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Effect of administering a diet contamined with fumonisins on the kidneys of wistar rats

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ABSTRACT. Fumonisins (FBs) are mycotoxins produced by *Fusarium* molds. Several works have shown contamination of maize by this toxin. Fumonisin B1 (FB-1) is found in greatest proportion (about 70%), resistant to several industrialization processes. In that context, the objective of this work was to analyze the effect of administering a diet contaminated with FB-$_1$ on the morphophysiology of the kidneys of 21-day old male Wistar rats. The animals were divided into 2 groups: G0 (with animals receiving feed free of FBs) and G6 (6mg of FB_1 kg^{-1} of feed). The diet was administered during 42 days. After that period, the animals were placed in metabolic cages for urine collection, blood was collected for analysis of plasma creatinine, and the kidneys were fixed and stained with Masson's trichrome. We observed that FB_1 administration did not affect feed intake, body weight gain and animal growth. The normal levels of plasma creatinine suggest that the toxin did not lead to glomerular lesion. There was also no change in water intake, osmolarity and excretion of sodium in urine. However, there was a significant increase in urine volume and potassium excretion in urine, with mild tubulointerstitial changes in the outer cortex for the group receiving the mycotoxin.

Keywords: nephrotoxicity, tubulointerstitial changes, morphophysiology of the kidneys.

Efeito da administração de ração contaminada com a micotoxina fumonisinas sobre os rins de ratos wistar

RESUMO. Fumonisinas (FBs) são micotoxinas produzidas por fungos do gênero *Fusarium*. Diversos trabalhos demonstraram a contaminação do milho por essa toxina. A fumonisina B1 (FB-1) é encontrada em maior proporção (cerca de 70%), sendo resistente a vários processos de industrialização. De acordo com este contexto, o trabalho em foco teve como objetivo analisar o efeito da administração de dieta contaminada com FB-1 sobre a morfofisiologia renal de ratos Wistar machos, com 21 dias de idade. Os animais foram divididos em 2 grupos: G0 (ração isenta de FBs) e G6 (alimentados com 6mg de FB1 kg-1 de ração). A dieta foi administrada por 42 dias. Após esse período, os animais foram colocados em gaiolas metabólicas para coleta da urina, o sangue foi coletado para análise da creatinina plasmática, e os rins fixados e corados pelo Tricrômico de Masson. Observou-se que a administração de FB1 não afetou o consumo de ração, o ganho de peso e crescimento dos animais. A normalidade nos níveis da creatinina plasmática sugere que a toxina não induziu lesão glomerular. Não houve alteração na quantidade de água ingerida, na osmolaridade e na excreção urinária do sódio. No entanto houve aumento significativo no volume urinário e na excreção urinária do potássio e presença de alterações tubulointersticiais de intensidade leve no córtex externo, no grupo que recebeu a micotoxina.

Palavras-chave: nefrotoxicidade, alterações tubulointersticiais, morfofisiologia renal.

Introduction

Fumonisins (FBs) represent a family of mycotoxins produced by genus *Fusarium*, which infest maize and other grains. The intake of grains contaminated with this mold is associated with harm to several body systems, including the kidneys (RILEY et al., 1994; POZZI et al., 2002).

Among fumonisins, B_1 (FB_1), produced by genus *Fusarium* is the most abundant and harmful to health. Because it is resistant to industrialization processes, FB_1 is found in industrialized foods, such as maize flour and corn meal (KAWASHIMA; SOARES, 2006;). Fumonisin B_2 and B_3 are produced by the same species that produce FB_1, have the same toxic effect of FB_1, but occur in much smaller amounts (RHEEDER et al., 2002).The toxicity of FB_1 lies in its structural similarity with sphingolipids, being capable of inhibiting the ceramide synthase enzyme. This inhibition results

in accumulated sphingosine and sphingamine in serum, urine and tissues, and reduces the biosynthesis of sphingomyelin. Fumonisin B_1 intoxication compromises important physiological processes, such as cell signaling and communication, incorporation of folic acid by cells, and is related to the onset of cancer (IARC, 1993; RILEY et al., 2001; NOUR et al., 2007; RILEY; VOSS et al., 2007).

The manifestations of FB_1 intoxication are specific to each animal species, such as leukoencephalomalacia in horses (SMITH et al., 2002) and pulmonary edema in pigs (DILKIN et al., 2004; SMITH et al., 2009). In lab animals, in general, the liver and kidneys are most affected, with sensibility varying according to species, lineage, sex and exposure dose (VOSS et al., 2007).

Although FB_1 hepatotoxicity is relevant in all studied species, studies indicate that in certain animals, such as rabbits (GUMPRECHT et al., 1995) and some species of rats (RYLEY et al., 1994), there is greater sensibility of the kidneys to that mycotoxin. In experiments with Sprague-Dawley rats, renal effects are more intense than in the liver, including inflammation, necrosis and apoptosis (RYLEY et al., 1994).

There is a close relation between kidney lesions caused by FB_1 with sphingolipid metabolism disorder. The presence of high levels of sphingosine and sphingamine in urine indicates the kidney as the target with the greatest accumulation of these precursors (RILEY et al., 1994; RILEY; VOSS, 2007).

Changes in renal structure, induced by FB_1, have been described in different studies (SUZUKI et al., 1995; HARD et al., 2001; MARTHUR et al., 2001; THEUMER et al., 2002) indicating effects on the glomerular and tubular region, the most frequent morphological change being individual cell necrosis, with small variations between species (BUCCI et al.,1998).

Riley et al. (1994) highlight that the nephrotoxicity offered by FB_1 could extend to humans. An initial renal lesion, as well as the physiopathological processes that unleashed it, can contribute to the development of chronic kidney disease (CKD), which is characterized by a slow, progressive and irreversible loss of kidney function, accompanied by glomerulosclerosis, tubulointerstitial fibrosis and vascular sclerosis. In the most advanced stage of CKD, the kidneys cannot maintain its functions, often leading to complications characteristic of functional loss, such as anemia, bone disease, malnutrition and metabolic acidosis (BECKER; HEWITSON, 2000; PASSOS et al., 2003; BASTOS et al., 2004; ROMÃO JÚNIOR, 2004; MIRANDA et al., 2009; PAIGE; NAGAMI, 2009; SCHNELLMANN, 2010).

Considering that context, the objective of this work was to analyze the effect of a diet contaminated with B_1 on the morphophysiology of the kidneys of male adult Wistar rats.

Material and methods

The study used male 21-day-old Wistar rats. The animals were kept in a vivarium at constant temperature around 23ºC, with automatically controlled photoperiod (12h dark $12h^{-1}$ light) and divided into two groups: G0 (n = 8)with animals receiving feed free of FBs; and G6 (n = 8), receiving feed with addition of 6 mg fumonisin B_1 kg^{-1} of feed.

To prepare the basic diet (Table 1) the corn, wheat bran and soybean meal were ground separately in knife mill with sieve particle size of 0.50 mm in diameter and manually mixed with other ingredients. Shortly after, total amount of the basal diet was divided into two parts and one of them received incorporation of the culture medium of the fungus *F. verticillioides* strain MRC 826 (LAMIC-UFSM, Santa Maria, Brazil), being resubmitted to mixing and homogenization. Diets with desired fumonisin concentrations were obtained by mixing appropriate proportions of basal diet with and without incorporation of the culture medium of the fungus. The diets were pelleted in an electric mill, adding water in the proportion of 30% of the mass, and then dried in a forced air oven (55°C) for 24 hours. Food and water were provided *ad libitum* to the animals throughout the experiment.

Table 1. Composition of the basal diet given to the rats during the experimental period.

Ingredient	(%)
Corn	33.63
Soybean meal	33.10
Wheat bran	27.20
Soybean oil	2.30
Limestone	2.07
Dicalcium phosphate	0.73
Common salt (iodized)	0.50
Premix vitamínico	0.10
Premix mineral	0.35
BHT3	0.02
Dry matter (%)	93.60
Gross energy (kcal kg^{-1})	4120.46
Crude protein (%)	22.37

1 vitamin supplement, composition per kg: ác. Folic 200 mg; ác. nicotinic 3,000 mg, biotin 20 mg, 1.600 mg calcium pantothenate, pyridoxine HCl 700

mg, 600 mg riboflavin, thiamine HCl 600 mg, Vitamin A 4,000,000 IU; 2,500 mg vitamin B12, vitamin D3 100,000 IU, 100,000 IU vitamin E; vitamin K1 75 mg.

2 Mineral Supplement, composition per kg: 14.26 mg boron, calcium 142.94 g, 44.9 g chlorine, copper 72.41 mg, 28.65 mg chromium, sulfur 8.6 g, 1,000 mg iron, fluorine 28.72 mg, 56.9 g phosphorus, iodine 5.95 mg, 2.85 mg lithium, magnesium 14.48 g, 300 mg manganese, molybdenum 4.32 mg, 14.31 mg nickel, potassium 102.86 g; 4.28 mg selenium, silicon 143.26 mg, sodium 29.38 mg, 2.87 mg vanadium, zinc 860 mg.

3 Butylhydroxytoluene

4 According to the bromatological analysis performed.

The animals received the diet for 42 days and they were kept in polypropylene cages (30 x 20 x 13 cm) with two animals per cage. After that period, they were placed in a metabolic cage, drawn galvanized wire and galvanized sheets (27 x 19 x 20 cm) with one animal per cage., to measure water intake, urine volume over 24 hours and collect urine. Blood was also collected to measure plasma creatinine. Body weight and naso-anal length were measured before diet administration and at the end of diet administration (42 days). Feed intake was measured weekly to estimate the daily intake in the first, second, penultimate and final week of the experiment.

To euthanize the animals, sodium thiopental (Thionembutal®) was used in intraperitoneal injections, at a concentration of 40 mg kg^{-1} of body weight. After euthanasia, the kidneys were collected, fixed, embedded in paraffin, sectioned at 5μm and strained using Masson's trichrome. The images obtained under light microscopy were captured using a video camera (Moticam1000 – 1.3M Pixel USB 2.0) and transmitted to the computer. Five fields of outer and five of inner renal cortex were evaluated with light microscopy, per animal. We quantified the number of foci / field / animal with presence of lesions such as glomerular sclerosis, tubulointerstitial fibrosis, inflammatory infiltrate or intratubular cylinders.

Plasma creatinine was quantified using the endpoint colorimetric method (Analisa Kit). In that method, creatinine reacts with picrate in an alkaline medium, originating a colored complex that is photometrically measured at 510 nm and is directly proportional to creatinine concentration.

To analyze urine osmolarity, an osmometer (VAPRO 5520) was used, and a flame spectrometer (B262) was used to quantify Na and K+ in urine.

Data were analyzed with Student's t test using the GraphPadPrism statistical package (*GraphPad Software*, version 5.0) and expressed as mean ± standard deviation.

The experiments were carried out in accordance with the norms set by the National council for the control of animal experimentation (CONCEA) and approved by the Animal Ethics Committee of the State University of Maringá (CEAE) (Protocol 068/2009).

Results

Feed intake, body weight and naso-anal length

The animals featured uniform body weight and naso-anal length (Table 2).

The analysis of daily feed intake showed no significant difference between the groups (Table 3), suggesting that fumonisin B_1, at 6 mg kg^{-1} of feed, did not interfere in the feed intake pattern. Moreover, the standard deviation of feed intake was low, indicating that ingestion of the toxin was uniform for all animals.

It was also observed that ingestion of the toxin, at the studied dose and period, did not cause any change in body weight gain and animal growth (Table 2).

Table 2. Body weight and naso-anal length in rats of the groups G0 (with animals receiving feed free of FBs- n = 8) and G6 (with a 6 mg FB_1 kg^{-1} of feed – n = 8).

Groups	Body weight (g)			Naso-anal length (cm)	
	Before diet administration	At the end of diet administration (42 days)	Body Weigh gaint	Before diet administration	At the end of diet administration (42 days)
G0	42.38±5.37 [a]	244.8±20.25 [a]	201.8±20,59 [a]	10.94±0.62 [a]	21.38±0.52 [a]
G6	46.75±4.03 [a]	239.6±7.19 [a]	192.8±13.99 [a]	11.44±0.56 [a]	21.13±0.64 [a]

Data are expressed as mean ± SD . Different letters in the same column indicate significant statistical difference ($p < 0.05$).

Table 3. Feed intake (g day^{-1}) in rats of the groups G0 (with animals receiving feed free of FBs- n = 8) and G6 (with 6 mg FB_1 kg^{-1} of feed – n = 8).

Groups	Feed intake (g day^{-1})			
	First Week	Second week	Penultimate week	Last week
G0	10.03±0.38 [a]	12.50±0.38 [a]	19.13±0.35 [a]	20.13±0.52 [a]
G6	10.00±0.38 [a]	12.63±0.52 [a]	19.38±0.35 [a]	20.56±0.42 [a]

Data are expressed as mean ± SD. Different letters in the same column indicate significant statistical difference ($p < 0.05$).

Plasma creatinine

Normal levels of plasma creatinine were detected in animals from the group that received FB_1 (G6) (Figure 1), suggesting that the mycotoxin did not influence glomerular function to the point of compromising plasma creatinine clearance.

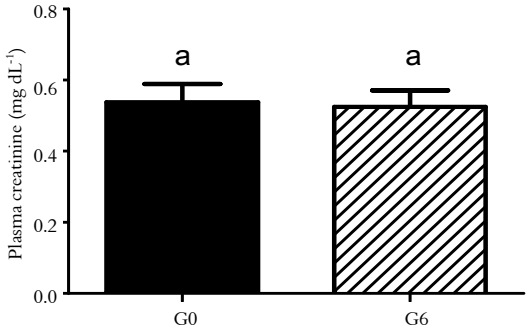

Figure 1. Plasma creatinine (mg dL-1) in rats of the groups G0 (with animals receiving feed free of FBs – n = 8) and G6 (diet with 6 mg FB1 kg^{-1} of feed – n = 8). Data are expressed as mean ± SD. Equal letters indicate there is no significant statistical difference (p = 0.6186).

Water intake, urine volume and urine osmolarity

The water intake of the animals in group G0 was not statistically different from those in group G6 (Figure 2A). However, the 24-hour urine volume of animals in group G6 was significantly greater than controls (Figure 2B).

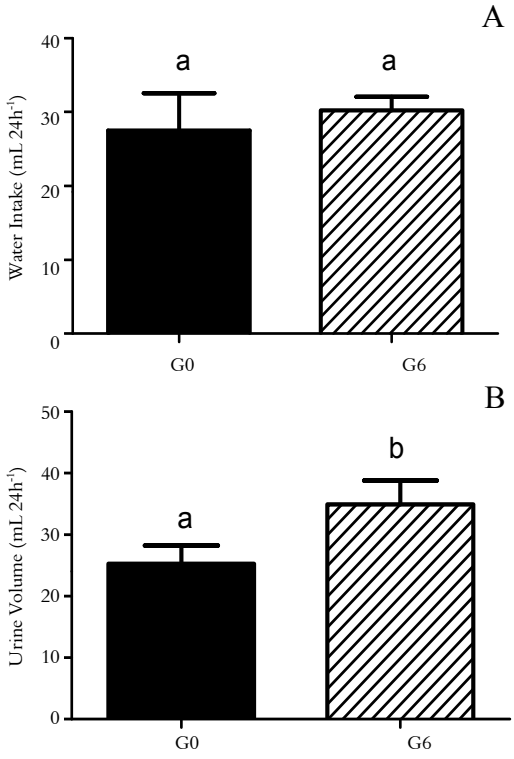

Figure 2. (A) Water Intake (mL $24h^{-1}$). (B) Urine Volume (mL $24h^{-1}$) in rats of the groups: G0 (with animals receiving feed free of FBs – n = 8) and G6 (diet with 6 mg FB_1 kg^{-1} of feed – n = 8). Data are expressed as mean ± SD. Equal letters indicate there is no significant statistical difference (in "A" p = 0.3467 and in "B" p = 0.0048).

The analysis of urine osmolarity showed that there was no significant difference between animals that received mycotoxin (G6) and controls (G0) (Figure 3).

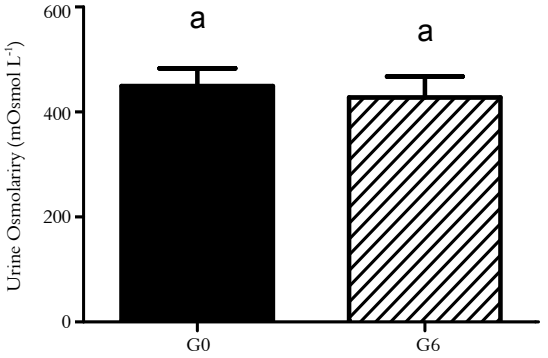

Figure 3. Urine Osmolarity (mOsmol L^{-1}) in rats of the groups: G0 (with animals receiving feed free of FBs – n = 8) and G6 (diet with 6 mg FB_1 kg^{-1} of feed – n = 8). Data are expressed as mean ± SD. Equal letters indicate there is no significant statistical differences (p = 0.7388).

Urinary excretion of sodium and potassium

There was no significant difference in Na^+ excretion in urine (Figure 4A) between the groups. However, a significant increase was observed in the excretion of K^+ in the animals that received the toxin (Figure 4B).

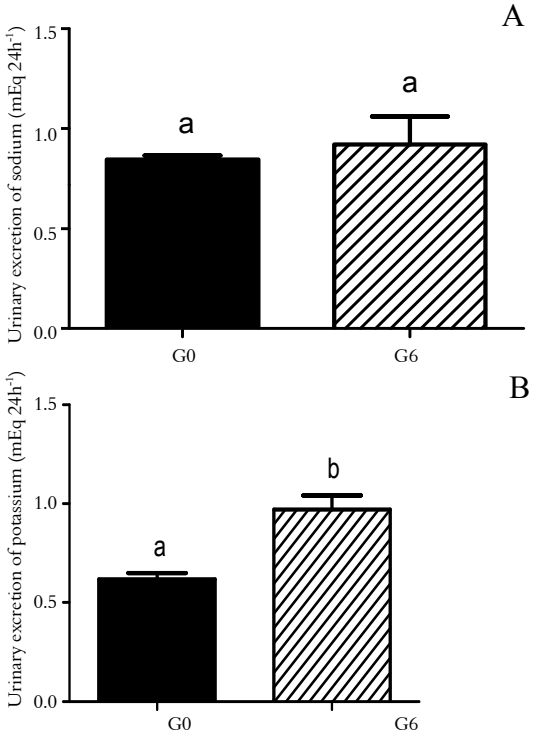

Figure 4. (A) Urinary excretion of sodium (mEq $24h^{-1}$). (B) Urinary excretion of potassium (mEq $24h^{-1}$) in rats of the groups: G0 (with animals receiving feed free of FBs – n = 8) and G6 (diet with 6mg FB_1 kg^{-1} of feed – n = 8). Data are expressed as mean ± SD. Equal letters indicate there is no significant statistical differences (in "A" p = 0.4022 and in "B" p = 0.0002).

Analysis of renal tissue

The analysis of the glomerular region showed glomeruli with well-preserved loops, with no

inflammatory infiltrate or sclerosis in either group (Figure 5A and B).

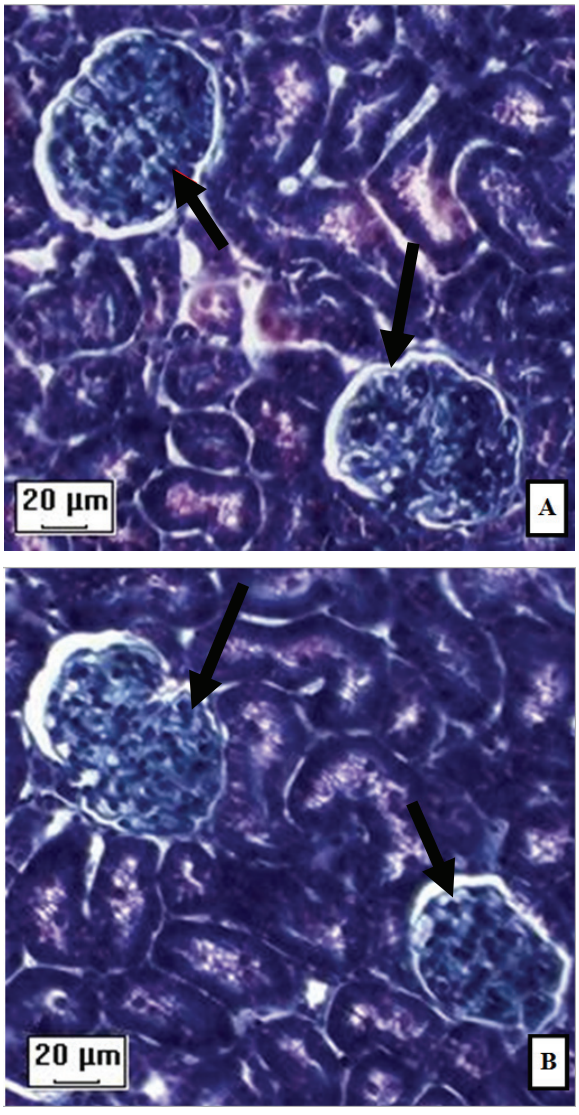

Figure 5. Histologic sections of renal cortex, stained with Masson's Trichrome Original magnification: 10x. Images representing the glomerular region of renal tissue in rats of the groups: A) G0 (with animals receiving feed free of FBs – n = 8). B) G6 (diet with 6 mg FB_1 kg^{-1} of feed- n = 8). Note, in both images, the arrows indicate glomeruli with loops well preserved, without sclerosis and inflammatory infiltrate.

With regard to the tubulointerstitial region, the presence of inflammatory infiltrate and fibrosis was observed, with mild intensity, in the outer renal cortex of the animals that received the toxin (G6) (Figure 6B). Figure 7 shows the quantification of these foci. No foci with changes in the inner cortex were observed.

Discussion

Several studies have shown an increase in plasma creatinine in different models of animals acutely exposed to FB_1 (EDRINGTON et al., 1995; SUZUKI et al., 1995; BONDY et al., 1996; BONDY et al., 2000; GELDERBLOM et al., 2001; ORSI et al., 2009).

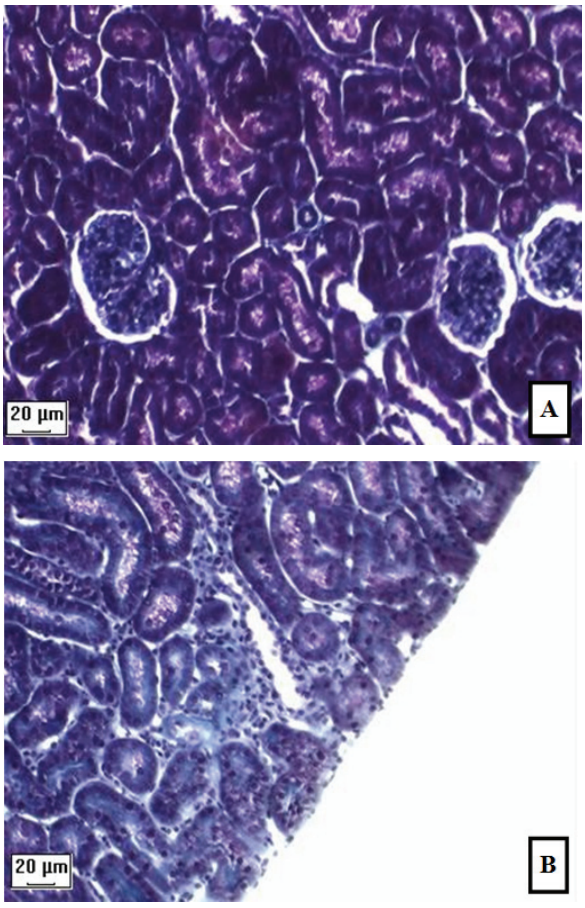

Figure 6. Histologic sections of renal cortex, stained with Masson's Trichrome. Original magnification: 10x. Images represent renal tubulointerstitium, in rats of the groups: A) G0 (with animals receiving feed free of FBs – n = 8). B) G6 (diet with 6 mg FB_1 kg^{-1} of feed- n = 8). Observe presence of inflammatory infiltration and fibrosis in the outer cortex in (B).

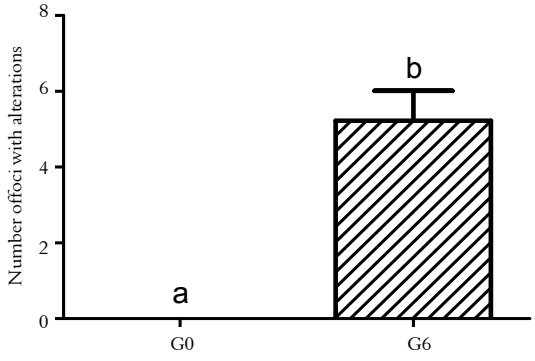

Figure 7. Number of foci with alterations in renal tubulointerstitium, in rats of the groups G0 (with animals receiving feed free of FBs FB_1- n = 8) and G6 (diet with 6 mg FB_1 kg^{-1} of feed – n = 8). Data are expressed as mean ± SD. Differents letters indicate significant statistical difference ($p < 0.05$).

Creatinine is a product of the metabolization of creatine in skeletal muscle, with constant synthesis, constantly excreted by the kidneys, thus maintaining adequate plasma levels. Plasma creatinine is used to rapidly evaluate glomerular function, as it is freely filtered in the glomeruli and is not significantly resorbed and secreted in the renal tubules[1]. Therefore, adequate clearance of plasma creatinine depends on the integrality of glomerular function. (WYSS; KADDURAH-DAOUK, 2000).

Edrington et al. (1995), working with lambs, observed an increase in plasma creatinine for animals that received, for 4 days, fumonisins B_1, B_2 and B_3, via gavage, at the doses of 11.1, 22.2 and 45.5 mg of fumonisins kg^{-1} of body weight, in the 7 days after the last dose.

In 2009, Orsi et al., working with rabbits (males), verified that oral administration of a single dose of fumonisin B_1 kg^{-1} of body weight, at the concentration of 31.5 mg, caused an elevation in plasma creatinine in 7 days, and proteinuria in 72 hours, following administration of the toxin.

Bondy et al. (2000), using male Sprague Dawley rats, in which the kidneys are considered the main targets of FB_1-induced nephrotoxicity, observed that daily intraperitoneal administration of 0.75 mg of FB_1 kg^{-1} of body weight caused a significant increase in plasma creatinine in the 4th and 6th consecutive days the toxin was administered. A study by Gelderblom et al. (2001), administering FB_1 at 10 and 25 mg FB_1 kg^{-1} for 24 months in male BD IX rats, showed an elevation in plasma creatinine. Those authors related the increase to histopathological lesions found in the kidneys.

We did not observe changes either in plasma creatinine or glomerular structure in the animals that received mycotoxin. Our results were different from the studies conducted with acute administration of the toxin, possibly because in those cases, in addition to acute administration, other animal models and administration methods were used, as well as higher doses of the toxin. We used a dose of 6mg of FB_1 per kg of feed, because it is near the contamination levels of food items in the Brazilian market, as indicated in studies performed in different states of the country (MALLMANNT et al., 2001; KAWASHIMA; SOARES, 2006;

Kawashima and Soares (2006) showed that samples of corn-based products available for sale in the city of Recife, Pernambuco state, between 1999 and 2001, showed a mean concentration of 0.615 mg of FB_1 kg^{-1}.

We also observed that administration of fumonisin B_1 at the dose of 6 mg kg^{-1} of feed, for 42 days, did not alter feed intake, weight gain and body growth of animals (Tables 2 and 3). These results are in accordance with the study by Theumer et al. (2002) with Wistar rats, in which FB_1 was administered in the diet, at the concentration of 100 mg kg^{-1} for 30 and 60 days.

Our results showed that administration of the toxin led to an increase in 24-hour urine volume, with no increase in water intake. Studies by Bondy et al. (1995), with the Sprague Dawley lineage, intraperitoneal (ip.) administration of the toxin at higher doses – 7 mg and 10 mg kg^{-1} – and acute treatment for 5 days, showed an increase in urine volume without increase in water intake. The authors suggested that the increase in urine volume was temporary, and argued that the kidney is capable of functionally adapting, therefore being able to recover after a brief period of polyuria. Confirming the argument of Bondy et al. (1995), the work of Suzuki et al. (1995), detected a significant increase in urine volume for animals that received the toxin (at the doses of 7 and 10 mg kg^{-1}), and a return of urine volume to normal levels on the 4th day in animals that received 10 mg of FB_1 kg^{-1}. The authors suggested that this recovery was related to homeostatic mechanisms to reduce liquid loss.

Our results show that, despite the increase in urine volume for animals that received the toxin, urine osmolarity remained stable. In the study by Suzuki et al. (1995), the increase in urine volume was accompanied by a reduction in urine osmolarity, in that the reduced urine osmolarity in the animals that received the dose of 10 mg of FB_1 kg^{-1} occurred until the 3rd day, with a slight increase in the 4th day, accompanying the normalization in water excretion observed in that period.

When we quantified urine potassium, we observed a significant increase in K^+ excretion in urine for animals that received the mycotoxin. This increase may have contributed to the maintenance of urine osmolarity, even with the increased urine volume observed in animals that received FB_1.

We did not observe a significant difference in sodium excretion in urine for animals that received fumonisin B_1. Sodium is the main cation of extracellular fluid (ECF), and the kidneys are their main path of excretion. Changes in ECF volume are corrected by mechanisms that involve sodium excretion or conservation by the kidneys; these mechanisms are regulated by the renin-angiotensin-aldosterone system, sympathetic nervous system and

[1]A small fraction of creatinine is secreted by the cation secretory system in the proximal tubule; however, as the dosage method stains a small amount of chromogens at the same rate as creatinine secretion, this method is used in practice to analyze renal function (STANTON; KOEPPEN, 2009).

natriuretic peptides, among others. Therefore, the analysis of sodium excretion in urine helps in evaluating renal tubular function (GUYTON; HALL, 2011).

Another parameter that makes it possible to evaluate tubular function is potassium excretion in urine, as the kidneys regulate their body concentration through mechanisms of control of reabsorption and/or secretion, located in the distal and collecting tubules (STANTON; KOEPPEN, 2009). The significant increase in K^+ excretion in urine for the animals that received the mycotoxin suggests that fumonisin B_1 may have affected the potassium transport mechanisms in the tubulointerstitial region.

Alterations in tubular transport caused by FB_1 administration were described by Suzuki et al. (1995) and Bondy et al. (1996). Those authors suggested that FB_1 could interfere in the tubular secretion and reabsorption of organic molecules, dependent on ionic transport along the nephron. Suzuki et al. (1995) suggest that the interruption of the metabolism of sphingolipids, unleashed by FB_1, would cause structural disturbances in the cell membrane, affecting its transporters and ion excretion through the kidneys.

When analyzing the tubulointerstitial region, we observed mild alterations in the region of the outer cortex, in the animals that received the mycotoxin. This observation is in agreement with studies that indicate subtle changes in the proximal tubules in the early stages of FB_1 exposure, and more drastic changes in chronic exposure, affecting especially the corticomedullary region (SUZUKI et al., 1995; BUCCI et al., 1998; POZZI et al., 2000; HARD et al., 2001; MARTHUR et al., 2001; THEUMER et al., 2002). It is possible that the change in the potassium excretion in urine observed in the group that received the toxin is related to the tubulointerstitial lesion evidenced by the presence of mild inflammatory infiltrate and fibrosis.

Normal interstitial space is compact. This space is occupied by fenestrated peritubular capillaries and a small number of fibroblast-like cells. Any evident expansion of the cortical interstice is generally abnormal. This expansion may be due to edema or infiltration by acute inflammatory cells, as in interstitial diseases, or can be caused by the accumulation of chronic inflammatory cells and fibrous tissue, as in chronic interstitial diseases (KUMAR et al., 2005). The presence of mononuclear infiltrate can be associated with toxic and infectious injury in the interstice. From this initial injury can result an irreversible chronic lesion, characterized by interstitial fibrosis and tubular atrophy (RIELLA, 2003). The occurrence of these tubulointerstitial changes can be linked to a decline in kidney function, meaning there is an association between histopathological alterations in the kidneys and modifications in biomarkers of kidney function. (RIYUZO; SOARES, 2002; RODRÍGUEZ-ITURBE et al., 2005).

The action mechanism of fumonisins is not yet fully known. However, these mycotoxins are structurally similar to sphingosine, which contains a long chain (sphingoid) that serves as the basic structure for several sphingolipids. Therefore, according to Wang et al. (1991), the toxicity mechanism consists of the inhibition of ceramide synthase, the enzyme responsible for the synthesis of sphingolipids. Acknowledging the importance of sphingolipids in cellular regulatory processes, including those related to proliferation and apoptosis, investigators proposed that ceramide synthase inhibition is a critical step in the toxic mechanism of fumonisin, unleashing a sequence of molecular events that eventually lead to cytotoxicity or neoplasia (WANG et al., 1991; SCHROEDER et al., 1994; HUNNAN; OBEID, 1995; YOO et al., 1996; MERRILL et al., 1997; RILEY et al., 1998).

Conclusion

Ingestion of the FB_1 mycotoxin at the dose of 6 mg kg^{-1} of feed for 42 days induced a small inflammation in the tubulointerstitial region of the outer cortex in the kidneys of Wistar rats and influenced potassium excretion from the kidney.

Acknowledgements

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