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A retrospective analysis of the need for methylprednisolone in addition to IVIG for treating multi-system inflammatory syndrome in children

Rheumatology key message

- MIS-C patients with low ejection fraction will require aggressive therapy with IVIG and MP.

DEAR EDITOR, After the onset of the SARS COV2 pandemic, a new hypercytokinemic disease, multisystem inflammatory syndrome in children (MIS-C) was identified. Cardiac cause has been noted to be a major cause of morbidity. Lesions ranged from myocarditis with decreased ejection fraction, arrhythmia to coronary artery dilatation [1–3]. However, due to the novelty of the disease, there is no uniformly accepted consensus guidelines for its management. Management of MIS-C has been extrapolated from Kawasaki disease. Treatment with IVIG alone or in combination with steroids is given. As in Kawasaki disease aspirin is also instituted. In many cases, interleukin 1 blocker, anakinra has also been used. Due to lack of evidence, a British Delphi consensus study proposed IVIG as the initial therapy for MIS-C [4, 5]. Therefore, the management of MIS-C needs to be optimized.

We conducted this study with the aim to retrospectively analyse the treatment data to decide on the need for methylprednisolone (MP) in addition to IVIG. Seventy-one patients admitted between July and December 2020 in the Institute of Child Health, Kolkata and satisfying the WHO MIS-C criteria were evaluated. Ethical clearance was taken from the institutional ethical committee (IEC/250/2021 DATED 25.08.2021) and written informed consent was taken from the parents/guardian. Because CRP and echocardiography are done in all, and myocarditis was the most common cardiac affection, ejection fraction (EF) along with CRP was used for analysing the data. A logistic regression model was fitted to the data to classify MP usage based on CRP and EF. A χ^2 test of dependence was carried out to test dependence of EF on MP administration.

Seventy-one patients were admitted with a median age of 6 years, interquartile range 3–8. A total of 57.7% (41) of the children had myocarditis, 30.9% had low EF. In patients with normal EF, myocarditis was diagnosed

by disproportionate tachycardia, ECG showing ST/T wave change and echocardiography showing regional wall motion abnormalities, systolic or diastolic dysfunction. In total, 30.9% (22) received IVIG only, 60.6% (43) received IVIG and MP, 8.5% (6) received steroid only. Following therapy, inotropes could be tapered off over 48–72 h. Normalization of EF was noted by 5–7 days. All patients responded to therapy and there was no mortality.

Based on a logistic regression model to classify MP administration according to CRP and EF (reduced or normal), the coefficient for CRP had a P -value >0.05 , signifying it does not significantly affect MP requirement. However, the coefficient for EF had a P -value <0.05 , which means that EF has a significant relation to MP administration, and a change in EF value from normal to reduced will change the probability of MP requirement.

Twenty-four children with normal EF were given MP and IVIG, and 25 were not. Nineteen children with reduced EF (<55) received MP and IVIG whereas three did not (Table 1). To statistically test this dependence of MP administration on EF values, we carried out the χ^2 test of dependence of categorical values. The test gave a P -value <0.05 , which means that there is a relation between EF (reduced/normal) and MP administration.

Therefore, there was a significant association of children with low ejection fraction with combination therapy with IVIG and MP, whereas no significant association was found with CRP and combination therapy.

In a study conducted by Ouldali *et al.* for the French COVID 19 Pediatric Inflammation consortium, among 106 treated children, treatment with MP and IVIG was associated with a lower rate of treatment failure and second line treatment as compared with IVIG alone. They also noted that combination therapy was associated with less severe complications [4].

Another single-centre study on 40 children with MIS-C noted that combination therapy was associated with a shorter recovery time of cardiac functions [6].

The drawback of our study is that it is a retrospective observational study without any control arm.

TABLE 1 Distribution of patients according to therapy received in those with normal ejection fraction and reduced ejection fraction

	EF normal (>55)	EF reduced (<55)
MP and IVIG: NO	25	3
MP and IVIG: YES	24	19

EF: ejection fraction; MP: methylprednisolone.

We could conclude that patients with low EF will require MP in addition to IVIG, irrespective of CRP values.

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Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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References

- 1 Verdoni L, Mazza A, Gervasoni A *et al.* An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020;395:1771–8.
- 2 Feldstein LR, Rose EB, Horwitz SM *et al.* Multisystem inflammatory syndrome in US children and adolescents. *N Engl J Med* 2020;383:334–46.
- 3 Pignatelli R, Antona CV, Rivera IR *et al.* Pediatric multisystem SARS COV2 with versus without cardiac involvement: a multicenter study from Latin America. *Eur J Pediatr* 2021;180:2879–88.
- 4 Ouldali N, Toubiana J, Antona D *et al.* Association of intravenous immunoglobulins plus methylprednisolone vs immunoglobulins alone with course of fever in multisystem inflammatory syndrome in children. *JAMA* 2021;325:855–64.
- 5 Valverde I, Singh Y, Sanchez-de-Toledo J *et al.* Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in Europe. *Circulation* 2021;143: 21–32.
- 6 Belhadjer Z, Auriau J, Méot M *et al.* Addition of corticosteroids to immunoglobulins is associated with recovery of cardiac function in multi-inflammatory syndrome in children. *Circulation* 2020;142:2282–4.