NITROGEN, FAT AND MINERAL BALANCE STUDIES IN PATIENTS WITH PROTEIN MALNUTRITION

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Several papers have been published on nitrogen and fat balance in infants with protein malnutrition. Much less is known about mineral salt balances and the relationship between the retention of nitrogen and the retention of the major intracellular ions.

It has become increasingly evident that infants with kwashiorkor are depleted not only of protein, but also of several minerals, including potassium,[1, 2] phosphorus,[3] and magnesium.[4] In view of the importance of these minerals as intracellular ions, and their essential role in many metabolic processes, a study was undertaken of the nutritional state of kwashiorkor patients in our area with regard to these minerals. Nitrogen, fat, calcium and sodium balances were carried out concomitantly.

MATERIALS AND METHODS

The investigations formed part of a more comprehensive study[5] designed to assess the effect of milk fat and sun-

TABLE I. RESULTS OF BALANCE STUDIES (MEAN VALUES WITH STANDARD DEVIATIONS)

Element	Balance period	Intake	Urinary excretion	Faecal excretion	Retention	Retention (as percentage of intake)	Absorption (as percentage of intake)
Nitrogen (mg./kg./day)	1st 2nd	544±57·0 593±57·9	173±54·3 367±72·1	90±35·9 97±57·0	281±51·5 129±97·1	52±11·9 22±19·8	83± 6·3 84±10·6
Fat G./kg./day)	1st 2nd	3·44±1·109 3·59±1·269	— —	0·69±0·409 0·51±0·365	2·75±1·161 3·05±1·190	80±14·5 86±10·4	80±14·5 86±10·4
Calcium (mg./kg./day)	1st 2nd	127·2±15·83 139·1±14·39	2·2±1·06 2·8±1·51	96·0±34·18 121·3±32·70	29·0±19·03 15·0±33·83	23±15·8 11±25·3	25±16·3 12±25·2
Phosphorus (mg./kg./day)	1st 2nd	100·0±10·8 112·0±12·2	15·8±9·02 38·1±23·02	47·4±17·34 45·3±19·34	36·8±15·58 28·6±27·14	37±14·7 26±23·2	53±16·6 60±16·9
Magnesium (mEq./kg./day)	1st 2nd	1·07±0·186 1·18±0·122	0·05±0·036 0·11±0·056	0·85±0·343 1·03±0·384	0·17±0·212 0·04±0·347	16±19·3 3±27·1	21±21·2 13±28·2
Potassium (mEq./kg./day)	1st 2nd	4·46±1·256 3·72±0·661	1·50±0·792 2·18±1·007	1·21±0·614 0·49±0·238	1·75±1·729 1·05±1·156	39±37·7 28±30·7	73±21·7 87± 5·6
Sodium (mEq./kg./day)	1st 2nd	1·87±0·348 2·10±0·298	1·52±1·004 1·44±0·502	0·49±0·401 0·16±0·092	−0·14±1·055 0·50±0·370	— 24±18·1	74±21·9 92± 4·0
Statistical comparisons between first and second balance periods							
Nitrogen		P<1%	P<1%	NS* (P>10%)	P<1%	P<1%	NS* (P>10%)
Fat		NS* (P>10%)	—	NS* (P>5%)	NS* (P>10%)	NS* (P>5%)	—
Calcium		P<1%	NS* (P>10%)	NS* (P>5%)	NS* (P>10%)	NS* (P>5%)	NS* (P>10%)
Phosphorus		P<1%	P<1%	NS* (P>10%)	NS* (P>10%)	P<5%	NS* (P>5%)
Magnesium		P<2%	P<0·2%	NS* (P>5%)	NS* (P>10%)	P<5%	NS* (P>10%)
Potassium		NS* (P>10%)	P<3%	P<1%	NS* (P>40%)	NS* (P>50%)	P<1%
Sodium		P<2%	NS* (P>50%)	P<1%	NS* (P>10%)	NS* (P>20%)	P<0·1%

*NS = Not significant

flower-seed oil on the rate of recovery of kwashiorkor patients.

The balance technique, dietary regimen and analytical methods are described in detail in the previous report.[5] The diets were based on milk, each patient receiving one of the following formulae: dried skimmed milk with added sugar, dried whole milk, acidified dried whole milk, or dried skimmed milk with added sunflower-seed oil. No statistically significant difference was found between the 4 groups of patients in respect of nitrogen and mineral balance.[5] Retention of fat in the 3 groups of patients who received fat or oil was also not significantly different. It was therefore deemed justifiable to combine the results obtained in the different groups for the purpose of the present report.

Three-day balance studies were carried out on 31 Bantu kwashiorkor patients. Nitrogen and phosphorus balances were determined on all 31 patients, fat balances on 24, magnesium balances on 20, calcium balances on 19, sodium balances on 13, and potassium balances on 12. All balances were commenced within 6 days of admission and repeated 2½ - 3 weeks after admission.

RESULTS

The results of the balance studies are set out in Table I. Table II gives the wet weight, dry weight and ash content of the faeces. The results were analyzed by means of the two-tailed Wilcoxon matched-pairs signed-ranks test,[6] all values for intake, urinary excretion, faecal excretion, retention in mg. per kg. per day, percentage retention and percentage absorption obtained in the two balance periods being compared. The wet weights, dry weights and mineral contents of the faeces obtained during the two collection periods were compared by means of the same test. In all the tests a probability level of less than 5% was regarded as significant.

The finding most worthy of note was the very low urinary excretion not only of nitrogen but also of phosphorus, magnesium and potassium during the first balance period. This probably indicates that in addition to protein depletion a concomitant depletion of these minerals also existed, especially as a sharp increase in the urinary excretion of these elements occurred during the second balance period.

TABLE II. WET WEIGHT, DRY WEIGHT AND ASH CONTENT OF FAECES (MEAN VALUES WITH STANDARD DEVIATIONS)

	Wet weight in G./day	Dry weight in G./day	Ash content in G./day
During 1st collection period	204±165·2	15·3±8·48	3·02±0·797
During 2nd collection period	81± 65·2	11·2±5·36	2·16±1·118
Statistical comparisons between the two collection periods	P<1%	P<5%	NS* (P>10%)

*NS = Not significant

Apparent absorption of all the nutrients studied was impaired. This was especially marked for potassium and sodium during the first balance periods. During the second balance periods a great improvement occurred in the absorption of both these electrolytes, the differences being statistically significant. The differences in absorption between the two balance periods were not significant for nitrogen, fat, calcium, phosphorus and magnesium.

Diarrhoea was a prominent symptom during the initial stages of treatment. As can be seen in Table II, the stool weights (wet weights and dry weights) were much higher in the first balance periods than in the second, the differences being statistically significant.

DISCUSSION

The very high values for nitrogen retention in spite of some impairment in absorption observed during the first balance periods confirm the findings of several other workers.[3,7,8] During the second balance periods much lower values for retention were obtained, a finding also well documented for kwashiorkor patients.[3,8] The reduced avidity for nitrogen later in treatment presumably reflects the replenishment of the tissues with protein.[3,8]

Although the wet- and dry-weight values of the stools were much lower in the second collection period than in the first, the differences in the values for apparent absorption of nitrogen for the two periods were not statistically significant. The relationship between the faecal excretion of nitrogen and the wet-weight values of the stools obtained during the first balance period was also found to be not significant when the rank correlation coefficient was tested.[6] This seems to indicate that diarrhoea *per se* had little effect on the absorption of nitrogen in most of the patients. It agrees with the findings of Cravioto,[9] who was unable to show a significant difference in nitrogen absorption between kwashiorkor patients excreting more than 400 G. of fresh faeces per day and those with less than 100 G.

A finding of interest that emerges from Tables I and II is that, while the dry weight of the stools was increased during the first balance period when diarrhoea was severe, faecal nitrogen excretion during this period was less than during the second balance period. The increased dry weight of the stools during the first balance period must therefore have been due to the presence of additional non-nitrogenous matter, of which only about one-fifth can be accounted for as minerals (Table II).

Nitrogen absorption in most of our patients appeared to be only slightly impaired (Table I). The average value for apparent absorption in normal American children 4 - 12 years old is 90% of intake.[10] It is not known whether the same figure is applicable to normal South African Bantu children, but work carried out in the Congo indicates that the figure may well be lower in normal African children.[11,12]

Children normally absorb about 97% of the ingested dietary fat.[10] Absorption in our patients was impaired during both balance periods, the differences in the values obtained for the 2 periods not being significant (Table I). The values we obtained in our patients agree closely with those reported from other centres.[7,13] In spite of the impaired absorption of milk fat and sunflower-seed oil, considerable quantities were nevertheless absorbed. The diets containing fat or oil were very well tolerated and no adverse effects on the patients were observed.[5]

The values obtained during the two balance periods for faecal excretion of calcium, phosphorus and magnesium were not significantly different, suggesting that, as with nitrogen and fat, absorption of these minerals was not appreciably affected by the severity of the diarrhoea. In fact, whereas only 2 calcium and 3 magnesium balances were negative during the first balance periods, 6 calcium and 9 magnesium balances were negative during the second balance periods. This was at a stage when a great improvement of the diarrhoea, as reflected by the wet weights of the stools, had already occurred in most of the patients.

The mean values for apparent absorption of calcium (25% during the first balance period and 12% during the second), phosphorus (53 and 60%), and magnesium (16 and 3%) were considerably lower than the corresponding values—calcium 30%, phosphorus 69%, magnesium 46%—obtained by Macy[10] in normal American children 4 - 12 years old. In this respect our results are different from those of Holemans and Lambrechts,[14,15] whose values for apparent absorption of calcium in normal and malnourished Congolese children were even higher than those of Macy. However, the intakes of calcium in their subjects were much lower than in our patients. Waterlow and Wills[3] noted only a slight impairment in the absorption of phosphorus by malnourished Jamaican infants during their first days in hospital.

The urinary excretion of calcium, phosphorus and magnesium was very low during the first balance periods. In the normal children studied by Macy[10] 10% of the dietary calcium, 55% of the dietary phosphorus, and 30% of the dietary magnesium, was excreted in the urine. The corresponding mean values obtained in our patients were: calcium 2% of intake, phosphorus 16%, and magnesium 5%.

The average urinary excretion of both phosphorus and magnesium was more than doubled during the second balance period as compared with the first, suggesting that deficiencies of both these minerals existed at least during the time when the first balances were carried out. Our magnesium balance results have been described in detail elsewhere.[16] Evidence suggesting magnesium depletion in malnourished infants, as reflected by a low urinary excretion of magnesium, has also been obtained in Jamaica[17,18] and in Cape Town.[19]

Low urinary excretion of phosphorus, resulting in large initial retention that diminished progressively with treatment has been described in other centres.[3,15] A low urinary excretion of phosphorus naturally is not necessarily an indication of phosphorus depletion. However, it seems a likely explanation in our patients, particularly since low values for inorganic serum phosphorus in kwashiorkor patients have been observed in several areas,[3] including Pretoria.[20] Moreover, the phosphorus content of muscle biopsy specimens of malnourished infants has sometimes been found to be low.[3]

Although the intakes of magnesium and phosphorus were greater during the second than during the first balance periods, the increased urinary excretion during the second balance period was not due merely to increased intake. While the average amounts of both minerals excreted showed an increase of more than 100% in the second balance period as compared with the first, the average increase in intake amounted to no more than 12%.

The potassium and sodium retention values given in Table I should be regarded with reserve, for the interpretation of electrolyte balances is, for several reasons, not easy.[10] It has been pointed out, for instance, that as much as 30% of the potassium apparently retained by infants may be lost through the skin.[10] Again, a large and apparently physiological variation in electrolyte balance has been observed to occur in infants over a period of days by

Gamble and co-workers.[21] Again, the body adjusts itself slowly to a change in the level of intake, so that sometimes it probably takes from 2 weeks to a month for equilibrium to become established.[10] However, as can be seen from Table I, it is at least evident that absorption of both sodium (average = 74% of intake) and potassium (average = 73% of intake) was grossly impaired during the first balance periods and that it improved vastly during the second balance periods. Healthy children normally absorb about 87% of dietary potassium and 98% of dietary sodium.[10]

During the first balance periods, in spite of the large faecal loss of potassium that occurred in most patients, only 2 negative potassium balances were encountered, the reason being that urinary excretion of potassium was low. The initial low urinary excretion of potassium, and the subsequent increased excretion that was evident in most of the patients during the second balance period, suggest a potassium deficiency during the first balance periods. Several workers, using different techniques, such as serum estimations,[1, 22, 23] balance studies,[1] isotope-dilution methods,[2] and analysis of muscle biopsy specimens,[24] have shown that potassium deficiency often exists in kwashiorkor patients. The differences between the values for urinary excretion of potassium during the two balance periods were significant, but retention of potassium did not differ significantly. This can probably be explained by the large faecal losses of potassium that occurred during the first balance periods.

In contrast with potassium no significant differences were observed in the urinary excretion of sodium during the two balance periods. No evidence of depletion of sodium was therefore observed. Hansen's work[1] indicated that in the acute stage of kwashiorkor potassium depletion was usually accompanied by an accumulation of sodium in the body. After 1 - 2 days of treatment a sodium diuresis, which closely paralleled loss of weight and oedema, was observed. In all 7 patients studied this resulted in negative balances at the end of the balance periods, which lasted from 7 to 14 days. Serum-sodium values were within the accepted normal range, a finding also observed elsewhere.[23] In the present series of 13 patients studied, 6 negative sodium balances were observed during the first balance periods, and only 2 negative sodium balances during the second balance periods. Our findings are therefore consistent with the occurrence of a transient sodium diuresis during the initial stage of recovery.

Conclusion. The results obtained in the present study show that large quantities of water are lost in the stools during the acute stage of kwashiorkor, and suggest that in addition to protein depletion kwashiorkor patients may also suffer from depletion of several minerals. In treating these patients the possibility of such deficiencies should be kept in mind.

SUMMARY

Three-day balance studies were carried out on 31 Bantu kwashiorkor patients within 6 days after admission to hospital and repeated 2½ to 3 weeks after admission. Nitrogen and phosphorus balances were determined on all 31 patients, fat balance on 24, magnesium balance on 20, calcium balance on 19, sodium balance on 13 and potassium balance on 12 patients.

The finding most worthy of note was the very low urinary excretion during the first balance period not only of nitrogen, but also of phosphorus, magnesium and potassium. This suggests that, in addition to depletion of protein, a depletion of these minerals also existed, especially as a marked increase in the urinary excretion of these elements occurred during the second balance periods.

Diarrhoea, as reflected by the high wet weights of the stools, was a prominent symptom during the first balance periods. Apparent absorption of all the nutrients studied was impaired during the first balance periods. This was particularly marked for potassium and sodium. During the second balance periods a marked improvement was seen in the absorption of these two electrolytes. For nitrogen, fat, calcium, phosphorus and magnesium the differences in apparent absorption during the two balance periods were not significant.

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