COMPARISON OF CARDIOTOXICITY OF TWO OSMOLAR CONTRAST AGENTS IN WISTAR RATS

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ABSTRACT

Introduction: The benefits of low osmolar contrast media to clinicians is important in radiological care. Evidence have suggested that contrast media have a variety of adverse effects on the cardiovascular system but few have directly compared low osmolar contrast media group.

Objectives: This study therefore compared the structural effect of intravenously administered low osmolar contrast medias Iohexol with Iopromide on the Heart of Wistar Rats.

Methodology: The study was experimental, Iohexol (350mg,700mg,1400mg I/mL) and Iopromide (300mg, 600mg, 1200mg Iodine/mL) were administered via the tail vein. 72 hours and 1 week after the initial administration heart organs were harvested and processed for histopathological laboratory evaluation.

Results: No obvious histomorphological changes of Wistar Rats' heart exposed to iohexol and iopromide was noted 72 hours and 1 week after initial intravenous administration even at a relatively higher dose.

Conclusion: The study showed both iohexol and iopromide have no obvious adverse cardiac effect even when administered at a relatively higher dose up to 1 week after initial administration.

Keywords: Cardiotoxicity, Iohexol, Iopromide, contrast media, histomorphological

INTRODUCTION

Cardiotoxicity is associated with several cytotoxic drugs and may be responsible for long term side effects and severe morbidity [1]. A wide range of cardiac toxicity exist from small changes in blood pressure and arrhythmias to cardiomyopathy. Different mechanisms of chemotherapy induced cardiotoxicity have been postulated including cellular damage due to the formation of free oxygen radicals and the induction of immunogenic reactions with the presence of antigen presenting cells in the heart [2]. There is evidence to suggest that contrast media may have a variety of adverse effects on the cardiovascular system. They have primary central effects on myocardial contractility, electrophysiology and coronary blood flow and primary effects on the peripheral vasculature including blood pressure fall/hypotension, bradycardia, angina pectoris, and shock [3]. The effects on the heart itself are obviously greatest when injection is directly into the coronary arteries, as during coronary arteriography. There are marked depressant effects on cardiac pump function which are dose dependent and most persistent in the ischaemic heart. Osmolality, chemotoxicity, oxygen displacement and ionic content all contribute to these effects [4]. Compared with high osmolar contrast media, nonionic low osmolar contrast media have been shown to decrease the incidence of major complications associated with diagnostic cardiac catheterization. This study therefore compared the structural effect of intravenously administered low osmolar contrast medias Iohexol with Iopromide on the Heart of Wistar Rats.

MATERIALS AND METHODS

Ethics

The experimental study was consistent with ethical principles of animal's experimentation and guidelines as established by the National Institute of Veterinary Research Vom Jos Plateau State.

ANIMALSTUDIES

A total of 80 Wistar rats aged 3-4 months and weighing between 120 – 152 grams were obtained from the Animal Center of the National Veterinary Research Institute Vom. These animals were randomly divided into 3 groups; Iohexol (group 1), Iopromide (group 2) and Control (group 3). Group 1 was further divided into 3 sub-groups according to contrast doses administered; Iohexol 350 mg I (group 1A), Iohexol 700 mg I (group 1B), and Iohexol 1400 mg I/kg body weight (group 1C). Group 2 was also divided further into subgroups; group 2A (Iopromide 300 mg I/kg), 2B (Iopromide 600 mg I/kg) and 2C (Iopromide 1200 mg I/kg). Each sub group contains at least 12 Rats housed in a medium cage in a well-ventilated room and allowed to acclimatize for three (3) weeks before the commencement of the study. During that period, they were monitored regularly to ensure a high level of hygiene and general cleanliness of the housing system and also to ensure that they were in good condition. Pellet diets (vital feed) were regularly and sufficiently given to them as food. They also have access to fresh, portable, uncontaminated drinking water. All the rats were weight before administration of contrast and sacrifice.

Contrast Administration: Each Wistar Rat in groups 1A, 1B, and 1C were respectively administered 350mg I, 700mg I, and 1400mg I/kg body weight of Iohexol through the tail vein while groups 2A, 2B, and 2C Rats were respectively administered 300ml I, 600ml I, and 1200ml I/kg body weight of Iopromide via the tail vein. The animals in Control group C were administered 600 ml of distilled water/kg body weight.

Animal Sacrifice and Sample Collections: Seventy-two (72) hours after the initial administration of contrast medias, six (6) Wistar Rats from each sub-group were euthanized by inhalation of anesthesia gas (chloroform) in a glass chamber. This renders the animal unconscious and insensitive to pain. The thorax was then opened through dissection and the heart organ harvested and stored in a container containing 1% formaldehyde solution for histopathological analysis. Similar procedure was applied to the remaining Wistar Rats in each sub-groups 1 week later.

RESULTS

Histopathological alterations

Normal cardiac tissues were seen in control group. Cardiac myocytes 72 hours after administration of iohexol and iopromide at low, medium and high doses appeared normal. Similarly, no obvious histomorphological changes were noted 1 week later with administration of both iohexol and iopromide at varying doses.

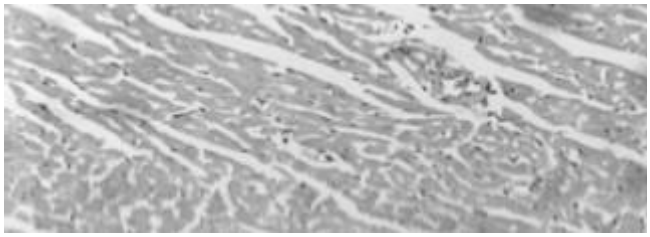

Plate 1: Control: Normal heart showing normal myocytes. H&E stain X200

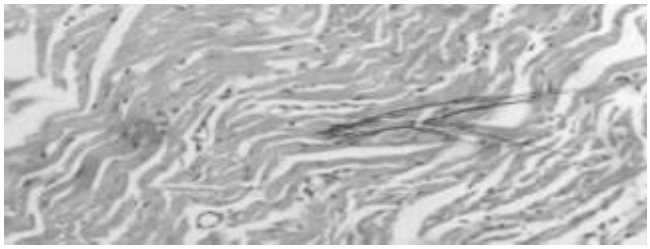

Plate 2: Micrograph of the heart 72 hours after intravenous administration of medium dose of Iohexol. The heart shows normal muscle fibres. H&E stain X200

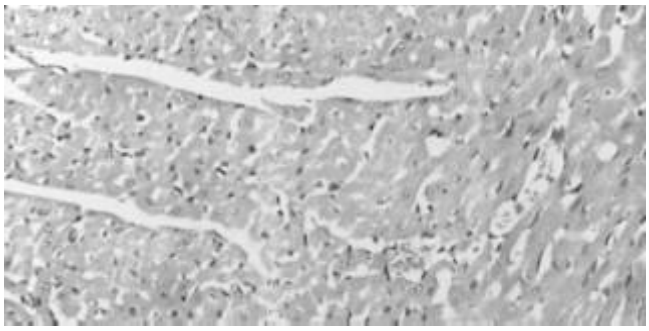

Plate 3: Micrograph of the heart 1 week after intravenous administration of medium dose of Iopromide. The heart shows normal myocytes. H&E stain X200

DISCUSSION

Although the heart is not a common target organ, many chemicals can affect it, either by damaging the myocardium or by acting indirectly through the blood vessels or nervous system. Cardiotoxicity or medication-induced damage to the heart muscle such as heart failure, structural damage, and hypertension are known adverse effect and affects quality of life and overall survival [5]. Thus, in this present study we evaluated and compared histomorphological changes of Wistar rats exposed to various doses of iohexol and iopromide after 72 hours and 1 week of intravenous administration.

Our result showed no obvious changes in the histomorphology of the heart regardless of the doses and up to 1 week after administration. This finding is in agreement with those of Bu-Chun *et al.* [6] in a meta-analysis of the risk of total cardiovascular events of iso-osmolar iodixanol compared with low-osmolar contrast media in which cardiovascular disease events were defined as a composite of death, stroke, myocardial infarction (MI), angina pectoris, new arrhythmias, congestive heart failure, and emergent need for revascularization. Result of the study showed cardiovascular events was not significantly decreased when iodixanol was compared with all LOCM pooled. Similarly, subgroup analysis showed no relative difference. Adverse drug reactions have also been reported to be very low with iopromide in cardiac catheterization in China [7]**.** This safety profile of iopromide is confirmed by a pooled analysis of data carried out by Petra *et al.* [8] in Asian and European countries and the united states of America. Seong *et al.* [9] reported iopromide as the most commonly implicated iodinated contrast medium, followed by iohexol in terms of general safety. For iopromide, the percentage of adverse effects of cardiovascular disorders, general was significantly higher while for iohexol, the percentage of adverse effects of body as a whole general disorder was significantly higher. These findings disagree with our own study.

CONCLUSION

The present study, implied that low osmolar contrast media iohexol and iopromide have no risk of developing cardiac adverse effect up to 1 week of intravenous administration at higher doses.

Conflict of Interest: Nil

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