High-dose steroids in the management of Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2 (PIMS-THS): Considering the hypothalamo-pituitary-adrenal axis

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INTRODUCTION

- Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2 (PIMS-THS) remains a relatively new condition.
- Steroid therapy has been used as a therapeutic strategy to good effect. 1-4
- Consensus guidelines for PIMS-THS suggest that young children, children with coronary artery changes, and children who remain unwell after 24 hours of intravenous immunoglobulin (IVIG) should receive high-dose intravenous methylprednisolone (10-30mg/kg). 5
- As is always the case with prolonged or high-dose steroid administration, this treatment carries a risk of iatrogenic adrenal insufficiency.

AIM

We aimed to characterise steroid therapy use in a cohort of children with PIMS-THS and consider implications for hypothalamo-pituitary-adrenal (HPA) axis function.

METHODS

- Retrospective observational study of children (<18 years) admitted to Great Ormond Street Hospital with PIMS-THS during the first (1st April 2020 to 30th June 2020) and second (1st October 2020 to 31st May 2021) wave of the COVID-19 pandemic in the UK.
- We analysed demographic data and clinical data on treatments used in PIMS-THS management including steroid type, treatment length, and cumulative dose (mg/m²/day).
- The approximate hydrocortisone equivalence was calculated to allow comparison between steroids used. A relative potency of hydrocortisone: dexamethasone: prednisolone: methylprednisolone = 1:30:4:5.
- SPSS 27.0.1 was used for analyses.

RESULTS

PIMS-THS management and steroid treatment

- A total of 127 children with a PIMS-THS diagnosis were included in this study: 48 from the first COVID-19 wave and 79 from the second COVID-19 wave.
- Median age was 7.9 years (IQR 7.0-12.0).
- The majority of children were admitted to the Paediatric Intensive Care Unit (PICU) (82.7%, n=105) for a median length of stay of 3.0 days (IQR 2.0-5.0).
- COVID-19 IgG positivity and polymerase chain reaction (PCR) positivity were 91.3% (n=116) and 16.5% (n=21), respectively.
- Most children received intravenous and/or oral systemic steroid therapy (84.9%, n=104).
- Other treatments received included intubation and ventilation (16.5%, n=21), anaesthesia (7.1%, n=9), tocilizumab (4.7%, n=6), IVIG (64.5%, n=83), therapeutic anticoagulation (8.4%, n=12), and prophylactic anticoagulation (83.5%, n=108).
- Steroid therapy varied in length, type, and total dose (Figure 1).
- The most common treatment regime was high-dose methylprednisolone for three days followed by oral prednisolone tapered once the patient’s clinical condition and inflammatory markers had improved.

CONCLUSIONS

- Prolonged, high-dose steroids are often used in the management of PIMS-THS with the potential for HPA axis suppression.
- We suggest a low threshold for discussing steroid weaning with paediatric endocrinology teams.
- Measurement of early morning cortisol and ACTH concentrations can be useful to assess adrenal axis recovery.
- Dynamic testing of the HPA axis should be considered if concerns arise regarding adrenal insufficiency secondary to suppression.
- There is a need for steroid management advice to be incorporated into national and international PIMS-THS guidance.

Impact on the HPA axis

- No child had a known history of adrenal insufficiency nor pituitary dysfunction.
- Early morning serum cortisol concentrations were checked in 11.8% (n=15) of children during the acute phase of their illness (mean 496.7nmol/L, SDS 315.9).
- Thyroid function tests were performed in 15.0% (n=19) and all were within normal range (mean free thyroxine 15.1 (SDS 4.7).
- Five patients (3.9%) were referred to endocrinology for advice.
- One of these children had an undetectable early morning cortisol concentration taken during prednisone weaning and was maintained on physiological hydrocortisone treatment until endogenous adrenal axis recovery.
- Four other children were referred to endocrinology: two for consultation on tapering regimens of steroids and two for other endocrine issues (hyperglycaemia, abnormal thyroid function tests).
- One child developed posterior reversible encephalopathy syndrome (PRES) as a result of steroid treatment.
- To our knowledge, no child has developed endocrine dysfunction during follow up.

REFERENCES