SIGNIFICANTLY LOW LEVELS OF URINARY PEPSINOGEN IN TYPE 1 DIABETES

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ABSTRACT

Pepsinogen has been implicated in autoimmune disorders. To verify the hypothesis that it may have a role to play in type 1 diabetes mellitus, 24 hour urinary pepsinogen was estimated in 45 subjects of type 1 diabetes, 31 subjects with type 2 diabetes and 14 control subjects. The mean values in the respective groups were 397.77 ± 45.5; 927.67 ± 224.72 and 793.37 ± 325.37 units per ml respectively. The mean values of 24 hour urinary pepsinogen were lower in type 1 diabetes when compared to type 2 diabetes and controls ($P<0.05$ & $P<0.05$ respectively). Estimation of 24 hour urinary pepsinogen may be used as a marker for type 1 diabetes.

KEW WORDS: 24 hour urinary pepsinogen : Type 1 diabetes, Type 2 diabetes.

INTRODUCTION

Pepsin is implicated in self / non-self discrimination by macrophages during phagocytosis in a hypothesis proposed by Ohnishi [1]. Pepsin has also been shown to act as an "immune complexase" because it selectively decomposes immune complexed at neutral pH. Thus pepsin / pepsinogen has been shown to play a role in autoimmune abnormalities [2]. The effects of pepsin in autoimmune glomerulonephritis in mice was also investigated [2]. It was found that administration of pepsin resulted in reduction of serum levels of immune complexes and suppressed progressive increase in urinary excretion of proteins. It is well known that pepsinogens in the serum are grouped into two classes : PGA (formerly PG I) and PGC (formerly PG II) [3-4]. Human PGA displays highly polymorphic isozymogen patterns, some of which are active at near neutral pH. Moreover pepsin / pepsinogen irrespective of its origin (from macrophages or chief cells of gastric mucosa) has the same immunoregulatory properties [1]. PGA is excreted in the urine because of its relatively low molecular weight and therefore pepsinogen activity in urine represents PGA activity. In contrast to this PGC has high molecular weight and is not excreted in the urine. This urinary pepsinogen quantitation provides and indirect reliable estimate of PGA activity. The choice of urinary pepsinogen estimation is also relevant from the genetic point of view because the gene cluster fro PGA on autosome 11 q, is in close linkage with insuling gene [5]. In view of this urinary pepsinogen levels were determined in type 1 and type 2 diabetes cases for comparative analysis. We are unaware of any such studies in diabetic cases using urinary pepsinogen as a marker. Thus this study contributes new information relating to pepsinogen activity in diabetic cases.

MATERIALS AND METHODS:

Patients visiting the Endocrinology unit of Gandhi General Hospital, and Princess Durru Shehvar Hospital (Hyderabad) were selected. The clinical diagnosis as suffering from diabetes mellitus as well as classification of cases into type 1 and type 2 diabetes was according to the criteria laid down by World Health Organization [6]. Blood sugar levels were estimated according to glucose oxidase method (Glucose oxidase kit, GOD –PAP/End point, Kaizen Diagnostics, Hyderabad). None of the cases were suffering from malnutrition. The type 1 cases were found to be positive for ketosis upon withdrawal of insulin while none of the type 2 cases showed ketosis. A total of 45 cases of type 1 diabetes, 31 cases of type 2 diabetes and 14 control subjects were studied. Urinary pepsinogen values were determined in both the types of diabetes mellitus i.e. type 1 and type 2 and compared with that of control subjects. The method followed for estimation of urinary pepsinogen was that described by Mirsky et al (1948) employing acidified haemoglobin as a substrate [7].

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RESULTS:

The mean urinary pepsinogen levels in type 1 and type 2 cases were 397.77 ± 45.5, 927.67 ± 224.72 respectively while the control group had a mean level of 793.37 ± 325.37 units per ml per 24 hours (Table 1).

Table 1 : Urinary pepsinogen levels in Diabetes mellitus cases and control subjects

Category	Number	Mean ± S.E.
Type 1 (IDDM)	45	397.77 ± 45.5 *
Type 2 (NIDDM)	31	927.67 ± 224.72
Control	14	793.37 ± 325.37

* $P < 0.05$ - Type 1 vs Type2
* $P < 0.05$ - Type 1 vs Controls

The mean level in type 1 diabetes cases was found to be significantly low compared to controls and type 2 diabetes group ($p < 0.05$). The urinary pepsinogen values in type 2 diabetes (927.67 ± 224.72) ($p<0.05$) were higher than that of control subjects as well as type 1 dibetes cases.

DISCUSSION:

An important observation is the significantly low levels of urinary pepsinogen activity in type 1 diabetes. It is known that pepsin serves as an "immune complexase" and low levels observed in this group indicate augmentation of autoimmune process by less efficient clearance of circulating immune complexes and certain other unknown mechanisms that may contribute to autoimmunity in type 1 diabetes cases. This marker is also of potential importance of being used as a parameter to distinguish type 1 diabetes cases from type 2 diabetic subjects. Thus this study reports new information regarding decreased urinary pepsinogen activity in type 1 diabetes and its possible role in immuno-regulation.

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