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Anaphylaxis associated with the mRNA COVID-19 vaccines: Approach to allergy investigation

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ABSTRACT

Reports about cases of anaphylaxis to mRNA vaccines have created anxiety in the community and could increase vaccine hesitancy in the population. There are no standardized protocols for allergy testing to mRNA vaccines. PEG is currently the only excipient in both vaccines with recognized allergenic potential. Allergy to PEG has been reported with increasing frequency over recent years, often in patients who had repeated systemic allergic reactions/anaphylaxis to several classes of drugs before diagnosis. Proposed protocols are based on current knowledge about potential mechanisms of anaphylaxis associated with the mRNA vaccines, and the assumption that polyethylene glycol (PEG) is the most likely culprit. Allergy testing to PEGs and mRNA vaccines is complex and carries the risk of anaphylaxis and should be conducted in a specialist drug allergy center. Appropriate PEG-free emergency medical treatment and supervision should be readily available.

1. Introduction

1.1. The COVID-19 mRNA vaccines

With the introduction of vaccination programs with the new Pfizer/BioNTech's and Moderna's mRNA vaccines, more allergic reactions including vaccine-associated cases of anaphylaxis are reported, but overall remain rare. However, the information has created anxiety in the community. Allergies in general are so common (10–40%) that this could increase the vaccine hesitancy or resistance against the vaccines in the population [1,2]. Conversely, patients with allergies are concerned about the possibility that they may not be able to get vaccinated. Anaphylactic reactions can occur with any vaccine but are usually extremely rare—about one per 1 million doses [3]. The U.S. Centers for Disease Control and Prevention (CDC) reported a rate of 11.1 per million doses administered for Pfizer/BioNTech's mRNA vaccine [4]; however, new data indicate a lower rate of 5.5 per 1 million doses for the COVID-19 vaccines (29 cases out of more than 5.3 million doses that have been administered as of Jan 5, 2021) [5]. The reported rate for the Moderna COVID-19 vaccine is 2.5 per million doses administered [6].

1.2. Is polyethylene glycol the culprit?

The COVID-19 mRNA vaccines consist of non-infectious, non-replicating RNA in a lipid-based formulation, which delivers the RNA to cells in the immunized person. The lipid nanoparticles are chemically attached to polyethylene glycol (PEG) molecules (PEGylated) that cover the outside of the particles and increase their stability and life span. Protein expression from the RNA is transient, and as is RNA itself. The vaccines do not contain adjuvants and the vaccine vials do not contain latex [7].

PEG is currently the only excipient in both vaccines with recognized allergenic potential [8]. PEGs, also called macrogols, are hydrophilic polymers with molecular weight (MW) in the 300–35,000 g/mol range. They are found in everyday products such as cosmetics, and medications, industrial and food products. PEGylation is a process used to extend half-life and limit volume of distribution of nucleic acid, peptide, and small molecule therapeutics. In pharmaceuticals, the number included in the name indicates the average molecular weight (e.g., PEG4000) but in in the cosmetics industry, the number refers to the average number of ethylene oxide units in each molecule (e.g., PEG40). Cross-reactivity exists with polysorbates [9]. Allergy to PEG has been reported with increasing frequency over recent years, often in patients

Abbreviations: PEG, polyethylene glycol; MW, molecular weight; SPT, skin prick test; IDT, intradermal test.

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