CARE FOR CHILDREN AND ADOLESCENTS WITH SUSPECTED OR CONFIRMED PIMS-TS / MIS-C

NATIONAL CLINICAL EVIDENCE TASKFORCE
COVID-19

FORMS OF GUIDANCE

Evidence-Based Recommendation **(EBR)**
Consensus Recommendation
Good Practice Point

Types of EBRs: RECOMMENDATION FOR USE | RECOMMENDATION AGAINST USE | CONDITIONAL RECOMMENDATION FOR USE | CONDITIONAL RECOMMENDATION AGAINST USE

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General

MULTIDISCIPLINARY CARE

CONSENSUS RECOMMENDATION

Children and adolescents who have suspected or confirmed PIMS-TS should be managed by, and their care discussed with, a multidisciplinary team. Because of the potential for rapid deterioration, early consultation with experts and consideration of early transfer to a hospital with intensive care facilities able to manage children is recommended for patients with suspected or confirmed PIMS-TS.

GOOD PRACTICE POINT

Seek expert advice and multidisciplinary involvement to exclude other hyperinflammatory presentations, including sepsis, malignancy, rheumatological disease and Kawasaki disease.

DEFINITION OF SYNDROME

Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS), also known as multisystem inflammatory syndrome in children associated with COVID-19 (MIS-C), is a rare, hyperinflammatory condition involving many organ systems.

A child may present with:

- persistent fever
- inflammation (neutrophilia, elevated CRP and lymphopenia)
- evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder)
- additional features.

This may include children fulfilling full or partial criteria for Kawasaki disease.

Refer to:

- PAEDS network definition for case reporting and identification of suspected cases.

Treatments

IMMUNOMODULATORY AGENTS

CHILDREN UNDER 5 YEARS OF AGE

CONSENSUS RECOMMENDATION

With PIMS-TS and no haemodynamic compromise

- give **IV immunoglobulin** 2 g/kg/dose – single dose (max 100 g/dose)

AND

- give **IV methylprednisolone** 2 mg/kg/day (max 1000 mg) for 3 days^^

CONSENSUS RECOMMENDATION

With PIMS-TS and haemodynamic compromise and/or no/limited improvement with above

- consider the following, in order, until improvement – consult a specialist as soon as possible:
  - **increase dose of IV methylprednisolone** 10 mg/kg/day (max 1000 mg) for 3 days^^
  - **add IV immunoglobulin** 2 g/kg/dose – single dose (max 100 g/dose)
  - **add biologics** anti IL-1, anti IL-6 or anti-TNF**

CONSENSUS RECOMMENDATION

With possible PIMS-TS and Kawasaki disease-like clinical features##

- give **IV immunoglobulin** 2 g/kg/dose – single dose (max 100 g/dose)

CONSENSUS RECOMMENDATION

Antiplatelets

For children with PIMS-TS who are treated with IV immunoglobulin, steroids (e.g. methylprednisolone), or biologic agents (e.g. anti IL-1; anti IL-6; anti-TNF), low-dose aspirin should be prescribed (3–5 mg/kg once daily for at least 6 weeks).

GOOD PRACTICE POINT

Children with myocardial dysfunction

The oncotic load from a large IVIG dose should be considered when administering this agent to children with myocardial dysfunction. For selected cases of PIMS-TS with severe myocardial dysfunction, corticosteroid treatment alone and/or delayed use of IVIG may be beneficial.

CHILDREN AND ADOLESCENTS 5 YEARS AND OLDER

CONSENSUS RECOMMENDATION

With PIMS-TS and no haemodynamic compromise

- give **IV methylprednisolone** 2 mg/kg/day (max 1000 mg) for 3 days^^

CONSENSUS RECOMMENDATION

With PIMS-TS and haemodynamic compromise and/or no/limited improvement with above

- consider the following, in order, until improvement – consult a specialist as soon as possible:
  - **increase dose of IV methylprednisolone** 10 mg/kg/day (max 1000 mg) for 3 days^^
  - **add IV immunoglobulin** 2 g/kg/dose – single dose (max 100 g/dose)
  - **add biologics** anti IL-1, anti IL-6 or anti-TNF**

CONSENSUS RECOMMENDATION

With possible PIMS-TS and Kawasaki disease-like clinical features##

- give **IV methylprednisolone** 2 mg/kg/day (max 1000 mg) for 3 days^^

AND

- give **IV immunoglobulin** 2 g/kg/dose – single dose (max 100 g/dose)

CONSENSUS RECOMMENDATION

If thought to be Kawasaki disease##

- give **IV methylprednisolone** 2 mg/kg/day (max 1000 mg) for 3 days^^

AND

- give **IV immunoglobulin** 2 g/kg/dose – single dose (max 100 g/dose)

CONSENSUS RECOMMENDATION

Antiplatelets

For children with PIMS-TS who are treated with IV immunoglobulin, steroids (e.g. methylprednisolone), or biologic agents (e.g. anti IL-1; anti IL-6; anti-TNF), low-dose aspirin should be prescribed (3–5 mg/kg once daily for at least 6 weeks).

Please refer to footnotes located on page 2 of this flowchart.

VTE PROPHYLAXIS

CONSENSUS RECOMMENDATION

Thromboprophylaxis

Based on age and risk assessment:

- In **children under 12 years** who are hospitalised specifically for PIMS-TS/ MIS-C treatment and **with either D-dimer levels > 5 x upper limit normal, or additional thrombosis risk factors**^ (including hospital-associated VTE), use prophylactic doses of LMWH* and mechanical thromboprophylaxis (TED stockings or calf compressors) where suitable based on size and mobility until discharge from hospital.
- In **children and adolescents aged 12 years and over** who are hospitalised specifically for PIMS-TS/ MIS-C treatment and with no contraindications to anticoagulants#, use prophylactic doses of LMWH* and mechanical thromboprophylaxis (TED stockings or calf compressors) until discharge from hospital.

GOOD PRACTICE POINT

In children with PIMS-TS/ MIS-C, the presence of myocardial dysfunction or giant coronary artery aneurysms might be an indication for extended duration therapeutic anticoagulation that continues post discharge.

Key source

National Clinical Evidence Taskforce – Australian guidelines for the clinical care of people with COVID-19.

^ Thrombosis risk factors

- Admission to PICU
- Obesity (BMI > 95th centile)
- Central venous catheter
- Length of stay anticipated > 3 days
- Immobility that is not longstanding
- Personal history of VTE
- Known thrombophilia
- First degree relative with VTE
- Active malignancy
- Recent surgery / trauma
- Severe dehydration
- Underlying medical condition: nephrotic syndrome, cystic fibrosis, sickle cell disease, cardiac disease, chronic inflammatory disorder (juvenile idiopathic arthritis, inflammatory bowel disease), post splenectomy

* Dose of low molecular weight heparin (LMWH)

- ≥ 3 months old – enoxaparin 0.5 mg/kg BD (max 60 mg BD, or at the standard adult prophylactic dose for your centre)
- < 3 months old – enoxaparin 0.75 mg/kg BD
- Unfractionated heparin (UFH) is an alternative to LMWH and can be considered if there is potential for surgical intervention, renal impairment or other clinical factors that would normally favour UFH over LMWH. Dosing should be advised by paediatric haematology.
- Where eGFR is < 30 mL/min/1.73 m^2, UFH or clearance-adjusted doses of LMWH may be used (discuss with paediatric haematologist).

Contraindications to thromboprophylaxis

- Stroke / intracranial haemorrhage
- Any bleeding from any site / uncontrolled bleeding
- Likely to need surgery in < 24 hours
- Congenital bleeding disorder (e.g. Von Willebrand Disease, haemophilia)
- Platelets < 50 x 10^9/L and/or INR > 1.8
- Uncontrolled hypertension

Consider UFH

^^ After 3 days of IV methylprednisolone, continue with oral prednisolone 2 mg/kg daily (max 60 mg/day) when tolerating oral intake and wean over a total of 2-3 weeks. Children with mild illness and rapid response to therapy may be able to cease therapy after 3 days rather than having oral continuation therapy with prednisolone. Some children with milder illness who can tolerate oral prednisolone can commence therapy with oral prednisolone at 2 mg/kg/day (max 60 mg/day) in place of methylprednisolone.

** Consider testing for infections that may be unmasked by the use of these agents.

Kawasaki disease-like phenotype is more common in patients < 5 years of age.