2. IVIG hospital administration – in children

Every country and institution may have different regulations regarding immunoglobulin therapy administration. Some of the steps/measures given below may not be necessary. Please follow your local and national guidelines.

Intravenous IgG (IVIG), depending on the indication, is prescribed and given on regular basis at various doses.

IVIG is well tolerated by the majority of patients. However, if it is not tolerated (i.e. in the presence of adverse events), patients may be switched to another product (1). The first infusion with a new product should be monitored carefully for adverse events.

Each patient may require an individualized infusion regimen in order to minimise adverse events and to achieve the desired therapeutic response (2). Once a successful regimen has been established, it should be adhered to at every infusion.

Prior to every infusion, a review of the administration route, adverse events observed with previous infusion, premedication and patient treatment satisfaction should be made.

At the hospital, IVIG is usually administered *via* an IV pump. However, patients who are trained for IVIG home-therapy may be trained to use gravity drip administration sets.

Check in each product's package insert if a filter is required.

The patient/legal representative(s) should:
- Be aware of the possible adverse events (including delayed and late adverse event)
- Know what to do in case of adverse event
- Have a telephone contact to call for advice

For detailed rationales, please see explanations below the list.

Before the first infusion
- Check the patient's identity and the prescription according to the hospital policy
- Assess the understanding of therapy with the child and its legal representative(s)
- It is advisable to have a written informed consent from the child (from 16 years onwards, please refer to national legislation), and/or from their legal representative(s); please check with your local guidelines

- Describe possible adverse events to the patient or the legal representative, including possible flu-like symptoms after the first 2 to 3 infusions, and record any adverse events
- Complete pre-treatment blood tests (according to local protocol/agreement) (Rationale 1)
- Check immunoglobulin trough levels regularly in antibody deficient patients (Rationale 2)
- Assess the patient's general health, including temperature, pulse and blood pressure (for vital signs, please refer to your local guidelines to see when assessment is required)(Rationale 3)

Pre-infusion assessment for the next infusions

- Check the patient's identity and the prescription according to the hospital policy
- Advise the patient to drink water before, during and after the infusion (Rationale 4)
- Assess the patient's well-being and do not start an infusion if the patient has an infection, a temperature, or flu-like symptoms (Rationale 3)
- Assess for any weight loss or gain (Rationale 5)
- Assess that the immunoglobulin product ordered is the product prescribed for the patient, check the product name, dose, and expiry date
- Inspect product for clarity and colour (Rationale 6)
- The immunoglobulin should be at room temperature before the infusion (Rationale 7)
- Assess the need for premedication (Rationale 8)
- Assess if pre-treatment blood tests are required

Equipment

- Local anaesthetic cream/spray may be applied to the venous access site
- Immunoglobulin product for intravenous use
- Intravenous (IV) infusion pump
- IV infusion set (flush with 0.9% NaCl solution, according to your hospital guidelines and product package insert)
- IV cannula: gauge size 24G (or 22G)
- Disinfectant
- Cannula dressing
- Gauze
- Post-infusion dressing
- Sharps container

Infusion (3)

(Please see troubleshooting in Appendix 6)

- Wash and disinfect your hands and working surface thoroughly (Rational 9)
- Prepare the patient for cannulation using appropriate topical anaesthetics and distraction therapy if needed (4)
- Prime the administration set with immunoglobulin and start infusion (increase the rate to the maximum rate tolerated by each patient or to the maximum rate advised in the product package insert)
    - For the first two infusions, increase the infusion rate slowly as advised in the package insert (Rationale 7)
    - Note that the maximum rate is lower for the first two infusions than for the following ones (Rationale 7)
- Please refer to local guidelines with regard to vital signs before each rate increase
- Do not leave the child unattended during the infusion
- Check the peripheral infusion site half-hourly for inflammation (tenderness, swelling, redness) and leakage. STOP the infusion if there are any signs of inflammation, extravasation or adverse events (Rationale 7)

• Assess for signs of anaphylaxis and adverse events and act accordingly (Rationale 7) • On completion of the infusion, you may flush the administration set with 0.9% NaCl solution to ensure that the total dose is administered (please refer to local guidelines) (Rationale 10) • Post-infusion, observe the patient as per local guidelines • Before patient discharge, remove the cannula and make sure that access site has completely stopped bleeding and that no haematoma is forming • Dispose of all items according to hospital policy
Is IV access difficult? The use of permanent indwelling ports or central venous lines in antibody deficient patients is strongly discouraged due to the risk of infections and/or thrombotic events. If peripheral access is consistently difficult, subcutaneous IgG therapy (SCIG) is a viable option.
Careful documentation of every IVIG infusion should include: • The patient's current health status, medications and any changes in this status in the period between infusions • The product name, dose and batch numbers of the products used (Rationale 10) • Any pre-medications which were given • Duration of infusion and any rate titrations made • Any problems experienced by the patient during infusion and what was done to address them • Patient treatment/infusion satisfaction • Next appointment

Rationale 1

Patients should be tested for exposure to known blood borne pathogens **before** starting IVIG therapy. Once immunoglobulin therapy has been started, serologic tests may become positive because of the passively transferred antibodies and not be informative of the patient's infection status. Normally, health centres test for HIV and hepatitis A, B, and C, and measure complete blood count, hepatic transaminases and renal function before initiating immunoglobulin therapy by any route. In hematologic disease, Coombs' testing should be done prior to IVIG therapy (www.uptodate.com/contents/general-principles-in-the-use-of-immuneglobulin?source=search_result&search=intravenous+immunoglobulin&selectedTitle). In immunodeficient patients, serologic tests are frequently not informative because patients are not able to form antibodies specific for these pathogens. A negative serologic test in a patient with immune deficiency does not mean that the patient has not been exposed to the pathogens. PCR tests are used to detect active infection with Epstein-Barr virus, CMV and Hepatitis B.

Rationale 2

To monitor the effectiveness of treatment.

Rationale 3

To establish what is normal for each patient and detect potential infusion-related abnormalities. During infusion, an alteration of vital signs could indicate an adverse event. If fever is present and/or other signs of an acute infection the infusion may need to be postponed until antibiotic treatment is started and/or fever settles. Infusing when a patient has an acute infection can lead to antigen-antibody reaction by formation of immune complex. This effect is most common

on first infusion as the concentration of antigens is highest at that time. It is important not to confound this effect with systemic adverse events, and to educate patients about the difference so that they do not fear future treatment sessions.

Rationale 4
Patients receiving IVIG should be well hydrated prior to the infusion. This is particularly important for patients with risk factors for thrombosis and/or renal complications of IVIG therapy, such as pre-existing renal insufficiency, diabetes mellitus, paraproteinaemia, heart disease, and/or concomitant use of nephrotoxic agents. In patients who are not able to drink, and if their condition permits, additional IV hydration may be considered. Good hydration reduces the risk of adverse events.

Rationale 5
Immunoglobulin therapy depends on patient weight, among other parameters. Any significant change in weight may indicate a need for dose increase or (less likely) reduction. The weight is also important to calculate the infusion rate.

Rational 6
The liquid should be clear and transparent; if it is cloudy or has deposits, the product should not be used.

Rationale 7
Systemic adverse events are more likely to occur with cold immunoglobulin solutions (fridge temperature), with the first infusion, a fast infusion, a large infusion, a long interval since the prior infusion, a switch to a new product or batch number, or the presence of a current infection (5, 6). The most common immediate reactions are headache, cold sweat, light dizziness, chills, fever, and muscular pain. These are usually mild and occur within an hour of starting an infusion and disappear within 6 hours. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.

Rationale 8
Premedication is usually only given if there has been a recent systemic adverse event. Many adverse events can be minimized or prevented by oral premedication, for example with antihistamines, steroidal or non-steroidal anti-inflammatory agents (6).

Rationale 9
Good hygiene is an important aspect in infection prevention.

Rationale 10
Although the risk of transmission of blood-borne infections with currently licensed IVIG products is minimal, it is still present. The dose, brand, batch number, expiration date, and manufacturer of any immune globulin product infused into any patient should be carefully recorded in the medical record, as is done for all blood products. In addition, patients should be trained to keep their

own logs of this information, as it is often required by law to have donor-to-recipient traceability.

References

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