Nigerian Journal of Paediatrics 1989; 16 (1 & 2): 1-6

The Thyrotropin and Prolactin Reserves in Kwashiorkor and Marasmus

DOE ESANGBEDO* AND F A AKESODE**

SUMMARY

Esangbedo D O E and Akesode F A. The Thyrotropin and Prolactin Reserves in Kwashiorkor and Marasmus. Nigerian Journal of Paediatrics 1989; 15:0. Twenty four children were studied to determine the state of thyroid stimulating hormone (TSH) and prolactin (PRL) reserve in the pituitary gland in kwashiorkor and marasmus. The basal serum TSH was raised in the kwashiorkor ($3.8\mu U/ml \pm 2.2$, $p<0.05$) and marasmus groups ($3.9 \pm 1.8\mu U/ml$, $p<0.025$) when compared with the controls ($2.4 \pm 0.6\mu U/ml$). There was a prompt and significant rise of TSH in response to intravenous synthetic thyrotropin releasing hormone (TRH) in kwashiorkor ($p<0.005$) and marasmus ($p<0.0005$) as with the controls ($p<0.0005$). The basal serum PRL levels in the kwashiorkor and marasmus groups were not significantly different from that of the control group ($12.1 \pm 4.5ng/ml$, $14.1 \pm 5.3ng/ml$ and $16.2 \pm 4.7ng/ml$ respectively). The response of the serum PRL to intravenous synthetic TRH showed prompt and significant rise in the kwashiorkor group ($p<0.0005$), the marasmus group ($p<0.0005$), and the controls ($p<0.0005$). It is therefore, concluded that the reserve of TSH and PRL in the pituitary gland is adequate in kwashiorkor and marasmus.

College of Medicine, University of Lagos, Lagos.

Department of Paediatrics

***Senior Registrar**

****Senior Lecturer**

Correspondence:

Professor F A Akesode,
Department of Paediatrics,
Ogun State University Teaching Hospital,
Sagamu.

Introduction

THE presence of a low serum thyroxine (T_4) level in protein energy malnutrition is a common finding.[1-3] Various reasons have been offered for this low level. Serum thyroxine binding globulin (TBG), thyroxine prealbumin (TBPA) and albumin concentrations are low in these clinical situations. In caloric deprivation, the T_4 production rate is unimpaired while triiodothyronine (T_3) generation from T_4

is impaired.[4] A minimum intake of carbohydrate is essential for the maintenance of 5–deiodinase activity, the enzyme required in the conversion of T_4 to T_3. However, the reversed triiodothyronine (rT_3) is increased during starvation because of increased conversion of T_4 to rT_3 and a decreased clearance rate of rT_3 secondary to a decrease in 5'-deiodinase activity. Free T_4 is either unchanged or increased in protein energy malnutrition. The increased free T_4 level may due to the effect of free fatty acids which may decrease the binding of T_4.

Various workers have shown that the basal thyroxine stimulating hormone (TSH) and the response to thyrotropin releasing hormone (TRH) may be blunted in protein energy malnutrition. The possible explanations are that the pituitary gland may be more sensitive to the negative feed back effects of circulating T_4 and T3 or that there is depletion of pituitary TSH in these clinical situations. This study therefore, aims at determining the state of TSH and prolactin (PRI) reserve in the pituitary gland of children with kwashiorkor and marasmus.

Materials and Methods

The subjects were eighteen 6–24 months old children; ten were cases of kwashiorkor, eight of marasmus. The classification into kwashiorkor and marasmus was based on the Wellcome classification.[6] The controls were 6 apparently healthy children aged 6–24 months who showed no signs of malnutrition and whose weights were above 80% of the expected weight for age and sex.

Thyroid releasing hormone stimulating test was performed between 9 a.m. and 12 noon within twenty-four hours of admission. The children were fasted for six hours prior to the study. Immediately after the first venepuncture to determine the basal serum hormone levels, 100ug of synthetic TRH (thypinone) (donated by *Abbot Laboratories,* North Chicago) was given intravenously. Two mililitres of blood was withdrawn at the 20th, 40th and 60th minutes. The serum was separated immediately, in all the samples and stored at -20°C before the assay. Serum TSH and PRL levels were measured in each sample, using radioimmunoassay kits from Amersham International of UK *(Amerlex TSH RIA Kit* and *Prolactin RIA Kit*). Counting was done using gamma scintillation counter *(Parkard Auto-gamma scintillation spectometer, Model No. 5210 by Nuclear Chicago).*

The TSH concentrations in 97 sera from euthyroid adults who are not on thyroid treatment were determined using the *Amerlex-M TSH RIA Kit.* The range of TSH concentrations in these euthyroid patients was 1.0 to 5.5 μlU TSH/ml.

Results

The basal serum TSH levels were significantly elevated in kwashiorkor (3.8 ± 2.2μU/ml, $p<0.05$) and marasmus (3.9 ± 1.8μU/ml, $p<0.025$) when compared with the controls (2.4 ± 0.6 μU/ml (Table I). The basal serum prolactin level did not show a significant difference between the kwashiorkor group (12.1 ± 4.5ng/ml), the marasmus group (14.1 ± 5.3ng/ml) and the controls (16.2 ± 4.7ng/ml) (Table II).

There was a prompt and significant rise of serum TSH in response to intravenous synthetic TRH in the kwashiorkor ($p<0.0005$). The peak values were obtained at the 20th minute in all the groups (Fig. 1). There was no significant difference between the peak values in all the three groups. There was also no significant difference between the values of serum TSH of the PEM groups and the controls at the 40th and 60th minutes.

Table I

Mean Serum Levels of TSH in response to TRH stimulation

	No of cases	Time (minutes)			
		0	20	40	60
Marasmus	8	3.9* ± 1.9	18.6 ± 8.2	16.0 ± 8.7	12.5 ± 6.0
Kwashiorkor	10	3,8 ± 2,3	15.2 ± 9.7	13.0 ± 6.6	11.8 ± 7.3
Controls	6	2.7 ± 1.1	16.3 ± 5.2	13.0 ± 4.0	9.4 ± 2.1

*Figures (μU/Ml) are mean values ±1 standard deviation

TSH = Thyrotropin

TRH = Thyrotropin-releasing hormone.

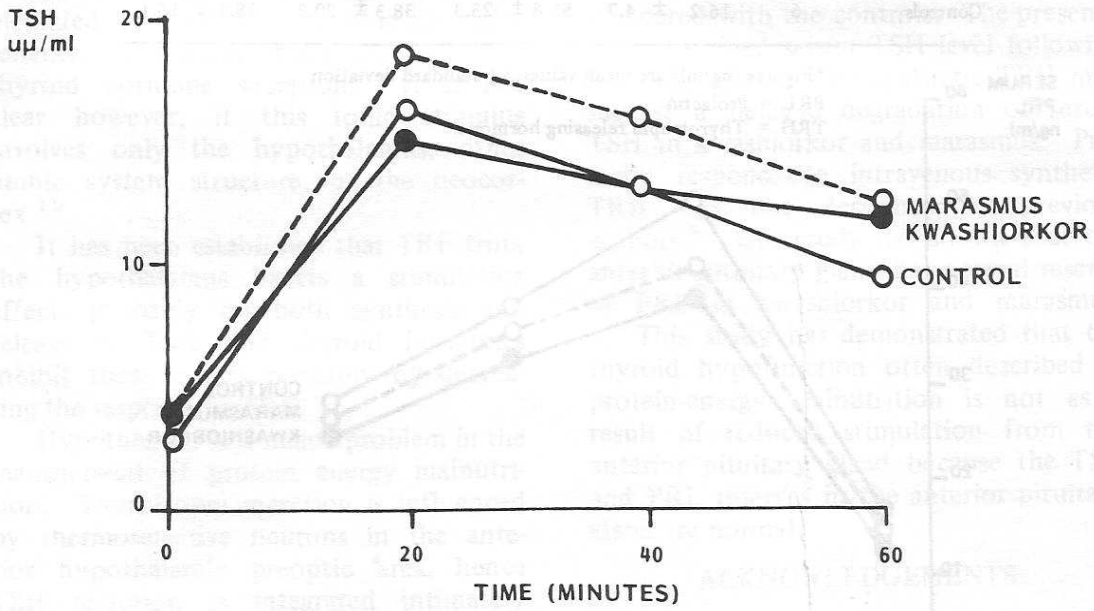

Fig. 1. Serum TSH response to intravenous injection of TRH.

The kwashiorkor and marasmus groups did not show a significant fall of serum TSH at the 60th minute when compared with the peak response at the 20th minute. However, the control group demonstrated a significant fall ($p<0.005$) in serum TSH level at the 60th minute when compared to the peak value at the 20th minute.

There was a significant rise of serum PRL level for the kwashiorkor and marasmus groups and controls following intravenous synthetic TRH administration (Table II, Figure 2). The peak value at the 20th minute for the kwasiorkor and marasmus groups and the control group were not significantly different. The PRL response at the 40th and 60th minutes were also not significantly different for the three groups (Fig. 2). The fall from the peak at the 20th minute to the level at the 60th minute were all significant in the PEM groups and the controls.

Table II

Mean Serum Levels of PRL in response to TRH stimulation

	No of cases	Time (minute)			
		0	20	40	60
Marasmus	8	14.1* ± 5.7	42.8 ± 16.1	35.6 ± 17.5	26.4 ± 10.8
Kwashiorkor	10	12.1 ± 4.8	39.3 ± 12.8	32.8 ± 17.1	24.7 ± 14.2
Controls	6	16.2 ± 4.7	51.8 ± 25.3	38.3 ± 20.3	28.3 ± 15.1

*Figures (ng/ml) are mean values ±1 standard deviation
PRL = Prolactin
TRH = Thyrotropin releasing hormone.

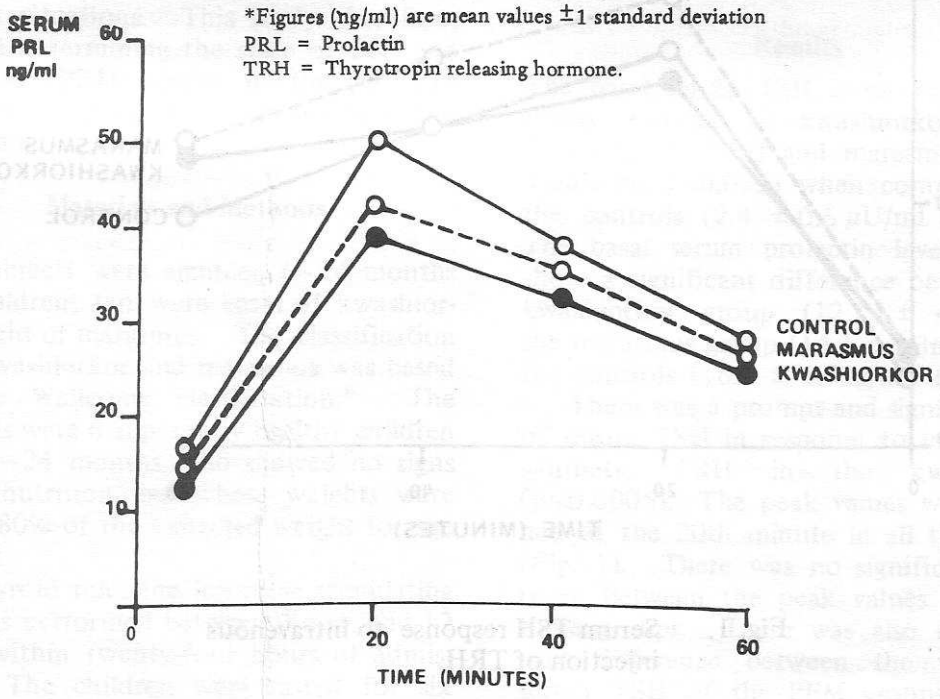

Fig. 2. Serum PRL response to intravenous injection of TRH.

Discussion

There have been reports of depressed serum TSH level in kwashiorkor and marasmus[1] and in marasmus.[2 3] Normal serum TSH level has also been reported in kwashiorkor[2] and PEM.[7] These are contrary to the finding in this study in which the serum TSH levels in the children suffering from kwashiorkor and marasmus were significantly higher than that of the controls. Similar reports of elevated serum TSH level in kwashiorkor have been made.[8]

An intact hypothalamus is necessary for a basal level of secretion of TSH by the anterior pituitary gland. The control of TSH within the hypothalamic-pituitary system appears to be influenced in three ways. Evidence exists which shows that the first control is mediated by the hypothalamus.[9] A tonic neural influence mediated by TRF is responsible for maintenance of normal levels of TSH and thyroid hormone secretion. It is not clear however, if this tonic stimulus involves only the hypothalamus, other limbic system structure, or the neocortex.[10]

It has been established that TRF from the hypothalamus exerts a stimulating effect, probably on both synthesis and release of TSH, and thyroid hormones inhibit these events probably by decreasing the response to TRF.

Hypothermia is a major problem in the management of protein energy malnutrition. Thyrotropin secretion is influenced by thermosensitive neurons in the anterior hypothalamic preoptic area, hence TSH secretion is integrated intimately with the control of body temperature and food intake. In cases where there is hypothermia and inadequate food intake, TSH secretion is increased.[10]

There is paucity of information on the basal serum prolactin levels in children suffering from severe protein-energy malnutrition. This study has demonstrated that the level remains normal. This is not surprising because even though TRH stimulates the secretion of both TSH and PRL from the anterior pituitary gland, there is also a dissociation in their secretion. Only some cases of primary hypothyroidism demonstrate hyperprolactinaemia.[11 12] The significant rise of serum TSH level following intravenous bolus administration of synthetic TRH agrees with the finding of others who also demonstrated a normal response of TSH in two thirds of the children with kwashiorkor that they studied. However, an exaggerated and sustained response in kwashiorkor has been described.[8] In this study, the TSH response was not exaggerated but there was a relatively sustained serum TSH level after the peak response when compared with the controls. The presence of a sustained serum TSH level following the peak response to synthetic TRH may suggest a delayed degradation of serum TSH in kwashiorkor and marasmus. Prolactin response to intravenous synthetic TRH was not described by previous authors.[8] Our study has shown that the anterior pituitary gland has normal reserve of PRL in kwashiorkor and marasmus.

This study has demonstrated that the thyroid hypofunction often described in protein-energy malnutrition is not as a result of reduced stimulation from the anterior pituitary gland because the TSH and PRL reserves in the anterior pituitary gland are normal.

ACKNOWLEDGEMENTS

We are grateful to Professor Fregene of the Department of Radiation Biology and to Mr Sanyaolu of the Department of Obstetrics and Gynaecology for their help in measuring Thyroid Stimulating Hormone and Prolactin levels respectively. The

assistance given by Matron Akinrimisi and her Nursing Staff of Ward D2 is also appreciated. We are grateful for the secretarial help of Mr J C Usifoh and Mrs C I Daramola.

References

1. Olusi S O, Orrell D H, Morris P M and McFarlane H. A study of endocrine function in protein-energy malnutrition. Clinica Chimica Acta 1977; 74: 261–5.
2. Graham G G, Braertl J M, Claeyssen G, Suskind R, Greenberg A H, Thompson R G and Blizzard R M: Thyroid hormonal studies in severely malnourished Peruvian infants and small children. J Pediatr 1973; 83: 321–7.
3. Godard C. Plasma thyrotropin levels in severe infantile malnutrition. In: Gardener L I and Amachree P, eds. Endocrine Aspects of Malnutrition. California: Kroe Foundation, 1973: 221.
4. Eisenstein Z, Hagg S and Vagenakis A G. Effect of starvation on the production and peripheral metabolism of 3, 3, 5–tri-iodothyroine in euthyroid, obese subjects. J Clin Endocrinol Metab 1978; 47: 889–93.
5. Leung A K C. Euthyroid sick syndrome. Annals of Royal College of Physicians and surgeons of Canada 1987; 20: 245–48.
6. Wellcome Trust Working Party. Classification of Infantile Malnutrition. Lancet 1970; 11: 302–3.
7. Ingenbleek Y and Becker C. Triiodothyronine and thyroid stimulating hormone in protein calorie malnutrition in infants. Lancet 1975; 2: 845–9.
8. Walumbe J M. Thyrotropin secretion in protein-energy malnutrition in Ugandan children. E Afr Med J 1982; 59: 560–2.
9. Schally A V, Bowers C Y and Redding T W. Purification of thyrotropic hormone – releasing factor from bovine hypothalamus. Endocrinology 1966; 78: 726–9.
10. Fisher D A and Hughes E R. Disorders of the Hypothalamus. In. Kelley V C, ed. Endocrine and Genetic Disorders of Children. New York: Harper and Row (Publishers) Inc. 1974: 143–65.
11. Van Caal L, Abs R, De Leenw I and Bakaretl J. Hypothyroidism and Prolactin. Europ J Obstet Gynaec Reprod Biol 1981; 12: 315–7.
12. Suter S N, Kaplan S L, Aubert M L and Grumbach M M Plasma prolactin and thyrotropin and the response to thyrotropin-releasing factor in children with primary hypothalamic hypothyroidism. J Clin Endocrinol Metab 1978; 47: 1015 – 7.

Accepted 18 November, 1987