Original Article

Adverse Reactions of Low Osmolar Non-Ionic and Ionic Contrast Media When Used Together or Separately During Percutaneous Coronary Intervention

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Background: **Due to perceived advantages in the use of non-ionic contrast agents for diagnostic angiography and ionic agents for percutaneous coronary intervention (PCI), patients often receive various combinations of both types of agents.**

Aim: **To assess potential adverse effects of non-ionic and ionic contrast media when used together or separately during percutaneous coronary intervention.**

Methods: **We retrospectively evaluated the outcomes of 532 patients undergoing percutaneous coronary intervention in our institution. Patients were divided into two groups: those that underwent diagnostic angiography and "follow on" PCI; and those that underwent "planned" PCI. The groups were subdivided on the basis of the use of the ionic agent ioxaglate or the non-ionic agent iopromide during PCI. The frequency of allergic reactions and major adverse cardiac events (MACE) were noted.**

Results: **With respect to the "follow on" group, allergic reactions occurred in 9 of 150 patients (6.0%) who received the combination of ioxaglate and iopromide versus 1 of 93 (1.1%) who only received iopromide ($p = 0.094$). There was no difference with respect to MACE [6 (4.0%) ioxaglate and iopromide versus 4 (4.3%) iopromide alone, $p = 1.00$]. In the "planned" group, 7 of 165 patients (4.2%) receiving ioxaglate had an allergic reaction as opposed 0.0% (0 of 124 patients) in the iopromide group ($p = 0.021$). All contrast reactions were mild. The incidence of a MACE was similar in both groups [1 (0.6%) ioxaglate versus 2 (1.6%) iopromide, $p = 0.579$]. The incidence of allergic reactions was similar if ioxaglate was used alone or in combination with iopromide ($p = 0.478$).**

Conclusions: **Whilst combining ionic and non-ionic contrast agents in the same procedure was not associated with any more adverse reactions than using an ionic contrast agent alone, the ionic contrast agent ioxaglate was associated with the majority of allergic reactions. With respect to choice of contrast agent, using the non-ionic agent iopromide alone for coronary intervention is associated with the lowest risk of an adverse event.**

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Keywords. Ioxaglate; Iopromide; Angioplasty; Complications

Introduction

Contrast media are essential components of the performance of percutaneous coronary intervention (PCI), but their contribution to complications occurring during these procedures has been debated. Non-ionic low osmolar contrast agents have been shown to decrease the incidence of adverse reactions associated with diagnostic procedures when compared to high osmolar ionic compounds.[1–4] Allergic reactions also appear to occur more frequently in patients receiving low osmolarity ionic compounds when compared to non-ionic compounds.[5,6] Studies in vitro have shown that non-ionic low osmolar agents have less inherent anticoagulant activity than ionic agents.[7,8] A few randomised clinical trials have supported the conclusion that the ionic low osmolar compound

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ioxaglate is associated with fewer ischaemic complications of coronary intervention than are non-ionic agents.[9,10] Based on the perceived better tolerability and cheaper cost of non-ionic agents in our environment, our laboratory routinely uses these compounds for diagnostic angiography and reserves the ionic agent, ioxaglate, for percutaneous coronary interventions. This policy meant that many patients who "followed on" from their diagnostic procedures to coronary interventions received two different classes of agents in rapid succession during the same procedure. Due to a lack of data concerning the safety of "mixing" different classes of contrast agents, we sought to determine whether this practice resulted in more adverse clinical events than would a policy of continuing the same type of contrast agent. In order to establish a baseline risk of adverse reactions, we ascertained the incidence of such events in patients undergoing "planned" percutaneous coronary intervention that received exclusively either ioxaglate or iopromide (the non-ionic agent).

Materials and Methods

Study Population

All 532 patients who underwent PCI from January 2001 to February 2002 in our institution were included in the study. We performed a retrospective analysis of our prospective, observational percutaneous coronary intervention database. Three operators using standard techniques performed all coronary interventions during the study period and patients' details were prospectively entered into our database. It is our policy for patients to receive at least 300 mg of aspirin within 24 h of the procedure and to continue on 100–150 mg daily after the intervention. Intracoronary stent implantations were performed using standard techniques of high-pressure balloon inflations and patients generally received a loading dose of 300 mg of clopidogrel (if not previously on it) and 75 mg daily thereafter for 4 weeks. Heparin was administered as a weight-adjusted dose. Patients routinely had blood drawn for creatine kinase (CK) enzyme (and MB isoenzyme) the morning after the procedure and more frequently if there was a reason to suspect an adverse cardiac event. Data on the occurrence of thrombotic stent occlusion (TSO), emergency target vessel revascularisation (TVR) and periprocedural myocardial infarction (MI) are routinely collected in our institution prospectively and entered into our database. In addition, the occurrence of allergic reactions is noted and routinely entered into our database. As is the policy of our institution, all patients undergoing diagnostic coronary angiography received the low osmolar non-ionic monomer contrast agent iopromide (Ultravist, Schering, Berlin, Germany). During coronary intervention the choice of contrast medium was at the discretion of the operator and all patients received either the low osmolar ionic dimer compound ioxaglate (Hexabrix, Guerbet, Paris, France) or iopromide. For the purpose of this study we divided patients into two groups. The first group comprised patients who underwent diagnostic coronary angiography and "follow on" coronary intervention, which was defined as unplanned percutaneous coronary intervention directly after the diagnostic angiogram. All patients received iopromide during the diagnostic procedure and either iopromide or ioxaglate during the coronary intervention. The second group of patients had their diagnostic angiogram (using iopromide) performed some time before their "planned" percutaneous coronary intervention. This group was divided into two subgroups based on whether or not they received iopromide or ioxaglate during their coronary intervention. Finally, we compared the incidence of allergic reactions in patients who received ioxaglate alone or in combination with iopromide.

Procedural Variables

The number of attempted lesions, stent usage, fluoroscopy time, volume of contrast media used and use of glycoprotein IIb/IIIa antagonists were recorded for each patient.

Study Endpoints

The primary endpoint was the development of an allergic reaction requiring treatment with H1 and H2 antagonists, corticosteroids or catecholamines. Allergic reactions could include cutaneous manifestations of urticaria with or without pruritus, erythema, maculopapular rash, conjunctival symptoms and facial or peripheral angioneurotic oedema. This data was obtained from the database and where necessary correlations were obtained from the clinical record.

The secondary endpoint was a composite of cardiovascular death, non-fatal myocardial infarction and urgent target vessel revascularisation at 30 days. Urgent TVR was defined as the occurrence of emergency coronary bypass surgery or repeat PCI of the treated vessel for recurrent ischaemia within 30 days of the initial procedure. Non-fatal myocardial infarction was defined as an increase in the creatine kinase concentration to three times the upper limit of normal with a concomitant rise in the CK–MB isoenzyme above the upper limit of normal or the appearance of new Q waves after the procedure. If a patient reached more than one cardiac endpoint, only the most severe endpoint was counted as a major adverse cardiac event (MACE) for the final analysis. Thrombotic stent occlusion was defined as angiographically proven total occlusion (TIMI flow <2), or flow-limiting thrombus formation inside the stent within 30 days after initially successful stenting.

Statistical Analysis

All values are reported as mean $\pm$ one standard deviation unless otherwise stated. Categorical variables are compared with χ^2-test or Fischer's exact test as appropriate. Continuous variables with a normal distribution are compared with unpaired Student's *t*-test and continuous variables not normally distributed are compared with the Mann–Whitney Wilcoxon test. Statistical analysis was performed using SPSS for Windows (version 10). Statistical significance was defined as a two-tailed p value of <0.05.

Results

During the study period there were 243 patients who had "follow on" PCI. Of these 93 received iopromide alone