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Study of Some Hormones in Protein Energy Malnutrition

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Abstract

Forty patients with protein energy malnutrition (25 males and 15 females) in addition to 20 healthy normal control subjects were included in the study. Both patients and control groups were subjected to full history taking, complete clinical examination and investigations that included complete blood picture, total plasma proteins and serum albumin, blood glucose level, estimation of serum T_3 , T_4, TSH and cortisol by radioimmunoassay. Results showed that levels of thyroid hormones; T_3 and T_4 were significantly lower in PEM patients than controls; T_3 mean was 60.63 ± 21 in marasmus, 43.95±27 in KWO, 47.52±18 in M. KOW versus 195.1±40 in controls while T_4 mean was 4.75±24, 4.03±1, 4.5±1 in marasmus, KWO and M. KWO respectively versus 8.92+1 in controls. TSH was around normal with mean of 10.57±8.02±2, 9.75±3 versus 7.51±4 in control. On the other hand cortisol was significantly higher in PEM patients than controls. Its mean was 24.46±5 in marasmus, 19.82±7 in KWO 20.3±8 in M. KWO versus 9.73±3 in controls. Hypoglycemia was found in KWO cases (mean blood glucose was 59.5±5 mg/dl) but not in marasmus or M. KWO. Also hypoalbuminemia was present in both KWO where means of plasma albumin were 2±0.11 mg/dl and 2.12±0 mg/dl respectively.

Introduction

PROTEIN Energy Malnutrition (PEM) constitutes a major pediatric problem in most developing countries including Egypt where the syndrome is quite common. It stands as major threat to infant's health growth and development [1].

PEM is not a clearcut disease entity but a syndrome in which all organs and tissues are involved. It results from either deficiency of total caloric intake or deficiency of protein diet or deficiency of both [2]. Multiple system affection and several metabolic derangements are thus to be expected.

Standard pathological descriptions of the endocrine glands in PEM are those of atrophy affecting particularly the pituitary and adrenal glands as well as reduction in

the number of secretory cells of these glands [3]. The most of these descriptive endocrinal and metabolic changes are adaptive in nature [4]. Accordingly serum levels of related hormones are expected to be affected by reduction.

Several investigators reported, surprisingly, a rise in the growth hormone level in children suffering PEM [5] while others reported low values of somatomedins, the growth promoting peptides produced by the liver in response to growth hormone stimulation [6].

Growth failure, hypothermia and mental apathy can be attributed to deterioration in thyroid function [7].

Some of the biochemical features of PEM highly suggest the implication of adrenal cortex. While hypoglycemia favours hypofunction, other features like 'edema and salt retention as well as the slight tendency to moon face appearance suggest hyperfunction. Alleyne et al. [8] reported that plasma cortisol is constantly high in malnourished children and falls with recovery. On the other hand there are some authors whose findings point to adrenal cortical hypofunction rather than hyperfunction [9].

In view of the controversial previously published data, the present work was done to assess some of the hormonal changes that may occur in PEM especially those of Triidothyronine (T_3), tetraiodothyronine (T_4), thyroid stimulating hormone (TSH) and cortisol.

Subjects and Methods

The study was carried out in Zagazig University Hospital, Pediatric Department, on 40 patients suffering from PEM. They were 25 males and 15 females. Their ages ranged from 3 to 30 months. In addition, 20 healthy normal subjects sex and age matched with the patients group (10 male and 10 females) served as a control group patients were classified into three groups according to their clinical findings [10]:

1- Marasmus group: included 28 patients
2- KWO group: included 8 patients.
3- Marasmic KWO Group: 4 patients.

Both patients and control groups were subjected to:

a- Full history and thorough clinical examination.

b- Routine investigations including:

1- Complete blood picture.
2- Serum proteins (total and albumin) by Biuret method.
3- Random blood glucose level.

c- Estimation of serum level of:

1- Tri-idothyronine (T_3).
2- Tetra-iodothyronine (T_4).
3- Thyroid stimulating hormone (TSH). The three hormones were estimated by kits: T_3 (I^{125}), T_4 (I^{125}) TSH IRMA (I^{125}) coated tubes immunoradiomtric assay provided by "Farmos Diagnostica", Finland.
4- Plasma cortisol: The kit used was cortisol immunocoat (I^{125}) provided by RANTEX, Monica.

Results

Table (1) shows the mean (x) and standard deviation (± SD) of hematological and hormonal variables among the different groups using ANOVA test.

The table shows that there was significant difference ($p < 0.01$) of different variables between the different groups.

Table (2) shows the correlation between cortisol and anthropometric meas-

urements in the different groups.

It shows that in marasmus, KWO and marasmic KWO there was -ve correlation between plasma cortisol and growth indices i.e. + ve correlation between cortisol and growth retardation.

Discussion

Among the several aspects of the metabolic derangement in PEM are the endocrinal ones which have recently received more attention. One of the endocrinal organs that received much interest is the thyroid gland. Hypothyroidism was detected in PEM by many authors, [11,12,13,14].

In the present study results showed significant decrease in the circulating T_3 in KWO (mean 43.95±27) in marasmus (mean 60.63±21) and in M. KWO (Mean 47.52±2) relative to normal control group (mean 195.7±4). Similarly T_4 levels were lower in KWO (mean 4.03±1.7), marasmus (mean 4.75±1.2) and in M. KWO (mean 4.5±1.6) relative to control (mean 8.95±1.1). These findings are in agreement with El-Mahdy [15] whose study showed significant lowering of T_3 and T_4 in KWO patients. Also this reduction of T_3 and T_4 in PEM patients was proved by Gabr et al. [1] who found that T_4 was significantly lower in KWO than control and by others [16,17,18]. This drop in T_3 and T_4 may be explained by the presence of hypothyroidism which was evidenced by the low level of radioactive iodine uptake [19], low protein bound iodine [20], low butanol extractable iodines [12], decreased basal metabolic rate and diminished O_2 consumption [21], low serum thyroxine [7] and decreased free thyroxine [22].

Our study showed also that there was positive correlation between T_3 and T_4 levels in KWO patients and their serum albu-

Table (1): The Mean (x) and Standard Deviation of Hematological and Hormonal Variables among the Different Groups (Using ANOVA Test).

Variable	I (x ± SD)	II (x ± SD)	III (x ± SD)	IV (x ± SD)	F	p
Hb (gm%)	8.41 ± 1.07	8.41 ± 1.7	9.8 ± 1.24	10.89 ± 0.73	22.17	< 0.01
Total plasma protein (gm%)	6.3 ± 0.41	4.91 ± 0.6	5.10 ±0.14	8.09 ± 0.24	75.584	< 0.01
Serum albumin (gm%)	3.21 ± 0.30	2.00 ± 0.11	2.12 ± 0.23	3.95 ± 0.18	149.979	< 0.01
Blood glucose (gm%)	80.25±6.12	59.5 ± 5.55	60.75 ± 6.65	86.55 ± 4.09	61.379	< 0.01
T_3	60.63±21.23	43.95 ± 27.5	47.52 ±18.06	195.1± 40.38	92.172	< 0.01
T_4	4.75±1.24	4.03 ± 1.68	4.5 ± 1.60	8.95 ± 1.10	46.908	< 0.01
TSH	10.57 ±2.69	8.02 ± 2.57	9.75 ± 3.92	7.51 ± 1.40	6.990	< 0.01
Cortisol	24.46±5.8	19.82 ± 7.6	20.30 ± 8.9	9.73 ± 2.57	28.146	< 0.01

Table (2): The Correlation between Cortisol and Ahthropometric Measurements in the Different Groups.

Group	Dependent variable	Weight		Length		HC		NAC		Triceps S.F.	
		r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Marasmus *r* : 0.05 ± 32 *r* : 0.01 ± 37	Cortisol	- 0.446	< 0.01	- 0.412	< 0.01	- 0.381	< 0.01	- 0.395	< 0.01	- 0.430	< 0.01
KWO *r* : 0.05 ± 0.63 *r* : 0.01 ± 0.70	Cortisol	- 0.762	< 0.01	- 0.652	< 0.05	0.713	< 0.01	- 0.633	< 0.05	- 0.552	N.S
M. KWO *r* : 0.05 ± 0.93 *r* : 0.01 ± 0.96	Cortisol	- 0.994	< 0.01	- 0.856	< 0.01	- 0.972	< 0.01	- 0.980	< 0.01	- 0.936	< 0.05
Controls *r* : 0.05 ± 0.38 *r* : 0.01 ± 0.44	Cortisol	- 0.285	N.S	0.236	N.S	- 0.280	N.S	0.226	N.S	- 0.097	N.S

HC : Head circumference
MAC : Mid-arm circumference

min levels (r = 0.731 and 0.761 respectively). No correlation was found in the other groups suggesting that low albumin level may be responsible for the T_3 and T_4. Both hormones are transported into the blood stream by carrier proteins serum albumin (SA), thyrobinding pre-albumin (TBPA) and thyrobinding globulin (TBG). The same positive relation between T_4 and serum albumin in KWO patients was also reported [1].

While T_3 level in patients of all groups was significantly diminished when compared to normal control (T_3 was 25.98% of control levels), T_4 level was slightly diminished (T_4 was 49.38% of control). This is in agreement with Ingenbleck [16] who found that T_3 level in PEM was about 23.3% of controls while T_4 was about 41.7% of controls.

Normally 80% to 90% of the circulating T_3 (which is metabolically more active than T_4) is derived from peripheral deiodinization of T_4, the remaining 10-20% of T_3 is derived from direct thyroidal T_3 secretion [23,24]. An alternative pathway for peripheral T_4 metabolism is its conversion to reverse T_3 (r T_3) which is calorigenically inactive [25]. It appears that in PEM later pathway is more stimulated resulting in energy conservation and hypometabolism in order to protect the malnourished child with reduced lean body from an otherwise earlier demise [26].

This reduction of T_3 in PEM patients could be also explained by impaired liver function [27], carbohydrate deficiency since glucose is an important factor for the liver microsomal enzyme responsible for conversion of T_4 to T_3 [28] or interestly due to vitamin deficiencies which are usually present in PEM [29]. lastly, cortisol which was found to be elevated in the acute stages of PEM also inhibits T_3 generation from T_4 be inhibiting the 5-deiodinase system [16].

As regards the functions of the pituitary gland in PEM conflicting data were reported. While some [30] demonstrated normal concentration of TSH in KWO patients indicating no alteration in the pituitary thyroid axis, others [13] had found high basal TSH level patients of PEM. In the present study TSH levels were around normal in all groups (mean in marasmus 10.57±2.7, in KWO 8.02±2.6, in M. KWO 9.75±3.9 while in normal controls 7.51±1.4). According to ANOVA test and LSD there was no significant difference in the level of TSH between KWO, M. KWO and control group, while in the marasmic group there was slight elevation of TSH level when compared to the control group. This normal TSH level runs with most studies done [31,32,33].

One of the hormones which was also estimated in the present study was serum cortisol. It was significantly elevated in all PEM groups when compared with normal control (mean in marasmus was 24.46±5.8, in KWO 19.82± 7.6 in M. KWO 20.3±8.99 while in control it was 9.73±2.6). These results of elevated serum cortisol level in malnourished children are concordant with results of others [34,35,36]. This rise of serum cortisol in PEM patients may be partly explained by some impairment of cortisol conjugation by the malfunctioning hepatic cells [8] and partly by decreased binding of cortisol in the plasma of malnourished children [37].

On the other hand, the identical serum levels of cortisol in both marasmus and KWO may have been due to similar extent of exposure to infection [38].

Table (2) shows a +ve correlation be-

tween the high level cortisol in PEM and growth retardation. Physiologically high level of circulating glucocorticoids causes growth retardation though the divergent views as to the mode of actions [35]. This may be caused by any of these four mechanisms; a decrease in growth hormone release, a decrease in growth hormone induced somatomedin genera, a decrease in somatomedinm action on cartilage or a direct inhibitory effect on cartilage [39].

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