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RESEARCH PAPER

Adverse reactions following administration of contrast media for diagnostic imaging in anaesthetized dogs and cats: a retrospective study

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Abstract

Objective To evaluate incidences of adverse reaction after the administration of contrast media.

Study design Retrospective observational study.

Animals Animals included 356 dogs and 58 cats receiving non-ionic iodinated contrast agents, and 425 dogs and 49 cats receiving gadolinium-based contrast agents.

Methods Anaesthesia records of dogs and cats receiving intravenous (IV) gadobutrol for magnetic resonance imaging (MRI) or IV iohexol for computed tomography (CT) were reviewed. Changes in pulse rate, respiratory rate and mean arterial pressure at 5 minutes after administration of the contrast medium were evaluated. Changes of 10–20% were considered mild, those of >20% moderate, and reactions that required immediate treatment were considered severe. Associations of sex, age and weight with contrast reaction were investigated using logistic regression. Differences in the incidences of reactions to CT and MRI contrast media were examined with chi-squared tests. A p-value of <0.05 was considered to indicate statistical significance.

Results Of cats receiving iohexol, eight (13.8%) had mild and 10 (17.2%) had moderate reactions. Of cats receiving gadobutrol, six (12.2%) had mild and six (12.2%) had moderate reactions. No cats had severe reactions and the risk for reaction was not associated with type of medium, age, weight or sex ($p > 0.2$). Of dogs receiving iohexol, 64 (18.0%) had mild, 65 (18.3%) had moderate and three (0.8%) had severe reactions. Of dogs receiving gadobutrol, 42 (9.9%) had mild, 87 (20.5%) had moderate and one (0.2%) had a severe reaction. When dogs receiving iohexol were compared with those receiving gadobutrol, the odds ratio of a moderate reaction was 2.0 (95% confidence interval 1.34–3.10; $p = 0.001$). These estimates did not change substantially after adjustment for age, weight and sex.

Conclusions and clinical relevance Severe reactions to iohexol and gadobutrol are rare in dogs and cats; moderate reactions are more likely with iohexol than with gadobutrol.

Keywords cat, contrast media, dog, reaction.

Introduction

Magnetic resonance imaging (MRI) and computed tomography (CT) are diagnostic imaging modalities that are widely used in veterinary medicine, in which a contrast study is often required for diagnosis. Contrast media administration can cause adverse reactions which can be classified as acute or delayed based on their onset, as mild, moderate or severe based on their clinical features and the severity of symptoms (Namasivayam et al. 2006; Bohm et al. 2012), and as hypersensitivity (Type B)

or non-hypersensitivity (Type A) reactions based on their pathogenesis (Bohm et al. 2012).

Gadolinium-based contrast agents (GBCAs) and iodinated contrast agents (ICAs) are the most commonly used contrast agents in MRI and CT, respectively. At the study institution, gadobutrol is administered for contrast studies in MRI and iohexol is used in CT.

Gadobutrol is a second-generation, extracellular, non-ionic macrocyclic GBCA that is used in patients undergoing MRI for visualization of pathological lesions in the central nervous system and other body regions, and is formulated at twice the gadolinium ion concentration of other currently licensed GBCAs. This reduces the injection volume and provides a narrower bolus, thereby facilitating image enhancement (Scott 2013). The use of GBCAs is considered relatively safe, but adverse reactions have been reported in both human (Murphy et al. 1996; Li et al. 2006; Dillman et al. 2007; Abujudeh et al. 2010; Bruder et al. 2011; Jung et al. 2012; Cohan et al. 2013) and veterinary (Pollard et al. 2008a; Girard & Leece 2010) medicine.

Iodinated contrast agents can be divided into ionic ICAs (IICAs) and non-ionic ICAs (NIICAs). Iohexol is a monomer NIICA commonly used in veterinary medicine. Studies in human (Morcos et al. 1998; Namasivayam et al. 2006; Singh & Daftary 2008; Cohan et al. 2013) and veterinary (Pollard et al. 2008a,b) medicine have reported that incidences of mild, moderate and severe reactions are decreased with the use of NIICAs in comparison with the use of IICAs.

In human medicine, reactions to contrast media have been extensively investigated; conversely, in veterinary medicine there are few studies, all of which have included small numbers of animals. Anaesthetists are increasingly required to deal with patients undergoing advanced diagnostic imaging, and hence awareness of possible adverse reactions, their incidence and their clinical presentation can be useful in facilitating the immediate recognition and adequate treatment of these adverse events. The aim of the present study was to investigate the frequency and severity of immediate reactions to contrast agents in dogs and cats receiving gadobutrol for MRI or iohexol for CT studies under general anaesthesia.

Materials and methods

The study was approved by the University of Liverpool Committee of Research Ethics (RETH00065). A retrospective analysis was performed to review the medical records database of the Small Animal Teaching Hospital of the University of Liverpool for anaesthetized dogs and cats that had received intravenous (IV) gadobutrol for MRI or IV iohexol for CT between January 2011 and April 2013. Dogs and cats were included in the study population if their anaesthetic records contained information on heart rate (HR), respiratory rate (f_R) and mean arterial pressure (MAP) measured at 5 minutes before (baseline) and 5 minutes after contrast administration. Contrast agent was administered at doses of 600 mg kg^{-1} of iohexol (Omnipaque 300 mg mL^{-1}; GE Healthcare, NJ, USA) at 37 °C for CT, and 0.1 mmol kg^{-1} of gadobutrol (Gadovist 1.0 mmol mL^{-1}; Bayer Plc, UK) at 4 °C for MRI. All dogs received fluid therapy (Hartmann's solution, Aquapharm, No. 11; Animalcare Ltd, UK) during the procedure; the rate of administration was at the discretion of the anaesthetist in charge of the case.

Dogs were excluded from the study if they had received any other drugs, if the fluid rate had been changed or if other actions (e.g. hyperventilation) had been taken at the same time as contrast agent administration.

For each species separately, the following data were recorded: age; sex; breed; weight; pulse rate (PR); f_R, and MAP. In all MRI cases, PR was obtained using a pulse oximeter (Magnitude 3150 MRI Monitor; Invivo Research, Inc., FL, USA). Because electrocardiography (ECG) was unavailable in MRI, f_R was obtained using a capnograph (Capnomac Ultima; Datex-Ohmeda Inc., WI, USA) and MAP was measured non-invasively with an oscillometric method (Cardell Veterinary Monitor; Paragon Medical, Inc., IN, USA). In CT cases, all parameters were monitored with a multiparameter monitor (Dynascope DS 7100; Fukuda Denshi Co. Ltd, Japan), and PR was recorded from the pulse oximeter. Any anaesthetist's comments on the anaesthetic record indicating a perceived response to contrast medium administration were also recorded.

Reaction was defined as a change in PR, f_R or MAP of >10% from baseline occurring during the 5 minutes immediately after contrast administration. Reactions were then divided into three classes and categorized as mild when changes in PR, f_R or MAP ranged between 10% and 20%, as moderate when changes in PR, f_R or MAP exceeded 20%, and as severe when haemodynamic or respiratory alterations required immediate treatment. Statistical

