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Outcomes of premedication for non-ionic radio-contrast media hypersensitivity reactions in Korea

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ABSTRACT

Background: Radio-contrast media (CM)-related adverse reactions are important clinical problems that may cause fatal anaphylaxis. Accordingly, it has been common practice to premedicate patients who have had previous reactions to CM with corticosteroids, antihistamines, and H2 blockers to prevent hypersensitive reactions. However, the effectiveness of premedication has not been properly demonstrated, especially in cases related to non-ionic CM. In this study, we evaluated the effectiveness of premedication at preventing of non-ionic CM immediate-type hypersensitivity reactions.
Methods: A total of 30 patients who had been pretreated with corticosteroid and H1 antihistamines and/or H2 blockers in a 3-year period were enrolled. The results of premedication were evaluated in terms of clinical characteristics and the features of breakthrough reactions.
Results: Hypersensitivity reactions were not prevented in 5 of the 30 patients who had experienced prior CM reactions (overall recurrence rate after premedication 16.7%; 4/17 patients with mild previous reactions, and 1/13 patients with severe previous reactions). The recurrence rate after premedication was significantly higher in patients with mild previous reactions than in those with severe reactions (23.5% vs. 7.7%; $p < 0.001$). The breakthrough reactions were similar to the prior reactions in terms of severity and clinical manifestations.
Conclusion: Premedication with corticosteroid and H1 antihistamines and/or H2 blockers effectively prevent non-ionic CM-related adverse events in most patients who have had severe previous reactions to CM. However, physicians should be aware of the possibility of premedication failing and of breakthrough reactions, even in cases in which the previous reactions were mild.

1. Introduction

Radio-contrast media (CM) are intravascular pharmaceuticals that are used in approximately 75 million procedures annually [1]. In addition to computed tomography, many recent radiological and cardiologic interventional procedures require contrast media to obtain more accurate information and, indeed, the use of contrast media is crucial for diagnosis in many cases. However, contrast media are composed of highly concentrated solutions of tri-iodinated benzene derivatives, which can cause various types of immediate (≤1 h) and non-immediate (>1 h) adverse reactions [2]. Although low-osmolar, non-ionic CM have been used since the mid-1970s to reduce such side-effects, adverse reactions to them have also been reported (in 2.0–3.1% of cases) [3,4]. Furthermore, large-scale observational studies have demonstrated that severe immediate adverse reactions such as anaphylactic shock occur in 0.1–0.4% of patients receiving ionic CM and 0.02–0.04% of patients receiving non-ionic CM [5]. Considering the large num-

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Table 1
Clinical characteristics of and previous adverse reactions in the study subjects.

Subject number	Gender	Age	Underlying disease	Previous adverse reaction			Risk factors[b]
				Type[a]	Severity	Contrast media	
1	M	59	UTI	S	Mild	Iomeprol	
2	F	54	Pancreatic mucinous cystic tumor	S	Mild	Iopromide	
3	M	21	Nutcracker syndrome	S, G	Mild	Iopromide	
4	F	40	Breast cancer	S	Mild	Iopromide	
5	F	43	Breast cancer	S, N	Mild	Iopromide	
6	F	55	Angina	S	Mild	Iopromide	
7	F	77	Cholangiocarcinoma	S	Mild	Iomeprol	
8	F	35	Takayasu's arteritis	S	Mild	Unknown	
9	F	49	Brain aneurysm	S	Mild	Iopamidol	
10	M	68	CVA	S	Mild	Unknown	
11	M	25	Hypertension	S, G	Mild	Iopromide	
12	M	47	Angina	S	Mild	Iodixanol	
13	F	67	Hepatocellular carcinoma	S	Mild	Iomeprol	
14	F	57	Acute pancreatitis	S	Mild	Iopromide	AR
15	F	35	Gross hematuria	S	Mild	Iopromide	
16	F	50	Renal cell carcinoma	S	Mild	Unknown	
17	M	69	Angina	S	Mild	Iodixanol	BB
18	F	30	Asthma	R	Severe	Iopromide	BA
19	F	43	Cervix cancer	S, R, C	Severe	Iopromide	
20	F	58	Hepatocellular carcinoma	S, C	Severe	Iopromide	
21	F	74	Duodenal cancer	S, C	Severe	Iopromide	
22	F	68	Hepatocellular carcinoma	S, C	Severe	Iopamidol	
23	F	24	Spine tumor	S, R, C	Severe	Iomeprol	
24	F	68	Hepatocellular carcinoma	S, C	Severe	Iopamidol	
25	M	72	Angina	C, N	Severe	Iopromide	
26	M	55	Colon caner	S, R, C	Severe	Iopromide	
27	F	38	Rectal cancer	S, R, C	Severe	Iopromide	
28	F	48	Unstable angina	S, R	Severe	Iodixanol	
29	F	56	Colon caner	S, C	Severe	Iopromide	
30	F	59	Carotid aneurysm	S, C	Severe	Iopamidol	

[a] S: skin manifestations such as urticaria, angioedema, pruritus, facial flushing, or redness; G: gastrointestinal manifestations such as nausea or vomiting; N: neurological manifestations such as dizziness or syncope; R: respiratory manifestations such as rhinorrhea, dyspnea, laryngeal edema, bronchospasm, or hypoxemia; C: cardiovascular manifestations such as hypotension, arrhythmia, or cardiac arrest.
[b] AR: allergic rhinitis; BB: concomitant use of beta-blockers; BA: bronchial asthma.

ber of patients who receive CM annually, this incidence rate has a significant impact in clinical practice.

Premedication with corticosteroid, either alone or in combination with antihistamines and/or H2 blockers, is commonly used in patients that have previously experienced CM-related immediate adverse reactions [5]. However, the efficacy of combination prophylaxis regimens in these high-risk patients has not been fully evaluated to date, and supporting data are still lacking [6], especially in cases of non-ionic CM-induced reactions. Moreover, the outcome of using premedication to prevent CM hypersensitivity reactions has never been evaluated in an Asian or Korean population.

In this study, we evaluated 30 patients who had experienced prior immediate-type CM-related adverse reactions and who received premedication to prevent non-ionic CM hypersensitivity. We analyzed the effectiveness of premedication and the features of breakthrough reactions according to the patients' clinical characteristics.

2. Methods

2.1. Study subjects

We retrospectively reviewed patients who, in a 3-year period, were referred to the allergy clinics of the Seoul National University Hospital and Seoul National University Bundang Hospital for the prevention of CM-induced hypersensitivity reactions, due to a history of CM-related adverse reactions. The patients' clinical characteristics, including the characteristics of prior reactions, severity of prior reactions, contrast media associated with prior reactions, underlying disease, allergic disease history, and concomitant use of beta-blockers, were examined. This study included patients who had experienced only immediate-type (<1 h) hypersensitivity reactions and excluded patients with other types of previous reactions, such as delayed hypersensitivity reactions, vasovagal reactions, and chemotoxicity-related reactions. Prior CM-induced adverse reactions were classified as being either 'mild' or 'severe'. Severe reactions were defined by the presence of one or more of the following systemic symptoms: dyspnea, sudden drop in blood pressure, cardiac arrest, loss of consciousness. This study was approved by the institutional review boards of both hospitals.

2.2. Contrast media and procedures

All patients evaluated in this study had undergone intravascular radiological procedures, including various kinds of contrast CT scans, angiographies, and radiological interventions requiring the use of CM. Patients who had undergone non-vascular procedures, such as urological or intrabiliary procedures, were excluded. The CM used in these procedures included Ultravist™ (Iopromide), Iomeron™ (Iomepril), Pamiray™ (Iopamidol) (all low-osmolar, non-ionic), and Visipaque™ (Iodixanol) (iso-osmolar, non-ionic). Patients treated with high-osmolar and ionic CMs were excluded.

2.3. Premedication

Premedication formulations comprised combinations of modified forms of previously described systemic steroids, antihistamines, and H2 blockers [5,7,8]. In most patients, systemic steroids (prednisolone, 50 mg or methylprednisolone, 40–50 mg) were administered three times (13, 7, and 1 h prior to the procedure). As a result of factors including infection with hepatitis B virus, poor