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Does the Measles, Mumps and Rubella (MMR) Vaccine Enhance One or More Specific Functions in Children and Can it Help against this Novel Paediatric Inflammatory Multisystem Syndrome?

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Introduction

On 31st December 2019, the World Health Organisation (WHO) was informed of a novel virus known as Covid-19. This virus originated from Wuhan, China, where it rapidly started to spread to different parts of the world and become a global pandemic. Covid-19 mainly affected elderly and vulnerable adults. However, In April 2020 children started to present with a rare dangerous reaction which was unknown to healthcare providers. The novel syndrome seen in children has now been named Paediatric Inflammatory Multisystem Syndrome (PIMS). Some experts say that this new syndrome seen in children is related to Covid-19 and resembles Kawasaki Disease (KD) and Toxic Shock Syndrome (TSS). According to the Centers for Disease control and Prevention [1] it is recommended that all children receive two doses of the measles, mumps and rubella (MMR) vaccine. This editorial will be analysing key concepts from variable research collected through different studies, in order to gain a better understanding of the MMR Vaccine and if it has any benefit in a child's immune response when fighting against this new novel PIMS.

What is Covid-19?

According to the WHO [2] Covid-19 is a viral infectious disease which causes Severe Acute Respiratory Syndrome. Ferretti [3] states that the virus can be transmitted through exhaled droplets and contamination of surfaces. According to Singal [4] symptoms of Covid-19 include fever, sore throat, cough followed by breathing difficulties. Furthermore, Singal [4] explains that symptoms of Covid-19 in neonates, infants and children are significantly milder than they are in adults. Roser [5] states that as of May 14th 2020 there are (4,477,573) reported cases which includes (299,958)

reported deaths, with 2.2% of those deaths being related to children aged 0-17 years of age. Verdoni [6] that in children, the respiratory involvement in Covid-19 takes on a more benign course. According to Mehta [7] stated that Covid-19 carried a 3.7% mortality rate compared to less than 1% mortality rate from influenza. Furthermore, Mehta [7] mentions that Covid-19 can cause cytokine storms within the body, and that it is advantageous to identify and treat they hyper inflammation using existing approved therapies where possible, in order to reduce the rise in mortality.

What is Paediatric Inflammatory Multisystem Syndrome?

According to Herman [8] approximately a month after the first surge of Covid-19 cases in New York, where at that time at least 50 children developed a Multisystem Inflammatory Syndrome, suggesting it is a post infectious immune response related to Covid-19. The European Centre for Disease Prevention and Control [1] stated that a total of 230 suspected cases of this novel PIMS associated with Covid-19 has been reported within Europe with ages ranging between 0-19 years of age. Riphanean [9] explains that symptoms of this PIMS in children include fever, rash, conjunctivitis, peripheral oedema, extremity pain, abdominal pain, gastrointestinal symptoms and cardiac problems. Verdoni [6] States that there is evidence which proposes that tissue damage from Covid-19 is mediated by the innate immunity, however, this novel PIMS causes a similar reaction when compared to Covid-19 as cytokine storms are caused from macrophage activation. According to Ford [10] these new cases of the novel PIMS have common overlapping features of TSS and KD. In Riphanean [9] study, 8 children were admitted into the Paediatric Intensive care

Unit (PICU), none of them had any underlying health issues and all were tested negative for Covid-19, however, all children had known family exposure to Covid-19. 6 were of Afro-Caribbean descent and 5 were boys. Furthermore, in Riphæan [9] study, it mentions that the children were given intravenous (IV) Immunoglobulin 2g/kg in first 24 hours of arrival in PICU followed by aspirin if needed. Shekerdemian [11] conducted a study in Italy on this novel PIMS and found that children in group 2 were older than those who are typically seen with KD, had a higher rate of cardiac involvement and macrophage activation syndrome (MAS). Furthermore, Shekerdemian [11] states that all children made a full recovery, however, all patients received immunoglobulin, but 80% required further treatment with steroids.

What is Kawasaki Disease?

Ramphul & Mejias [12] state that Kawasaki Disease (KD) was first reported in 1961, and usually occurs in children under 5 years of age. Furthermore, Ramphul & Mejias [12] mention that KD is categorised as an acute systemic vascular disease, which typically affects medium and small sized vessels within the body. Hedrich [13] states that memory T cells increase in numbers during the acute phase of KD as effector T cells reduce during the convalescent phase which indicates adaptive immunity. Moreover, Hedrich [13] explains that due to the adaptive immunity against hyper inflammation Intravenous Immunoglobulin treatment is essential as it coincides with increased memory T cells and helps reduce the inflammatory responses. Lewin [14] States that Dr Stock believes the symptoms that are being presented from this novel PIMS has a unique resemblance to KD. Moreover, Lewin [14] also mentions that there is a difference with KD and the multisystem inflammatory syndrome which comes down to the in age group that has been affected, as KD occurs in children between 6 months to 5 years of age and PIMS is being presented in older children more.

What is the MMR Vaccine?

Public Health England [15] introduced a vaccine in the UK in 1988 and since then, mumps, measles and rubella has become rare. Bowes [16] states that the MMR vaccine is a multi-dose live vaccine where the CDC recommends that a child receives their first dose a few months after their first birthday, and a second dose when the child is between the ages 4 -6 years of age. Letley & Ramsay [17] explains that due to the ages that children receive their first and second dose, in the UK, this results in approximately 90% effectiveness after the first dose and 97% effectiveness after the second dose which also boosts herd immunity. According to the CDC [1] the US vaccination Schedule state that any child who receives both doses of the MMR are considered to be protected for life against MMR, however,

there have been cases where children who have had the vaccine has still been infected by mumps, measles or rubella, but it only caused mild symptoms. Cardermil [18] measured the effect of a third dose of MMR vaccine on university students after the mumps outbreak in 2015-2016 in Iowa. Cardermil [18] used fisher's exact test to compare unadjusted attack rates, where they found out that students who had been given their second dose of the MMR vaccine 13 or more years prior to the mumps outbreak, had 9-14 times more risk of mumps compared to those who had received their second dose more recently.

How can the MMR Vaccine Increase Immunity?

According to Gans [19] the MMR vaccine could prime the adaptive immunity by sensitising T cells which are needed to make critical cytokine. Miller [20] further reiterates that the MMR vaccine assumes a transient protective effect against heterologous viral infections. Welsh [21] explains that heterologous immunity is something that can develop to one type of pathogen after the host has been exposed to non-identical pathogens. Moreover, Welsh [21] mentions that certain studies with MMR Vaccine has shown beneficial effects towards morbidity and mortality with other diseases unrelated to the vaccine. Souquette & Thomas [22] states that influenza viruses recurrently mutate which can cause it to evade pre-existing immunity leading to epidemics and pandemics. However, Souquette & Thomas [22] further states that certain studies have shown Vaccines have helped boost T cell which can cause them to confer protection during an acute heterologous challenge [23].

Conclusion

There are still unanswered questions in relation to this novel PIMS virus and more research is needed to help find answers. However, it seems that PIMS is associated with the Covid-19 outbreak and bares a strong resemblance to KD and TSS. It also appears that although there is no substantial proof, there is a possibility that the MMR vaccine can boost the child's immune system through heterologous immunity, which could help fight off other non-identical pathogens, especially during a pandemic. Cardemil [18] explained that older children may need a third dose in order to boost up their immunity which may help older children fight off these novel viruses. Although the risk to children compared to adults is still seen as substantially low, PIMS along with Covid-19 can still become life threatening and as a result due to hyper inflammation, certain approved therapies such as immunoglobulin, aspirin and steroids must be used in the treatment and management of PIMS in children.

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Dedicated to Millie

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