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Evaluation of dexamethasone and methylprednisolone administration on visceral organs prior to contrast radiography in Nigerian indigenous breed of dogs

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Abstract

The number of medical procedures using iodinated contrast media has increased in recent decades, though contrast media are regarded as safer. Nine Nigerian indigenous breed of dogs were acquired and housed in the Small Animal Kennel of the Nigerian Veterinary Research Institute Veterinary Hospital. The nine dogs were grouped into three groups of three animals each. Group A was the control, and were given urografin at 370 mg/kg, ten minutes before exposure to x-ray. Group B were given dexamethasone at 1 mg/kg 2 hours before x-ray and urografin ten minutes before exposure to x-ray. Group C were given methylprednisolone at 1 mg/kg 2 hours before exposure to x-ray, and urografin ten minutes before exposure to x-ray. All groups were given urografin 24 hours later at 370 mg/kg. Pathological changes in the liver and the kidney were more severe in the methylprednisolone treated group, followed by dexamethasone treated group. While, the dexamethasone treated group recorded more pathologies in the spleen. The use of anti-inflammatory drugs (dexamethasone and methylprednisolone) tends to be more protective in the heart. We recommend that the use of steroids such as dexamethasone and methylprednisolone be avoided in contrast radiography except where heart pathology exist

Keywords: Contrast radiography Dexamethasone; Methylprednisolone; Nephrotoxic; Urografin

1. Introduction

Radiographic contrast media are a group of medical drugs used to improve the visibility of internal fluid, organs and structures in medical imaging, such as angiography, computed tomography, diagnostic X-ray (radiology) and in radiotherapy for treatment planning (Therapeutically in hyperthyroid patients, to rapidly correct severe hyperthyroidism prior to thyroidectomy). The currently available contrast media are indispensable in the practice of radiology, for both diagnostic and therapeutic purposes [1, 2, 3]. The number of medical procedures using iodinated contrast media has dramatically increased in recent decades [3]. They are usually excreted within 24 hours [4]. During radiotherapy, they are recommended in intestinal obstruction due to postoperative intra-abdominal adhesion, Urografin may be safely administered via a nasogastric tube or oral route to decrease the need for surgical operation; furthermore, this may help the physician to operate on the patients who need surgery as early as possible [5]. Recent products are now safer, yet with mild potential risk associated with their use, especially the intravenous contrast agents. An ideal contrast media should be highly soluble, with low viscosity, low toxicity and rapidly excreted from the system. [6,7]. Although intravenous contrast mediums are well-tolerated and safe compounds, with rare adverse effects [3], one

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of such is Contrast-induced nephropathy, a well-known adverse reaction associated with the use of intravenous or intra-arterial contrast material. Other forms of adverse reactions include delayed allergic reactions, anaphylactic reactions, and cutaneous reactions [2,7]. Previous allergic reactions to contrast material is known to increase the risk of developing adverse reactions to contrast agents. Hence, the need to premedicate with corticosteroid and diphenhydramine to reduce the chance of life-threatening emergencies. Examples of these premedication drugs are, prednisone at 50 mg orally, 13 hr, 7 hr, and 1 hr before contrast media administration; hydrocortisone at 200 mg intravenously, 1 hr before contrast media administration; methylprednisolone 32 mg orally, 12 and 2 hr before contrast media administration is used [3]. The mechanisms leading to contrast media nephrotoxicity have not been fully elucidated, but it is generally attributed to severe reduction in medullary blood flow, leading to hypoxia and direct tubular damage due to toxicity of contrast media. The intravenous injection of radiographic contrast medium causes an initial increase in renal blood flow, followed by a more prolonged decrease in blood flow, which is, accompanied by a decrease in glomerular filtration rate, with the extra-renal vessels showing transient vasoconstriction followed by decrease in vascular peripheral resistance. The result is renal ischaemia. Other intrinsic causes of medullary ischemia include, increased oxygen consumption, increased intra-tubular pressure secondary to contrast-induced diuresis, increased urinary viscosity, and tubular obstruction. Note that, oxygen delivery to the outer medulla is less compared to that in the medulla, even under normal conditions [3]

The administration of urografin causes significant alterations in the renal histological structure that are irreversible. These changes were in the form of glomeruli shrinkage, widening of the urinary space and capillary congestion. Dilated renal tubules, pyknotic nuclei, partial loss of the apical brush border, cytoplasmic vacuolations, and interstitial peritubular exudates in the renal medulla. Nephrotoxicity as a result of the administration of urografin affects the cortex and the medulla [8].

2. Material and methods

Nine Nigerian indigenous breeds of dogs were acquired and housed in the Small Animal Kennel of the Nigerian Veterinary Research Institute (NVRI), Veterinary Hospital Vom. The nine dogs weighing between 14-18 kg, were accommodated and acclimatise in the kennel for two weeks. The dogs were physically examined, blood and faecal samples were screened at the clinical pathology and parasitology laboratories respectively, for haemoparasite, haemogram and helminthes. The haemogram from the clinical pathology were all within normal range, and the samples taken to Parasitology Laboratory were negative for helminths. Feed and water were provided *ad li-bitum* throughout the period of the experiment as fasting was not required. The dogs were grouped into three groups of three animals each. Group A were the control, and were given urografin at 370 mg/kg [9, 10] ten minutes before exposure to x-ray. Group B were given dexamethasone at 1 mg/kg, 2 hours before x-ray and urografin ten minutes before exposure to x-ray. Group C were given methylprednisolone at 1 mg/kg, 2 hours before exposure to x-ray, and urografin ten minutes before exposure to x-ray. Urografin alone at 370 mg/kg was administered 24 hours later to all the three groups. Twenty-four hours after the second administration of urografin. The animals were euthanised using xylazine at 4 mg/kg intravenously. The visceral organs of the experimental animals were harvested for evaluation of gross and histopathological lesions.

Table 1 Experimental design

Group	Treatment (2 hrs before x-ray)	No. of dogs	Treatment with urografin day zero before evaluation
I	Control	3	Second dose after 24 hours from the first dose
II	Dexamethasone 1 mg/kg IM. 1/7	3	First dose 2 hours after steroid administration second dose 24 hours after first administration
III	Methylprednisolone 1 mg/kg IM. 1/7	3	First dose 2 hours after steroid administration second dose 24 hours after first administration

KEY:- No.= Number; IM= Intramuscular

3. Results

All experimental animals were apparently healthy and active prior to onset of the experiment. However, following the administration of urografin and exposure to x-ray, the dexamethasone treated group were normal, while the control and the methylprednisolone treated groups were dull, with less activities especially with the control group. The reduced

activities in the control group observed after the first dose of the urografin, was more after the second dose of the urografin. Fed intake was minimal (scanty) in the control group and was moderate in the steroid treated groups after the administration of urografin.

3.1. Gross lesions

After euthanasia, organs in the abdominal and the thoracic cavities (Figure 1) were evaluated. Hydrothorax was observed to be severe in the control group, mild and brownish in the dexamethasone treated group and absent in the methylprednisolone treated group. Representative gross images, of the evaluated organs are presented (Figures 2-5). Hydro-pericarditis was also absent in the methylprednisolone treated group, mild in the dexamethasone treated group but, severe in the control group. The fluid in the thoracic cavity of the control group had blood sting, hence, was pinkish in colour. Furthermore, the thorax had about one-fifth of its volume fluid filled. Interestingly fluid accumulations within the abdominal cavities were not observed in any of the experimental group, except for the normal peritoneal fluid. Consequently, the urinary bladder of all the experimental groups were void of urine as they were all apparently empty.

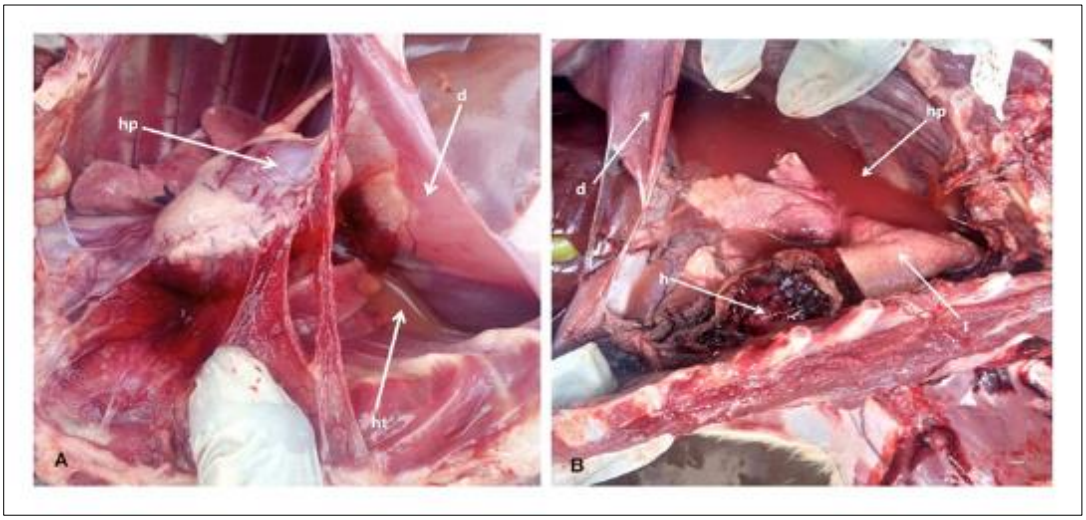

Figure 1 The thoracic cavity of group treated with dexamethasone (A); control (B) showing: - hp= hydropericardium; d= diaphram; ht= Hydrothorax; h= Heart; l= Lungs

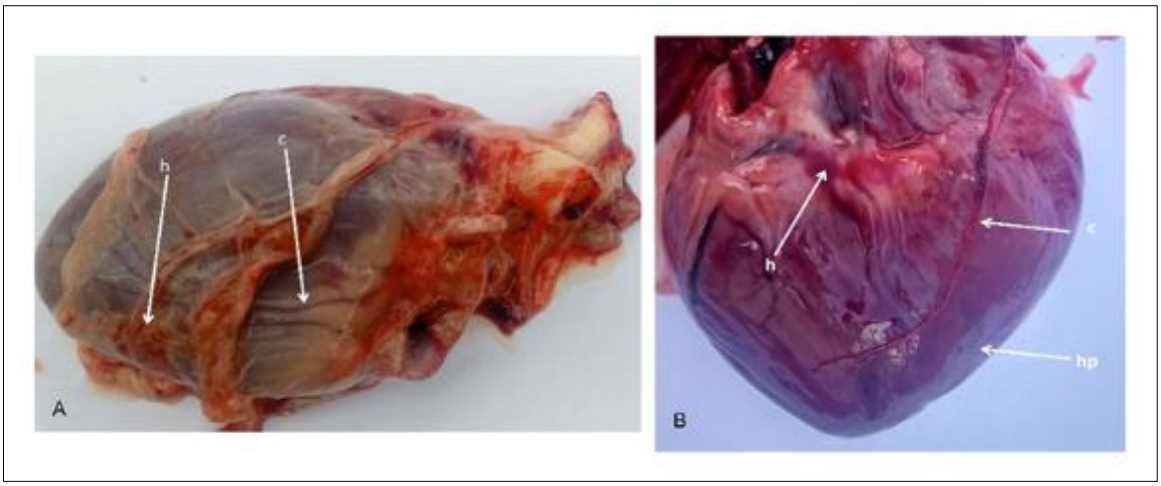

Figure 2 Photograph of the heart of group treated with dexamethasone (A); control (B) showing:- c= Congested coronary vessel; h= Haemorrage; hp= Hydropericardium

The heart was the first specific organ evaluated for pathological lesions (Figure 2). Congestion of the coronary vessels were severe as observed in the control group with more than 66% highly congested. Petechial and ecchimotic haemorrages were also observed in more than 50% of the myocardium, while, moderate spots were recorded within the atrium and ventricles. The dexamethasone treated group also recorded severe coronary vessels congestion of about

10% while, most of the vessels were moderatly congested. Heamorrages in this group was also moderately seen with majorly petechial haemorrages observed in approximately 10% of the cardiac surface, while the cardiac chambers only recorded mild haemorrages. The methylprednisolone treated group recorded mildly congested coronary vessels of less than 7%, cardiac haemorrages were also mild and were relatively absent in all the cardiac chambers.

The second specific organ evaluated for pathological lesions was the liver (Figure 3). Hepatomegaly was apparently absent in all the experimental groups as all edges of the liver were sharp. Normal size gall bladder without any obvious distentions in any of the experimental group were observed. Moderate hepatic congestions were recorded in all the experimental groups, but were more predominant in the control group. Haemorrages in the control group were seen ranging from affecting only the edges of the liver and to approximately half of the liver surfaces. The dexamethasone treated group also recorded haemorrages on the liver edges to approximately one-fifth of the liver surface which was similar to the methylprednisolone treated group. The methylprednisolone treated group had some portions of the edges of the liver without any haemorrages.

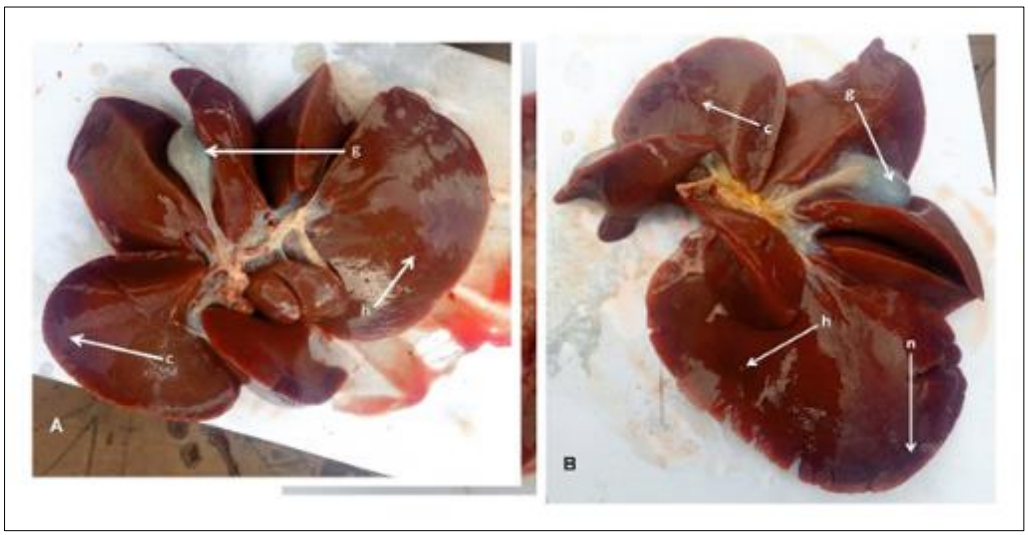

Figure 3 The liver from group treated with methylprednisolone (A) dexamethasone (B); showing: - g= Gall bladder; h= Haemorrage; c= haemorrhages

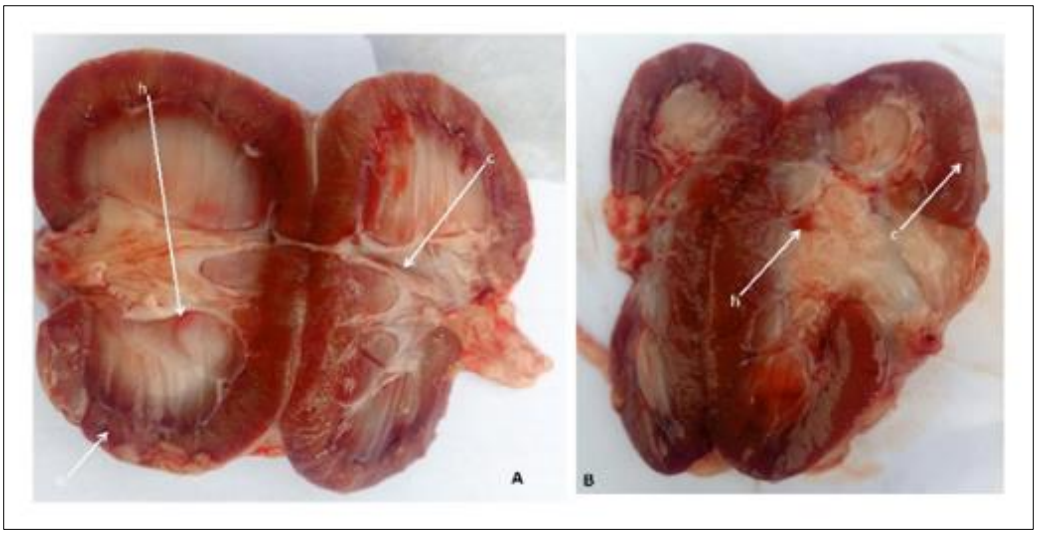

Figure 4 The kidney from group treated with methylprednisolone (A)dexamethasone (B); showing:- n= necrosis; h= Haemorrages; c= Congestion

The kidney was also evaluated for pathological lesions (Figure 4). The medullar of the kidney in the control group, had mildly congested vessels which was apparently uniform in the cortex. haemorrages were also absent in the renal cortex. The dexamethasone group showed severely congested kidney vessels with haemorrages affecting approximately 80%

of the corticomedullary junction, while about 30% of the cortex was haemorragic. In the methylprednisolone group, the renal vessels were congested, haemorrages observed affects about 90% of the junctions between the renal medullar and the renal cortex, while approximately 50% of the renal cortex were haemorragic. Furthermore, the cortex in the steroid treated group had variations in size as some portions appeared to have shrinked with relatively more firm texture compared to that in the control group

The spleen (Figure 5) was also evaluated for pathological lesions. All the experimental groups recorded spleenomegally. The control group was found to have the least magnitude of haemorrages with less than 20% of the spleen affected, while the methylprednisolone treated group had more haemorrages with about 40% of the spleen affected. The haemorrages in the dexamethasone treated group affected about 30% of the spleen.

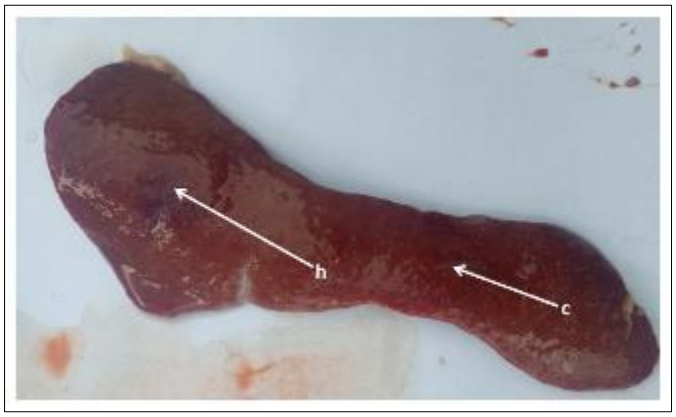

Figure 5 The spleen treated with methylprednisolone showing:- h= Haemorrage; c= Congestion

3.2. Histopathological lesions

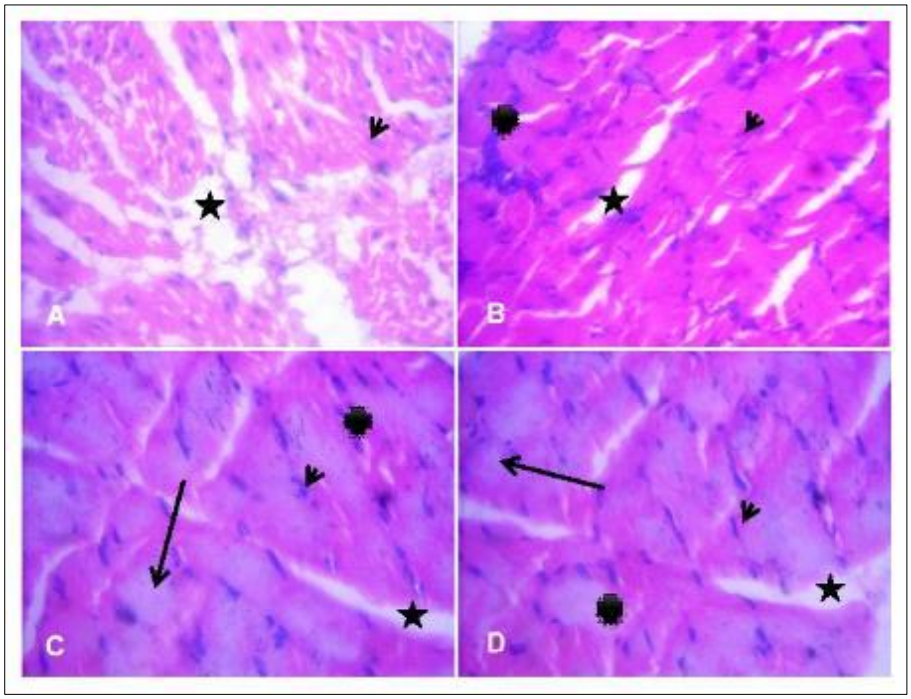

Figure 6 Representative photomicrographs of the heart after the second dose of urografin. A – control showing oedema (asterisk), mild cellular degeneration (arrow head); B – dexamethasone treated group showing mild oedema (asterisk), cellular degeneration (arrow head) and moderate infiltration of inflammatory cells; C and D – methylprednisolone treated group showing mild oedema (asterisks), cellular degeneration (arrows) and mild infiltration of inflammatory cells (cross):

Histolopathological lessions observed in the heart is shown in Figure 6. predominant lesions in the heart of the control group oedema with diffused infiltation of inflammatory cell. The magnitude of the infiltration of inflammatory cells was higher in the methylprednisolone and the dexamethasone treated groups. Degeneration of cardiac cells were more obviously recorded in the mmethylprednisolone treated group.

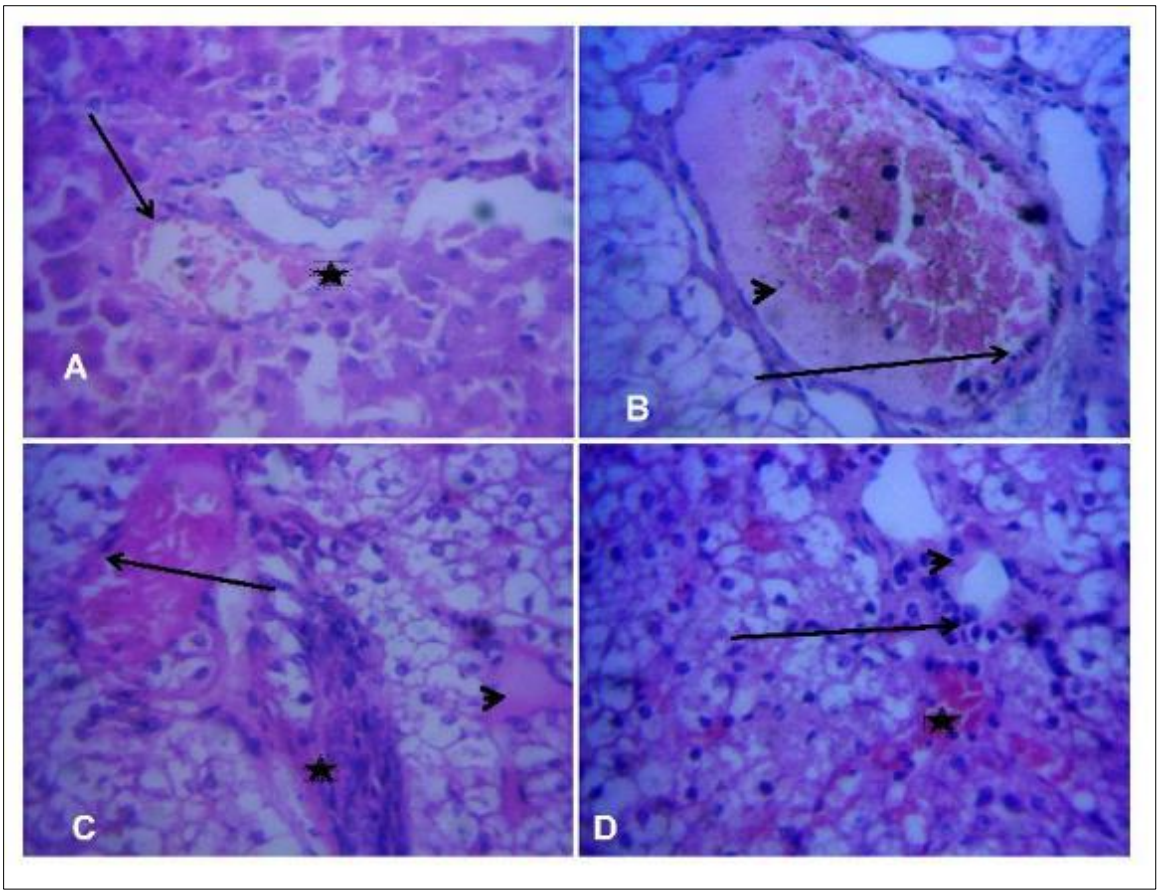

Figure 7 Representative photomicrographs of the liver after the second dose of urografin. A – control showing mild congestion (asterisk), mild perivascular inflammation (arrow); B – dexamethasone treated group with severe congestion (asterisk), moderate perivascular inflammation and contrast media (arrow head); C and D – methylprednisolone treated. showing severe congestion (arrow), marked infiltration of inflammatory cells (asterisk), marked vacuolation and contrast media (arrow head)

Histopathological lesions observed in the liver are depicted in Figure 7. The liver showed moderate infiltration of inflammatory cells in the steroid treated groups, especially in the methylprednisolone treated group that recorded more perivascular inflammation. Congestion was seen in all the groups, least observed in the methylprednisolone treated group, and more in the dexamethasone treated group

The renal capsule (Figure 8), was relatively normal as observed in the control group, less lesions in the dexamethasone treated group. The renal tubules were conspicuous in the control group unlike in the steroid treated groups especially with the methylprednisolone treated. There was mild perivascular infiltration of inflammatory cells in the control, moderate in the dexamethasone treated group and severe in the methylprednisolone treated group. Congestion was however, more with the dexamethasone treated group, followed by methylprednisolone and almost absent in the control group. Capillary haemorrhages was severe in the dexamethasone treated, mild in the methylprednisolone and absent in the control group.

The spleen (figure 9) was slightly depleted of lymphoid cells in the dexamethasone treated group and also congestion was severe in same group. The control and the methylprednisolone treated group showed apparently normal distribution of lymphoid cells.

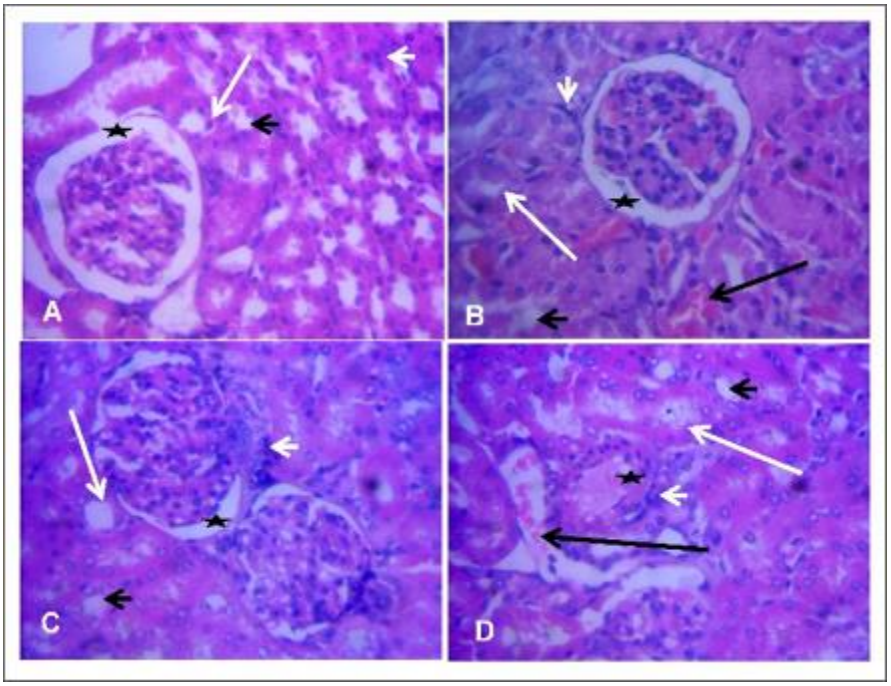

Figure 8 Representative photomicrographs of the kidney after the second dose of urografin. A – control showing mild infiltration of inflammatory cells (white arrow head), mild degeneration of tubular epithelial cells (red arrow); B – dexamethasone treated group showing moderate congestion (black arrow), mild infiltration of inflammatory cells (white arrow head); C and D – methylprednisolone treated group showing mild infiltration of inflammatory cells, mild vacuolar degeneration and obliteration of the lumen of the renal tubules:

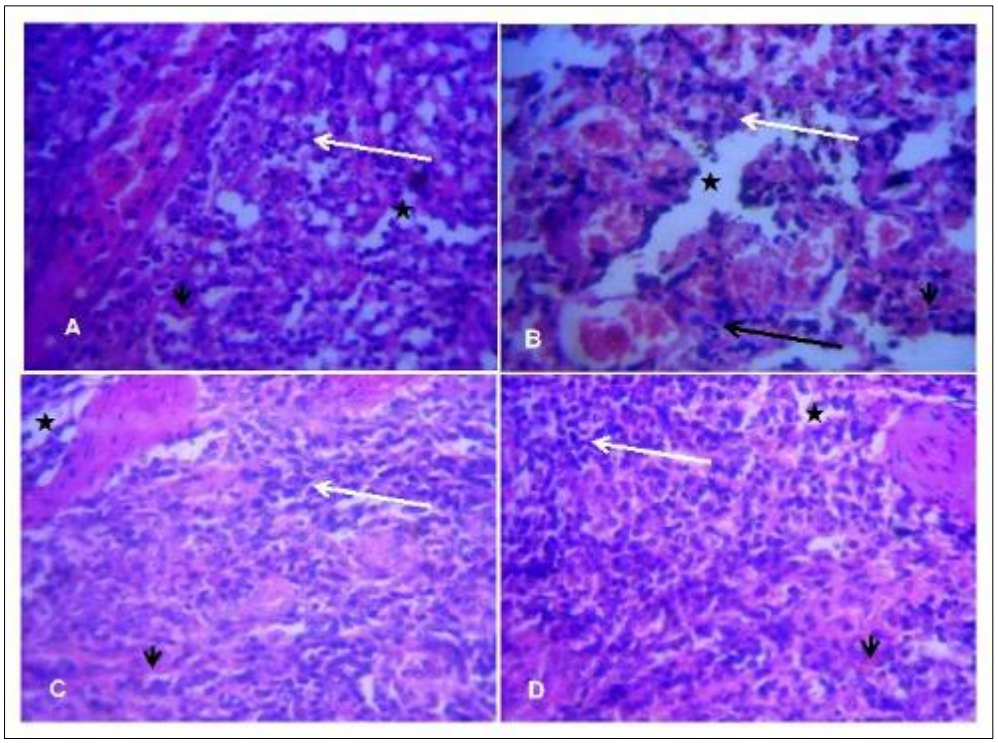

Figure 9 Representative photomicrographs of the spleen after the second dose of urografin. A – control showing relative lymphocyte depletion (white arrow), mild haemorrhages (arrow head); B – dexamethasone treated group showing oedema (asterisk), moderate congestion (?) and mild haemorrhages (arrow head); C and D – methylprednisolone treated showing mild haemorrhages and normal distribution of lymphoid cells:

4. Discussion

Steroids are usually recommended in contrast radiography to prevent the side effects of urografin Amer and Elabd [11]. Grossly in all the groups, the heart appeared to be least affected and grossly appeared normal. We observed moderate oedema in the control group. Although Weil [12], documented that, steroids are vital in the treatment of cardiovascular diseases, tissue degeneration was observed in the methylprednisolone treated group in this study. Infiltration of inflammatory cells were least observed in the methylprednisolone treated; vascular congestion was more in the dexamethasone treated group followed by that in the methylprednisolone group. Steroid are relevant in the maintenance of the normal cardiac activities White et al., [13]. The liver in all the experimental animals had mild haemorrhages grossly and histologically, with congested blood vessels, most likely due to the interaction between the tissue and the contrast media, as also documented by Moreno [3]. Perivascular infiltration of inflammatory cells were also observed but were common to all the experimental groups even though it was more in the steroid treated groups especially in the methylprednisolone treated group. Vascular congestion were observed in the control group but more in the steroid treated groups especially in the methylprednisolone treated. Although methylprednisolone was observed in this study to have induced varying degrees of pathologies, paradoxically corticosteroids, most specifically methylprednisolone has been recommended in the treatment of liver pathology [14,15]. While Urografin had been documented in the management of sensorineural hearing loss alongside with steroids Tottonchi et al., [16], its side effects on the visceral organs should also be considered as observed in this study.

Congestions in the kidney were observed to be more in the renal medulla of the dexamethasone treated group and more at the medullary cortical junctions in the methylprednisolone treated group. Evaluation of the kidney, being the major excretory organ of parenteral contrast medium excretion, is very critical Dure-Smith et al., [17]. The sensitivity of urography in the diagnosis of renal conditions is very imperative, hence, they cannot be replaced by the relatively recent imaging techniques like the ultrasonography [9,18,19]. The use of steroids prior to contrast media administration to mitigate allergy due to contrast media had been documented [20]. Methylprednisolone, dexamethasone or adrenaline administration 2 hrs prior to the administration of contrast media has been recommended [21,22,23]. The control group had a relatively normal histological feature of renal tubules with obvious vacuole and epithelial cells. Similar report was also documented by Iliya *et al*., [24], that structural and functional activities of the kidneys were unaltered with the use of urografin. However, Ahmed et al., [8], Ikamaise [25], reported shrinkage of glomeruli, widening of the urinary space and capillary congestion. In this study, these observations were very mild in the control group which could be due to the low dose used relative to the high dose used by the other authors. However, we also observed capillary congestion, which was moderate in the steroid treated groups, and mild in the control. The congestion could be due to the aggregation of red blood cells in the kidney as a normal kidney response to urografin, as stated by Liss *et al*., [26]. However, those lesions were severe with the steroid treated groups where vascular congestion occurred more in the steroid treated groups. These groups also had more obliterated kidney tubules than in the control, and the renal tubules were not readily distinguished from the kidney stroma in the steroid treated groups. Atrophy of the glomerulus was observed in the steroid treated groups especially in the methylprednisolone treated, the anti-inflammatory effects of these steroids could be responsible for the reduced oxygen supply that supposed to be compensated through the normal inflammatory response. Leow [4] state that, nephrotoxicity arises, due to medullary ischaemia that occurs as a result of increase in the consumption of oxygen by the kidney tubular cells and due to decline in the perfusion to the outer medulla. Inflammatory cells infiltration as observed in this study were more in the methylprednisolone treated group. Urografin results in nephrotoxic changes in both the kidney cortex and the medulla. This organ was severely affected as the major excretory organ of the contrast media [9]. Measures should also be put in place as documented by Sengar and Vijayanandan [27], that the unmetabolized contrast media used in contrast radiography have been found to be in high concentration especially in ground water than in surface water.

The spleen in all the groups were with blunt edges, signifying splenomegaly. In the spleen, all the groups recorded haemorrages, and oedema and the oedema was more in the dexamethasone treated and control groups. Consequently, depletion of the lymphoid cells was seen in all the groups but more predominantly in the dexamethasone treated group. Lymphoid cells were more evenly distributed in the methylprednisolone treated group and this finding corroborates those reported by Fitzpatrick and Greenstein [28], that steroids help in the restoration of normal immunological response of the lymphoid tissues.

5. Conclusion

This study revealed more cellular pathology in the methylprednisolone treated group on the liver and the kidney followed by dexamethasone treated group. It was also discovered in this study that dexamethasone treatment prior to administration of contrast media induces pathologies in the spleen. Based on the findings in this study, it was concluded

that the use of anti-inflammatory drugs (like dexamethasone and methylprednisolone) was more protective on the heart compared to other visceral organs. It was therefore recommended that the use of steroids like dexamethasone and methylprednisolone be avoided in contrast radiography except where heart pathology exist or is suspected.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest

Statement of ethical approval

Ethical approval was obtained from the animal ethics and and welfare committee of the Nigerian Veterinary research institute Vom, Plateau state, Nigeria

References

[1] Belle, M. B. B., Leffa, D. D., Mazzorana, D. and De Andrade, V. M. Evaluation of the mutagenic effect of the iodinated contrast medium Urografi na® 292 using the micronucleus test in mouse bone marrow cells Anais da Academia Brasileira de Ciências 2013, 85(2): 737-744

[2] Andreucci, M. Solomon, R. Tasanarong, A.. Side effects of radiographic contrast media: pathogenesis, risk factors and prevention. Biomed research international. 2014, article ID 741018, 20 pages. https://doi.org/10.1155/2014/741018

[3] Moreno, E. M., Gracia-Bara, T., Mayorga, C., La´zaro, M. M., Campano´n, V. and Da´vila, I. Hypersensitivity reactions to iodinated contrast media: Is it a true allergy? Curr Treat Options Allergy, 2018, 5:103–117

[4] Leow, K. S., Wu, Y. W. and Tan, C. H. Renal-related adverse effects of intravenous contrast media in computed tomography. Singapore Medical Journal, 2015, 56(4): 186-193

[5] Yagci, G., Kaymakcioglu, N., Fatih Can, M., Peker, Y., Cetiner, S. and Tufan T. Comparison of urografin versus standard therapy in postoperative small bowel obstruction. Journal of Investigative Surgery, 2005,18:315–320

[6] Lee, S. Y., Rhee, C. M., Leung, A. M., Braverman, L. E., Brent, A. and Pearce, A. N. A review: Radiographic iodinated contrast media-induced thyroid dysfunction. Journal of Clinical Endocrinology and Metabolism, 2015, 100(2): 376–383.

[7] Chibuzo, A. l., Uche, E. C. and Jerome, N. Intravascular contrast media in radiography: Historical development and review of risk factors for adverse reactions. South American Journal of Clinical Research, 2016, 3(1): 1-10

[8] Ahmed, ERM. Effect of urografin on the kidney of adult female albino rat and the possible protective role of nebivolol: a morphological and ultrastructural study M.Sc. Thesis in anatomy and embryology faculty of medicine Fayoum University. 2013. pp 10-50

[9] Moulvi, B. A., Parrah, J. D., Athar, H., Ansari, M. M. and Khan, Q. Excretory urography in animals: A review. Research Journal for Veterinary Practitioners, 2013, 1 (3): 23 – 30.

[10] Wilford, S., Weller, R. and Dunkel, B. Case report: Successful treatment of a horse with presumed parasitic encephalitis. Equine Veterinary Education, 2013, 25(12): 601-604.

[11] Amer, R. M., Elabd, S. S. Deleterious effect of urografin on the renal tubules of adult albino rats and the possible protective effect of N-acetylcysteine light and electron microscopic study. Egyptian Journal of Histology, 2019, 42(3): 730-739.

[12] Weil, N. H. The cardiovascular effects of corticosteroids. Cardiovascular, 1962, 25(1): 718-725.

[13] White, K. P., Driscoll, M. S., Rother, M. J. and Grant-kels, J. M. Severe adverse cardiovascular effects of pulse steroid therapy: Is continuous cardiac monitoring necessary? Journal of the American academy of dermatology, 1994, 30(5): 768-773.

[14] Powell, L. W. and Axelsel, E. Corticosteroids in liver disease: Studies on the biological conversion of prednisone to prednisolone and plasma protein binding. Gut, 1972, 13(1): 690-696

[15] Díaz-García, J. D., Córdova-Gallardo, J., Torres-Viloria, A., Estrada-Hernández, R. and Torre-Delgadillo, A. Lesión hepática inducida por fármacos secundaria al uso de esteroides anabólicos. Revista de Gastroenterología de México, 2020, 85(1):92-94.

[16] Totonchi, J. S., Nayadkazem, M., Ghabili, K., Ayat, S. E. and Rad, S. R. Urografin in the treatment of sensorineural hearing loss. Pakistan journal of biological sciences, 2008, 11(13): 1759-1763

[17] Dure-Smith, P. The dose of contrast medium in intravenous urography: A physiologic assessment. American journal of roentgenology, 1970, 108(4): 691-697.

[18] Brockowa, K. and Ring, J. Anaphylaxis to radiographic contrast media. Current opinion in allergy and clinical immunology, 2011, 11(4):326-331

[19] Cha, M. J., Kang, D. Y., Lee, W., Yoon, S. H., Choi, Y. H., Byun, J. S., Lee, J. Kim, Y., Choo, K. S., Cho, B. S., Jeon, K. N., Jung, J. and Kang, H. Hypersensitivity reactions to iodinated contrast media: A multicenter study of 196081 Patients. Radiology, 2019, 293:117–124

[20] Baerlocher, M. O., Asch, M., and Myers, A. Allergic-type reactions to radiographic contrast media. CMAJ: Canadian Medical Association journal, 2010, 182(12), 1328. https://doi.org/10.1503/cmaj.090371

[21] Thomas, G. M. Adverse Reactions to Contrast Material: Recognition, Prevention, and Treatment. American Family Physician, 2002, 66(7): 1229-1234.

[22] Sikka, A., Bista, J. K., Rajan, P. V., Chalifoux, L. A., Miller, F. H., Yaghmai, V. and Horowitz, J. M. How to manage allergic reactions to contrast agents in pregnant patients. American Journal of Roentgenology, 2016, 206(2): 247-252. https://www.ajroline.org/doi/10.2214/AJR.15.14976

[23] Onyambu, C. K., Aywak, A. A., Osiemo, S. K., and Mutala, T. M. Anaphylactic reactions in radiology procedures. in (ed.), Recent advances in asthma research and Treatments. 2021, IntechOpen. https://doi.org/10.5772/intechopen.95784

[24] Iliya, M. S., Leonid, P. L., Mikhail, G. Z. and Elena, Y. Z., The Problem of nephropathy induced by endocavitary administration of iodine-containing X-ray contrast Agents. International Journal of Medical Imaging. 2016, 4(3): pp. 17-22.

[25] Ikamaise, V. C., Ekanem, T. B., Eduwen, D. U., Paulinus, S. O. and Archibong, B. E. Effects of urografin of the morphology of the kidney cells of adult wister rats. Palgo Journal of Medicine and Medical Science, 2016, 3(3):83-90.

[26] Liss, P. Nygren, A. Olsson, U. Ulfendahl, Hs R. Erikson, U. Effects of contrast media and mannitol on renal medullary bloodflow and red cell aggregation in the rat kidney. Kidney International, 1996, 49(1): 1268—1275

[27] Sengar, A. and Vijayanandan, A. Comprehensive review on iodinated x-ray contrast media: complete fate, occurrence and formation of disinfection by-products. Science of the total environment, 2021, 769(2021). https://doi.org/10.1016/j.scitotenv.2020.144846

[28] Fitzpatrick, F. T. A. and Greenstein, B. D. Effects of various steroids on the thymus, spleen, ventral prostate and seminal vesicles in old orchidectomized rats. Journal of endocrinology, 1986, 113(1): 51-55.