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**Management of radio-contrast allergy in radio-contrast allergic patients undergoing coronary angiography and intervention**

**Objectives**
Radiocontrast agents (RCA) allergy occurs in 0.04% – 0.22% of patients. However, the risk of allergic reaction increases as 16% to 35% in patients with prior RCA allergy. Herein we reported our experience in patients with a prior history of RCA induced anaphylaxis who underwent coronary angiography (CAG) and intervention.

**Methods**
This retrospective study included 11 patients with prior history of RCA anaphylaxis who underwent CAG and/or intervention at our clinic between May 2016 and September 2019. The mean age of the patients was 61.8±8.99 years, 8 (72.7%) were female, 9 (81.8%) had hypertension, 6 (54.5%) – diabetes mellitus, 11 (100%) – dyslipidemia, 8 (72.7%) patients were current smokers, 4 had prior history RCA allergy after i.v. RCA administration in contrast enhanced computed tomography and 7 patients experienced RCA allergy after CAG. All patients had prior severe anaphylaxis reaction. All patients were pretreated with intravenous feniramin maleat 45.5 mg and methylprednizolone 80 mg one hour before the procedure and dexametazon 8 mg after the procedure.

**Results**
CAG and intervention was successfully completed in all patients. Two patients had breakthrough RCA induced anaphylaxis, they had urticarial, itching, dyspnea and chest tightness, angioedema during coronary artery stenting. Additional dose of i.v. methylprednisolone 80 mg, salbutamol nebulae and i.v. adrenalin 1 mg administration rapidly stabilized the patients. All patients were successfully treated and uneventfully discharged after percutaneous coronary intervention.

**Conclusion**
Management of patients with prior RCA adverse drug reaction may be complex. However when CAG and/or intervention is required in such patients it may be safely performed with premedication.

**Keywords**
Radiocontrast; allergy; coronary angiography; premedication protocols

**For citation**
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**Introduction**
Adverse drug reactions are unexpected, noxious, unintended and dose-independent reactions occurring after the administration of drugs [1]. Systemic allergic reactions are classified as IgE-mediated anaphylaxis and systemic non-IgE-mediated anaphylaxis (anaphylactoid reactions) [2, 3]. Radiocontrast agents (RCA) allergy is a severe life-threatening condition requiring prompt intervention. It was reported that severe RCA allergy occurs in 0.04% – 0.22% of patients [3–9].

However the risk of allergic reaction increases as 16% to 35% in patients with prior RCA allergy [5–9]. There is no completely protective pretreatment regimen from RCA anaphylaxis. However some pretreatment regimens including prednisone, diphenhydramine, and occasionally cimetidine and ephedrine are commonly used [1, 8]. These regimens reduce the risk of repeat reactions to 3.1% – 9% [5, 6]. Allergic reactions occur 2.1% to 18% of patients despite pretreatment with these regimes [9–12].

Coronary artery disease is still the leading cause of death. Coronary angiography (CAG) and intervention is the integral part of management of coronary artery disease. Current guidelines suggested the use of steroids and antihistamines in patients with a prior history of RCA anaphylaxis prior to cardiac catheterization. However the data regarding the management of such patients is scarce. Herein we reported our experience in patients with a prior history of RCA adverse drug reactions who underwent CAG and intervention.

**Methods and study design**
This retrospective study included 11 patients with prior history of RCA anaphylaxis who underwent CAG and/or...
Способствует:

- Увеличению времени выполнения физической нагрузки и всех показателей нагрузочных проб
- Снижению частоты госпитализаций по поводу фатального и нефатального инфаркта миокарда
- Снижению числа госпитализаций в связи с усилением симптомов течения ХСН
intervention at our clinic between May 2016 and September 2019. This study confirms the principles of Helsinki declaration. All patients were pretreated with intravenous (i.v.) feniramin maleat 45.5 mg and methylprednizolone 80 mg one hour before the procedure and dexametazon 8 mg after the procedure. All patients underwent CAG and/or intervention with iohexol 350 mgI/200 mL (Omnipaque; Opakim, Istanbul, Turkey) in compliance with PCI guidelines. RCA was administered via intracoronary injection. The volume of RCA was at the discretion of the treating physician according to operative requirements.

Results
The data of 11 patients were evaluated retrospectively. The mean age of the patients was 61.8±8.99 years, 8 (72.7%) were female, 9 (81.8%) had hypertension, 6 (54.5%) – diabetes mellitus, 11 (100%) – dyslipidemia and 8 (72.7%) patients were current smokers. Four had prior history RCA allergy after i.v. RCA administration in contrast enhanced computed tomography (CT) and 7 patients experienced RCA allergy after CAG. All patients had prior severe anaphylaxis reaction (Table 1). Four of patients presented with acute coronary syndrome and the remaining 7 patients had critical large ischemia on myocardial perfusion sintigraphy. CAG and intervention was successfully completed in all patients. Two patients had breakthrough RCA induced anaphylaxis, they had urticarial, itching, dyspnea and chest tightness, angioedema during coronary artery stenting. Additional dose of i.v. methylprednisalol 80 mg, salbutamol nebulae and i.v. adrenalin 1 mg administration rapidly stabilize the patients. All patients were successfully treated and uneventfully discharged after percutaneous coronary intervention.

Discussion
Adverse drug reactions occur up to 0.4% of patients after intra-arterial RCA exposure [1]. Luckily most of these reactions were mild. However the severe adverse reactions to RCA are life threatening requiring emergent intervention. RCA are used in CAG. Prior RCA allergy, age, beta-blocker therapy, cardiovascular disease, asthma, allergy history (medication, food, environmental), hematological diseases and female sex were identified risk factors for RCA [8, 9, 13]. Therefore performing CAG in these high risk patients may be problematic. However CAG is the gold standard for the diagnosis and management of coronary artery disease. The pros and cons of the CAG and intervention should be decided on patient bases. In this study we performed CAG and intervention in 11 patients – 4 with acute coronary syndrome and 7 with critical large ischemia on myocardial perfusion sintigraphy. Therefore the CAG could not be postponed. History of severe RCA allergy, drug allergy, allergy to 4 or more allergens and chronic corticosteroid usage were related to severe breakthrough of RCA [9, 14]. All our patients had prior severe RCA adverse reaction and 8 of them were on beta blocker therapy prior to CAG.

Current guidelines recommended to use diphenhydramine and steroid before the procedure. Oral administration of prednisone 50 mg at 13, 7 and 1 hour to procedure or hydrocortisone 200 mg i.v. every 4 hours till to procedure were suggested as the choice of steroid [1, 4, 5, 15]. RCM induced anaphylaxis is through direct stimulation of mast cells and basophils degranulation causing systemic mediator release [3]. Steroids may stabilize cell membrane and the release and production of mediators [1]. H1 and H2 antihistamines are used as adjunctive therapy for acute anaphylaxis and for prevention of anaphylaxis in allergen immunotherapy pretreatment protocols [1, 14]. Furthermore it has been shown that addition of montelukast in pretreatment protocols is effective in reducing RCA reactions [15]. Isoosmolar RCA are generally used in CAG. High osmolar RCA have higher risk of RCA allergy [4, 7]. We used isoosmolar agents in our cath lab. Only 2 of 11 pa-

| Patient no | Previous modality | Previous history |
|-----------|------------------|-----------------|
| 1         | Contrast CT      | Urticaria, pruritus, dyspnea, angioedema |
| 2         | Contrast CT      | Urticaria, pruritus, dyspnea, vomiting, dizziness, chest tightness |
| 3         | CAG              | Urticaria, pruritus, dyspnea, vomiting, dizziness |
| 4         | CAG              | Flushing, diaphoresis, urticaria, pruritus, dyspnea |
| 5         | CAG              | Urticaria, pruritus, dyspnea, vomiting, dizziness, chest tightness |
| 6         | Contrast CT      | Urticaria, pruritus, dyspnea, chest tightness |
| 7         | Contrast CT      | Flushing, diaphoresis, urticaria, pruritus, dyspnea |
| 8         | CAG              | Urticaria, pruritus, dyspnea, vomiting, dizziness |
| 9         | CAG              | Urticaria, pruritus, dyspnea, vomiting, dizziness, chest tightness |
| 10        | CAG              | Flushing, diaphoresis, urticaria, pruritus, dyspnea |
| 11        | CAG              | Urticaria, pruritus, dyspnea, vomiting, dizziness |

CT, Computed tomography; CAG, coronary angiography.
Patients experienced severe RCA induced anaphylaxis reactions during CAG. We administered i.v. additional dose of methylprednisolone 80 mg and adrenalin 1 mg.

Patients also received salbutamol nebulae and oxygen. After the administration of adrenalin dyspnea and angioedema were resolved in all patients. It is important that adrenalin is always presented in cath lab and in emergent situations it is life saving.

Our study had some limitations. Firstly our study population is small. However, anaphylaxis secondary to RCA is an infrequent disease. Hence, the small sample size of this study is valuable. Secondly, we did not test the efficacy of different premedication regimens, and did not evaluate the different RCA on the recurrence of RCA allergy. Therefore, further large scaled multicenter study may give valuable information regarding this issue.

**Conclusion**

Management of patients with prior RCA adverse drug reaction may be complex. However when CAG and/or intervention is required in such patients it may be safely performed with premedication.

No conflict of interest is reported.

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