Commentary

Chromium: can it be useful in treatment of DHF?

Dengue haemorrhagic fever (DHF) is caused by dengue viruses, members of family *Flaviviridae*. The dengue viruses are of 4 antigenic types called DEN 1-4. It has been estimated that over 50 million dengue virus (DENV) infections occur globally each year. Among symptomatic cases, the majority of subjects experience uncomplicated dengue fever (DF), an acute febrile illness typically lasting 3-7 days, accompanied by headache, myalgias, and less often, a maculopapular rash. Laboratory findings in patients with DF include leucopaenia, thrombocytopaenia and mild elevations in serum hepatic transaminases. DHF represents the severe clinical manifestation of DENV infection, which occurs in no more than 3 per cent of infected individuals. DHF is distinguished from DF on clinical grounds, with the three primary criteria being the occurrence of a vascular permeability defect resulting in plasma leakage; multifactorial haemostatic abnormalities, including marked thrombocytopaenia; and a bleeding diathesis. When severe, the plasma leakage leads to hypotension and circulatory collapse, and this is the most important concern for triage and therapy. Thrombocytopaenia is quite severe in DHF, with a platelet count of less than 100,000 cells/mm³ required to fulfill the case definition.

The principle mechanisms by which DENV infection causes DHF have been a subject of controversy ever since the syndrome was first recognized. Opposing views have focussed on the effect of viral and host factors on disease severity. Differences in virulence between naturally circulating DENV strains had been suspected based on differences in clinical profiles observed during isolated DENV outbreaks in Indonesia and the Pacific Islands. More recently, studies in Peru and Sri Lanka have provided more convincing data demonstrating the association of DHF with specific viral genotypes and not with others. Key seroepidemiological studies by Halstead and colleagues in Thailand first suggested an association of increased risk for DHF with a secondary DENV infection; that is, a new DENV infection in an individual who had previously experienced one or more DENV infections. The occurrence of DHF during primary DENV infection in the first year of life in children born to DENV-immune mothers, and who therefore acquire antibody against DENV transplacentally also supports the idea of an in vivo role for ADE. Immune complex formation in vivo has been detected in association with complement activation in patients with severe disease. However, the exact mechanism of DHF still remains elusive. At present, there is no specific therapy available for DHF. Appropriate fluid management to correct hypovolaemia has been successful in reducing the mortality of DHF.

Chromium on the other hand occurs naturally in the environment and humans are widely exposed to this metal. Chromium can affect various immune cells. In a study on Wistar rats it was shown that the effect of chromium on alveolar macrophages was dose dependent. With smaller doses, it activated the macrophages whereas in higher doses it inhibited phagocytic functions of macrophages. Similarly in another study inhalation of soluble chromium led to greater levels of total recoverable cells, neutrophils, and monocytes in bronchopulmonary lavage of rats compared to rats exposed to insoluble Cr6.16.
In this issue Shrivastva et al. have shown that by giving chromium to dengue infected mice there was less reduction in platelet counts compared to normal mice inoculated with dengue virus alone. Thus, the authors have opened a new area of interest whether chromium can protect against DHF caused by dengue virus. More studies are required on this aspect to prove or disprove this hypothesis.

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References


