Clinical experience of intramuscular immunoglobulin for measles prophylaxis in children: is it practical?

Leanne Philips¹,²

Megan K Young³,⁴

Janet Wallace¹

Hazel C Dobinson¹

¹Children’s Health Queensland, Queensland Children’s Hospital,

²School of Nursing, Midwifery and Social Work, University of Queensland,

³Metro North Hospital and Health Service, Metro North Public Health Unit, Brisbane

⁴School of Medicine and Menzies Health Institute Queensland, Griffith University, Gold Coast, Queensland, Australia
Abstract

Measles continues to be a public health concern worldwide. Vulnerable individuals including those in which vaccinations is contraindicated, may be reliant on normal human immunoglobulin prophylaxis in an aim to prevent disease. This paper will summarise and discuss a tertiary paediatric hospital’s clinical experience and the practicalities of administering intramuscular normal human immunoglobulin to paediatric patients as per the current measles prophylaxis guidelines in Australia. Following potential exposure within the emergency department, seventeen paediatric patients (0-15 years) were recommended intramuscular normal human immunoglobulin for prophylaxis. The dose of normal human immunoglobulin ranged from 0.6mL to 15mLs and required multiple (2-8) injections. Two patients required sedation for staff to safely administer the injections. Staff involved with these cases reported administering multiple injections to paediatric patients to be a traumatising experience. They also expressed views that the injection of large volumes via the intramuscular route was an impractical method of administration. Based on this experience, we recommend intravenous immunoglobulin be considered when large volumes of normal human immunoglobulin are recommended intramuscularly.

Key words: pediatrics, intramuscular, immunoglobulin, infectious, disease, measles
Introduction

In 2014, Australia was one of the first countries declared by the World Health Organization to have eliminated measles. Containment of the disease can be credited to overall high population-wide vaccination rates, active surveillance systems and rapid public health responses to new cases. With the frequency of travelers to and from endemic countries around the world, outbreaks in Australia remain a concern, especially in areas with low vaccination rates and vulnerable populations including the immune suppressed and those too young to be vaccinated.

In Australia, surveillance and management of measles cases is coordinated by state public health units supported by national guidelines. The guidelines were last reviewed in 2019 and provide public health and local authorities with nationally consistent guidance in responding to a case. Included in the guideline is a management plan for healthcare facilities and recommendations for those requiring prophylaxis. This paper summaries and discusses a tertiary paediatric hospital’s clinical experience and the practicalities of administering intramuscular (IM) normal human immunoglobulin (NHIG) as post-exposure prophylaxis for vulnerable patients exposed to measles. Queensland Human Research Ethics Committee granted a waiver of ethics as this project meets the requirements of Section 5.1.22 and 5.1.23 of the National Statement as a low and negligible risk quality activity.

Our experience

In March 2018, 123 patients at a tertiary paediatric emergency department were potentially exposed to measles. The measles case was a seven month old child, had acquired the disease overseas, had not previously received a measles vaccine and was not isolated on presentation to the emergency department. The Australian Immunisation Handbook currently recommends measles vaccination in this age group prior to travel, however, in 2018 no such recommendation was in place.

Those potentially exposed were contacted to confirm immunisation status and vaccination was offered if required, in the absence of contraindications. Any families unable to be contacted by phone were sent a letter (hard copy). Seventeen children were identified as potentially exposed and met criteria for immunoglobulin
prophylaxis as per National Guidelines. Ages ranged from 6 days to 14 years. Four patients were immune compromised and required 0.5mL/kg (to a maximum of 15mL). The remaining 13 patients were unvaccinated and required 0.2mL/kg. Based on the mL/kg dosages, total NHIG volumes for intramuscular injection ranged between 0.6mL and 15mLs. One family declined prophylactic treatment for their child and one child received NHIG at their local service provider. No child developed measles following this exposure.

The large volumes recommended for IM injection created the first challenge for clinical staff as the volumes exceeded the maximum for IM injection according to hospital guidelines, see Table 1. Consequently, each patient received between two and eight injections with injection volumes ranging from 0.3mL to 2.5mL per injection determined by age and the muscle group to be injected. Administering multiple injections to paediatric patients posed two further challenges.

Firstly, our staff had limited to no experience injecting into some of the sites recommended in the hospital guideline (for example the gluteal region). While IM injections are within the scope of a registered nurse, it is a procedure rarely undertaken within our paediatric organisation outside of vaccinations. Most of the nursing staff were experienced with IM injections into the vastus lateralis and deltoid but not experienced in injecting into the ventrogluteal and gluteus maximus muscles. As a result, patients were administered multiple injections into different areas of the vastus lateralis and deltoid muscles. There were no reports of soft tissue complications following IM NHIG injection.

Secondly, the ability to safely administer multiple intramuscular injections to paediatric patients was challenging. Two patients aged six years and 12 years required conscious sedation with nitrous oxide to enable staff to safely administer more than one injection. A clinical hold (utilizing the parent to hold and support the child) was used for patients who were developmentally unable to remain immobile for the procedure. Although the manufacturer’s product information supports adding lignocaine solution to NHIG injection to reduce injection pain, this technique was not used as it would have increased the volume to be injected. Staff reported administration of multiple injections and the volumes injected to be a “traumatising
experience”. Staff used techniques such as simultaneous injections (two staff administering at the same time) to reduce the length of the procedure.

Discussion

Systematic review has concluded the administration of immunoglobulin is effective for preventing measles and it is a necessary intervention for those most at risk of measles complications. However, the challenges of administration in a paediatric population posed by the volumes required, particularly in light of current local intramuscular guidelines, should be subject to further consideration.

We identified few primary studies of injection technique in children. Those available considered assessment of needle length and gauge, complications from intramuscular injections, and site of injection in relation to muscle mass, but no studies specifically examined maximum volumes for IM injection in children. Two narrative literature reviews offer references for their recommendations, but reference to primary research evidence on the maximum volume for IM injection in children is again lacking.

There are many publicly available clinical guidelines, both in Australia and internationally, that recommend maximum injection volumes at different muscle sites and / or to patients of different ages. None of the guidelines that we identified, nor our own current hospital guideline includes references to primary studies or systematic reviews on injection volumes in children. When referencing is used, most cite other guidelines or text books of nursing practice. One guideline goes so far as to say there is no universal agreement on optimum injection site or injectable volumes for children. Despite the lack of primary research evidence, most guidelines and reviews recommend a maximum volume of 2mLs for IM injection in children which is dependent on age and injection site. Given this volume limitation, the number of injections of IM NHIG required to complete measles post-exposure prophylaxis can be large; as was our experience.

Further, there is emerging evidence that the current volumes of IM immunoglobulin recommended for vulnerable groups may be insufficient to ensure effectiveness for preventing measles. Internationally, declining measles antibody levels in immunoglobulin products, most likely due to high levels of vaccine-derived (as
opposed to infection-derived) immunity among donors, have prompted alterations to public health guidelines\textsuperscript{21,22}. If the recommendations from a recent Australian modelling study are adopted\textsuperscript{20}, volumes larger than 15mLs could be required for some children. Due to the impracticalities identified during the clinical experience reported here, we support recent recommendations from England and Canada that suggest the use of intravenous immunoglobulin (IVIG) in certain instances\textsuperscript{19,21}, and would recommend its use in children be considered when the volume required exceeds two IM injections. Inherent with this consideration should be an assessment of the benefits versus risks of intravenous compared to intramuscular dosing for the individual, including if access to IVIG will be timely and any impacts on the timing of receipt of active vaccination against measles.

UK guidelines recommend 0.15 g/kg of IVIG\textsuperscript{21} and Canadian guidelines recommend 400 mg/kg (0.4 g/kg) of IVIG\textsuperscript{19} for measles post-exposure prophylaxis. The concentration of measles antibodies in the IVIG products used by these countries have been estimated at 80-330 IU/g\textsuperscript{21} and 330 IU/g\textsuperscript{19} respectively. Australian IVIG has a measles antibody concentration of 100-400 IU/g\textsuperscript{23}. If IVIG is to be used for measles post-exposure prophylaxis in Australia it would seem reasonable to adopt the more conservative dose of 0.4 g/kg in the absence of further evidence on the minimum effective dose of immunoglobulins administered by the intravenous route.

Given the paucity of primary research in this area, further studies examining the maximal volumes for IM injection as well as use of intravenous immunoglobulin for measles prophylaxis in children with emphasis on effective and efficient dosing, including an examination of the cost effectiveness to this approach would be valuable to inform clinical practice in the future.
References


Table 1. Local guideline for maximum amounts of solution to be injected into each muscle tissue.

<table>
<thead>
<tr>
<th>Muscle Group</th>
<th>0 - 18 months</th>
<th>18 months - 3 years</th>
<th>3 - 6 years</th>
<th>6 - 15 years</th>
<th>&gt;15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vastus lateralis</td>
<td>0.5mL</td>
<td>1mL</td>
<td>1.5mL</td>
<td>1.5-2mL</td>
<td>2-2.5mL</td>
</tr>
<tr>
<td>Deltoid</td>
<td>Not recommended</td>
<td>Not recommended unless other sites not available 0.5mL</td>
<td>0.5mL</td>
<td>0.5mL</td>
<td>1mL</td>
</tr>
<tr>
<td>Ventrogluteal</td>
<td>Not recommended</td>
<td>Not recommended unless other sites not available 1mL</td>
<td>1.5mL</td>
<td>1.5-2mL</td>
<td>2-2.5mL</td>
</tr>
<tr>
<td>Gluteus maximus</td>
<td>Not recommended</td>
<td>Not recommended unless other sites not available 1mL</td>
<td>Not recommended unless other sites not available 1.5mL</td>
<td>Not recommended unless other sites not available 1.5-2mL</td>
<td>Not recommended unless other sites not available 2-2.5mL</td>
</tr>
</tbody>
</table>

Volumes over 2mL may be considered in some circumstances e.g. PEG-Asparaginase where a volume of 2.4mL is often required. Volumes of up to 2.4mL in one injection are used in exceptional circumstances with documented informed consent where the risk of muscle necrosis is discussed with the parent/carer.