Article Title: **Anaphylactoid Reactions From Iopromide In Patient With Angina Undergoing Angiography**

Article Keywords: Iopromide, Contrast Media, Anaphylactic, Anaphylactoid Reactions, Adverse Reactions

Key Points:

- Iopromide, a non-ionic iodinated contrast media, is known to have the highest occurrence in causing anaphylactoid reactions.
- The use of Iopromide in patient with history of angina undergoing angiography need to be monitored intensively as the adverse reactions are likely to occur.
- Healthcare professionals who are using iodinated contrast media need to recognise and treat anaphylactic reactions immediately and appropriately.
- In patients with previous hypersensitivity to contrast media, premedication with antihistamines and/or corticosteroids is recommended.

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BRIEF REPORT

Anaphylactoid Reactions From Iopromide In Patient With Angina Undergoing Angiography

SUMMARY/ABSTRACT

A 55yr old patient with a history of angina is being assessed for a coronary bypass. Undergoing an angiography, on infusion of non-ionic iodinated radio contrast media (Iopromide), incidence is occurred. Clinical manifestations are consistent with anaphylactoid reactions. The patient becomes confused, appears flushed and also develops palpitations, angioedema, hypotension and bronchoconstriction. Following treatment with sympathomimetics and anti-histamines, the patient recovers and is returned to the ward. Non-ionic iodinated radio contrast media has commonly caused adverse reactions. Iopromide-induced anaphylactoid reactions has the highest occurrence among the same drug class. Cardiologists and Radiologists should be aware in the use of Iopromide in severely ill cardiovascular patients, as the adverse reactions are likely to occur. It is crucial to recognise and treat anaphylactoid reactions immediately and appropriately.

Key Words - Iopromide, Contrast Media, Anaphylactic, Anaphylactoid Reactions, Adverse Reactions

INTRODUCTION

Iopromide is a non-ionic iodinated contrast media, with osmolality of 0.6-0.7/kg water, considered as low osmolar contrast media. Intravascular iodinated contrast media are commonly used in imaging modalities. Iopromide is indicated mostly for angiography, arteriography, aortography, venography, urography, and tomography. [1]

Contrast media is known to commonly cause incidence of anaphylactoid reactions. Based on the adverse reaction frequencies happened during hospitalisation, the risk is categorised as significance, compare to other drug categories. Within low osmolality iodinated contrast media, iopromide shows the highest number of incidence. The aetiology of causality remains unclear. The most affected organs or systems are skin and respiratory, followed by gastrointestinal and cardiovascular.[2] The risk probability is higher among elderly and patient with cardiovascular disease and adverse reactions are more likely to happen. A precaution should be taken by cardiologist and radiologist for patients with recent myocardial infarction, severe coronary artery disease, unstable angina or coronary artery bypass graft and in patients with low output left ventricular failure.[3]

Many studies has been conducted to observed the adverse reactions of iopromide administration, which is categorised into three classifications: pharmacological toxicity; hypersensitivity divided into two sub classifications: immediate (within one hour) and delayed (more than one hour up to one week); and unrelated event.[2] Unrelated event may happen in angiography as contrast media solutions were infused through catheters into

the heart chamber. Due to the catheterisation procedure, may also cause serious adverse reactions, such as myocardial infarction and cerebral embolism.

CASE REPORT

A 55yr old patient with a history of angina is being assessed for a coronary bypass. Undergoing an angiography, on infusion of non-ionic iodinated radio contrast media (Iopromide), incidence is occurred. Clinical manifestations are consistent with anaphylactoid reactions. The patient becomes confused, appears flushed and also develops palpitations, angioedema, hypotension and bronchoconstriction. Following treatment with sympathomimetics and anti-histamines, the patient recovers and is returned to the ward.

DISCUSSION

Delayed reactions to iodinated contrast media are most likely caused by immune reactions to this drug. Using in vitro and ex vivo test, a study demonstrates a T cell-mediated mechanism to the iodinate contrast media,[4] whilst the aetiology of immediate reactions still remains unclear. The term used whether “anaphylactoid reactions” or “anaphylactic” for immediate reactions explains the mechanism of physiology response, specifically related to immunology reaction. Anaphylactic involves Ig-E while anaphylactoid reaction is not mediated by Ig-E but express the similar clinical manifestation. [5]

The mechanism of parasympathetic activity on smooth muscle induced by the release of endothelium-derived relaxing factor, which is decreasing rate of the sinoatrial node and

delaying conductivity of the atrioventricular nodal conduction, and peripheral vasodilatation. This will cause hypotension and bradycardia, with the symptoms of palpitations. [5] All of these conditions match with patient's symptoms.

The pharmacological adverse reactions of iodinated contrast media are similar to the mechanism of histamine release of allergy. Histamine mediates its effects through activation of histamine 1 (H1) and histamine 2 (H2) receptors. Both H1 receptors and H2 receptors mediate glandular hyper secretion. smooth muscle contraction and increase mucosal secretions, which can lead to anaphylactoid reactions.[6] This explains the patient's symptoms of developing angioedema.

More recent study argues that no correlation between plasma histamine level and the severity of contrast media induced reactions. An Ig-E related mechanism is strongly suspected.[7] Whether by Ig-E or non Ig-E mediated mechanisms, histamine and leukotriene and prostaglandin are released, causing smooth muscle spasm in the respiratory tract. This mechanism results bronchoconstriction, with the signs and symptoms of pulmonary complication. This relate to the patient appears flushed, experiences short of breath, wheezing, that somewhat similar to acute asthma attack. These symptoms may further cause hypoxia. Lack of oxygen in the central nervous system may result in dizziness and confusion. This explains the patient's confuse feeling. Smooth muscle spasm also affects the gastrointestinal tract that lead to nausea, vomiting, abdominal cramps and diarrhoea as well. However, in this case, the patient does not demonstrate the symptoms.[8]

The hyper osmolar radio contrast media solution can stimulate vasopressin release, which is responsible for vasodilatation. This mechanism is known as dose-depending adverse reactions. Vasodilatatory effect results in decreasing systemic blood pressure. This mechanism explains the pain and heat sensation in angiography.[9] Researchers suggest to use the lower osmolar media for peripheral angiography to reduce the potential pharmacological toxicity that can direct to organ damage.[10] In conjunction with the osmolality of radio contrast media solution may also explains the nephrotoxicity of this agent. [11] Since the patient does not demonstrate the symptoms, the author supposes it is not necessarily discussed further in this article.

Management and Prophylaxis of Idiopathic Anaphylactic

Non-ionic iodinated contrast media-induced adverse reactions and common allergic reactions have much in common. This similarity underpins the similar treatment for both reactions. Management of anaphylactoid reactions should relieve the symptoms in acute episode. Recommended acute management of a patient with anaphylaxis is to place the patient in a supine position and give adrenaline and intravenous volume resuscitation (Level IV). The use of antihistamine is to correct the delayed allergic reaction. [12]

There has been pro and contra toward the prevention of anaphylactoid reactions of iodinated contrast media. Some studies show inefficacy, however some interventions with steroid pre-medication show the reduced symptoms. Oral double dose of methyl prednisolone is suggested to prevent a potentially major reaction of iodinated contrast media.[13] For antihistamines, since the mechanism of reaction is still being in debate

whether or not mediated by Ig-E, limited evidence shows they are beneficial. However, in some patients with a history of allergies, pre-treatment with corticosteroid and antihistamines is presumably helpful. Limited evidence is available about this regime. [14]

A further study about the structure activity relationship of this drug class need to be proceed to invent the high quality imaging radio medicine with lower adverse reactions.

Alternative (Non-Drug Induced) Explanation

- As the patient has a history of angina, there is a probability that the patient might have recurrent cardiovascular problem, such as: angina attack, atrial fibrillation or myocardial infarct.
- There is also a probability that the patient has certain severe allergy that is induced by certain food intake or insect bite before the angiography performance.
- Since the clinical manifestations of anaphylaxis/anaphylactoid reactions is similar to respiratory and pulmonary complications. It is crucial to examine whether or not it is an asthma attack of the patient that already suffer from severe asthmatic syndrome before the procedure take place.

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