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Letter to the Editor

Effect of a single dose of methyl prednisolone as rescue medication for patients who develop hypotensive dengue shock syndrome during the febrile phase: a retrospective observational study

The dengue fever (DF) epidemic in 2009 in Sri Lanka resulted in nearly 370 deaths (1.4% case fatality), mainly adults.[1] Although dengue shock syndrome (DSS) is thought to occur during the immediate afebrile phase of dengue infection, we encountered adult patients developing hypotensive DSS during the febrile phase. Although steroids have been shown to decrease cell infection rates and inhibit pro-inflammatory cytokines,[2,3] existing data do not recommend routine use of steroids in the management of DF.[4] However, due to the higher-than-usual mortality during the current epidemic here, many clinicians used steroids empirically, usually as rescue medication.

Studies that have assessed the effects of steroids in DF have all been in children.[5] Some show no benefit in established DSS,[6,7] while two have shown benefits with high-dose methyl prednisolone.[8,9] A possible role for steroids in complicated adult DF has not been investigated.

The management of dengue patients in our hospital in 2009 was based on the World Health Organization protocol, and regular meetings and audits were carried out in order to maintain uniform standards of care across medical units. In our unit a single dose of intravenous methyl prednisolone 1 g intravenous over 20 min was given as rescue medication to highly selected patients who developed hypotensive DSS (supine systolic blood pressure $<$100 mmHg and a postural drop of $\geq$20 mmHg with a pulse pressure $\leq$20 mmHg together with the presence of or rapidly developing ascites or pleural effusions and peripheral vascular collapse[10]) during the febrile phase (with no evidence of secondary bacterial infection), in addition to the currently recommended management. Clinical and management data of 23 such patients (group A) were retrospectively compared with 32 comparable patients from other units who did not receive methyl prednisolone (group B). The groups were comparable with regard to age, sex, duration of illness, and clinical and laboratory parameters at the time of admission and when hypotensive DSS was detected (Table 1). Out of patients with severe DSS, 3/23 died in group A compared to 15/32 in group B (p = 0.01). Group B required significantly more intensive care treatment and resuscitation fluids (crystalloids,

Table 1
Comparisons of clinical, biochemical, and hematological parameters, management and outcome. Statistical analysis was done using Stata 8.2 (Stata Corp., College Station, TX, USA). Statistical significance was assessed using the Wilcoxon rank sum test for numeric variables and Fisher's exact test for categorical variables

	Group A, mean (SD)	Group B, mean (SD)	p-Value
Parameters on admission			
Age (years)	31 (12)	34 (13)	0.42
Sex (M: male, F: female)	23 (M: 7, F:16)	32 (M: 13, F:19)	
Illness days	3.8 (1.2)/3 (2–6)	3.9 (0.71)/3 (2–6)	0.33
Fever (°F)	102 [=38.8 °C] (0.92 [=−17 °C])	101 [=38.3 °C] (2 [=−16 °C])	0.07
Pulse rate (per min)	93 (14)	101 (12)	0.20
Systolic BP (supine) mmHg	103 (15)	106 (13)	0.94
Diastolic BP (supine) mmHg	67 (9.9)	66 (14)	0.83
WBC ($\times 10^9$/l)	3.5 (1.5)	3.8 (1.3)	0.39
Hb (g/dl)	14 (2.9)	13 (0.71)	0.60
PCV (dl/l)	42 (8.6)	42 (4.2)	0.53
Platelet count ($\times 10^9$/l)	70 (63)	36 (30)	0.27
Parameters at diagnosis of severe illness requiring resuscitation			
Time since onset of illness (days)	5.6 (1.8)	5.9 (1.7)	0.69
Time since admission (days)	2.4 (1.6)	2.5 (1.5)	0.7
Fever (°F)	102 (1)	102 (2.6)	0.4
Pulse rate (per min)	94 (12)	101 (19)	0.06
Systolic BP (supine) mmHg	91 (12)	87 (38)	0.59
Diastolic BP (supine) mmHg	72 (11)	73 (22)	0.24
Hb (g/dl)	14.2 (3.1)	14.0 (0.8)	0.41
PCV (dl/l)	46 (7.2)	47 (6.3)	0.6
Platelet count ($\times 10^9$/l)	25 (13)	19 (6.2)	0.45
Pre-resuscitation IV crystalloids (l/24 h)	1 (0.13)	2 (0.6)	0.000
Resuscitation crystalloids, l/h	0.32 (0.098)	0.51 (0.093)	0.0003
Resuscitation FFP (units; 150 ml)	2 (1.1)	5 (2.4)	0.001
Resuscitation platelets (units)	2.3 (2)	6.8 (3.7)	0.027
Resuscitation colloids l/h	0.036 (0.13)	0.69 (0.46)	0.0007
SGPT (maximum) IU/l	286 (247)	762 (1349)	0.24
SGOT (maximum) IU/l	814 (1558)	2964 (3763)	0.04

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Table 1 (*Continued*)

	Group A, mean (SD)	Group B, mean (SD)	*p*-Value
Myocarditis	18/23	20/32	0.25
Encephalitis	2/23	1/32	0.565
Outcome			
Deaths (out of severe DSS)	3/23	15/32	0.010
Deaths (out of all dengue patients)	3/327	15/628	0.15
Time to defervescence (h)	1.4 (2.3) (n = 21)	17.2 (6.2) (n = 30)	0.000
Hemodynamic stability (h)	5.8 (5.8) (n = 20)	18.2 (10.2) (n = 17)	0.000
Hematological recovery (days)	2.1 (0.86) (n = 20)	3.4 (1.2) (n = 17)	0.013
Proportion needing intensive care	8/23	28/32	0.000
Total hospital stay (days)	7.9 (2.6) (n = 20)	12.2 (1.3) (n = 17)	0.001

SD, standard deviation; BP, blood pressure; WBC, white blood cell count; Hb, hemoglobin; PCV, packed cell volume; IV, intravenous; FFP, fresh frozen plasma; SGPT, serum glutamic pyruvic transaminase; SGOT, serum glutamic oxaloacetic transaminase; DSS, dengue shock syndrome.

colloids, fresh frozen plasma, and platelets) compared to group A. In survivors, the mean time to hemodynamic stability in group A was 5.8 h compared to 18.2 h in group B.

These preliminary observations seem to suggest that a timely single dose of intravenous methyl prednisolone may benefit adult patients who develop hypotensive DSS during the febrile phase of DF. We recommend randomized clinical trials to address this issue.

Ethical approval: Permission to present our data was obtained from the Ethics Committee, Faculty of Medicine, University of Kelaniya, Sri Lanka.

Conflict of interest: No conflict of interest to declare.

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