Plasma Prolactin Response to Thyrotropin Releasing Hormone in Children with Newly Diagnosed Insulin Dependent Diabetes

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ABE, K., M.ATSUURA, N., FUKUSHIMA, N., NOHARA, Y., FUJITA, H., FUJIEDA, K. and KATO, T. Plasma Prolactin Response to Thyrotropin Releasing Hormone in Children with Newly Diagnosed Insulin Dependent Diabetes. Tohoku J. exp. Med., 1983, 140 (1), 29-34 — The basal and TRH-induced prolactin (PRL) and TSH secretions were examined in 14 children aged 4 to 13 years with newly diagnosed insulin dependent diabetes (IDD) within three weeks after diagnosis. Basal PRL levels did not differ from the values of control. In response to TRH, 6 out of 14 patients showed an exaggerated PRL response and 8 a normal PRL response. The basal and TRH-induced TSH secretions were normal, while plasma triiodothyronine (T₃) and thyroxine (T₄) concentrations were significantly (p<0.001, p<0.02) lower in patients than in controls. These findings suggest that a significant proportion of children with newly diagnosed IDD has an exaggerated PRL response to TRH, and TSH secretion remains unchanged despite significant decreases of circulating thyroid hormone levels.

Since it was reported that the administration of prolactin (PRL) elicited hyperglycemia (Rathgeb et al. 1971) and that an impaired glucose tolerance and hyperinsulinemia were observed after glucose load in patients with hyperprolactinemia (Landgraf et al. 1977), PRL has been considered to exert a diabetogenic action. It, therefore, seems to be of interest to explore PRL release in diabetes mellitus. The previous results on PRL release under basal condition and in response to provocative stimuli have been controversial; PRL secretions in response to stimuli have been reported to be exaggerated (Hanssen et al. 1976), blunted (LeRoith et al. 1979) or unchanged (Frøland et al. 1977; LeRoith et al. 1980). Since PRL secretion has not been well studied in children with insulin dependent diabetes (IDD), we have examined plasma PRL and thyrotropin (TSH) concentrations in children with newly diagnosed IDD under basal condition and in response to thyrotropin releasing hormone (TRH) stimulation.

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PATIENTS AND METHODS

Fourteen children (8 males, 6 females), aged 4 to 13 years with mean age of 7.7 years, were admitted to Hokkaido University Hospital for evaluation of polyuria, polydipsia, lassitude and so on. On admission all patients were newly diagnosed as juvenile IDD based on clinical and laboratory findings and were immediately treated with insulin administration. None of them had signs or symptoms of emotional disturbances or diabetic angiopathy. Plasma PRL and TSH responses to TRH were examined within three weeks after diagnosis. After an overnight fast, TRH was administered in an intravenous bolus of 5 μg/kg and blood samples were collected at 0, 15, 30, 60, 90 and 120 min after TRH stimulation as previously described (Abe et al. 1979, 1982). All insulin was withheld on the morning of the tests. Plasma PRL, TSH, thyroxine (T₄), and triiodothyronine (T₃) levels were measured by commercially available radioimmunoassay kits (Daiichi Radioisotope Lab, Eiken Chemical Co., Tokyo) and human prolactin (h PRL, Lewis No. 3) was used as a reference standard. Statistical analyses were performed by using Student’s t-test.

RESULTS

The basal PRL levels in diabetic males and females were 7.9±1.6 ng/ml (mean±s.E.) and 7.3±2.3 ng/ml, respectively, which were similar to those of controls in both sexes. In response to TRH, 5 out of 8 male patients (63%) showed a normal PRL response and 3 (37%) exaggerated PRL response, while 3 out of 6 female patients (50%) had a normal PRL response and 3 (50%) an exaggerated PRL response (Figs. 1 and 2). Thus, 6 out of 14 children (43%) with newly diagnosed IDD showed an exaggerated PRL response to TRH. The basal and TRH-induced TSH levels in diabetic children were within normal ranges in both sexes and none of them had an exaggerated TSH response to TRH (Fig. 3). Although plasma T₄ and T₃ levels in control (n=30) were 9.2±0.4 μg/100 ml and 179.7±6.3 ng/100 ml, respectively, plasma T₄ and T₃ levels in diabetic males were 7.2±0.8 μg/100 ml and 97.6±6.8 ng/100 ml, both of which were significantly lower (p<0.02, p<0.001) than those of control. Plasma T₄ and T₃ levels in diabetic females were 7.7±0.6 μg/100 ml and 112.0±17.6 ng/100 ml, respectively. The plasma T₃, but not T₄, level in diabetic females was significantly lower (p<0.001) than that of control. As shown in Fig. 4, there was no significant correlation between the peak levels of plasma PRL in response to TRH and plasma T₄ or T₃ concentrations, unlike in hyperthyroid patients (Abe et al. 1982).

DISCUSSION

Since PRL has been considered to be a diabetogenic hormone (Landgraf et al. 1977), we thought it of interest to explore PRL secretion in children with newly diagnosed IDD. The previous reports on basal PRL release and the response to provocative stimuli in patients with IDD have been controversial. Hanssen and Torjesen (1977) reported elevated PRL levels in diabetic ketoacidosis and Hunter et al. (1974) showed high basal PRL levels in patients without or with only mild retinopathy as compared to those in patients with severe retinopathy and controls. On the contrary, Bratusch-Marrain et al. (1980) did not find any changes in serum PRL levels in diabetic precoma and Frøland et al. (1977) described normal
basal and TRH-stimulated PRL levels in patients with and without retinopathy. Although LeRoith et al. (1979) described a nonresponsiveness of plasma PRL to arginine in IDD, Gray et al. (1979) showed a normal PRL response to arginine. Moreover, Drejer et al. (1977) reported a loss of diurnal variation in plasma PRL, but Hanssen et al. (1978) did not confirm this finding. Thus, the previous results obtained from adult patients with IDD on PRL secretions have been conflicting. There is no study, to our knowledge, about PRL release in children with newly diagnosed IDDM. In this regard, the present study demonstrates that although basal plasma PRL concentrations were within normal ranges in children with newly diagnosed IDD, a significant proportion of the patients (43%) had an exaggerated PRL response to TRH.

This finding is in accord with the report from Hanssen et al. (1976) who described a high PRL response to TRH in juvenile IDD.

The reason for the exaggerated PRL response is unknown. Although our
Fig. 3. Plasma TSH responses to TRH in eight diabetic boys (■—■), six diabetic girls (○—○) compared to that in 41 healthy children (△—△).

Fig. 4. Correlation between peak levels of plasma PRL after TRH and plasma T₄ or T₃ in diabetic boys (●) and diabetic girls (○).
previous study (Abe et al. 1982) demonstrated a negative correlation between the peak levels of plasma PRL in response to TRH and plasma T₃ levels in hyperthyroid children, such a correlation was not observed in patients with newly diagnosed IDD. The clinical significance of the exaggerated PRL response to TRH remains unknown. In view of a diabetogenic action of PRL, it may be of interest to determine whether the high PRL responder is related to the likelihood of poor control and/or retinopathy in future.

The present study also demonstrates the decreases in blood thyroid hormone levels in children with newly diagnosed IDD. This is in agreement with previous reports that circulating thyroid hormone levels, particularly T₃ levels, are low in diabetic patients with metabolic derangement (Saunders et al. 1978). It may be of interest to note that the basal and TRH-induced TSH secretions were within normal ranges in children with newly diagnosed IDD and none of them did exhibit the high TSH response to TRH, despite the decreases of circulating thyroid hormone levels. This finding is in accord with previous results (LeRoith et al. 1980) that the basal TSH secretion and the response to TRH were normal in diabetic patients with IDD, and may be compatible with the view (Gardner et al. 1979) that the reduction in the extrathyroidal conversion of T₄ to T₃ in fasting and nonthyroidal conditions is accompanied by a lower set-point of pituitary TSH secretory activity.

In summary, the present study demonstrates that significant proportion of children with newly diagnosed IDD has an exaggerated PRL response to TRH, and TSH secretion remains unchanged despite significant decreases of circulating thyroid hormone levels.

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References


