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OPINION

Possible Correlations between the COVID-19 mRNA Vaccine and Contracting Myocarditis/Pericarditis in Young Adults

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ABSTRACT

mRNA vaccines have been pivotal in the management of global health in regulating the spread and severity of COVID-19 across the world. Approximately six months post vaccine, there was concerns raised by the Food and Drug Administration (FDA) over the adverse events of inflammatory heart conditions in the younger adult demographic aged between 18-24 years old following vaccination in particular mRNA. This article will look at possible correlations between the delivery of the mRNA vaccine and the effect it has had on the younger adult population.

INTRODUCTION

According to Greenwood [1] vaccinations were introduced to the world in the late 18th century by Edward Jenner and has had a major contribution to global health. Yu, et al. [2] states in December 2019 a novel outbreak of Coronavirus (COVID-19) was found in Wuhan China and rapidly spread across the world where it became a global pandemic. Joffe [3] states the Food and Drug Administration (FDA) recognised the threat to public safety and approved the first vaccine in December 2020, known as the Pfizer and BioNTech vaccination which has shown an efficacy of 95% in clinical trials. Yadegari, et al. [4] states there is a potential of reaching the herd immunity threshold when a high percentage of the population have recovered from the disease and have developed protective antibodies. However, it is estimated that 90% of the population must be immune to interrupt COVID-19 chain of transmission, due to its high contagious rate [4]. Hall, et al. [5] investigated the effectiveness immunity in health care workers in the United Kingdom (UK) after receiving vaccination within 10 months. Results showed that after two doses of the COVID-19 vaccine, there was evidence of high short-term protection, which decreased considerably after 6 months. However, infection acquired immunity which was boosted with vaccination acquired immunity remained high up to a year after infection (Appendix 1). Witberg, et al. [6] explain there has been an association between the development of inflammatory conditions of the heart after taking the mRNA vaccines, Pfizer and BioNTech and Moderna, which has mainly affected younger adults. According to Doshi [7] the results gathered in June 2021 relating to adverse effects from Pfizer affecting the heart were 26 cases (1 fatal) of pericarditis and 123 cases (24 fatal) of myocarditis affecting 18-24-year-olds since the vaccine rollout in December 2020. Patone, et al. [8] states as on November 2021 there was 1,783 reports to the United States Vaccine Adverse Event Reporting System (VAERS) of cases involving

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heart inflammation among the age group of 12–29 years of age following COVID-19 Vaccination, most commonly the mRNA vaccine. This article will explore how the lymphatic system works in terms of immunity and evaluate possible variables which could impact how an individual could obtain an adverse event following the mRNA vaccine for COVID-19.

THE LYMPHATIC SYSTEM

Cueni and Detmar [9] explain the lymphatic system was first discovered in the 17th century, where it works alongside the circulatory system and contributes to immune surveillance, regulation of tissue pressure and absorption of dietary fat in the intestine. Kataru, et al, [10] further explain the lymphatic system acts by adopting a passive role in the regulation of immune responses, where they transport pathogen cells to regional lymph nodes. Caroline [11] states the mechanism of the lymphatic system begins with lymph getting filtered through the capillaries into the tissues, where it gets picked up by lymph capillaries moving through the larger lymph vessels to the collecting ducts where it drains. Furthermore, Liao and Von der Weid [12] states the physiology of the lymphatic system is when fluid leaks through the pressure differential from the capillaries during gas exchange, which turns into lymph and gets picked up by the lymph vessels and taken to the nodes. When pathogens invade the peripheral tissues, the lymphatic vessels transport the pathogens to the nearest lymph node, where adaptive immunity is initiated with the production of antibodies that will remove the pathogen and create memory against it [12]. Capobianco, et al. [13] states lymph drains from either side from the axillary nodes located in the upper arms, where it passes through certain nodes which help cleanse the fluid prior to it returning to the venous blood supply. The right-side lymph travels through the lymphatic vessels to the right lymphatic duct located in the base of the neck, where it then enters the right broncho mediastinal trunk in the supra-area of the thoracic cavity [13]. From there It travels upwards to the right subclavian trunk leading to the right internal jugular vein, (venous angle), where the lymph is drained back into the venous blood stream [13]. Whereas on the left side lymph travels inferior to the thoracic duct where it starts to drain and continues to flow upwards towards the left broncho mediastinal trunk supra-area of the thoracic cavity to the left subclavian trunk, leading to the left internal jugular vein (venous angle) where the lymph is drained and returned to the venous blood supply [13]. However, Murakami, et al. [14] assessed the broncho mediastinal lymph vessels and their formation with the collecting trunks. The findings indicated the trunks on the left side were not always consistent with formation, as at times lymph showed it was travelling in varying courses [14]. This can be classified into three groups: the upper most paratracheal nodes (alongside the trachea), the anterior mediastinal nodes (anterior to the heart) and the left phrenic nodes (superior to the diaphragm) [14]. Crumbie [15] states that within the medial/anterior mediastinum resides the heart, which area lies the pericardium along with

segments of the great vessels. Sintou, et al. [16] explain in Mediastinal Lymphadenopathy, antibodies are activated from the mediastinal node, where it can cause antibodies to reach cardiac tissue in vivo and can result in cardiac tissue damage of the myocardium/pericardium.

How the lymphatic system reacts to the vaccination

Clem [17] states the immune system is separated into two divisions with one being the innate immune system, which is non-specific and provides general resistance, which makes up the body's first line of defence against pathogenic agents. The other division is known as the adaptive system, which is specific and has memory cells, which will allow this system to react more quickly to a particular pathogenic agent [17]. Knight and Nigam [18] states vaccines are utilised as vessels of low-risk infectious agents to stimulate the body's immune response, by targeting the memory cells within an individual's adaptive immunity. This will assist the body in fighting incoming invaders and prevent a potentially dangerous pathogenic agent from replicating and causing major infection [18]. Eliskova, et al. [19] explain when the vaccination has been administered, the body's innate system must primarily detect the threat as to whether it is a pathogenic agent or immunization, which could potentially trigger the body's inflammatory response. Marshall, et al. [20] further explain the inflammatory response allows products of the body's immune system in the area of infection. This enables Pattern Recognition Receptors (PRR) to provide a small range of immune cells to react and respond quickly to any pathogenic agents, which share common structures, known as Pathogen Associated Molecular Patterns (PAMPs) [20]. Lee and Ryu [21] explain mRNA vaccines such as Pfizer encode the viral protein and the immune-modulatory proteins as adjuvants, which stimulates the innate immune response, activating antigen-specific T-cell responses without inducing systematic inflammation.

Variables that could prevent reaction

Donnelly [22] states applicable vaccination administration is a crucial element to ensure successful vaccination, whereby most vaccines are delivered via subcutaneous or Intramuscular (IM) routes. Zuckerman [23] highlight vaccines are more commonly given through the IM route, as it maximises immunogenicity of the vaccine and minimises adverse reactions at the site of injection. Hypodermic injections can be associated with pain and distress by the patient, which can lead to poor compliance, which is why it's vital to have highly trained personnel for administration [22]. Deliberation of the needle gauge should be considered, as a larger bore needle allows the vaccine to be dispersed over a larger surface area and reduces the risk of localised redness and swelling [23]. Rhamimov, et al. [24] investigated the impact of skin bulging techniques via IM vaccination, where the findings highlighted skin bunching can prevent effective vaccination response in the minority of individuals, due to

increased skin to muscle distance. The results of the study showed 10% of all subjects, skin bunching increased the skin-to-muscle distance by approximately 20 mm or more [24]. Another point highlighted in this study was the angle of injection, as if the injection was not delivered at a 90-degree angle, the skin-to-muscle angle would increase causing an in-proper muscle penetration. Zhang, et al. [25] state the route of delivery can have an impact on vaccine localisation, which can result in consequential local and systemic immune responses. The site of injection has been known to affect the vaccine efficacy in relation to how a particular site will interact with antigen presenting cells, which can direct a different immune response [25]. Sepah [26] explain the World Health Organisation (WHO) and the Centers for Disease Control (CDC) no longer recommend aspiration, there are still many sources of literature published on advising aspiration prior to injecting a drug through the IM route. Moreover, it is crucial for aspiration to be effective, negative pressure must be applied for 5-10 seconds [26]. However, The US Advisory Committee on immunization practices has not given any advice on aspiration during vaccine administration, where they leave the decision up to the vaccinator [26]. Herraiz-Adillo [27] state a retrospective study on aspiration reported approximately 40% of nurses had aspired blood at least once, with blood aspiration occurring most frequently in the dorsal gluteal (15%) and the deltoid (12%) regions. This finding defies the logic of staff who are against aspiration, as there is meant to be minimal risk of aspirating blood in the deltoid muscle due to the low calibre of blood vessels [27]. Jayadevan [28] posted a picture on social media of the correct IM injection technique (Appendix 2) following a study on aspiration in Denmark, which highlighted the possibility of healthcare staff using a faulty technique during IM injection of the COVID-19 vaccine could be causing the rare clotting disorders. Merchant [29] state vaccines are not designed for administration into the circulatory system as it can lead to the distribution and transfection of tissues beyond the injection site, which can cause serious issues with the heart such as post immunisation thrombotic events or inflammatory conditions associated with the heart such as myocarditis and pericarditis.

CONCLUSION

Over the years, vaccinations have been proven to be an effective tool against pathogens. However, certain aspects of vaccination procedures need to be considered to improve patient safety and overall outcome. It is important to have a highly trained vaccinator's giving IM injections, who can use their autonomy to deliver the correct technique of 90-degrees angle injection and prevent skin bulging techniques. Although the WHO and CDC no longer recommend aspiration during IM injection, studies have shown there is still a potential risk, whereby it is more beneficial to follow guidance on aspiration prior to delivering the vaccination to help prevent vaccinated injuries. There have been studies related to possible avenues where the vaccination can affect

particular areas of the body, depending on the injection site. Although it cannot be proven and more research needs to be carried out on this topic, theoretically by injecting in the right arm, rather than the left arm could potentially help prevent the risk of an individual suffering from an adverse effect caused by the vaccine.

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