Cortisol and Growth Hormone in Kwashiorkor and Marasmus

J. M. Van Der Westhuysen, J. J. Jones, C. H. Van Niekerk, P. C. Belonje

SUMMARY

Cortisol and growth hormone concentrations in the plasma were determined in 26 children with kwashiorkor, 13 with marasmus, and 21 controls. Cortisol levels were high in babies with kwashiorkor and marasmus, but higher in the former, in relation to a constant body mass. The concentration of plasma cortisol correlated positively with the body mass deficit in kwashiorkor \( r = 0.66 \) and in children with low mass for age \( r = 0.75 \). Growth hormone levels were elevated in both kwashiorkor and marasmus. The proposed role of these hormones in metabolic adaptation to malnutrition is discussed.


Adaptation to deficient nutrition depends primarily on the endocrine control of the metabolic processes involved. The two ultimate forms of protein energy malnutrition, namely kwashiorkor and marasmus, have been described as forms of failure of adaptation and successful adaptation to protein energy malnutrition, respectively.\(^1\)

Failure of adaptation involves the inability of hormones to maintain normal metabolism because the malnutrition is too severe,\(^2\) or the individual is physiologically unable to adapt to the dietary deficiency. Hormonal changes, such as increases in cortisol and growth hormone, have been reported by many workers.\(^3\) Some workers\(^4\) ascribe the increase in plasma cortisol to the general stress of malnutrition, whereas others\(^5\) attribute it to infection. The increase in growth hormone is also related to changes in plasma amino acid concentration,\(^6\) particularly alanine\(^7\) and valine.\(^8\) Recently, Rao\(^9\) proposed that mal-adaptation to protein energy malnutrition (kwashiorkor) results from an inability of the adrenal cortex to respond sufficiently to mobilise enough amino acids for use by an abnormally high secretion of growth hormone. The successful adaptation in marasmus results from an adequately responsive adrenal and relatively low growth hormone. This experiment was performed to test this hypothesis, by comparing these hormonal concentrations in non-fatal and fatal kwashiorkor and marasmus, and to attempt to relate them to the severity of malnutrition.

PATIENTS AND METHODS

Thirty-nine patients between the ages of 12 and 48 months with protein energy malnutrition were studied. They were admitted to Harari Hospital, Salisbury, between December 1972 and March 1973 and were all underweight for age (Boston 50th percentile).\(^10\) Twenty-six patients with oedema and less than 80% of the expected body mass for age, were classified as kwashiorkor, and 13 without oedema and less than 60% of the expected body mass for age, as marasmus.\(^11\)

It is customary to take a venous blood sample from all children admitted to this hospital before treatment is started. The blood is collected between 08h00 and 09h00 in plastic syringes containing lithium heparin as an anticoagulant. Immediately after collection, blood samples are placed in ice and spun down in a refrigerated centrifuge within 2 hours of collection. Plasma is stored at \(-20^\circ\text{C}\), until it is analysed. Another venous blood sample is taken for analysis 1 week after the patient has been admitted to hospital and again during the patient's last week in hospital.

In this study, at each blood sampling, the child was examined and the age, body mass and height were recorded. Any signs of gastro-intestinal disturbance or of other infections were noted. Measurements were made of skinfold thickness over the triceps, using Harpenden skinfold calipers, and the mid-arm circumference was measured with a tape measure. From these measurements the 'mid-arm muscle circumference' was determined.\(^12\) Oedema was measured as the pitting depth, in millimetres, obtained after pressure for 15 seconds on the dorsum of the foot and by scoring (0 - 9) for the total degree of oedema in the limbs (0 - 3), face (0 - 3) and abdomen (0 - 3). Further observations included skin, hair and liver changes. Liver enlargement was measured in centimetres, in the right midclavicular line by palpation, with the child supine. Skin lesions and stomatitis were graded by M.Med.Vet., University of Stellenbosch, CP.
Plasma cortisol concentration was determined by competitive protein binding, and plasma growth hormone was estimated by radio-immunoassay. The antibodies were supplied by CEA-CIA Sorin. Total plasma protein was determined by the biuret method and albumin by cellulose acetate electrophoresis followed by flying-spot densitometry.

RESULTS

The mean plasma hormone concentrations of children suffering from protein energy malnutrition on admission to hospital, are summarised in Table I. Changes occurring in these concentrations during recovery in hospital, are presented in Table II.

In both kwashiorkor and marasmus, the mean plasma cortisol concentrations were significantly greater ($P<0.01$) in the controls, but did not differ from each other. In addition, kwashiorkor and marasmus patients who subsequently died in hospital had cortisol concentrations significantly greater ($P<0.05$) than those who recovered. In Table III the correlations of plasma cortisol with the severity of the clinical features are presented. It can be seen that severe clinical features are associated with higher concentrations of cortisol in the plasma. Fig. 1 presents the relationships of plasma cortisol and body mass deficit of children with a low body mass for age, but without oedema ($r=0.75$, kwashiorkor: $y = 159.607 + 6.301x$), and of those with kwashiorkor ($r=0.658$). Although the two regression lines did not differ in slope (low body mass/age: $y = 23.50 + 6.79x$; kwashiorkor: $y = 159.607 + 6.301x$), they differed significantly ($P<0.01$) in the y intercept. An analysis of covariance showed that kwashiorkor patients had a significantly higher ($P<0.01$) plasma cortisol concentration than malnourished children without oedema, when the effect of body mass deficit was made constant.

![Graph showing correlations and regressions of plasma cortisol concentrations and body mass deficit in malnourished children with oedema (kwashiorkor) and in those without oedema.](image)

**TABLE I. PLASMA ENDOCRINE CONCENTRATIONS IN KWASHIORKOR AND MARASMUS PATIENTS ON ADMISSION TO HOSPITAL AND IN CONTROLS**

<table>
<thead>
<tr>
<th></th>
<th>Kwashiorkor</th>
<th>Marasmus</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Lived 12</td>
<td>Died 14</td>
<td>21</td>
</tr>
<tr>
<td>Cortisol (ng/ml)</td>
<td>127.0 ± 13.13 *</td>
<td>163.3 ± 10.99 b</td>
<td>120.5 ± 10.41 *</td>
</tr>
<tr>
<td>Growth hormone (ng/ml)</td>
<td>71.45 ± 1.79 *</td>
<td>70.00 ± 2.58</td>
<td>76.00 ± 7.45 *</td>
</tr>
<tr>
<td>Plasma albumin (g/100 ml)</td>
<td>2.31 ± 0.10 c</td>
<td>1.99 ± 0.09 b</td>
<td>2.72 ± 0.10 b</td>
</tr>
</tbody>
</table>

* b c Figures with the same superscript are not significantly ($P<0.01$) different from each other.

**TABLE II. PLASMA ENDOCRINE CONCENTRATIONS IN CONTROLS AND IN KWASHIORKOR AND MARASMUS PATIENTS ON ADMISSION AND DURING RECOVERY IN HOSPITAL**

<table>
<thead>
<tr>
<th></th>
<th>Kwashiorkor</th>
<th>Marasmus</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Admission 11</td>
<td>7 days 11</td>
<td>Discharge 11</td>
</tr>
<tr>
<td>Cortisol (ng/ml)</td>
<td>112.3 ± 11.66 a</td>
<td>86.57 ± 7.32 b</td>
<td>82.00 ± 20.12 b</td>
</tr>
<tr>
<td>Growth hormone (ng/ml)</td>
<td>75.67 ± 5.97 a</td>
<td>36.67 ± 7.23 b</td>
<td>34.33 ± 5.70 b</td>
</tr>
<tr>
<td>Plasma albumin (g/100 ml)</td>
<td>2.19 ± 0.15 a</td>
<td>3.18 ± 0.22 b</td>
<td>3.95 ± 0.12 c</td>
</tr>
</tbody>
</table>

* a b c Figures with the same superscript are not significantly ($P<0.05$) different from each other.
of discharge than those of the controls.

Growth hormone concentrations were significantly elevated ($P<0.01$) in each child admitted to hospital with protein energy malnutrition, compared with the controls (Table I). Children with kwashiorkor or marasmus did not differ from each other in this respect, nor did those suffering from the fatal and non-fatal forms of the disease differ in growth hormone concentrations. During recovery in hospital, growth hormone concentration returned to the normal level within the first week of treatment.

**DISCUSSION**

Adrenal function in protein energy malnutrition has been the subject of investigation for many years. Owing to contradictory reports between histological studies and determinations of urinary steroid excretion, it was concluded that urinary excretion may be an unreliable guide to adrenal activity and that the plasma cortisol concentration should be used. In general, raised concentrations of plasma cortisol in protein energy malnutrition, regardless of type have been reported, although there have been conflicting results of adrenal activity being generally low in kwashiorkor, but high in marasmus.

Recently, Rao proposed that high adrenal activity may be essential for adaptation to protein energy malnutrition and that the main difference between the aetiology of marasmus (successful adaptation) and kwashiorkor (failure of adaptation) is not of dietary origin, but depends mainly on the ability of the adrenal cortex to respond adequately to maintain metabolic integrity. The results of this study do not agree with this theory nor with the work of Castellanos and Arroyave and Lunn et al, but show that plasma cortisol concentration is elevated in both types of protein energy malnutrition. The significant increase in cortisol levels of children with fatal protein energy malnutrition above those of surviving children, also makes it most unlikely for the magnitude of the adrenal response to be valid as an indication of successful adaptation. Moreover, high correlation was found between plasma cortisol concentration and the severity of the clinical features.

This study clearly showed that body mass deficit is correlated with cortisol concentration which is more elevated in kwashiorkor, the type of protein energy malnutrition that represents maladaptation. Cortisol concentration is higher in kwashiorkor than in marasmus, and still higher when the disease is fatal. It was also found that cortisol in experimental protein energy malnutrition (in pigs) was related to the clinical severity of the syndrome. Therefore, cortisol concentration is not so much an indication of an adaptive response, but simply represents the severity of the stress of protein energy malnutrition, a conclusion that is in marked contrast to Rao's theory. In agreement with Abass and with Rao et al., the highest cortisol concentrations were found in children with high body mass deficits, and more so in children with kwashiorkor.

It is generally agreed that in severe kwashiorkor serum growth hormone concentrations are raised. In marasmus, growth hormone concentrations have been reported as either normal or raised. The present results confirm those of Pimstone et al. that growth hormone concentrations are elevated in both kwashiorkor and marasmus. This elevated concentration of growth hormone is not significantly related to body mass deficit or to plasma concentrations of glucose or albumin. These results also are at variance with the theory of Rao. She reported growth hormone to be high in kwashiorkor and low in marasmus, and that the plasma amino acids showed opposite changes. The present study shows that growth hormone concentration is markedly elevated in both types of protein energy malnutrition.

From this it can be concluded that, although hypo-proteininaemia, and particularly hypo-albuminaemia, are expressions of the metabolic state during the maintenance of plasma albumin concentration and metabolic integrity in protein energy malnutrition, factors other than growth hormone and cortisol concentrations are primarily responsible for successful adaptation.

**REFERENCES**