

# Severe imported *Plasmodium falciparum* malaria in French paediatric intensive care units

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Severe *Plasmodium falciparum* (Pf) malaria is a major cause of morbidity and mortality worldwide, particularly in malaria-endemic areas. The paper by Lanneaux *et al*<sup>1</sup> aims to assess the relevance of WHO severity criteria for paediatric Pf malaria in an industrialised country. The authors retrospectively identified children with Pf malaria admitted to eight paediatric intensive care units (PICU) and paediatric emergency departments in France over a 6-year period and conducted a case-control study to analyse WHO severity criteria and major interventions (mechanical ventilation, blood transfusion, fluid challenge, treatment of cerebral oedema and renal replacement). The WHO severity criteria for paediatric Pf malaria were still found to be relevant for countries not endemic for Pf malaria. A similar spectrum of complications, although at lower frequencies than in malaria-endemic countries, was found. In particular, altered consciousness (70%) and circulatory collapse (23%) accounted for the bulk of severe disease requiring admission to PICU. Interestingly, there were no deaths reported in this study, similar to that of our study of PICU admissions in the UK.

Of particular interest in this study was that after altered consciousness, there was a significantly higher OR of circulatory collapse and acidosis in cases compared with controls. Furthermore, these severity criteria were also more likely to receive more than one intervention, which included mechanical ventilation, fluid challenge, catecholamine infusion and blood product transfusion. No deaths were observed in this study and only four children had long-term sequelae (toe ischaemia, post-encephalitic coma, pyramidal hypertonia and focal segmental glomerulosclerosis). This contrasts with the findings of the Fluid Expansion as Supportive Therapy (FEAST) trial where

African children with shock were randomised to early rapid fluid resuscitation with normal saline or 5% human albumin and showed a 3.3% increased absolute risk of death by 48 hours compared with no-bolus controls.<sup>2</sup> Pf malaria parasitaemia was present in 57% of 3123 children included in this trial. In a subsequent analysis of the FEAST study data exploring mechanisms of excess mortality, cardiovascular collapse and refractory shock rather than fluid overload appeared to contribute most to excess deaths with rapid fluid resuscitation. The FEAST trial was conducted in settings with no access to intensive care so the applicability of these findings, particularly to those with PICU facilities, will be limited. It may be that over and above fluid resuscitation, other supportive measures, such as mechanical ventilation and use of inotropes, may be important in the management of circulatory collapse due to Pf malaria. The management of severe imported malaria in children therefore should involve prompt emergency assessment and provision of supportive care, including respiratory and cardiovascular support, as outlined by Maitland *et al*<sup>3</sup> and supported by the present study.<sup>1</sup> This has resulted in the recommendation that all children with severe or complicated malaria in resource-rich countries be managed in a PICU or high dependency unit together with specialist support/advice in managing malaria.<sup>4</sup>

The rate of community-acquired bacterial co-infection has been estimated to have an overall prevalence of 8% in imported falciparum malaria among adults.<sup>5</sup> Pneumonia was the most common community-acquired coinfection occurring in 3% of cases. Bacteraemia was found in 3% of cases; most of these were caused by gram-negative organisms. Lanneaux *et al* found a similar prevalence of 5% in children with imported falciparum malaria but, interestingly, this was similar in cases and controls.<sup>1</sup> As it is often difficult to exclude or differentiate concurrent bacteraemia or meningitis from severe malaria, it is recommended

that empirical broad-spectrum antibiotics should be given to children with severe malaria until bacterial infection can be excluded.<sup>4</sup>

In this study, the majority of children with severe Pf malaria were treated with intravenous quinine and only four patients were treated with intravenous artesunate. There was no comparison made of differences in response to treatment and outcomes. However, there is now substantial evidence for the superiority of intravenous artesunate over intravenous quinine, demonstrating a mortality benefit in adults and children with severe Pf malaria.<sup>6</sup> Intravenous artesunate is now recommended as the treatment of choice for severe Pf malaria in adults and children in various national and international guidelines including WHO guidelines.<sup>4</sup> Intravenous quinine is still indicated if artesunate is not immediately available and treatment should not be delayed while awaiting artesunate therapy.

What messages should paediatricians take from this paper? Paediatricians should recognise that severe malaria still occurs and can kill even in resource-rich, malaria non-endemic countries. As the symptoms of malaria can be varied and non-specific, often mimicking other common childhood illnesses, it is important that malaria is promptly recognised and diagnosed. Early institution of supportive and specific antimalarial therapy will be imperative in preventing adverse outcomes, particularly death. All children with severe Pf malaria should be closely monitored and receive full supportive care, preferably on a PICU. Antimalarial therapy should be commenced as soon as possible and should include intravenous artesunate as the preferred option, although treatment should not be delayed while awaiting artesunate therapy.

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