

Role of Steroid in Complicated Dengue Fever Attending A Tertiary Care Hospital- A Therapeutic Challenge

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Abstract- Pathogenesis of complicated dengue fever is poorly understood but there is evidence that immunoactivation plays important role behind the manifestations of severe dengue. Currently no definitive therapy is available for the management of severe dengue. In this study complicated dengue fever patients specially with ARDS and multiorgan failure were treated with steroid therapy and patients showed significant improvement. Thus this study states successful use of steroid in complicated dengue, a therapeutic challenge.

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I. Introduction

Dengue is the most common vector-borne viral infection of humans, with around 50 million infections estimated to occur annually and some 2.5 billion people living in areas of risk. A broad spectrum of disease manifestations is seen, ranging from asymptomatic infection to a systemic plasma leakage syndrome typically accompanied by thrombocytopenia and coagulation derangements. Severe plasma leakage may progress to life-threatening dengue shock syndrome (DSS).¹

The pathogenesis of severe dengue is poorly understood. Much of the evidence points to severe manifestations of dengue having an immunological basis, rather than being due to direct tissue damage by the virus. Vascular endothelial cell dysfunction, induced by cytokine and chemical mediators, is thought to be an important factor leading to plasma leakage. Current limited evidence suggests that transient disruption of the surface glycocalyx lining the vascular endothelium takes place. The cytokines tumour necrosis factor alpha, interleukin (IL)-2, IL-6, IL-8, IL-10, IL-12, and interferon gamma are significantly elevated in severe dengue when compared with uncomplicated dengue fever. Complement activation is a feature of severe dengue, and complement levels correlate with disease severity.²

Corticosteroids are highly effective anti-inflammatory agents, frequently employed as adjunctive therapy in disease states where the host immune response is thought to contribute significantly to disease pathogenesis.¹ Their clinical use in septic or inflammatory shock has, however, been fraught with controversy. However, this controversy is yet unresolved, and currently the guidelines for the treatment of severe sepsis recommend corticosteroids in low doses only in patients with refractory shock, and, furthermore, do not recommend the differentiation between patients with and without an adequate adrenocortical response.² Among patients with less severe sepsis there is some evidence that early administration of corticosteroids improves outcome and/or reduces the need for hospitalization. There is also a growing body of work indicating that steroids modulate the function of the endothelial glycocalyx and may prevent damage to this layer.¹ Nonetheless, in sepsis, corticosteroids are generally safe, with hyperglycemia and hypernatremia the only clinically significant adverse effects. Though there have been concerns previously that corticosteroids may increase the incidence of superinfection and gastrointestinal bleeding, these are largely unsupported. The beneficial effects of low-dose corticosteroids in septic shock are presumed to be due to restoration of vascular reactivity to vasopressor agents and not their immunosuppressive effects. Lack of vascular reactivity to vasopressors is not considered to be the main mechanism of shock in dengue, and thus the evidence from severe sepsis cannot be directly extrapolated to dengue.²

II. Materials And Methods

We have given steroid therapy to dengue patients in the initial days of illness when disease complications just started to develop but not too early or too late.

Mrs Soma Manna, 38/F, presented to us with history of fever for 3 days associated with epigastric pain. Her BP was 90/60, PR- 110/min. She also c/o increased menstrual bleed both in duration and amount for this cycle. During her hospital stay she became drowsy. She also c/o respiratory distress. Chest examination revealed b/l basal crepitation with diminished breath sound. SpO₂ was 90% in room air. CXR showed b/l pleural effusion. USG W/A showed mild hepatomegaly with mild ascites. Platelet count diminished upto 11000. SGOT/SGPT was 8200/7600. LDH was 5100. Amylase/Lipase was 247/232. NS1Ag and Dengue IgM both were positive in high titre. Subsequently she developed ARDS with multi organ failure. After receiving steroid therapy her condition improved gradually though she developed bradycardia which also normalised subsequently. Patient was discharged in clinically and hemodynamically stable condition.

Mrs. Kalpana Mondal, 50/F, admitted with c/o fever for 10 days associated with weakness, respiratory distress, facial puffiness and pedal edema with decreased urine output. Dengue IgM was positive. Her PR was 136/min, BP- 100/70. JVP was raised. Chest examination revealed b/l crepitations with pleural effusion. Her platelet count was 75000. SGOT/SGPT was 185/156. Creatinine was 1.1. She was given steroid therapy along with other conservative management. Patient condition gradually improved. Pulse rate normalised. Swellings subsided. She was then later discharged in stable condition.

Mrs. Angurbala Mondal, 60/F, known hypertensive on tab. Amlodipine 5mg od, presented to us with c/o fever for 7 days along with weakness, anorexia and vomiting. She was off amlodipine for last 7 days. At presentation her BP was 90/60. PR 104/min. She was sick looking. Her chest examination revealed right sided diminished breath sound but no crepitations was present. CXR showed right sided pleural effusion. Her platelet count diminished upto 30000. SGOT/SGPT was 124/30. Amylase/Lipase was mildly elevated. She was given steroid therapy along with other conservative management. Patient condition gradually improved and later discharged in stable condition.

Mrs. Pratima Ghosh, 60/F, admitted with c/o fever for 6 days associated with hematuria. NS1Ag and Dengue IgM both were positive. Her platelet count was 10000. BP- 100/60. PR-86/min. Chest examination showed right sided diminished breath sound with mild crepitations. CXR showed right sided pleural effusion. SGOT/SGPT was 250/70. She was given steroid therapy along with other conservative management. She was also given 2 units of platelet transfusion. Patient condition gradually improved and later discharged in stable condition.

Mr. X, 55/M, presented to us with c/o fever for 2 days associated with weakness, myalgia. His BP was 90/60, PR was 110/min. Patient was sick looking. Chest was b/l clear. NS1Ag was positive. He was given steroid therapy along with other conservative management. Later dengue IgM also became positive. His condition improved gradually. BP became 130/80. General condition improved.

Mrs, Y, 40/F, presented to us with fever for 3 days associated with myalgia, arthralgia, generalised erythematous rash. PR was 106/min, BP was 100/60. Chest was b/l clear. During hospital stay patient condition deteriorated. Pleural effusion developed. Usg w/a showed grade I fatty liver with mild ascites. SpO₂ dropped upto 90% in room air. Platelet count became 30000. SGOT/SGPT was 752/842. Amylase/lipase was 424/524. 24 hour urinary protein was 750mg. BP became 90/60. PR became 64/min. Subsequently she developed ARDS with multi organ failure. She was on conventional conservative management. She was then given steroid therapy. Condition improved gradually and she was later discharged in clinically and hemodynamically stable condition. At follow up visit after 3 weeks 24 hour urinary protein was found to be 120 mg.

III. Discussion

The Dengue infection results in significant morbidity and mortality worldwide. The current recommended treatment is largely supportive, with careful fluid replacement and with no specific treatment being available at present.³ The earliest evidence of possible benefit of corticosteroids in dengue came from a small randomized controlled trial, in which children with dengue shock syndrome were treated with a tapering dose of hydrocortisone for 3 days; a statistically significant mortality benefit was seen in older children (8 years and over). Several clinical trials were conducted between 1973 and 1988, with varying results. Corticosteroids are not recommended treatment in the WHO dengue guidelines. The main criticism of this recommendation is that it is based on poor-quality evidence, thus the interest in corticosteroids for treating dengue has continued.²

There is a paucity of high-quality evidence regarding the effects of corticosteroids in dengue, either in prevention of complications or treatment of established shock. However, the apparent beneficial effects of corticosteroids given for severe shock cannot be ignored, given the high mortality associated with the most severe forms of dengue. There is a definite need for an adequately powered and carefully designed randomized controlled trial of high-dose corticosteroids in the treatment of patients with severe dengue shock syndrome. Justification for such a trial is supported by the fact that no major adverse effects have been demonstrated with the administration of corticosteroids in dengue. The controversy on the effects of corticosteroids in dengue arises from the lack of good-quality trials and the overemphasis of poor-quality evidence from early studies.²

In our study we found that timely steroid therapy can lower down both mortality and morbidity rates in patients with complicated dengue fever.

IV. Conclusion

Considering immune mediated pathogenesis, high mortality rate and non availability of any effective treatment of complicated dengue fever, steroid therapy may provide a glimmer of hope which may halt disease progression leading to decreased morbidity and mortality if given timely with appropriate patient selection. But along with its favourable effects steroid therapy may also bring an array of complications when given to acutely ill patients. Hence the efficacious role of steroids in complicated dengue fever can be confirmed when applied to a larger population and by conducting well designed studies which may eventually open a new horizon in management of dengue.

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