

## ALLERGIC REACTIONS TO COLLOID FLUIDS IN ANESTHESIA

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### SUMMARY

Allergic reactions in anesthesia are a rare event, however, might be life threatening when occurred. Clinical manifestations may not be indicative at first, and difficult to differentiate from different situations during operation and anesthesia. Colloids represent a group of fluids often used during perioperative period that, among other adverse reactions, have an allergic potential. Albumin is a natural colloid that has the lowest incidence of these reactions. However, it is found as an additional substance in other blood products, and, therefore, has to be taken into consideration if anaphylaxis occurs. Dextran cause the most severe reactions due to dextran reactive antibodies. Pretreatment with Dextran 1 may inhibit the reaction. Gelatins have the highest incidence of anaphylaxis among colloids. Patients with history of allergy to some food, vaccines, cosmetics containing gelatin are at greater perioperative risk for anaphylaxis. Not to forget, gelatins are also a part of topical haemostatic agents used in surgery. Testing for colloid allergies is limited due to their pathophysiologic mechanism, so the clinical assessment is usually essential. Treatment of anaphylaxis caused by colloids is the same as for any other cause. This is a review of the most common colloids and their association with allergic reactions in everyday practice.

**Key words:** albumin – gelatin – dextran - hydroxyethyl starch - anaphylaxis

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### INTRODUCTION

Allergic reactions in anesthesia are a rare occurrence, however, may be life threatening when come upon. They represent a unique situation not always recognized on time due to unpredictable course of anesthesia. It is not difficult to perceive in awake patient where the symptoms might be mild. However, in a patient during anesthesia it is much harder to distinguish certain changes that might be categorized as an allergic reaction.

Skin manifestations are usually not identified at first due to covered patient during the operation. Cardiovascular changes also might be misguided by the influence of drugs used during anesthesia. At last, there are many drugs administered and other substances used in the operating room that might induce similar symptoms which might later be difficult to classify as an allergic reaction to a certain drug.

The pathophysiology of anaphylaxis may be mediated by immunologic or nonimmunologic mechanism. Immunologic mechanism can be divided into immunoglobulin E (IgE) – dependant or non-IgE – dependant type, and nonimmunologic has direct influence on mast cell activation (Mali 2012). Regardless the mechanism, symptoms are similar and caused by release of mediators. One of the substances often used during anesthesia that might induce allergic reactions through all of the mechanisms are volume expanders known as colloids.

### COLLOIDS AS POTENTIAL ALLERGENS

Colloids are large molecular weight substances that are important in capillary fluid dynamics as only constituents effective at exerting an osmotic force across the capillary wall (Mitra & Khandelwal 2009). They contain water and electrolytes; however, a colloid is a large molecule that does not diffuse across semipermeable membranes. In normal plasma, the plasma proteins are the major colloids present. The colloids include natural (albumin) and synthetic (dextran, gelatins and starches) substances (Mitra & Khandelwal 2009). One of general problems with all of them is small but significant incidence of adverse reactions, especially allergic. According to the literature, the incidence of allergic reactions to these solutions in perioperative period is around 3-4%, where they most refer to gelatins (Mali 2012, Ryder & Waldmann 2004). In a French study incidence of allergic reactions to gelatin and dextran were much higher (0.34% and 0.27%), than to albumin and hydroxyethyl starches where they were less than 0.1% (Mali 2012, Laxenaire et al. 1994).

### ALBUMIN

Albumin is a natural colloid consisted of a single polypeptide chain and a molecular weight of approximately 69 000 Dalton, synthesized in the liver. Its primary role is to maintain the colloid osmotic pressure

in the intravascular space at the level of the capillaries (Mitra & Khandelwal 2009). It also serves as a carrier for variety of active substances. Unlike artificial colloids, it is associated with lower incidence of anaphylactic reactions. However, there have been cases reported where human serum albumin was most likely the cause of anaphylaxis. This should be kept in mind whenever albumin is being used.

It also has to be taken into consideration that albumin is a component of other products when dealing with potential allergic reaction. In a case of a 40-year old man who underwent an elective surgical replacement of a mitral valve, allergic reaction occurred after administration of fibrinogen concentrate and, few hours later, erythrocyte concentrate. The tests showed highly positive reaction that specific fibrinogen concentrate, and to its component albumin. That might possibly explain the second allergic reaction due to albumin presence in erythrocyte concentrate (Komericki et al. 2014).

## **DEXTRAN**

Dextran are highly branched polysaccharide molecules, which are produced from the bacterium *Leuconostoc mesenteroides*. Most widely used are Dextran 70 (70 000 Dalton), a 6% solution, and Dextran 40 (40 000 Dalton), a 10% solution (Mitra & Khandelwal 2009). Dextran 40 is used in microvascular surgery to improve microcirculatory flow, in prophylaxis of postoperative and posttraumatic thromboembolism. In comparison to other colloids, they cause far more and severe anaphylactic reactions as a result of the release of vasoactive mediators triggered by dextran reactive antibodies. Dextran-induced anaphylactic reactions (DIAR) were described more than sixty years ago. They can be mild with non-immunologic mechanism of action or severe anaphylactic reactions due to IgG class dextran-reactive antibodies (DRA). It has also been described that using the hapten (Dextran 1) may inhibit this reaction. The role of it is to combine with the antibodies at specific sites and, therefore, prevent the formation of large immune complexes when given the clinical dextran (Hedrin 1997). However, there have been cases of anaphylaxis reported despite the use of Dextran 1. Therefore, whenever using dextrans, regardless the pretreatment, it should, nevertheless, be with a precaution.

## **GELATIN**

Gelatins are large molecular weight proteins formed from hydrolysis of cattle or pork collagen. There are three types: succinylated or modified fluid gelatins, urea-crosslinked gelatins and oxypolygelatins (Mitra & Khandelwal 2009). They have the highest incidence of anaphylactic reactions of all the colloids. Since gelatin is also contained in food, vaccines, pharmaceuticals and cosmetics, patients with a history of allergic reaction to

these products are at greater perioperative risk of anaphylaxis. In one prospective study during a period between 1997 and 2011 the authors observed the positive correlation between allergy to red meat and sensitization to gelatin (Mullins et al. 2012).

In addition, previous exposure to the product does not guarantee safety administration later on. There was a case reported where an elderly female had to undergo a second surgery in two months period and had to be given the same gelatin as during the first surgery. Shortly after utilization she developed shock and ST elevation in ECG was recorded, suggesting anaphylactic reaction (Marrel et al. 2011). In another case of a young primigravida who underwent a caesarian section, after administration of gelatin-based colloid, symptoms of allergic reaction such as itching, tingling, shortness of breath and severe hypotension occurred (Karri et al. 2009). In both of these cases they confirmed the anaphylactic reaction, most likely IgE mediated, by elevated Tryptase level, high IgE titer and positive skin prick test.

Not to forget, anesthesiologists are not the only ones using the gelatin during the anesthesia. There are also several reports of serious reactions, from simple rash to severe anaphylaxis, during pediatric surgery after the surgeons' application of topical haemostatic agents, which are composed of bovine and porcine gelatin matrix.

## **HYDROXYETHYL STARCHES (HES)**

Hydroxyethyl starches (HES) are synthetic colloids derived from amylopectin, highly branched glucose polymer. Hydroxyethyl groups are attached to glucose at C-2, and to a lesser extent, at C-3 and C-6. These solutions are characterized by their molar substitution (0.4–0.7) and molecular weight that ranges from 70 000 to 450 000 Dalton. There are several generations developed, but first and second are associated with higher incidence of allergic reactions (Mitra & Khandelwal 2009). According to the literature, these reactions are rare. However, there have been cases described, not only with hetastarches and pentastarches, but also with tetrastarches.

## **DIAGNOSIS**

Testing for colloid allergies is limited and not always achievable. That is the reason why clinical judgment and time difference from application to manifestation is essential. Gelatin allergy may be confirmed by serum IgE testing. If that is negative, prick skin test might be performed. Intradermal testing can also be considered. If these tests are all negative, it is very unlikely that the reaction was IgE mediated. Evaluation of serum tryptase might help distinguishing the anaphylaxis from other perioperative events due to its characteristic elevation in these circumstances. However, it does not give us any information regarding the agent that caused the reaction (Mills et al. 2014).

## TREATMENT

Treatment of anaphylaxis caused by colloids does not differentiate from any other anaphylaxis. The infusion must be stopped as soon as there is any suspicion of possible allergic reaction, and immediate actions according to latest guidelines taken.

## CONCLUSION

Allergic reactions to colloids in perioperative period are rare, but possibly severe complication. They are not always easily recognized due to specific circumstances during operation and many other substances applied. However, it is important to take precaution whenever using them and be prepared to act immediately.

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