

Research Regarding the High Doses of Non-Ionic Contrast Substances in Cat Urography

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Abstract. Given the complexity and high frequency appearance of urinary disorders in cats, the aim of this paper was to establish the toxic dose of nonionic contrast agents in cat urography, following the administration of three times the normal dose. The study showed slight changes of the biochemical and hematological parameters and the life of the patient was never in peril. It was necessary to use non-ionic contrast agents, precisely because they reduce the harmfulness of these substances to the body, in comparison with ionic substances which are fatal to cats.

Keywords: toxic dose, urography, nonionic substances, cat

INTRODUCTION

X-ray contrast media are chemically inert drugs which are given intravascular in very high amounts within a very short time period. Although they are regarded as relatively safe drugs, adverse reactions can occur: these are normally divided into immediate and delayed reactions. The latter appear hours to days after injection. Immediate reactions have been drastically reduced since the introduction of non-ionic monomers and non-ionic dimers. However, the delayed reactions still occur in a frequency of 1–3% in X-ray contrast media exposed patients. Most of these reactions are mild and manifest themselves as skin eruption, but severe reactions can also occur. Further improvement of the safety of these drugs is only possible with a better understanding of etiologies behind the observed adverse reactions (1).

Optiray 160, 240, 300, 320, 350 solution for injection is a nonionic contrast medium used in radiology, mainly in cerebral angiography, peripheral, visceral and renal aortography, left ventriculography, venography and intravenous urography. Optiray is also indicated in computed tomography (CT) of the head and body.

Intravascular administration of Optiray makes the vessels opaque and facilitates radiographic visualization of internal structures until a significant haemodilution substance appears.

Optiray pharmacokinetic profile, with its hydrophilic properties and a very low level of serum and plasma protein binding, indicates that Optiray is distributed in the extracellular space and rapidly eliminated by the kidneys through glomerular filtration. This product contains a new entity in Romania, approved through the CEDRAC simplified procedure for the authorized products in the European Union (8).

METHODS AND MATERIALS

The research was conducted on an adult common breed female cat, weighing 3 kg and being clinically healthy.

The non-ionic contrast substance used in intravenous Urography in a direct push was Optiray, at a dose of 8 ml / kg (normal dose 2.3 ml / kg), containing ioversol. We observed the influence of the quantity of substance administered to the body, and we got good radiographic images of the urinary system.

The biological material was subjected to intravenous Urography in a direct push (as administrator of contrast);

We used the following methods of investigation: the individual was subjected to clinical examination, monitoring the significant semiological constants, as temperature pulse and respiration.

The next step was to establish a 48 hour diet before the investigation, removing bones from its food that could compromise the radiological image of the urinary tract. Instead, it received dry food, which was gradually reduced. 24 hours before the investigation the cat stopped receiving food, but it still received water ad libitum. This diet was necessary in order to increase the elimination of digestive content, of dense and gaseous composition, that might affect image quality, leading to false diagnosis.

15 minutes before the administration of the contrast substance, the cat has undergone a general toilette, by brushing, in order to remove any radio-opaque impurities (such as sand), which could affect the Urography image, leading to a negative influence on the interpretation.

Given the behavior of the cat near strangers, showing a reserved attitude, being rarely friendly or actually aggressive (showing its teeth or claws when the foreign person is trying to comfort her), the study required the tranquilization of the subject. The drug substance used was Xylazine, administered intramuscularly. Rubbing alcohol was used as a local antiseptic. The needles used to manage the substance had a very small diameter (0.2 mm), and the syringes used had a volume of 5 and 10 ml.

To avoid secondary reactions, before administrating the contrast agents to the patient, we used Atropine.

After the administration of the contrast agents, samples of blood were collected to carry out biochemical and hematological tests. The anticoagulant used was Heparin, which was deposited in special containers. The examination of the blood samples was done in the laboratory of the Faculty of Veterinary Medicine, the Department of Veterinary Pathology. The radiographs were performed in the Roentgen diagnostic laboratory of the Faculty of Veterinary Medicine, in Cluj-Napoca, using a SK-7.3.-MEDICAL camera with automatic exposure time.

Before using the contrast substance, it was warmed up at the body temperature, to avoid the appearance of certain side effects that could be due to colder solutions.

The dose used was according to the weight of the animal (8 ml / kg), and in the end we reached the quadrupled dose.

We chose to administrate the intravenous contrast substance in the cephalic vein. Before puncturing the vessel, the site was aseptically prepared. To highlight the vessel, it was necessary to conduct a local vein, using an elastic buttock as a tourniquet. The dye was extracted from the phial, preheated to body temperature, only when administered. Radiographic exposures were made at certain intervals of time after ceasing the

administration of the solution: 3 minutes, 15 minutes, 30 minutes and 1 hour and 15 minutes (Images 1, 2, 3, 4).

The administration in a direct push of Optiray was performed in the forearm cephalic vein, after the area was aseptically prepared. (7)

RESULTS AND DISCUSSIONS

In the study, it was observed that the patient behaved normally, there were no signs of intoxication and the physiological constants remained within physiological limits, except that of the body temperature that varied in hypothermia (table 1).

Table 1

The physiological constants were monitored during determinations

	Before tranquilization	After the administration of atropine and Xylazine	After the administration of Optiray	Blood harvesting 15 minutes after the administration of Optiray	Blood harvesting 30 minutes after the administration of Optiray	45 minutes after the administration of Optiray
Temperature	36.5 °C	37.4 °C	36.0 °C	35.8 °C	34.9 °C	35.4 °C
Puls	140/min	184/min	180/min	120/min	135/min	119/min
Breathing	30/min	44/min	48/min	40/min	35/min	36/min

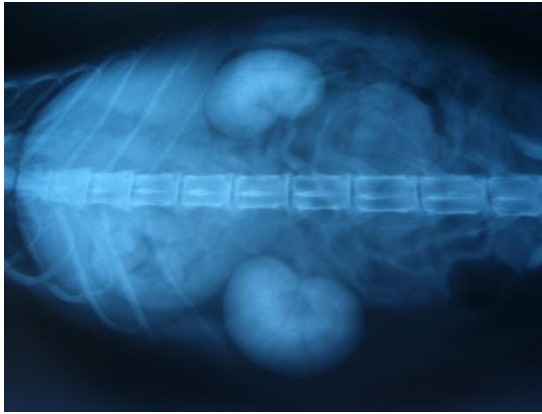


Image 1: Radiography, 3 minutes after the administration of the contrast substance



Image 2: Radiography, 15 minutes after the administration of the contrast substance;

Biochemical tests showed few changes, with the exception of a few parameters that were much higher or lower than normal.

15 minutes after the exposure, the glucose and the γ – amylase were high, and PAL, Ca^{2+} , Mg^{2+} , Na^+ , Fe^{3+} were low (table 2).



Image 3: Radiography, 30 minutes after the administration of the contrast substance;

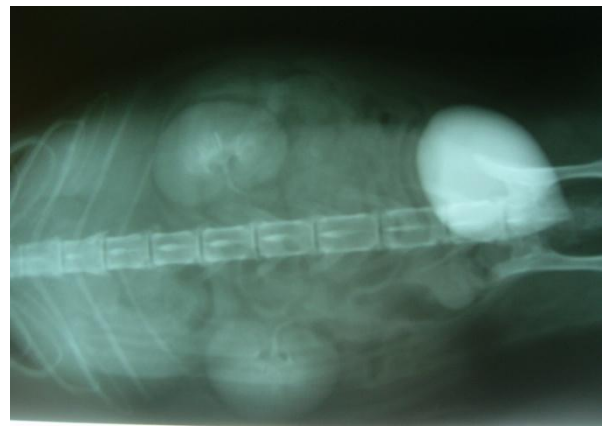


Image 4: Radiography, 1 hour and 15 minutes after the administration of the contrast substance.

Table 2.

Constant monitoring of blood serum biochemistry, 15 minutes after the administration of the contrast substance

Tests	Results	Unit	Minimum	Maximum	Observations
Glucose	230	mg/dl	72	105	High
Urea	65	mg/dl	30	66	
Creatinine	1.28	mg/dl	0.56	1.808	
ASAT	30	U/L		<35	
ALAT	47	U/L		<60	
GGT	5.1	U/L		<10	
PAL	210	U/L	60	190	High
Total protein	6.38	g/dl	5	7	
Albumin.	2.86	g/dl	1.5	2.947	
Total Cholesterol	88.31	mg/dl	77.3	251.3	
Triglycerides	46.5	mg/dl	43.75	140	
Uric Acid	0.381	mg/dl	-	-	
Total Bilirubin.	0.02	mg/dl		< 0.7	
γ - amylase	1100	U/I		<800	High
Ca ²⁺	7.0	mg/dl	8.22	0.92	Low
Mg ²⁺	1.72	mg/dl	2.1	3.2	Low
Na ⁺	120	mmol/l	140	155	Low
K ⁺	3.4	mmol/l	3.4	5.5	
Fe ³⁺	56.7	mg/dl	83	224	Low

30 minutes after the exposure, the glucose and γ - amylase remained high, PAL and the Total Protein appeared high as well, the Na⁺, Fe³⁺, Ca²⁺ appeared low, but reaching towards the normal values, and Mg²⁺ returned to the normal value (table 3).

Table 3.

Tests	Results	Units	Minimum	Maximum	Observations
Glucose	212.3	mg/dl	72	105	High
Urea	46.9	mg/dl	30	66	
Creatinine	1.022	mg/dl	0.56	1.808	
ASAT	27.3	U/L		<35	
ALAT	58.4	U/L		<60	
GGT	3.2	U/L		<10	
PAL	280.6	U/L	60	190	High
Total protein	9.09	g/dl	5	7	High
Albumin.	3.98	g/dl	1.5	2.947	High
Total cholesterol	82.9	mg/dl	77.3	251.3	
Triglycerides	43.4	mg/dl	43.75	140	
Uric acid	0.376	mg/dl	-	-	
Total bilirubin.	0.067	mg/dl		< 0.7	
γ - amylase	1300	U/I		<800	High
Ca ²⁺	8.0	mg/dl	8.22	0.92	Low
Mg ²⁺	2.65	mg/dl	2.1	3.2	
Na ⁺	132	mmol/l	140	155	Low
K ⁺	5.0	mmol/l	3.4	5.5	
Fe ³⁺	49.6	mg/dl	83	224	Low

Constant monitoring of blood serum biochemistry, 30 minutes after the administration of the contrast substance

Also, the histogram of blood components showed that everything was normal, with the exception of the MI, witch was high (table 4).

Table 4.

Histogram of blood components, 15 minutes after administrating Optiray

Tests	Results	Normal limits
WBC	12.2 $10^9/l$	(5.50 – 19.50)
LYM	2.56 $10^9/l$	(1.50 – 7.00)
MID	0.98 $10^9/l$	(< 1.50)
GRA	7.12 $10^9/l$	(2.50 – 14.00)
LY%	27.9 %	(20.0 - 55.0)
MI%	+8.7 %	(1.0 – 3.0)
GR%	63.6 %	(35.0 – 80.0)
RBC	8.72 $10^{12}/l$	(5.00 – 10.00)
HGB	11.7 g/dl	(8.0 – 15.0)
HTC	33.78 %	(24.00 – 45.00)
MCV	43 fl	(39 – 55)
MCH	16.1 pg	(12.5 – 17.5)
MCHC	35.9 g/dl	(30.0 – 36.0)
RDW _c	18.3 %	
PLT	543 $10^9/l$	(300 – 800)
PCT	0.53 %	
MPV	12.9 fl	(12.0 – 17.0)
PDW _c	36.6 %	

Also, the histogram of blood components showed that the MI was aiming for the normal values and it also showed an increase of the MCHC (table5).

Table 5.

Histogram of blood components, 30 minutes after administrating Optiray

est	Results	Normal limits
WBC	11.00 $10^9/l$	(5.50 – 19.50)
LYM	4.21 $10^9/l$	(1.50 – 7.00)
MID	0.72 $10^9/l$	(< 1.50)
GRA	7.26 $10^9/l$	(2.50 – 14.00)
LY%	31.0 %	(20.0 - 55.0)
MI%	+5.4 %	(1.0 – 3.0)
GR%	63.6 %	(35.0 – 80.0)
RBC	6.98 $10^{12}/l$	(5.00 – 10.00)
HGB	11.4 g/dl	(8.0 – 15.0)
HTC	29.11 %	(24.00 – 45.00)
MCV	39.3 fl	(39 – 55)
MCH	13.8 pg	(12.5 – 17.5)
MCHC	+ 38.1 g/dl	(30.0 – 36.0)
RDW _c	19.7 %	
PLT	411 $10^9/l$	(300 – 800)
PCT	0.43 %	
MPV	13.1 fl	(12.0 – 17.0)
PDW _c	32.0 %	

CONCLUSIONS

- The test showed that there are no significant changes in the biochemical and hematological parameters after the administration of four times the normal dose of Optiray.
- Due to the insignificant changes in the blood, and the well response of the cat after the exposure, Optiray is a suitable substance for urographies in cats. However, the study may continue on a larger number of cats and the dose can be increased five times to establish the toxic dose.

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