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Effect of Feeding Pearl Millet (*Pennisetum typhoides*), Potassium Iodate or Their Mixture to Nubian Goats

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Abstract: Pearl millet 1 g/kg day, potassium iodate 50 ppm, and the two combined were fed to male Nubian goats for periods up to 111 days. There was no evidence of any carcinogenic effect of Pearl millet on the thyroid gland or other vital organs, but the main features were goiter and entero-hepatonephropathy. In male goats, dietary potassium iodate was neither toxic nor protective against goiter. Severe damage to the thyroid follicles associated with prominent alopecia, nervous signs and exophthalmia were correlated with changes in serum AST, GGT and ALP activities and total protein, albumin, globulin, total lipid, cholesterol, creatinine, calcium, inorganic phosphate, magnesium, iodine and selenium concentrations and with alteration in thyroid, liver, kidneys, heart, spleen and semi-membranous muscles iodine and selenium levels and in hematology.

Key words: Potassium iodate, pearl millet, Nubian goats, thyroid gland

INTRODUCTION

Over the years, there has been a global awareness of the prevalence of iodine deficiency and its serious consequences on health. Some international organization such as UNICEF, Swedish Save the Children and International Science Program in the Chemical Sciences have provided financial assistance in order to identify causative factors and control iodine deficiency disorders in Western Sudan. El Tom *et al*. (1984, 1985) have shown that in Darfur State, Western Sudan, goiter prevalence is high in humans and that 85% of the school children are goitrous. These authors have suggested that the main cause of goiter is iodine deficiency and that other factors in food or water could contribute to its high endemicity.

Abdel Gadir (1995, 2001) have described the hazards associated with the occurrence of goitrogenic substances in the natural environment with particular emphasis on plant-derived compounds and also evaluated the nutritive value and goitrogenic activity of the graminaceous plant, Pearl millet (*Pennisetum typhoides*), a crop commonly known as Dukhn and cultivated in Western Sudan.

The present study was undertaken to investigate the role of orally administered potassium iodate, within the range to which the human beings could be exposed, in goitrogenicity and extra- thyroid effects of Pearl millet in the goat, an animal which lives in close association with man in the Sudan.

MATERIALS AND METHODS

Goats and Feed

Twelve clinically healthy, male Nubian goat kids, 5-18-month-old, were housed in pens within the premises of the Department of Veterinary Medicine, Pharmacology and Toxicology, University

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of Khartoum; they were fed on goat concentrate ration (up to 0.5 kg/head day), had free access to drinking water and allowed a 15 day preliminary period during which time they were injected with prophylactic doses of oxytetracycline (Agropharm Ltd., UK) and sulphamethazine (Havee Co., The Netherlands) for the control of bacterial infection and coccidiosis, respectively. At the end of the preliminary period, the goats were assigned to 4 groups, each of 3 animals. Goat kids 13, 14 and 15 were fed the untreated diet and served as controls (Group 1). Clean Pearl millet grains produced in Marrah Mountains Area, Western Sudan, were purchased from Khartoum-North Cereals Market, ground and thoroughly mixed with the basal ration and fed at 1 g kg^{-1} to male kids 16, 17 and 18 (Group 2). Potassium iodate (BDH Chemicals Ltd., UK) was thoroughly mixed with the goat concentrate diet at 50 ppm and fed to male kids 19, 20 and 21 (Group 3). A mixture of dietary millet at 1 g kg^{-1} and potassium iodate at 50 ppm was fed to male goats 22, 23 and 24 (Group 4). Feeding continued daily until the goats died or were slaughtered.

Laboratory Analyses

The goats were bled from the jugular vein on 3 occasions before feeding commenced and then at weekly intervals thereafter for hematology and serum analysis. Hemoglobin (Hb) concentration, Packed Cell Volume (PCV), Red Blood Cell (RBC) and White Blood Cell (WBC) counts, Mean Corpuscular Volume (MCV) and Mean Corpuscular Hemoglobin Concentration (MCHC) were estimated (Schalm *et al*., 1975).

Sera were analyzed for the Activities of Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP) and Gamma Glutamyl Transferase (GGT) and for the concentrations of total protein, albumin, total lipid, cholesterol, bilirubin, creatinine, calcium, phosphorus and magnesium by commercial kits (Randox Laboratories, UK). Serum and tissue (thyroid, liver, kidneys, spleen, heart and semimembranosus muscle) were analyzed for the concentrations of iodine and selenium by use of Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) as described by Beauchemin (1991).

Pathological Examinations

Necropsies were undertaken on all goats immediately after death or humane slaughter to identify gross lesions and specimens of the thyroid, liver, kidneys, intestine, spleen, heart, lungs, testicles, CNS and peripheral nerves were fixed in 10% neutral buffered formalin, embedded in paraffin wax, sectioned at 6 μm and stained with Hematoxylin and Eosin (H and E) for histopathologic examinations.

Statistical Analysis

The significance of differences between means was compared at each time point using Duncan's multiple range test after ANOVA for one- way classified data (Snedecor and Cochran, 1989).

RESULTS

Clinical Findings

The control goats 13, 14 and 15 (Group 1) remained clinically healthy throughout the experiment and were humanly slaughtered on day 62. In male goats 16, 17 and 18 (Group 2) fed millet at 1 g/kg/day, diarrhea was first observed within 2 days post feeding and continued for 6 days; it was severe in goat 18 with inappetence, dehydration, loss in condition and recumbency before death on day 10. Male goats 16 and 17 in Group 2 were slaughtered on day 33. Male animals 19, 20 and 21 (Group 3) receiving dietary potassium iodate at 50 ppm showed no clinical abnormalities and were slaughtered on day 33. Kids 22, 23 and 24 (Group 4) fed the mixture of 1 g/kg/day of millet plus 50 ppm of potassium iodate had diarrhea within 3 days post feeding, dehydration and weakness. Goat kid 23 died on day 7 and kid 24 was slaughtered in a moribund condition on day 27. Male goat kid 22 showed rough hair, alopecia, exophthalmia and diarrhea between day 80 and 100 and was slaughtered in extremis on day 111.

Pathological Changes

In animals of Group 4, there was pallor, enlargement and firmness of the thyroid gland, hepatic fatty change, congestion of the renal cortico-medullary junction, gelatinization of the kidney pelvis and patchy pulmonary cyanosis. Goat 22 in Group 4 showed gelatinization of the semi-membranous muscle. In kids of Group 2, the thyroid gland was slightly enlarged, pale and soft, the liver was fatty with distended gall bladder, the renal cortico-medullary junction was congested, the renal pelvis was gelatinous and the lungs were slightly cyanotic or emphysematous. In kids of Group 3, there was no change in the thyroid gland, but the liver revealed slight fatty change and the kidneys had congestion at the cortico-medullary junction. No lesions were detected in kids of the control (Group 1) or in other tissues including heart, testicles, brain or peripheral nerves of the test groups.

On microscopy, In Group 2, the thyroid follicles varied in size and colloid content with damaged follicles and lymphocytic infiltration. In Group 4 especially the goat kid which survived for 111 days, the thyroid follicles showed hyperplasia of the epithelial cells (Fig. 1) with interstitial fibroplasia. In goats fed potassium iodate alone (Group 3) and in the control goats (Group 1), there were no significant changes in the thyroid follicles. In goats fed millet alone or millet plus potassium iodate, there was catarrhal enteritis with packing of the intestinal lamina propria with lymphocytes. The liver showed cytoplasmic fatty vacuolation of the centrilobular hepatocytes and the epithelial cells of the renal proximal

Convoluted tubules were degenerated and some of the glomerular tufts were shrunken. The lumina of some of the degenerated renal tubules contained acidophilic homogeneous material and the red pulp of the spleen had hemosiderin deposits.

Hematological Changes

The values of Hb were lower ($p<0.05$) in Groups 2 and 4 and those of MCV were higher ($p<0.05$) in Group 2 and lower ($p<0.05$) in Group 3 than the controls (Group 1). The values of WBC were higher ($p<0.05$) in Group 4 than the controls and those of RBC, PVC and MCHC were not different among the treatment groups (Table 1).

Serobiochemical Changes

There was a significant increase ($p<0.01$) in the activity of AST in Groups 2-4 and in ALP ($p<0.001$) in Group 3 with no changes in that of GGT in any of the test groups (Table 2). The concentrations of total protein and globulin did not change in any of the test groups when compared to the controls (Group 1). Total lipid concentration was lower ($p<0.05$) in Groups 2 and 3 and that of creatinine was lower ($p<0.05$) in Groups 2 and 4. The concentration of cholesterol was lower ($p<0.05$-0.01) in Groups 2 and 3 than the controls. The concentration of selenium was lower ($p<0.05$) in Group 4 and that of iodine was lower ($p<0.05$) in Group 2 and higher ($p<0.05$-0.001) in Groups 3 and 4 than the controls. The concentration of bilirubin was lower ($p<0.05$) in Group 4 than other groups.

Changes in Tissue Iodine and Selenium Concentrations

Iodine concentrations in the liver, kidneys, heart, spleen and semimembranosus muscle of goats in group 4 were higher ($p<0.05$-0.001) than the controls (Group 1) (Table 3). The concentration of iodine in the liver and heart of Group 2 was lower ($p<0.05$-0.01) and that in the kidneys of Group 2 was higher ($p<0.05$) than the controls (Group 1). Although the concentration of iodine in the tissues of Group 3 varied, it did not show a significant change. The concentrations of selenium in the liver, kidneys, heart and spleen were not different among the treatment groups. However, selenium concentration in the semimembranosus muscle of Group 2 was higher ($p<0.05$) than other groups.

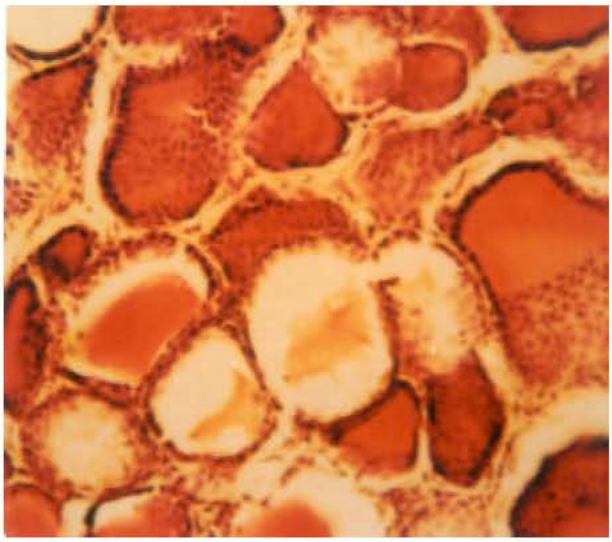

Fig. 1: Thyroid gland of male goat kid fed a mixture of dietary millet at 1 g/kg/day and potassium iodate at 50 ppm, showing follicular-cell hyperplasia H and E X 120

Table 1: Hematological changes in male goat kids fed Pearl millet, potassium iodate or their mixture

Group No.	Hb (g dL^{-})	PCV (%)	RBC (x 10^6 mm^3)	MCV (m^3)	MCHC (%)	WBC (x 10^3 mm^3)
1 (Control)	7.20±0.27	29.21±2.30	11.27±1.30	25.90±0.38	24.03±3.50	10.15±0.90
2 (1 g kg^{-1} millet)	5.83±0.14*	25.25±0.43^{NS}	8.43±0.03^{NS}	30.01±0.63*	23.08±0.10^{NS}	9.31±0.48^{NS}
3 (50 ppm potassium iodate)	6.16±0.06^{NS}	26.67±0.35^{NS}	11.98±0.52	22.26±0.12*	23.10±0.06^{NS}	11.50±0.29^{NS}
4 (1 g kg^{-1} millet + 50 ppm potassium iodate)	5.40±0.23*	21.40±2.03^{NS}	8.97±0.04^{NS}	23.80±0.43^{NS}	25.30±0.64^{NS}	16.50±0.29*

Values are means±SD; NS = Not significant; *p<0.05

Table 2: Serobiochemical changes in male goat kids fed Pearl millet, potassium iodate or their mixture

	Groups			
Parameters	1 (Control)	2 (1 g kg^{-1} millet)	3 (50 ppm potassium iodate)	4 1 g kg^{-1} millet + 50 ppm potassium iodate
ALP (iu)	74.60±6.90	51.10±7.90	393.10±19.8***	40.00±1.30**
GGT (iu)	32.80±3.00	36.00±0.49	41.50±4.40^{NS}	51.60±7.30^{NS}
AST (iu)	34.14±6.90	47.76±2.99**	59.13±6.21	79.17±10.31**
Total protein (g dL^{-1})	5.70±0.15	6.40±0.21^{NS}	50.50±0.30	5.32±0.40^{NS}
Albumin (g dL^{-1})	2.50±0.30	2.41±0.20^{NS}	1.38±0.05*	1.90±0.50^{NS}
Globulin (g dL^{-1})	3.20±0.40	3.99±0.22^{NS}	4.12±0.28^{NS}	3.42±0.50^{NS}
Total lipid (mg dL^{-1})	335.20±12.00	295.90±7.04*	292.50±7.50*	337.60±5.40^{NS}
Cholesterol (mg dL^{-1})	64.00±5.00	44.00±6.10	40.50±2.70**	56.0±1.90^{NS}
Creatinine (mg dL^{-1})	1.23±0.04	0.90±0.09*	1.06±0.09^{ns}	0.91±0.09*
Bilirubin (mg dL^{-1})	0.53±0.20	0.33±0.16^{NS}	0.56±0.17^{NS}	0.07±0.03*
Selenium (µg mL^{-1})	0.39±0.03	0.297±0.04^{NS}	0.32±0.95^{NS}	0.26±0.02
Iodine (µg mL^{-1})	0.14±0.03	0.064±0.006*	0.44±0.07**	0.254±0.036*

Values are means±SD; NS = Not significant; *p<0.05; **p<0.01; ***p<0.001

Changes in Thyroid Iodine and Selenium Concentration

Changes in the concentrations of iodine and selenium in the thyroid gland of the male goats on Pearl millet grain, potassium iodate or their mixture are presented in Fig. 2. The concentration of thyroid iodine was higher (p<0.05-0.001) in Groups 2 and 3 than the controls. The concentration of selenium in the thyroid gland of the test animals did not change.

Table 3: Iodine and selenium concentration in tissues of male goat kids fed Pearl millet, potassium iodate or their mixture

	Groups			
Tissue	1 (Control)	2 (1 g kg^{-1} millet)	3 (50 ppm potassium iodate)	4 1 g kg^{-1} millet + 50 ppm potassium iodate
Iodine (μg g^{-1})				
Liver	0.066±0.003	0.004±0.00**	0.210±0.13^{NS}	0.263±0.017**
Kidneys	0.058±0.005	0.133±0.007*	0.170±0.13^{NS}	0.326±0.06*
Heart	0.102±0.001	0.095±0.001*	0.085±0.03^{NS}	0.366±0.05*
Spleen	0.091±0.001	0.098±0.003^{NS}	0.125±0.007*	0.267±0.004***
S.M. Muscle	0.150±0.03	0.050±0.002^{NS}	0.181±0.30^{NS}	1.840±0.22*
Selenium (μg g^{-1})				
Liver	0.196±0.003	0.270±0.1^{NS}	0.170±0.035^{NS}	0.200±0.35^{NS}
Kidneys	0.644±0.03	0.520±0.1^{NS}	0.630±0.029^{NS}	0.450±0.11^{NS}
Heart	0.128±0.005	0.110±0.6^{NS}	0.230 ± 0.1^{NS}	0.100±0.17^{NS}
Spleen	0.201±0.001	0.200±0.006^{NS}	0.240±0.064^{NS}	0.230±0.02^{NS}
S.M. Muscle	0.066±0.003	0.210±0.02*	0.050±0.015^{NS}	0.040±0.01^{NS}

Values are means±SD; NS = Not significant; *p<0.05; **p<0.01; ***p<0.001

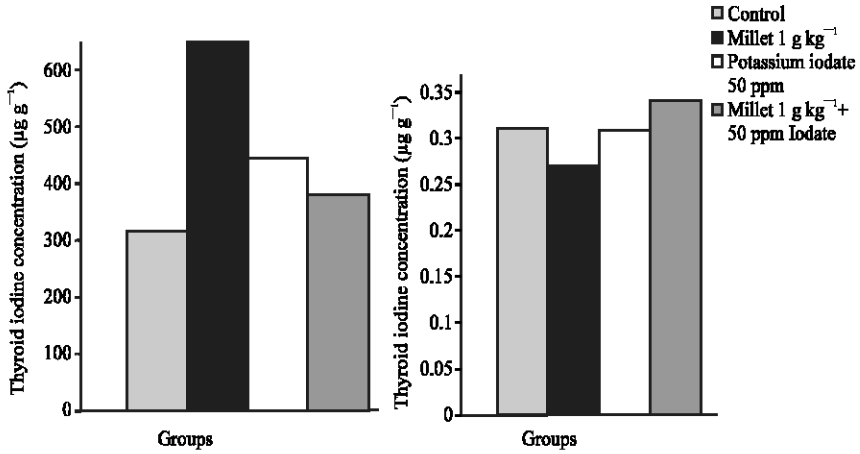

Fig. 2: Changes in concentration of iodine and selenium in the thyroid gland of male goat kids on millet, potassium iodate or their mixture

DISCUSSION

The present study has shown that Pearl millet (*P. typhoides*) is both goitrogenic and enterohepatonephrotoxic and is fatal to male Nubian goats when incorporated in the diet at 1 g/kg day. This study has also shown that dietary potassium iodate at 50 ppm is not toxic to goats and that it does not protect against millet goitrogenesis or extra-thyroid effects on male goats.

Indeed, the mixture of dietary millet and potassium iodate produced severe structural and functional changes in the thyroid gland as evidenced by the existence of damaged follicles, marked lymphocytic infiltration, hyperplasia of the epithelial cells of the thyroid follicles and fibroplasia. However, neoplasia was not detected in male goats fed dietary millet with or without potassium iodate. The alterations in total iodine and selenium concentrations in the thyroid gland of male goats on dietary millet with or without potassium iodate point to thyroid disease.

It has been found that toxins such as polyphenols and phytate occur naturally in millets (Hulse *et al*., 1980). It is likely that these goitrogenic substances in millet are concentrated in the thyroid gland and inhibit hormone synthesis at stages with the major effect being to block the release

of thyroid hormones. Unfortunately, we have not measured the concentration of T4, T3 or TSH in the serum of millet fed goats for lack of facilities.

Iodine prophylaxis was introduced a long time ago in several European countries, but endemic goitre is still present despite the efforts exerted for control.

In the present study, alopecia and exophthalmia were among the important signs in male goats fed the mixture of dietary millet and potassium iodate.

It is well known that selenium deficiency decreases iodine, T4 and T3 concentrations in the thyroid gland (Arthur *et al*., 1990).

The development of diarrhea in male goats fed Pearl millet may be a consequence of enteritis produced by the polyphenols and/or unknown substances contained in the millet grain and dehydration probably resulted from fluid loss from the alimentary tract. Ataxia might have been due to hepatopathy as the central and peripheral nervous systems showed no observable lesions. Furthermore, hepatic damage accompanied with alteration in serum enzyme activities and in the concentrations of total lipids and total cholesterol indicated liver malfunction. However, the absence of bilirubinemia suggested that millet feeding with or without potassium iodate is unlikely to interfere with the excretory ability of the hepatocytes, probably because none of the hepatic lesions was predominantly periportal. Likewise, the feeding to Nubian goats of *Jatropha curcas* and *Croton macrostachys* (Abdel Gadir *et al*., 2003) did not produce an increase in serum bilirubin concentration indicating that the ability of the liver to excrete bilirubin remained unchanged. The absence of hypoproteinemia in the millet-fed animals with or without potassium iodate was not a puzzle and it was interpreted as the result of mild dehydration. In spite of the occurrence of nephropathy in the test animals the concentrations of serum creatinine did not change. It has been found that fermented and processed fermented millets prevent the development of goitre but produce entero-hepatonephrotoxicty in Nubian goats (Abdel Gair and Adam, 2000).

We conclude that Pearl millet incorporated in the diet at 1 g/kg day produced in male goat kids goiter and extra-thyroid lesions mainly in the liver, kidneys and intestine and that incorporating potassium iodate at 50 ppm in the diet did not protect animals against Pearl millet goitrogenesis.

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