

The efficacy of single premedication with antihistamines for radiocontrast media hypersensitivity

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Background: Single premedication with antihistamines for radiocontrast media (RCM) hypersensitivity is frequently used in real world at the emergent situation although its efficacy is not proven.

Objective: To evaluate the effect of intravenous antihistamines as a premedication in general population who had experience of mild adverse reactions to iodinated RCM.

Methods: A retrospective observational study on 14,785 subjects who had RCM-enhanced computed tomography scans between January 2014 and December 2015 in Seoul National University Hospital Gangnam Healthcare Center, Seoul, South Korea.

Results: Among 453 subjects who had a history of mild RCM-induced hypersensitivity reactions, 273 subjects had a single premedication of intravenous antihistamine. When comparing antihistamine-premedication group and nonpremedication group, there is no protective effect of antihistamines on the incidence rate and severity of hypersensitivity (10.6% vs. 11.7%, $p = 0.729$).

Conclusion: The clinical efficacy of a single premedication of antihistamines for mild RCM-induced hypersensitivity was not confirmed.

Key words: Radiocontrast media; Hypersensitivity; Premedication

INTRODUCTION

Iodinated radiocontrast media (RCM) is widely used to obtain more accurate diagnosis during computed tomography (CT) scan. However RCM can sometimes cause various types of adverse reactions and the incidence rate of adverse reaction to

RCM has been climbing with increasing use of it [1].

A premedication with corticosteroid in combination with antihistamines is commonly used in patients with higher risk to prevent RCM-related hypersensitivity reactions (HRs) and has been thought to be effective in most cases [2]. In an emergency setting, the current guideline recommends that

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we may omit steroids and give intravenous antihistamines only to patients with a history of RCM-related HRs, because steroids have not shown positive results if they were administered less than 4 to 6 hours prior to contrast injection [3]. However, owing to the paucity of large-scale studies to prove the efficacy of premedication, global guidelines to prevent RCM-related HRs have not been standardized. For example, the efficacy of single premedication with antihistamines in subjects with a history of mild RCM-related HRs has not been fully assessed, although this way of prevention has been widely used in our daily practice.

The purpose of this retrospective study was to evaluate the effectiveness of single premedication with antihistamines in subjects with a history of mild RCM-induced HRs.

MATERIALS AND METHODS

Study populations

A total of 14,785 subjects who had RCM-enhanced CT scans between January 2014 and December 2015 in the Seoul National University Hospital Gangnam Healthcare Center (SNUHGHC), Seoul, South Korea, for a purpose of a routine health check-up were enrolled. We retrospectively reviewed medical records to find subjects who had a history of RCM-induced HRs and recorded their demographic factors, presence or absence of premedication, and outcomes of premedication including severity.

The Institutional Review Board of Seoul National University Hospital approved this retrospective cross-sectional study and waived the requirement for informed consent.

Premedication strategy in SNUHGHC

In SNUHGHC, we usually recommend that all subjects with a history of RCM-induced adverse events identified from medical records or questionnaires should see a physician before CT scan. Then the physician determined severity of RCM-induced HRs based on the American College of Radiology manual on RCM [3]. Mild reactions were defined as a history of limited urticaria, pruritus, cutaneous edema, nasal congestion, rhinorrhea, or conjunctivitis. As mentioned earlier, a single premedication with antihistamines in preventing mild RCM-induced HRs has not been proved so far and thus a prescription of antihistamines before CT scan in subjects with mild HRs to RCM is dependent on the physician's judgment.

Contrast media

The contrast media used in the SNUHGHC is all nonionic low-osmolar iodinated media and was administered intravenously by a power injector.

Adverse reactions

All adverse reactions detected during examination or reported by telephone afterward are recorded. Reactions are classified into immediate (<1 hour) or nonimmediate (>1 hour), mild, moderate, or severe reactions according to its manifestation with reference to the guideline [3].

Statistical analysis

A chi-square test for categorical variables and Student *t* test or analysis of variance for continuous variables were used to compare variables between subjects. All statistical analyses were conducted using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA). A $p < 0.05$ was considered to be statistically significant.

RESULTS

Among 14,785 subjects, 453 subjects who had a history of mild RCM-induced HRs were identified. According to the physician's judgment, a total of 273 subjects had a premedication of intravenous antihistamines (chlorpheniramine maleate 4 mg; Jeil Pharmaceutical, Seoul, Korea). The time gap between an injection of antihistamines and an administration of RCM ranged from 30 to 60 minutes.

There was no significant difference in clinical variables between premedication and nonpremedication groups except gender. There was no difference in the occurrence of RCM-induced HRs between premedication and nonpremedication groups (10.6% vs. 11.7%, $p = 0.729$) (Table 1). In addition, we could not find any significant differences between 2 groups according to the severity (mild vs. moderate, $p = 1.000$), and time interval (immediate vs. nonimmediate, $p = 1.000$).

DISCUSSION

In order to evaluate the clinical efficacy of a single premedication with antihistamines to prevent RCM-induced HR in subject with a history of mild RCM-induced HR, we

Table 1. Comparison of the study groups

Variable	Premedication	Nonpremedication	<i>p</i> value
Number	273	180	
Sex, male : female	168 : 105	129 : 51	0.026
Age (yr), median (range)	56 (36–76)	56 (31–77)	0.779
Adverse reaction	29 (10.6)	21 (11.7)	0.729
Time interval			1.000
Immediate	24 (82.8)	18 (85.7)	
Nonimmediate	5 (17.2)	3 (14.3)	
Severity			1.000
Mild	25 (86.2)	19 (90.5)	
Moderate	4 (13.8)	2 (9.5)	
Mild immediate			
Localized urticaria/ erythema/pruritus	20 (80)	14 (73.7)	
Localized itchy/scratchy throat/mild cough	1 (4)	2 (10.5)	
Mild nonimmediate			
Localized rash	4 (16)	3 (15.8)	
Moderate immediate			
Diffuse urticaria/erythema/pruritus	3 (75)	1 (33.3)	
Wheezing/bronchospasm, mild or no hypoxia	-	1 (33.3)	
Throat tightness/hoarseness without dyspnea	-	1 (33.3)	
Moderate nonimmediate			
Generalized rash	1 (25)	-	

Values are presented as number (%).

retrospectively reviewed medical records of 14,785 subjects visiting SNUHGHC for health check-up. In SNUHGHC, a premedication with antihistamines was done depending on the judgment of physicians in subjects with a history of mild RCM-induced HRs and thus this study might provide an unbiased perspective on the clinical efficacy of a single premedication with antihistamines in preventing mild RCM-induced HRs. Our retrospective analysis showed that a single premedication with antihistamines in subjects with a history of mild RCM-induced HRs was not clinically effective in preventing RCM-induced HRs.

The incidence rate of immediate HR to nonionic RCM is reported to be 0.7%–3% in the world [1] and especially in Asia Pacific region, it is reported to be 0.16%–2.21% in recent 10 years [4–8]. To use RCM safely, prevention strategies should be considered for those subjects who have a history of previous RCM-induced HRs before readministration of RCM because they are highly susceptible to recurrence [3]. As a part of

protective strategies against RCM-induced HRs, conventional premedication with antihistamines and corticosteroids is generally recommended [3]. In subjects with a history of moderate to severe RCM-induced HRs, coadministration of antihistamines and corticosteroids before re-exposure to RCM showed favorable outcomes [2, 9]. However, there have been limited evidences demonstrating clinical effects of a single premedication with antihistamines in subjects with a history of mild RCM-induced HRs. This uncertainty was well reflected in real practice. Most physicians recognized that a premedication of antihistamines would be helpful in preventing RCM-induced HRs, but our retrospective analysis revealed that actually about 60% of physicians recommended a single premedication of antihistamines in subjects with a history of mild RCM-induced HRs in a real situation. There must be lots of reasons to explain this discrepancy. However, a lack of strong guideline to prevent RCM-induced HR based on sound evidences might be the

most important one. In this point of view, our retrospective analysis provides a new view on the clinical efficacy of a single premedication of antihistamines in subjects with a history of mild RCM-induced HRs. Our observations suggest that we need to develop a new preventing strategy specified to subjects with a history of mild RCM-induced HR. However, there were some limiting points in generalizing our observations. The first and most important one was that our study used retrospective methods. A well-designed prospective study should be followed to confirm our findings. A range of time gap (30 minutes to 60 minutes) between an injection of antihistamines and an administration of RCM would be another limiting factor. The onset time of chlorpheniramine effect is known to be 30 minutes but a peak response are considered to be achieved between 1 to 2 hours [10]. Thus it is possible that RCM was administered before the time of full effect of chlorpheniramine in some subjects. In conclusion, this large retrospective study did not confirm the clinical efficacy of a single premedication of antihistamines in subjects with a history of mild RCM-induced HRs.

REFERENCES

1. Brockow K, Sanchez-Borges M. Hypersensitivity to contrast media and dyes. *Immunol Allergy Clin North Am* 2014;34:547-64.
2. Kim SH, Lee SH, Lee SM, Kang HR, Park HW, Kim SS, Cho SH, Min KU, Kim YY, Chang YS. Outcomes of premedication for non-ionic radiocontrast media hypersensitivity reactions in Korea. *Eur J Radiol* 2011;80:363-7.
3. ACR Manual on contrast media v10.2 [Internet]. Reston (VA): American College of Radiology; 2016 [cited 2016 Jun 1]. Available from: <http://www.acr.org/quality-safety/resources/contrast-manual>.
4. Lee SY, Lim KW, Chang YS. Radiocontrast media hypersensitivity in the Asia Pacific region. *Asia Pac Allergy* 2014;4:119-25.
5. Kim SS, Park CH, Park MJ, Choi SH, Kim YS, Park HW, Chang YS, Shin CS, Oh BH, Min KU, Kim YY, Cho SH. Adverse reactions to radiocontrast media in computed tomography (CT) in general population: incidence and clinical features. *Korean J Asthma Allergy Clin Immunol* 2007;27:157-61.
6. Kim MH, Park CH, Kim DI, Kim KM, Kim HK, Lim KH, Song WJ, Lee SM, Kim SH, Kwon HS, Park HW, Yoon CJ, Cho SH, Min KU, Kim YY, Chang YS. Surveillance of contrast-media-induced hypersensitivity reactions using signals from an electronic medical recording system. *Ann Allergy Asthma Immunol* 2012;108:167-71.
7. Bae YJ, Hwang YW, Yoon SY, Kim S, Lee T, Lee YS, Kwon HS, Cho YS, Shin MJ, Moon HB, Kim TB. The effectiveness of automatic recommending system for premedication in reducing recurrent radiocontrast media hypersensitivity reactions. *PLoS One* 2013;8:e66014.
8. Yang MS, Choi SI, Song WJ, Kim SH, Kang HR, Park HW, Cho SH, Min KU, Kim JH, Chang YS. Impact of an electronic consultant system on hypersensitivity reactions to iodinated radiocontrast media: an observational study. *Postgrad Med J* 2015;91:193-9.
9. Tramer MR, von Elm E, Loubeyre P, Hauser C. Pharmacological prevention of serious anaphylactic reactions due to iodinated contrast media: systematic review. *BMJ* 2006;333:675.
10. Micromedex Solutions. Medication, disease and toxicology management [Internet]. Ann Arbor (MI): Truven Health Analytics; c2012-2016 [cited 2016 Jun 1]. Available from: <https://www.micromedexsolutions.com/micromedex2/librarian>.