조영제 알레르기

고신의대 알레르기 내과
최길순

Case M/60 송O섭 06080110

◆ **C.C** : for evaluation of radiocontrast media induced allergic reaction

◆ **Present illness**

- no allergic disease history (drug allergy, bronchial asthma,...)
- 2006 년 abdominal aortic aneurysm 진단 후 본원 CS f/u 중
- 2010년 9월 chest pain으로 내원하여 NSTEMI 진단, 당시 stent insertion.
- 2012년 cough, sputum 으로 CI 입원 : 당시 evaluation 후 COPD with AE 로 treatment 시행함.
- 2013년 L-spine abscess 로 본원 OS 입원 치료함.
- 2014년 anal blood spotting 으로 본원 GI evaluation 진행함.

...

- 2015년 angio CT 시행후 syncope 병력
- 2018.7.12 premedication 으로 peniramine 1A, Dexamethasone 1A iv 시행 -> angio CT 시행함
  → 조영제 주입하자마자 nausea, dyspnea 호소, 5분 뒤 의식 소식 있으면서
  V/S BP 60/40 mmHg, PR 100회/min, RR 20 회/min, BT 36℃, SpO2 95%
  → 응급실로 refer 되어 N/S hydration 및 peniramine 1A, Dexamethasone 1A iv 투여
  의식 회복 후에도 목이 붓는 느낌, 호흡곤란, 흉통 호소
  → 1시간 반 후 BP 100/46 mmHg, PR 76 회/min 체크되어 병실로 이동

- 2018.7.18 abdominal aortic aneurysm dilatation 에 대해 intervention 예정으로 향후 조치?

Case

M/60 송O섭 06080110

◆ **2015년과 2018년 7월 event 사이에 radiocontrast media노출 병력**

- 2015년 angio CT
  - 2016.3.4 angio CT (이오메프롤;이오메론®)
  - 2016.8.8. abdominal CT (이오파미돌; 파미레이®)
  - 2017.5월 18 chest CT (이오파미돌; 레디센스®)
  - 2017.2월 외부 chest and abdominal CT
  - CAG 시행
- 2018.7.12 angio CT (이오메프롤;이오메론®)

Case

M/60 송O섭 06080110

- Impression : RCM induced anaphylaxis
- Evaluation : skin test using the radiocontrast media

Case

M/60 송O섭 06080110

◆ Skin prick test

Radiocontrast		Wheal (mm)	Erythema (mm)
Negative control (Saline)		0x0	0x0
Positive control(Histamine)		4x4	20x30
헥소슈어	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	0x0	0x0
파미레이	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	0x0	0x0
옴니헥솔	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	1x1	1x1
스캔룩스	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	1x1	1x1
제네틱스	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	0x0	0x0

Radiocontrast		Wheal (mm)	Erythema (mm)
옵티레이	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	1x1	1x1
레디센스	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	1x1	1x1
비지파크	1:100	0x0	0x0
	1:10	0x0	0x0
	1:2	0x0	0x0
이오메론	**1:100**	**1x1**	**1x1**
	1:10	**1x1**	**1x1**
	1:2	**2x2**	**2x2**

Case

M/60 송O섭 06080110

- 2018. 7.18 RCM(비지파크사용), premedication (methysol, peniramine)
  → peripheral angiogram, intervention, no side effect

- 2018. 7.20 angio CT : RCM(비지파크사용), premedication (methysol, peniramine)
  → no side effect

- 2018.8.14 brain MRI : no side effect

- 2018.8.15 chest, abdominal CT : RCM(비지파크사용), no premedication
- 2018.8.21 angio CT : RCM(비지파크사용), no premedication

Contrast Media

- **A <u>substance used to enhance the contrast of structures or fluids</u> within the body in medical imaging.**

- **<u>Radiocontrast media (RCM)</u>**

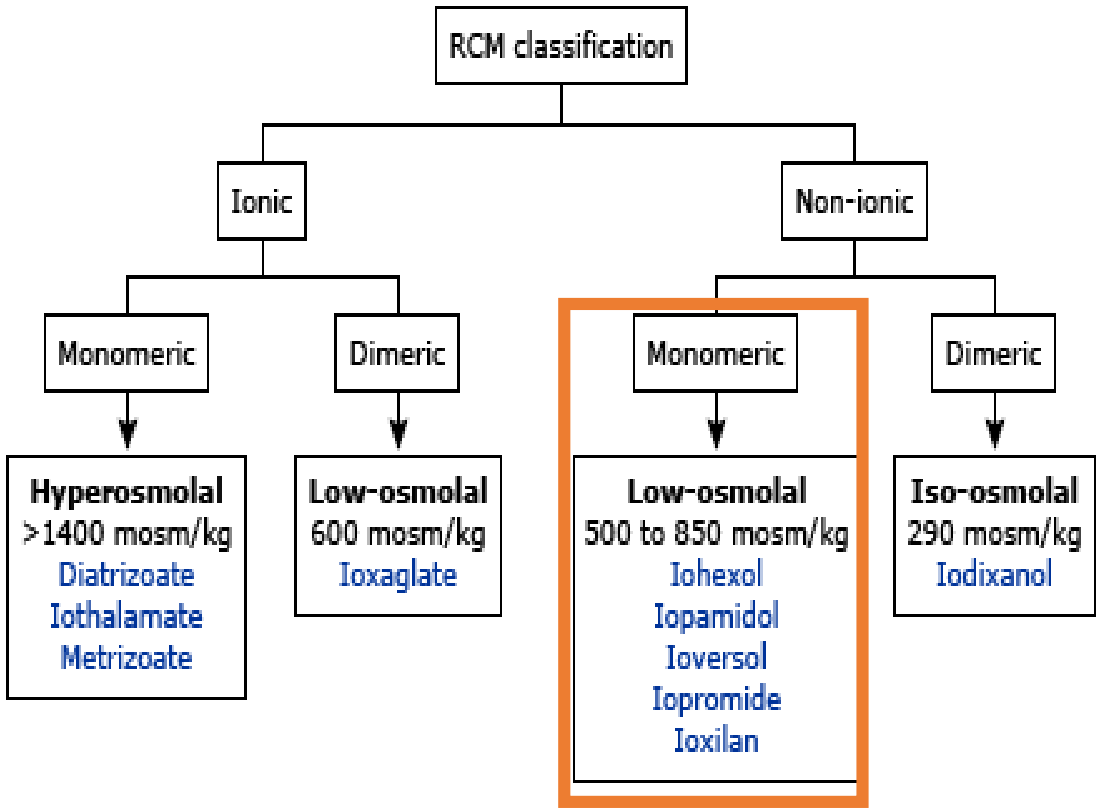
  - Iodinated **(ICM)**

  - Barium (gastro-intestinal)

- **<u>MRI contrast agent</u>**

  - Gadolinium

Iodine based contrast media (RCM, ICM)



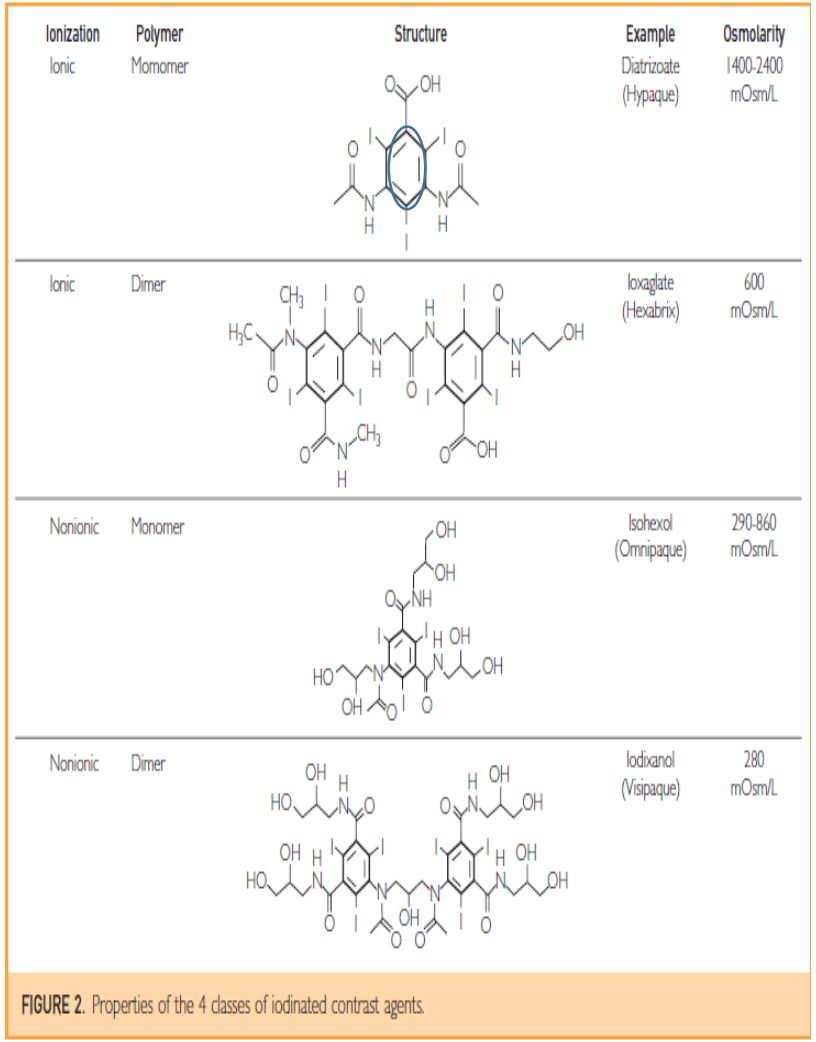


FIGURE 2. Properties of the 4 classes of iodinated contrast agents.

Iodine based contrast media (RCM)

- **Clinical Use**
  - more than 70 million exams/ year worldwide
    - Arthrography, myelography
    - **Angiography**
    - Venography
    - VCUG(voiding cystourethrography), IVU(intravenous urography)
    - HSG(hysterosalpingogram)
    - **ERCP(endoscopic retrograde cholangiopancreatography)**
    - **CT (computed tomography)**

Adverse Drug reaction(ADR)s to RCM

- **Adverse Drug reacton (약물 유해 반응)**
  : 약물을 사용하는 중 의도되지 않은 작용 중 약과의 인과 관계를 배제할 수 없는 경우

Type A 유해반응
: 의약품 자체의 특성에 의해 발생

- 다른 환자에서도 재현 가능
- 발생률이 비교적 높음

Type B 유해반응
: 환자의 개인적 특성에 의한 발생

- 환자의 개인적 특성과 관련
- 약물 투여량과 상관관계 없음
- 다른 환자에서 제현 불가능
- 발생률이 비교적 낮음

생리적 반응(기타 유해반응)	
경증	경미한 메스꺼움·구토 일시적인 화끈거림·열감·오한 두통, 어지러움, 불안, 맛의 변화 경증 고혈압 저절로 호전되는 혈관미주신경항진 반응
중등증	지속되는 메스꺼움·구토 흉통 고혈압성 긴급증(hypertensive urgency) 치료가 필요한 혈관미주신경항진 반응
중증	부정맥 경련 고혈압성 응급증(hypertensive emergency) 치료에 반응하지 않는 혈관미주신경항진 반응

Hypersensitivity reactions to RCM

- Idiosyncratic and largely **independent** of dose and infusion rate
- **Incidence**

  - a difference according the **type of RCM** and the **onset of the reaction**

  ➢ **Immediate hypersensitivity reactions (≤1 시간 발생, 수시간 안에 회복)**

  - 6.4~31.2% for ionic, 0.16~7.7% for non-ionic
  - severe reactions in 0.02% to 0.04% of intravenous procedures,
  - severe reactions: 0.04% for lower osmolar, 0.22% for ionic, high osmolar
  - fatality 1-2:100,000 exams

  ➢ **Non-immediate hypersensitivity reactions (1시간 ~10일 발생, 수일~ 수주 후 회복)**

  - 0.5% to 3% of RCM-exposed patients
  - high incidence in dimeric nonionic RCM

- **Clinical manifestations & Pathophysiology : different**

Immediate hypersensitivity reactions

Clinical manifestations

- 약물 투여후 1시간 이내에 발생
- 70%는 투여후 5분이내에 발생,
- **중증 또는 치명적인 반응의 96% : 20분 이내 발생**

- Flushing
- Pruritus
- Urticaria
- Angioedema
- Bronchospasm and wheezing
- Laryngeal edema and stridor
- Hypotension and rarely shock
- Loss of consciousness

- **Mild/ Moderate/ Severe**

	과민반응
경증	국소적인 두드러기·가려움증 국소적인 피부 부종 목(인후두) 가려움 코 충혈, 재채기, 콧물, 결막염
중등증	광범위한 두드러기·가려움증 광범위한 홍반 안면부종 목이 붓거나 쉼 저산소증이 없는 천명, 기도수축
중증	호흡곤란을 동반한 심한 부종과 안면부종 저혈압을 동반한 심한 홍반 그렁거림/저산소증을 동반한 후두부종 심한 저산소증이 있는 천명, 기도수축 아나필락시스 쇼크

Immediate hypersensitivity reactions

Pathophysiology

- Non IgE-mediated in the majority of cases,
  - Direct mast cell activation
  - Activation of the coagulation, kinin, and/or complement cascades
  - Inhibition of platelet aggregation with increased serotonin release
  - Inhibition of enzymes, such as cholinesterase

- rarely IgE-mediated

Delayed RCM Reactions

- Occur in 2% of patients
- Occur between 1 hour and 10 days after RCM administration
- Usually mild, cutaneous, self-limited
- Serious reactions 0.004-0.008%

- May be T-cell mediated
- **The majority are maculopapular, pruritic rashes with fever**
- **Desquamation is frequent**
- Cutaneous vasculitis, Erythema multiforme, SJS, TEN, DRESS: infrequent

- Often patient has multiple drug sensitivities

Risk Factors of hypersensitivity reaction to RCM

IHRs	Delayed HRs
• History of previous IHR to RCM (5x) • Female gender (up to 20x) • Increased incidence 20-50 yrs of age • Atopy (2-3x) • Asthma (10x, not all articles agree) • Possibly the use of certain medications : beta-blockers, aspirin and NSAIDs.	• Female • Patients being treated with IL-2 • Frequency of previous reaction (possible) but recurrence is not consistent • More frequent with non-ionic **dimers** • Equal frequency with ionic & non-ionic monomers

* More severe **reactions**

- Cardiovascular disease
- Beta-blockers
- Debilitated, unstable, or elderly

Treatment

*** Recognition of Early Clinical Manifestations** is essential to prevent further reaction or a fatal outcome.

- **IHRs**

  - depends upon the severity of the reaction

  - Mild : often self-limited, typically resolving fully in an hour or two

    diphenhydramine (50 mg intravenously to adults)

  - Severe : based on anaphylaxis (epinephrine IM)

    * corticosteroids : beneficial in preventing or reducing the severity of delayed Sx.

- **Delayed HRs**
  - most do not require treatment
  - no controlled studies
  - corticosteroids and H1 antagonists employed empirically for moderate severe and severe reactions

조영제를 사용한 검사를 진행해야 하는데..?

조영제 사용하고 부작용이 있었어요..

- Evaluation?
- Premedication?

Diagnostic approaches for RCM hypersensitivity

- **History taking and physical examination** : main stream in the diagnosis
- **Test is not required for diagnosis**

- **Immediate Reactions**
  - skin test
    : **not recommended,** could be useful to identify the causative RCMs in severe HRs.
  - basophil activation test (BAT)
  - tryptase or histamine

- **Delayed Reactions**
  - patch test
  - delayed reading of intradermal test.

Skin test in patients with hypersensitivity reaction to RCM

- 원인 조영제 확인?
- 조영제 사이의 교차반응?

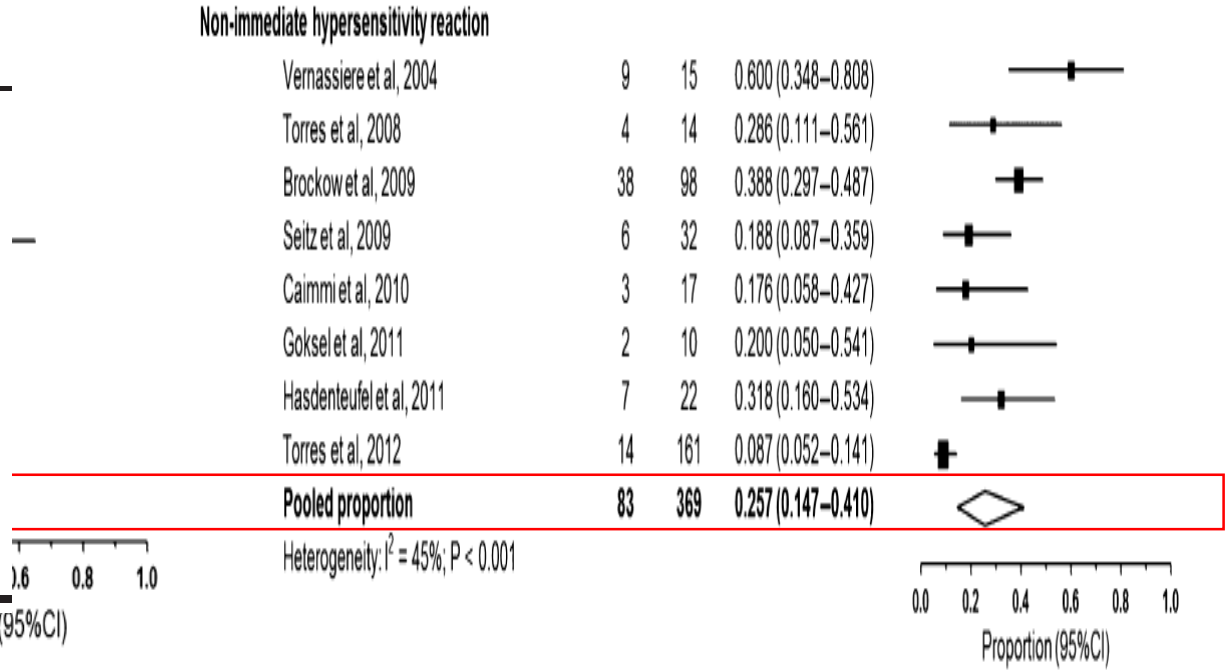
Allergy. 2015 Jun;70(6):625-37. doi: 10.1111/all.12589. Epub 2015 Mar 20.

Skin tests in patients with hypersensitivity reaction to iodinated contrast media: a meta-analysis.

Yoon SH[1,2], Lee SY[3,4,5], Kang HR[3,4], Kim JY[3,4], Hahn S[6], Park CM[1,2,7], Chang YS[3,5], Goo JM[1,2,7], Cho SH[3,4].

* Per-patient positive rates of skin tests in patients with immediate HSR to ICM

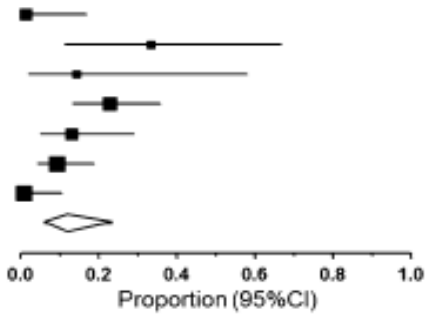
Source	Positive rate of skin tests, % SPT	IDT
Dewachter et al. (20)	50 (2/4)	100 (4/4)
Trcka et al. (22)	Not done	4 (4/96)
Brockow et al. (11)	3 (4/122)	26 (32/121)
Caimmi et al. (24)	0 (0/101)	15 (15/101)††
Dewachter et al. (25)	4 (1/24)	46 (12/26)
Goksel et al. (26)	0 (0/14)	14 (2/14)
Pinnobphun et al. (27)	0 (0/63)	24 (15/63)
Kim et al. (28)	3 (1/32)	26 (12/46)
Kim et al. (29)§§	2 (1/51)	65 (33/51)
Renaudin et al. (30)	14 (1/7)	57 (4/7)
Prieto-Garcia et al. (31)	0 (0/106)	10 (11/106)
Salas et al. (32)	3 (3/90)	6 (5/90)



- **Positive rates in Immediate reaction**

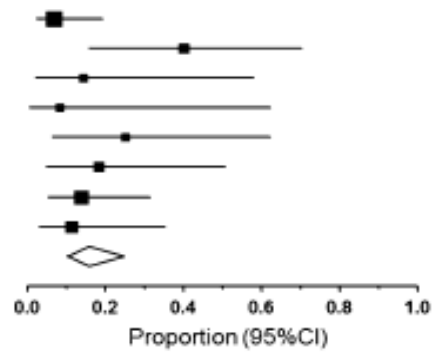
Mild immediate hypersensitivity reaction

Trcka et al, 2008	0	40	0.012 (0.001–0.167)
Dewachter et al, 2011	3	9	0.333 (0.111–0.667)
Goksel et al, 2011	1	7	0.143 (0.020–0.581)
Pinnobphun et al, 2011	12	53	0.226 (0.133–0.358)
Kim et al, 2013	4	31	0.129 (0.049–0.297)
Prieto-García et al, 2013	6	66	0.091 (0.041–0.188)
Salas et al, 2013	0	69	0.007 (0.000–0.104)
Pooled proportion	**26**	**275**	**0.122 (0.060–0.232)**
Heterogeneity: I^2 = 38%; P = 0.020			



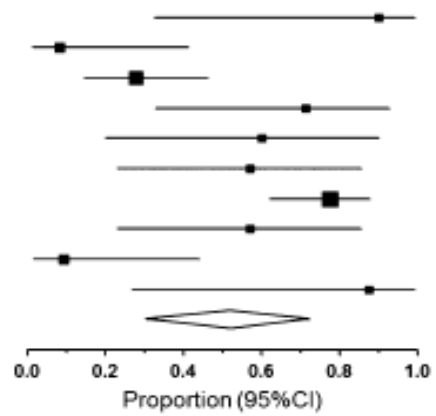
Moderate immediate hypersensitivity reaction

Trcka et al, 2008	3	44	0.068 (0.022–0.191)
Dewachter et al, 2011	4	10	0.400 (0.158–0.703)
Goksel et al, 2011	1	7	0.143 (0.020–0.581)
Pinnobphun et al, 2011	0	5	0.083 (0.005–0.622)
Kim et al, 2013	2	8	0.250 (0.063–0.623)
Kim et al, 2014	2	11	0.182 (0.046–0.507)
Prieto-García et al, 2013	4	29	0.138 (0.053–0.315)
Salas et al, 2013	2	18	0.111 (0.028–0.352)
Pooled proportion	**18**	**132**	**0.157 (0.099–0.241)**
Heterogeneity: I^2 = 6%; P = 0.274			



Severe immediate hypersensitivity reaction

Dewachter et al, 2001	4	4	0.900 (0.326–0.994)
Trcka et al, 2008	1	12	0.083 (0.012–0.413)
Brockow et al, 2009	8	29	0.276 (0.144–0.462)
Dewachter et al, 2011	5	7	0.714 (0.327–0.928)
Pinnobphun et al, 2011	3	5	0.600 (0.200–0.900)
Kim et al, 2013	4	7	0.571 (0.230–0.856)
Kim et al, 2014	31	40	0.775 (0.621–0.879)
Renaudin et al, 2013	4	7	0.571 (0.230–0.856)
Prieto-García et al, 2013	1	11	0.091 (0.013–0.439)
Salas et al, 2013	3	3	0.875 (0.266–0.993)
Pooled proportion	**64**	**125**	**0.519 (0.306–0.724)**
Heterogeneity: I^2 = 42%; P < 0.001			



- **Cross reactivity rate**

Immediate reaction

Immediate HSR		Ionic monomers		Ionic dimer	Nonionic monomers							Nonionic dimers	
		Amido-triozoate	Ioxita-lamate	Ioxaglate	Iobitridol	Iohexol	Iomeprol	Iopamidol	Iopentol	Iopromide	Ioversol	Iodixanol	Iotrolan
Ionic monomers	Amido-triozoate		12%‡ (3-44%)	10%†† (3-32%)	11%†† (3-35%)	8%†† (2-30%)	11%†† (3-34%)	10%†† (3-32%)	9%‡ (1-44%)	6%‡ (1-34%)	8%†† (2-30%)	8%†† (2-32%)	8%† (0-62%)
	Ioxita-lamate			7%†† (2-23%)	8%†† (2-24%)	8%†† (2-24%)	7%†† (2-23%)	10%†† (2-33%)	5%‡ (1-30%)	8%†† (2-27%)	4%†† (1-18%)	4%†† (1-18%)	6%† (0-54%)
Ionic dimer	Ioxaglate				11%††† (4-25%)	7%††† (2-19%)	8%††† (3-20%)	11%‡‡ (3-32%)	5%‡ (1-20%)	7%‡‡ (2-21%)	7%††† (2-20%)	6%††† (2-17%)	6%† (0-51%)
Nonionic monomers	Iobitridol					7%††† (3-18%)	10%††† (5-21%)	10%††† (5-22%)	9%‡ (2-35%)	12%††† (6-24%)	6%††† (2-15%)	7%††† (2-17%)	6%† (0-51%)
	Iohexol						11%†††† (5-22%)	8%††† (4-17%)	5%‡ (1-28%)	9%††† (4-18%)	7%††† (3-17%)	10%†††† (5-23%)	6%† (0-54%)
	Iomeprol							6%††† (2-15%)	13%†† (2-50%)	21%†††† (11-38%)	8%††† (3-20%)	11%†††† (5-24%)	6%† (0-51%)
	Iopamidol								7%†† (1-29%)	12%††† (6-22%)	5%††† (2-14%)	5%††† (2-14%)	6%† (0-51%)
	Iopentol									8%†† (2-31%)	5%‡ (1-28%)	6%‡ (1-32%)	6%† (0-54%)
	Iopromide										4%††† (1-14%)	9%††† (4-18%)	6%† (0-51%)
	Ioversol											5%††† (2-13%)	6%† (0-51%)
Nonionic dimers	Iodixanol												7%† (0-56%)
	Iotrolan												

Non-immediate reaction

Non-immediate HSR		Ionic monomers		Ionic dimer	Nonionic monomers							Nonionic dimers	
		Amido-triozoate	Ioxita-lamate	Ioxaglate	Iobitridol	Iohexol	Iomeprol	Iopamidol	Iopentol	Iopromide	Ioversol	Iodixanol	Iotrolan
Ionic monomers	Amido-triozoate		7%‡ (1-29%)	7%‡ (2-24%)	7%‡ (1-29%)	10%‡ (3-26%)	7%‡ (1-28%)	7%‡ (2-24%)	13%‡ (4-33%)	9%‡ (2-29%)	8%‡ (2-27%)	11%‡ (3-29%)	9%† (1-44%)
	Ioxita-lamate			24%†† (8-52%)	20%†† (9-39%)	24%†† (8-52%)	21%†† (9-42%)	28%†† (12-53%)	34%‡ (5-84%)	30%‡ (7-71%)	32%‡ (6-77%)	31%†† (11-61%)	3%† (0-35%)
Ionic dimer	Ioxaglate				16%‡‡ (7-32%)	26%†† (12-48%)	21%‡‡ (11-36%)	25%†† (10-49%)	37%‡ (8-80%)	24%†† (8-54%)	28%†† (8-65%)	28%‡‡ (12-51%)	7%† (1-35%)
Nonionic monomers	Iobitridol					25%‡‡ (10-48%)	13%††† (6-26%)	18%‡‡ (9-33%)	25%†† (8-56%)	22%‡‡ (8-48%)	19%‡‡ (5-49%)	22% ††† (12-37%)	9%‡ (2-35%)
	Iohexol						36%‡‡ (21-55%)	39%‡‡ (20-62%)	74%‡† (44-91%)	48%†† (15-83%)	61%‡† (25-88%)	59%‡‡ (25-88%)	24%‡ (9-50%)
	Iomeprol							33%‡‡ (16-55%)	42%†† (17-72%)	33%‡‡ (17-54%)	51%‡‡ (34-67%)	41%‡‡† (26-57%)	22%‡ (5-57%)
	Iopamidol								60%†† (20-90%)	40%†† (15-72%)	49%†† (12-87%)	51%‡‡ (25-77%)	21%‡ (5-59%)
	Iopentol									52%†† (18-84%)	66%†† (20-94%)	74%†† (39-93%)	24%‡ (9-50%)
	Iopromide										42%‡‡ (17-71%)	52%‡‡ (23-80%)	19%‡ (2-74%)
	Ioversol											64%‡‡ (33-87%)	16%‡ (1-63%)
Nonionic dimers	Iodixanol												24%‡ (9-50%)
	Iotrolan												

Outcomes According to Changes in Contrast Media

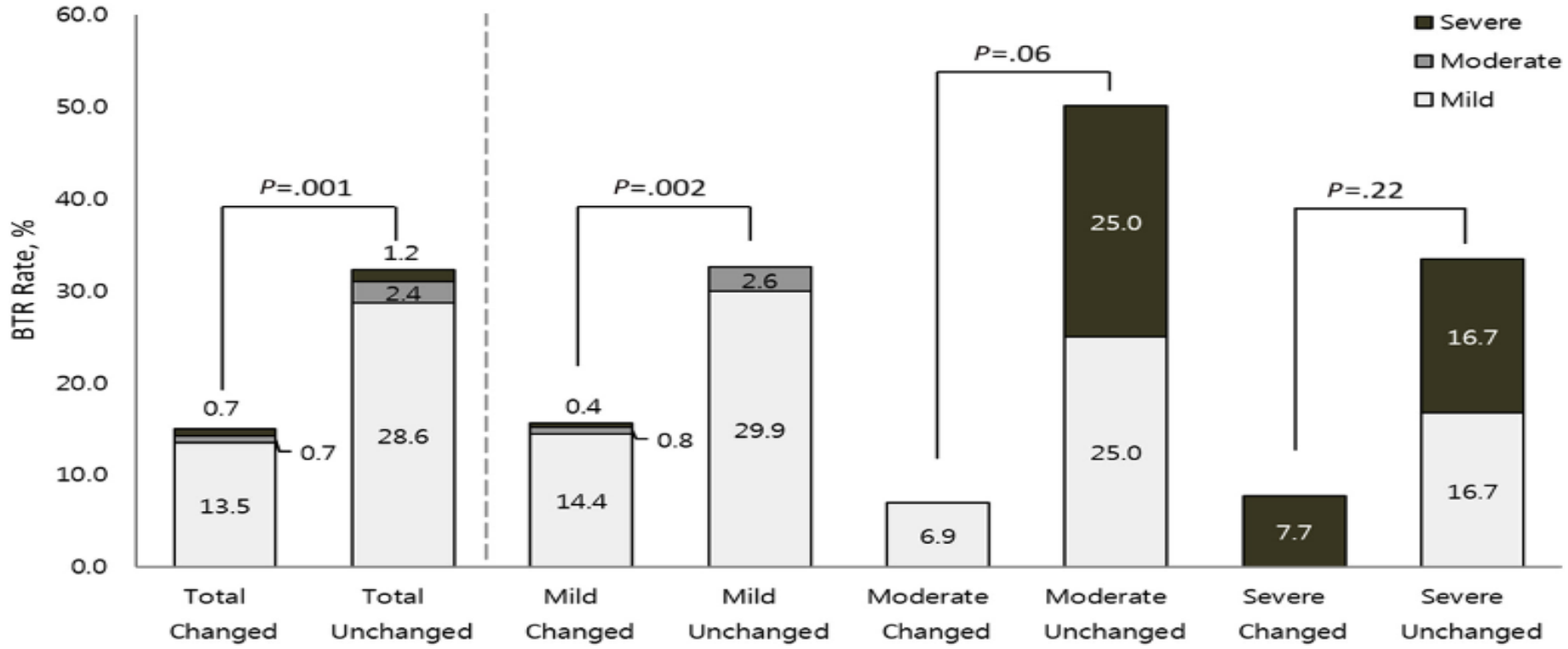


Figure 3. Breakthrough reaction (BTR) rates according to the use of the causative contrast agents: changing the iodinated contrast media agent decreased the overall BTR (14.9% vs 32.1%, $P = .001$) and the BTR rate in those with a mild (15.6% vs 32.5%, $P = .002$) index reaction.

Lee SY et al. Ann Allergy Asthma Immunol. 2017 Mar;118(3):339-344

Skin Testing for Suspected **Iodinated Contrast Media Hypersensitivity**.
Schrijvers R, Breynaert C, Ahmedali Y, Bourrain JL, Demoly P, Chiriac AM.
J Allergy Clin Immunol Pract. 2018 Jul - Aug;6(4):1246-1254. doi: 10.1016/j.jaip.2017.10.040. Epub 2018 Jan 19.
PMID: 29371073
Similar articles

Skin test positivity, n (%)	80 (13.4)
IHR	56 (70.0)
NIHR	20 (25.0)
Undetermined chronology	4 (5.0)

TABLE II. Challenges to negatively skin-tested ICM

		Initial chronology			Skin test result		
	Total	IHR	NIHR	UC	ST positive	ST negative	ST negative for a known culprit ICM
Total	597	423	118	56	80	517	125
Re-exposed, n (%)	233 (39.0)	172 (40.6)	43 (36.4)	18 (32.1)	17 (21.2)	216 (41.8)	51 (69.7%)
Tolerated, n (%)	217 (93.1)	162 (94.2)	37 (86.0)	18 (100)	16 (94.1)	201 (93.1)	43 (84.3%)
Not tolerated, n (%)	16 (6.9)	10 (5.8)	6 (14.0)	0 (0)	1* (5.9)	15 (6.9)	8 (15.7%)

Number of re-exposed patients and percentage (%) from total or subgroup is shown.
ICM, Iodinated contrast medium; *IHR*, immediate drug hypersensitivity reaction; *MPE*, maculopapular exanthema; *NIHR*, nonimmediate drug hypersensitivity reaction; *ST*, skin test; *UC*, undetermined chronology.
*Patient 330 experienced an MPE on rechallenge with a skin test positive ICM.

Skin testing for potential ICM hypersensitivity can **identify safe alternative(s) for ICM re-exposure** especially in patients with an immediate hypersensitivity reaction and/or skin test-proven ICM drug allergy

Skin test in patients with hypersensitivity reaction to RCM

- 이전에 중증의 반응을 경험했다면 skin test 를 고려해봐야....
- negatively Skin tested RCM

Cross-reactivity

Strong association	Frequents Association	Limited Association
Idixanol	Iodixanol	Iosaglate
Iohexol	Iohexol	Iopamidol
	Iopentol	Iobitridol
	Ioversol	Iopromide
	Iomeprol	

Recurrence of RCM Hypersensitivity

- Prevalence : 4% ~18%

Table 3

Relationships between Index and Breakthrough Reaction Severity

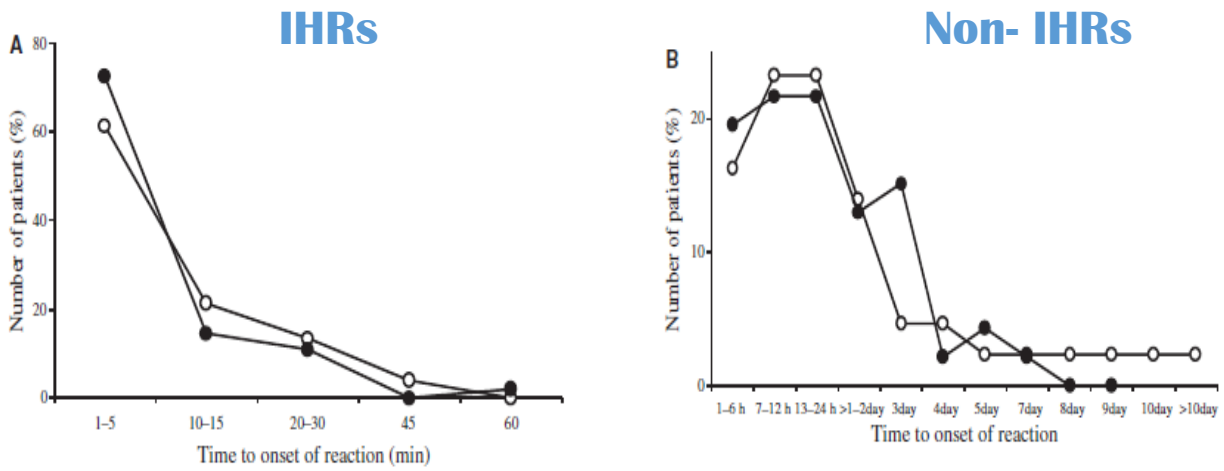
Index Reaction	Breakthrough Reaction			Change*
	Mild	Moderate	Severe	
Initial severity				
Unknown	45	17	0	. . .
Mild	94	9	0	. . .
Moderate	11	7	1	. . .
Severe	2	2	2	. . .
Change in severity*				
Unknown				62
Less severe				15
Same severity				103
More severe				10

Note.—Data are numbers of reactions (n = 190).

* Severity of breakthrough reaction compared with severity of index reaction.

Davenport MS et al. Radiology 2009, 253:372

Onset time of recurrent reaction



a European multicenter study, Allergy 2009: 64: 234–241

Prevention for RCM hypersensitivity reactions

- 비이온성 저장성/등장성(non-ionic low/iso-osmolar) 조영제 사용
- 조영제 주입 후 최소 30분 이상 영상의학과에서 관찰
- 소생술을 위한 약물과 장비를 즉시 사용할 수 있도록 구비

- **고위험 환자의 경우**
  - 반드시 필요한 경우가 아니라면 요오드화 조영제를 사용하지 않는 검사로 대체 고려
  - 과거에 유해반응을 일으켰던 조영제가 아닌 다른 조영제를 사용

- **피부검사:** 모든 환자에서 임상 적용을 권고할 근거는 부족,
  하지만, **중증의 반응을 경험한 환자의 경우 고려**
- 예방을 위해 **전처치 요법?**

Premedication ?

Arguments in Favor of and Against Premedication

In favor of premedication

- A serious anaphylactic reaction, even if not life-threatening, may contribute to major morbidity, a prolonged hospital stay, and high costs.
- Although controversial, pre-medication is widely used in clinical practice.
- Pharmacological and clinical data on the efficacy of anti-H1 plus anti-H2 agents and corticosteroids as single drugs indirectly suggest the utility of this classical association.
- Medical-legal and opportunity considerations

Against premedication

- The large number of unselected patients who need to receive the therapy to prevent a potentially life threatening event
- The cost
- The potential risk of side effects in some patients
- Delay in performing radiological or surgical procedures
- Encourages overconfidence on the part of physicians who inject contrast media or general or local anesthetics
- Possible neglect of appropriate measures to assess patients and to treat anaphylaxis

Recurrence of RCM Hypersensitivity, following premedication

Jingu et al. BMC Medical Imaging 2014, 14:34
http://www.biomedcentral.com/1471-2342/14/34

BMC Medical Imaging

RESEARCH ARTICLE Open Access

Breakthrough reactions of iodinated and gadolinium contrast media after oral steroid premedication protocol

Akiko Jingu[1*†], Junya Fukuda[2†], Ayako Taketomi-Takahashi[1†] and Yoshito Tsushima[1†]

Table 1 Severity of IR and severity of BTR to iodinated contrast media (CT)

Initial reaction (IR; n =134)		Breakthrough reaction (BTR)		
		Mild	Moderate	Severe
Iodine	Mild (n =113)	7	1	0
	Moderate (n =4)	0	0	0
Gadolinium	Mild (n =4)	0	0	0
	Moderate (n =2)	0	0	0
Others* (n =11)		0	0	0

*Suspected delayed adverse reactions to iodinated contrast media (n =11).

Table 4 Severity of IR and severity of BTR to gadolinium contrast media

Initial reaction (IR; n =33)		Breakthrough reaction (BTR)		
		Mild	Moderate	Severe
Iodine	Mild (n =15)	0	0	0
	Moderate (n =2)	0	0	0
	Severe (n =6)	0	0	0
Gadolinium	Mild (n =6)	0	0	0
Others* (n =4)		0	0	0

*In two patients, drug eruption was clinically suspected, but the causal medication was not identified. In another two patients, mild delayed reaction to iodinated contrast media was clinically suspected.

BTR after premedication

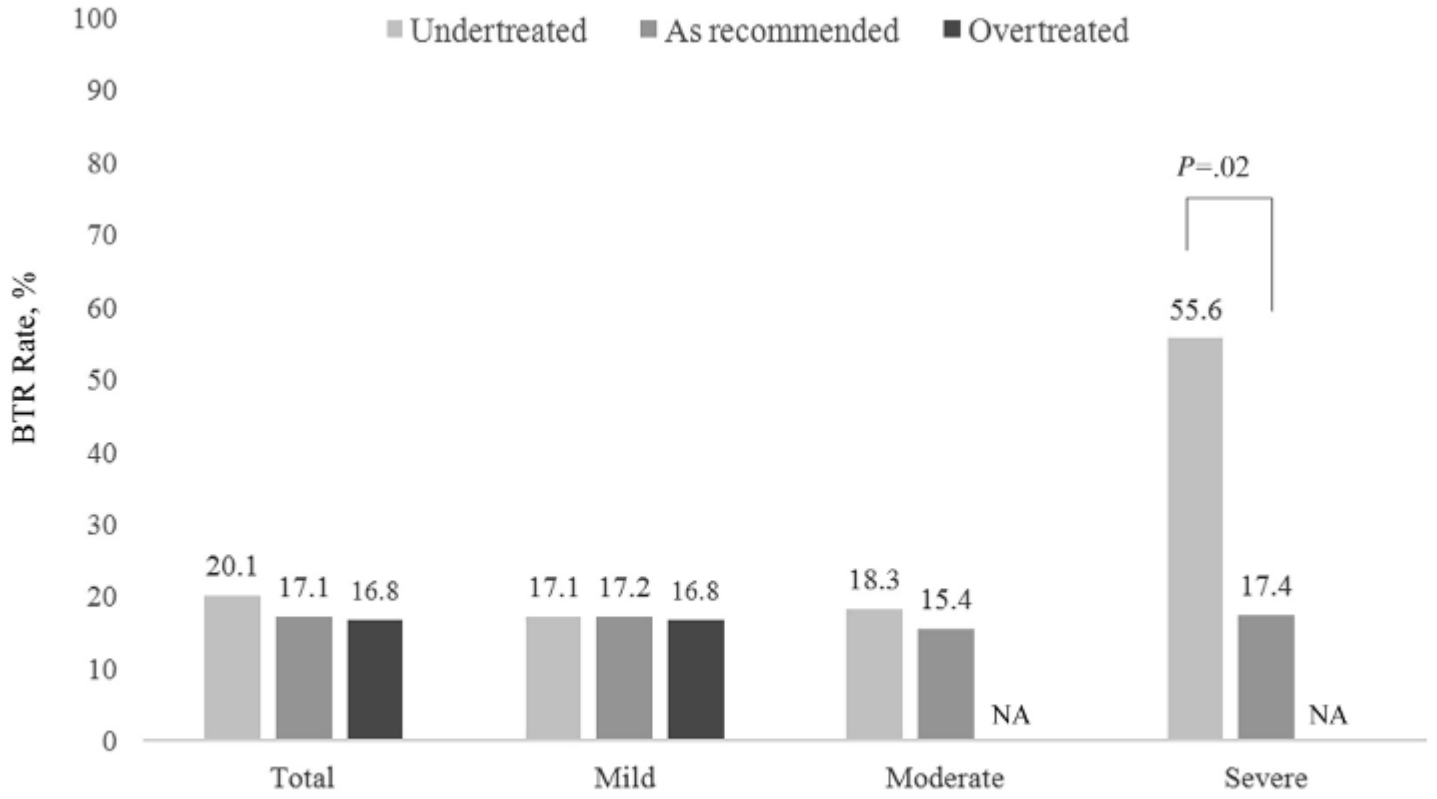


Figure 2. Patients with a severe index reaction had a significant decrease in the breakthrough reaction (BTR) rate when they were appropriately treated as per the recommendation compared with undertreated patients. There were no overpremedicated cases among patients with moderate and severe index reactions.
NA, not applicable.

Lee SY et al. Ann Allergy Asthma Immunol. 2017 Mar;118(3):339-344

Premedication

- 예방을 위해 **전처치**
  - 일반적인 전처치 및 고위험군에서의 전처치는 근거는 약함
  - 전처치 약물에 대한 부작용이나 과민반응 위험성이 높지 않다면 고위험군에서는 전처치를 고려

Risk factor of IHRs
• History of previous IHR to RCM (5x) • Female gender (up to 20x) • Increased incidence 20-50 yrs of age • Atopy (2-3x) • Asthma (10x, not all articles agree) • Possibly the use of certain medications : beta-blockers, aspirin and NSAIDs.

Premedication – 급성 반응

- 구역, 구토와 같은 생리적 반응에 대해서 항히스타민제나 전신 스테로이드제를 이용한 전처치는 불필요하며,
  과민반응의 경우에만 전처치를 시행
- 스테로이드제와 항히스타민제의 병용 투여가 가장 효과적인 것으로 알려져 있으나, 모든 중증반응을 예방할 수는 없다.

- **ACR 지침**

  [예정된 검사에 대한 전처치]
  - 조영제 주입 13시간, 7시간, 1시간 전 프레드니솔론 50 mg을 경구투여하고,
    조영제 주입 1시간 전 클로르페니라민 4 mg 주사(근주 혹은 정주)하거나 경구용 항히스타민제를 복용한다.
  - 조영제 주입 12시간, 2시간 전 메칠프레드니솔론 32 mg을 경구 투여하고, 항히스타민제를 추가해 볼 수 있다.
    * 환자에게 경구투여가 불가능한 경우, 대신 히드로코르티손 200 mg을 정주한다.

  [응급 상황에서의 전처치]
  - 조영제 주입 전까지 매 4시간 마다 메칠프레드니솔론 40 mg 혹은 히드로코르티손 200 mg을 정맥주사를 하고,
    조영제 주입 1시간 전에 클로르페니라민 4 mg을 정주한다.

- **ESUR 지침**

  : 조영제 주입 12시간, 2시간 전 프레드니손 30 mg (혹은 메칠프레드니솔론 32 mg)을 경구투여하고 항히스타민제를 함께 사용할 수 있다.

Premedication – 지연성 반응

- 아직까지 전처치의 효과가 객관적으로 입증되어 있지 않으며,
- 지연성 유해반응의 경우 중증 반응이 극히 드문 점을 감안할 때 경증 지연성 유해반응 환자에서 전처치는 현재 추천되지 않음

- 이전에 심각한 지연성 유해반응을 겪은 경우 경구 스테로이드제 예방요법을 시도해 볼 수 있음

  : 프레드니솔론 50 mg을 검사 당일, 이후 25 mg을 3일간 예방적으로 투여하고, 증상이 발생하면 프레드니솔론 용량을 50 mg으로 증량하여 치료를 하는 것이 제안된 바 있음

요약

- MRI 용 가돌리늄 조영제와 요오드화 조영제 사이의 교차반응은 보고된 바 없다.
- ADR to RCM : Type A, Type B(hypersensitivity reaction)
- Hypersensitivity reaction
  - 고위험군: 이전 과민반응 병력, 아토피, 천식, 고령, 특정 약물 사용환자
  - 반응이 발생하였을 때 빨리 인지하고 중증도에 따른 적절한 치료를 하는것이 중요
  - 조영제 주입 후 최소 30분 이상 관찰, 소생술을 위한 약물과 장비를 즉시 사용할 수 있도록 구비

  - 예방을 위해?

    비이온성 저장성/등장성(non-ionic low/iso-osmolar) 조영제 사용

    고위험 환자의 경우 : 반드시 필요한 경우가 아니라면 요오드화 조영제를 사용하지 않는 검사로 대체 고려

    과거에 유해반응을 일으켰던 조영제가 아닌 다른 조영제를 사용

피부검사: 모든 환자에서 임상 적용을 권고할 근거는 부족, 하지만, **중증의 반응을 경험한 환자의 경우 고려**

전처치 약물에 대한 부작용이나 과민반응 위험성이 높지 않다면 고위험군에서는 예방적 전처치를 고려

감사합니다.

TABLE III. Reactions on rechallenge

Patient number	Age/sex	Atopy	Initial reaction	IHR/NIHR	Grade	Initial culprit ICM	Skin test result (times performed)	Readministered product (n)	Reaction-scheme	Description (immediate/nonimmediate)	Grade	Premedication	Concordance with initial reaction
73	61/F	Yes	Loss of conscience	IHR	3	UD	neg	Iomeprol (n)	R R … R	Heat sensation and impending doom, no objective elements (immediate)	/	No	Yes (less severe)
528	63/M	Yes	General discomfort, loss of conscience	IHR	3	Ioxaglate or ioversol	neg (2)	Iohexol (4)*	0 0 R 0	Cough, heat sensation, dyspnea, urticaria (immediate)†	2	No (since R yes)	Yes
464	44/F	No	AE, dyspnea, nausea	IHR	2	UD	neg	Iobitridol (4)	R R R R	Identical reactions as first episode yet less intense (immediate)	1	Yes (chronic urticaria)	Yes (less severe)
284	71/F	Yes	Heat sensation, dyspnea	NIHR		UD	neg	Iobitridol (>5)	R R … R	Altered taste, facial redness for 1 wk (immediate)	1	Yes	Yes (less severe)
358	39/M	No	U, general discomfort, dyspnea	IHR	2	UD	neg	Iomeprol (4), iobitridol (1)	0 0 0 R 0	Self-limiting rash (immediate)	1	UD	Yes (less severe)
46	56/F	Yes	Anaphylaxis	IHR	2	Iomeprol	neg	UD (n)	R R … R	Redness upper body, self-limiting <1 d (immediate)	1	Yes	Yes (identical despite premedication)
424	58/F	No	Anaphylaxis	IHR	2	Iomeprol	neg	Iohexol	R	Anaphylaxis‡ (immediate)	3	No	Yes (more severe, uncertain diagnosis)
588	70/F	UD	MPE or U	IHR	1	Iomeprol	neg	Iobitridol (1)	R	Itch, possible urticaria (immediate)	1	UD	Yes (less severe)
269	54/F	No	U	IHR	1	Iobitridol	neg	Iobitridol (5)	0 0 0 R 0	Cough (immediate)	2	No before R (yes before 0)	Yes (UD)
199	22/M	Yes	MPE, AE	NIHR		Iomeprol	neg	Iomeprol (2), iodixanol (1)	R R R	MPE (immediate)	/	Yes	Yes (less severe)
116	50/F	No	U	IHR	1	UD	neg	UD	R	Redness back self-limiting (immediate)	1	Yes	Yes (less severe)
293	70/F	Yes	EMP	IHR	1	UD	neg	Ioversol (1), iohexol (1)	R 0	Self-limiting facial redness/rash <1 h (immediate)	1	UD	Yes (less severe)
292	53/F	UD	AE, dyspnea	NIHR		Ioversol	neg (2)	Iopromide (1)	R	AE (nonimmediate)		No	Yes (less severe)
176	32/F	No	MPE	NIHR		UD	neg	Iomeprol (1)	R	MPE (nonimmediate)		No	Yes
330	53/F	Yes	MPE	NIHR		Iomeprol	pos§	Iomeprol (1)	R	Erythema/AE (nonimmediate)		UD	Yes
460	59/F	UD	MPE, AE	NIHR		Iodixanol	neg	Iodixanol (2)	R R	MPE (nonimmediate)		Yes	Yes (less severe)

AE, Angioedema; *ICM*, iodinated contrast medium; *IHR*, immediate drug hypersensitivity reaction; *NIHR*, nonimmediate drug hypersensitivity reaction, *MPE*, maculopapular exanthema; *0*, no reaction on rechallenge; *R*, reaction; *U*, urticarial; *UD*, undetermined.

Table 1 Per-patient positive rates of skin tests in patients with immediate HSR to ICM

	Positive rate of skin tests, %		Positive rate of IDT according to, %						
			Tested ICM		Severity of HSR			Time interval*	
Source	SPT	IDT	Culprit ICM†	Only alternative ICM‡	Mild	Moderate	Severe	1–6 months	>6 months
Dewachter et al. (20)	50 (2/4)	100 (4/4)	100 (4/4)	0 (0/4)			100 (4/4)	100 (4/4)	
Trcka et al. (22)	Not done	4 (4/96)	NS		0 (0/40)	7 (3/44)	8 (1/12)	NS	
Brockow et al. (11)	3 (4/122)	26 (32/121)	38 (24/63)	7 (8/121)	26 (24/92)§		28 (8/29)	37 (17/46)¶	19 (14/74)**
Caimmi et al. (24)	0 (0/101)	15 (15/101)††	NS		††			NS	
Dewachter et al. (25)	4 (1/24)	46 (12/26)	46 (12/26)	0 (0/26)	33 (3/9)	40 (4/10)	71 (5/7)	NS	
Goksel et al. (26)	0 (0/14)	14 (2/14)	20 (2/10)	0 (0/4)	14 (1/7)	14 (1/7)		20 (2/10)	0 (0/4)
Pinnobphun et al. (27)	0 (0/63)	24 (15/63)	24 (15/63)	0 (0/63)	23 (12/53)	0 (0/5)	60 (3/5)	24 (8/34)	24 (7/29)
Kim et al. (28)	3 (1/32)	26 (12/46)	22 (10/46)	4 (2/46)	13 (4/31)	25 (2/8)	57 (4/7)	37 (7/19)‡‡	21 (3/14)
Kim et al. (29)§§	2 (1/51)	65 (33/51)	48 (22/46)	22 (11/51)		18 (2/11)	78 (31/40)	NS	
Renaudin et al. (30)	14 (1/7)	57 (4/7)	NS				57 (4/7)	NS	
Prieto-Garcia et al. (31)	0 (0/106)	10 (11/106)	14 (11/78)	0 (0/106)	9 (6/66)	14 (4/29)	9 (1/11)	¶¶	
Salas et al. (32)	3 (3/90)	6 (5/90)	6 (4/65)	2 (1/90)	0 (0/69)	11 (2/18)	100 (3/3)	***	

Table 1. The prevalence of immediate reaction to radiocontrast media

Author [ref.]	Year	Country	Contrast agents	No. of patients	Overall incidence (%)	Severe reactions (%)
Jacobsson et al. [27]	1988	Qatar	Ionic	493	31.2	0
			Nonionic	491	7.7	0
Katayama et al. [10]	1990	Japan	Ionic	169,284	12.7	0.22
			Nonionic	168,363	3.1	0.04
Yoshikawa [28]	1992	Japan	Nonionic	2,382	3.8	NA
Oi et al. [15]	1997	Japan	Ionic	472	23.9	NA
			Nonionic	512	6.4	NA
Thomas et al. [9]	1999	India	Ionic	1,798	21.1	0.28
Kim et al. [7]	2007	Korea	Nonionic	12,177	2.0	NA
Goksel et al. [16]	2011	Turkey	Ionic/nonionic	1,131	2.2	NA
Ho et al. [13]	2012	Australia	Nonionic	29,962	0.2	NA
Kim et al. [2]	2012	Korea	Mostly nonionic	9,862	0.5	NA
Bae et al. [6]	2013	Korea	Not described	70,542	1.1	0.21
Pradubpongsa et al. [12]	2013	Thailand	Ionic/nonionic	55,286	1.0	NA

Table 2. The prevalence of delayed reaction to radiocontrast media

Author [ref.]	Year	Country	Contrast agents	No. of patients	Overall incidence (%)
Yoshikawa [28]	1992	Japan	Nonionic	2,052	8.0
Oi et al. [15]	1997	Japan	Ionic	242	16.5
			Nonionic	215	14.9
Akiyama et al. [19]	1998	Japan	Nonionic	1,801	1.5
Yasuda and Munechika [18]	1998	Japan	Nonionic	2,370	12.4
Hosoya et al. [20]	2000	Japan	Nonionic	11,121	9.5
Kim et al. [7]	2007	Korea	Nonionic	12,177	0.3
Goksel et al. [16]	2011	Turkey	Ionic/nonionic	1,131	1.4
Kim et al. [2]	2012	Korea	Mostly nonionic	9,862	2.0
Pradubpongsa et al. [12]	2013	Thailand	Ionic/nonionic	55,286	0.03