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Gari Based Kwashiorkorigenic Diets Compromised Some Renal Functions in Albino Rats

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Abstract: Nigeria is still considered one of the countries with the highest prevalence of protein energy malnutrition. Cassava is a staple food in many parts of Nigeria and it is processed into different forms in different parts of the country, among the commonest of which is gari, which is often consumed by many people without being supplemented explaining partly the prevalent malnutrition. In this study, we investigated the possible effects of gari-based kwashiorkorigenic diet on the renal function which is central to maintenance of homeostasis. We used 24 weanly albino rats divided into two groups. One group was fed with Low Protein Diet (LPD) while the other was fed with normal Commercially Produced Diet (CPD), for 8 weeks. The results showed significant negative effects on both the growth, as shown by the body weight and the kidney size and function in the rats fed with the gari-based low protein diet. The percentage weight change (% + SD) and relative kidney weight for CPD and LPD groups were +340.95±2.63 and 0.51±0.02; -2.03±0.49 and 1.03±0.07, respectively. The Blood Urea Nitrogen (BUN) (mg dL⁻¹), serum creatinine (mg dL⁻¹) and the BUN/creatinine ratio were found to be 19.1±0.84, 0.81±0.11 and 24.47±1.18 in the CPD group but 93.42±6.68, 1.92±0.04 and 24.47±1.18 in the LPD group. Similarly, blood pH tended towards acidity in the test group, 6.80±0.04 compared with the control, 7.40±0.03. Therefore, we concluded that during chronic protein-energy malnutrition due to consumption of poorly supplemented gari-based diet, certain renal functions are compromised.

Key words: Gari, protein deficiency, renal excretion, acidosis, weanly rats

INTRODUCTION

An estimated 852 million people are undernourished worldwide and most (815 million), are living in developing countries (FAO, 2004). The World Health Organization (WHO, 2000) estimated in year 2000 that malnourished children numbered 181.9 million in developing countries. In addition, an estimated 149.6 million children younger than 5 years are malnourished when measured in terms of weight for age.

Poverty and ignorance have been highlighted as two of the greatest causative factors of protein malnutrition (Prentice *et al.*, 2008). In the areas where protein malnutrition is endemic, people are often of low economic status and are therefore, unable to afford many of the foods that can provide the daily required amount of protein. On the other hand, in these endemic areas, ignorance is often prevalent such that people don't know that there are cheap and affordable alternative sources of protein and more so, what a good nutrition

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entails. These people often feel that once they get enough calorie for their often highly energy intensive daily activities, that's all about nutrition.

Several pathological conditions have been associated with protein energy malnutrition and it has reportedly affected many organs including the kidney, adversely (Benabe and Martinez-Maldonado, 1998). The kidney is a versatile organ with a variety of functions which include elimination of metabolic waste and maintenance of homeostasis and acid-base balance (Arroyo, 2008).

Cassava is a staple food in many part of Nigeria. It is processed in various forms such as mere boiling, which are particularly common in the Northern part. It as also processed into fufu, lafun and gari which are the main forms in the Southern part. Gari is a staple for many of the 374 ethnic groups in Nigeria (Akoroda, 1992). It is popularly referred to as the common man's bread (Meludu *et al.*, 2001). Gari generally contains less than 2% protein (Ashaye *et al.*, 2005), so a diet based on gari has to be well supplemented with other protein sources. However, ignorance and poverty often prevent many from this supplementation. This explains part of the reasons why protein-energy malnutrition is prevalent many parts of the country.

In this experiment, we aimed at finding out what the effect gari-based kwashiorkorigenic diet would have on such a vital organ such as the kidney. Data on the effect of PEM on renal functions are scanty, though there are more data on renal dysfunctions leading to state of protein-energy malnutrition (Akner and Cederholm, 2001). Data from this experiment were expected to shed more light on the possible effects of diets consisting mainly of gari, which is a staple in many malnutrition endemic areas of Nigeria, on renal function in human especially the children with high protein requirement for growth.

MATERIALS AND METHODS

Animals

Twenty four male albino rats of the Wister strain were purchased from the Department of Physiology, University of Ibadan, Nigeria in July 2007. The rats were acclimatized for seven days. They were 21 days old at the time of commencement of the experiment. The rats were divided into 2 groups of 12 each. The control group animals were fed with Commercially Produced Diet (CPD) purchased from Ladokun Feeds Limited, Ibadan. The other group which was the test group was fed with gari-based low protein diet containing only 3% protein as described by Olowookere (1994). The animals were fed *ad libitum* and were also allowed free access to water. The rats were weighed at the beginning of the experiment and on weekly basis for eight weeks.

Formulation of Low Protein Diet

This was done according to Olowookere (1994). The feed was composed mainly from gari which made up 92% of the total weight in grams of the feed. Three grams protein was added per 100 g of the feed in the form of casein powder from bovine milk (Sigma-Aldrich Co, USA). Four grams of corn oil was added to serve as the lipid source and 1.5 g of vitamin and mineral premix (Animal Care Nigeria Ltd.) was added.

At the end of 8 weeks of feeding the animals were dissected under anesthesia and the blood samples were collected by venipuncture into heparinized tubes. The kidneys were also collected and washed in 150 mM KCl and weighed.

Biochemical Assays

Blood Urea Nitrogen (BUN) was determined according to the method of Weatherburn (1967) using RANDOX kit (RANDOX Laboratories Ltd., United Kingdom). Plasma creatinine level was measured by the method of Henry (1974) using RANDOX kit (RANDOX Laboratories Ltd., United Kingdom). The plasma pH was determined by the method of Rodkey (1961).

RESULTS AND DISCUSSION

The reduction in weight as revealed by the weight profile (Fig. 1) and other physical signs indicated that the condition induced was marasmic-kwashiorkor. In contrast to human in whom PEM can present in the form of kwashiorkor with the attendant edema which may result in false weight gain, it has been reported that the PEM present in rodents is marasmic-kwashiorkor (Olowookere *et al.*, 1980). This is in line with our result as shown that there was a significant reduction in the weight of the animals fed with low protein diet ($p < 0.05$). Despite that the animals in the LPD group were allowed unlimited access to food and water, we observed that their food consumption was significantly lower compared to the control group.

The central role played by the kidney in elimination of metabolic waste and the maintenance of pH balance cannot be contended (Arroyo, 2008). Our findings showed a significant reduction in renal excretory and acid-base regulation functions (Table 1). Since, renal excretion is an endergonic process (Saba *et al.*, 2007; Assadi *et al.*, 2008), the observed reduction in urea and creatinine clearance ($p < 0.05$) might be due at least in part to low calorie intake in the group on LPD. Apart from the calorie deficiency, the cellular energy generation is also negatively affected by protein energy malnutrition. Low dietary protein intake has

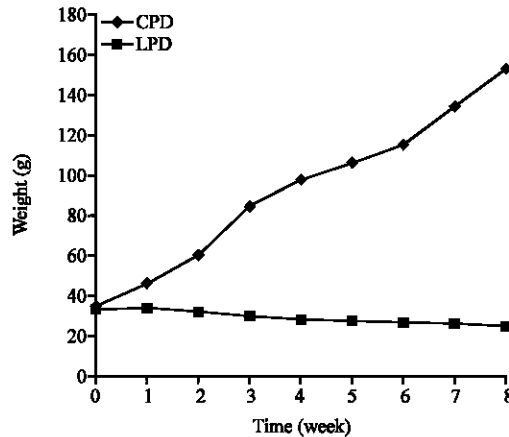


Fig. 1: Weight changes during the induction of marasmic-kwashiorkor

Table 1: Result of the percentage weight changes, relative kidney size, blood urea nitrogen, creatinine BUN/creatinine ratio and blood pH

Groups	Percentage weight changes (%)	Relative kidney weight (g)	BUN (mg dL ⁻¹)	Creatinine (mg dL ⁻¹)	BUN/creatinine ratio	Blood pH
CPD	+340.95±2.63	0.51±0.02	19.1±0.84	0.81±0.11	24.47±1.18	7.40±0.03
LPD	-2.03±0.49*	1.03±0.07*	93.42±6.68*	1.92±0.04*	50.23±5.18*	6.80±0.04#

+: Denotes weight gain; -: Denotes weight decrease; *Significant, $p < 0.05$ when compared to the control; #Not significant, compared to the control

been reported to adversely affect the mitochondrial oxidative phosphorylation and membrane permeability changes in a way that diminished energy generation (Olowookere *et al.*, 1991). Moreover, since the renal excretory apparatus is composed of membranous structures, oxidative damage to these structures would probably impair the excretory function. An increased oxidative injury during protein-energy malnutrition has been reported in growing rats (Rana *et al.*, 1996). Besides, the excretion process also involves certain membrane transport proteins (Otsuka *et al.*, 2005) which could be adversely affected by protein deficiency.

Blood urea level is one of the routinely assessed markers of kidney function, but its reliability in assessment of kidney function is often compromised in the face of factors that significantly elevate it (Mark *et al.*, 2005). We made similar observation in our experiment as the difference in blood urea levels between the test and control groups compared to the difference in serum creatinine between these same groups. We used weanly rats in our experiment because they were still at the stage of active growth with high demand for protein (Kabir *et al.*, 1998). Restriction in protein would lead to breakdown of tissue protein to meet other important body protein and calorie requirements. The observed reduction in kidney size and an increase in the relative kidney size (Table 1) found in the rats fed with LPD could be explained by the tissue protein breakdown which also contributed to the muscle wasting and the wasting of other tissues. This agrees with the result of Ece *et al.* (2007), who also reported a significant reduction in kidney size but a higher relative kidney size in malnourished children.

This protein breakdown contributed to the observed high urea nitrogen and decrease in body weight seen in the group fed with LPD in line with the finding of Klein *et al.* (2008). Moreover, since urea is not only filtered, but is also reabsorbed along the tubules and the collecting ducts, its clearance is also dependent on the rate of urine formation (Sands, 2003). We noticed that the rats on LPD were sluggish and also consumed less water which could contribute to diminished rate of urine flow and consequently higher blood urea levels. This agrees with the report of Berl and Schrier (2002) that as urine flow decreases, larger amounts of urea are reabsorbed leading to a significant decrease in urea clearance even in the face of normal glomerular filtration.

Unlike urea, serum creatinine is freely filtered at the glomerulus, not reabsorbed, but undergoes tubular secretion and its clearance exceeds inulin clearance which is considered as the gold standard for glomerular filtration rate (Robert, 2008). The higher BUN/creatinine ratio we found in the malnourished rats ($p < 0.05$) was consequently due more to the factor that raised BUN than the factors that lowered creatinine. We found that the blood volume was significantly smaller in the LPD group, this might lead to renal plasma underperfusion and consequently, reduced renal excretion according to Benabe and Martinez-Maldonado (1998).

Acid loads are poorly handled by malnourished patients (Kalantar-Zadeh *et al.*, 2004). This agrees with our result as we found a lower plasma pH in the malnourished rats compared to the rats on CPD. This difference was not statistically significant ($p > 0.05$) but was physiologically significant as it represents approximately ten fold increase in hydrogen ion concentration. Like the glomerular filtration, acid-base regulation is also an active process (Saba *et al.*, 2007) subject to negative impact of diminished calorie intake and energy generation.

In conclusion, apart from the effects due to low protein contents of the diet, the observed adverse effects including the renal function impairment seen in the rats on LPD might be due to the peculiarity of gari other than been deficient in protein. Gari is a food made

from cassava which is known to contain cyanide, a known inhibitor of the respiratory chain, the major source of ATP (Ramsey *et al.*, 2004). The processing method for the gari may not eliminate effectively enough the cyanide present in the cassava (Asegbeloyin and Onyimonyi, 2007). Also the ability to detoxify cyanide may have been compromised due to the malnutrition. The presence of cyanide may account for the defective renal glomerular filtration, acid regulation and other energy intensive processes in the LPD group, since mitochondrial electron transport has been negatively affected (Ezeji *et al.*, 2009). It may therefore be possible that the severity of renal dysfunction and perhaps that of the other signs of protein energy malnutrition will not be as much when another carbohydrate rich food substance other than gari is consumed.

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