the maintenance dose of the drug in the therapy for this disease.

Material and Methods

Twenty cases of proven pemphigus with typical clinical features of pemphigus vulgaris were selected for this

* Professor of Biochemistry, Coimbatore Medical College, Coimbatore.
† Professor of Dermatology.
‡ Tutor in Pathology, Thanjavur Medical College, Thanjavur-613004.
Request for reprints : Dr. L. Padmanabhan, MBBS., DD., Department of Pathology, Thanjavur Medical College, Thanjavur-613004
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study. The age group of patients varied from 30 to 45 years and they were treated with corticosteroid and broad spectrum antibiotics to prevent secondary infection.

Blood samples were collected under sterile conditions before the administration of corticosteroid and β-glucuronidase was estimated on fresh, non-haemolyzed and non-icteric sera. The patients were treated with doses varying from 30–50 mgm of prednisolone per day depending on the severity of the disease. Successive estimation of this enzyme in the serum of each patient was carried out on every 10th day.

Serum β-glucuronidase was estimated by the method described by Plaice et al[10], using phenolphthalein mono-β-glucuronic acid as substrate (obtained from Sigma, U.S.A)., with a slight modification in the incubation time which was reduced from 16 hours to 5 hours.

Results

The enzyme activity is expressed as U/L. One unit is the enzyme activity that liberates 1 μmol of phenolphthalein from phenolphthalein glucuronide/minute from one litre of serum at 38°C.

U/L is calculated as follows :

$$U/L = \frac{\text{n.mole phenolphthalein}}{t \times 60 \times 0.2}$$

t = time of incubation in hours.
Normal value for adults is 0.525 ± 0.142.

The patients were divided into 2 groups, depending on the decrease in the activity of the enzyme as a response to the therapy.

First group : Cases showing clinical improvement with significant decrease in serum β-glucuronidase within 10 days of 30–50 mgms per day prednisolone.

Second group: Cases showing clinical improvement in the old lesions, but failing to show decrease in enzyme activity on 30-50 mgms of daily prednisolone within 10 days of starting treatment and also developing fresh lesions. These cases showed decrease in serum β-glucuronidase on further increase in the dose of corticosteroid at which time all the lesions also improved.

Fifteen out of twenty patients fall under the first group and five in the second group. In the first group gradual decrease in serum β-glucuronidase was noticed within 10 days and reached the normal range in a period of 40 days. In the second group patients failed to show decrease in serum β-glucuronidase in the first 10 days, but on further increase in corticosteroid therapy they showed gradual decrease in the enzyme activity although failing to reach the normal range even on 40th day. Recurrences were seen frequently in this group (Table 1).

Discussion

Initial treatment and an effort to determine the maintenance dose of corticosteroids are necessary to perpetuate remission of the disease. It is known that corticosteroid is the drug of choice for pemphigus, which stabilizes the lysosomal membrane and thereby prevents the spillage of lysosomal enzymes into blood. As β-glucuronidase is one of the acid hydrolases present in lysosome, estimation of this enzyme in serum will be a good index to assess the lysosomal membrane stability. Elevated enzyme level is due to spillage of enzyme into the blood and is an indication for further increase in dosage of corticosteroid. A large number of patients have been maintained in a constant state of remission over a period of several years on adequate corticosteroid therapy. On the other hand, death usually occurs in two years, if corticosteroid therapy is not continued and recurrences invariably develop when adequate dose of corticosteroid is not administered.

TABLE 1

Successive estimation of serum β-glucuronidase before and after oral corticosteroid therapy in pemphigus vulgaris (Mean ± SE).

Group	No. of cases	B. glucuronidase U/L				
		Before Steroid therapy	10th day of steroid therapy	20th day of steroid therapy	30th day of steroid therapy	40th day of C. S. therapy
First group Cases showing immediate response to therapy with 50 mgm of prednisolone	15	0.957 ± 0.308	0.866 ± 0.166	0.766 ± 0.122	0.673 ± 0.137	0.550 ± 0.142
Second group * Cases not showing immediate response to therapy with 50 mgm of prednisolone	5	0.996 ± 0.250	0.990 ± 0.286	0.868 ± 0.220	0.740 ± 0.182	0 650 ± 0.198

* Prednisolone dose was increased to 60 mgm from 50 mg/day after 10 days.

In this study, 5 out of 20 cases have not shown significant decrease in β-glucuronidase activity on the routine dose of corticosteroid therapy for a period of 10 days even though there was distinct improvement of the lesions clinically. Further increase in the dose of corticosteroid decreased the enzyme activity in these cases. This indicates that the dose of corticosteroid was inadequate to achieve the lysosomal stability and these cases require further increase in the dose, to prevent relapse. 15 cases in the first group showed distinct decrease in the enzyme activity. The enzyme activity is proportional to the severity of the lesions and reflect the instability of lysosomal membrane.

It is concluded that the estimation of serum β-glucuronidase is a good index in assessing the dose for the initial treatment and also maintenance therapy with corticosteroid in pemphigus.

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ABSTRACT

Contact dermatitis due to calcium ammonium nitrate. J. S. Pasricha and Ramji Gupta, Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi - 110029.

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A 60 year old farmer developed generalized dermatitis after using calcium ammonium nitrate as a fertilizer. Relapses of the dermatitis generally coincided with his visits to the field and especially during the sowing season. Contact hypersensitivity was confirmed by repeated patch tests with the aqueous paste of calcium ammonium nitrate. The same paste did not produce a positive patch test reaction in any of the 13 controls.