Vitamin E and Vitamin C Supplementation does not Improve the Clinical Course of Measles with Pneumonia in Children: a Controlled Trial

Pneumonia is an important cause of measles-associated deaths [1]. We evaluated two dietary anti-oxidants, vitamins E and C as adjunct therapy of pneumonia in children with severe measles in a randomized double masked placebo controlled trial.

Children aged 1–10 years admitted with illness compatible with measles (generalized maculopapular rash with fever and at least one of cough, coryza or conjunctivitis) and associated pneumonia at the Infectious Diseases Hospital, Kolkata were randomized to (a) vitamin E and vitamin C (each 200 mg twice daily for 6 days) and (b) placebo supplemented groups and the impact on the clinical course of illness was evaluated. Outcome measures were, time to resolution of fever (skin temp 98°F), tachyponea (rate <40/min for 1–5 yrs and <30/min for 6–10 yrs), difficulty to eat and/or drink, and a very ill status (as judged by the clinician not aware of treatment allocation) during the 6 days of treatment. The Ethical Review Committee of the Institution approved the study. Parents gave informed consent. All patients received a single oral dose of vitamin A 200 000 IU at admission. A child was considered clinically 'cured' or 'much improved' based on, (a) alertness and general well being, (b) resolution of tachypnoea and or respiratory distress, (c) how well the child eats/drinks, and (d) resolution of fever. We measured serum α-tocopherol in a sub-sample using HPLC and TBARS (thiobarbituric acid reacting substances) by methods described earlier [2] at admission and discharge. We used Cox proportional hazards regression model to compare the duration of the illness indicators.

Seventy one children were recruited, 36 in the treatment and 35 in the placebo group. For two children in the placebo group consent was withdrawn. The patients had poor immunization record. All were clinically diagnosed to have pneumonia. After adjusting for age and sex there was no significant difference in the recovery rate ratios (Cox proportional hazards model) between the treated and control groups for the illness indicators (Table 1). None died.

Serum α-tocopherol concentration was 2.3-fold higher in the treated group compared to controls at discharge (Table 2). In both groups it increased from

TABLE 1

Effect of vitamins E & C treatment on the recovery from measles pneumonia: Cox proportional hazards model with duration of 'illness indicators' as dependent variables

Indicators	Very ill*	Feeding difficulty*	Fever*	Tachypnoea*
†Recovery rate ratio (95% CI)	1.11 (0.61–2.04)	0.83 (0.50–1.36)	0.61 (0.34–1.08)	0.87 (0.49–1.54)
p value	0.74	0.45	0.09	0.63

*Separate models were fitted for each illness indicator, adjusted for age group (1–5 yrs, 6–10 yrs) and sex.
†Ratio of the hazards rate for recovery in the group supplemented with vitamins E & C to the group supplemented with placebo. Values >1 favour vitamin E & C supplemented group. The value indicates the recovery rate ratio at any given time point during the period of observation.

TABLE 2

Serum α-tocopherol (on a sub-sample) and TBARS (thiobarbituric acid reacting substances) values in the two groups

	Study	Control
Serum α-tocopherol (mcg/dl)*		
Admission	[2]330.1 ± 187.2 ($n=13$)	[1]383.8 ± 143.9 ($n=15$)
Discharge	[2]1226 ± 643[3] ($n=14$)	[1]527.2 ± 276.4[3] ($n=11$)
TBARS (μm/l)		
Admission	5.3 ± 1.81 ($n=36$)	5.5 ± 1.23 ($n=31$)
Discharge	[4]4.9 ± 1.44[6] ($n=33$)	[4]5.5 ± 1.57 ($n=30$)
Difference between admission & discharge values	[5]0.604 ± 1.30 ($n=33$)	[5]−0.090 ± 1.45 ($n=29$)
Healthy children of same age group	3.42 (0.82)[6] ($n=29$)	–

[1]$p=0.17$, [2]$p=0.0002$, [3]$p=0.002$, [4]$p=0.12$, [5]$p=0.051$, [6]$p=0.0001$.

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the admission values. TBARS values were high at admission and remained high and comparable between the two groups at discharge. The decrease in TBARS values tended to be less in the study group compared to the controls ($p=0.051$). Both admission and discharge values were significantly higher compared to a group of non-diseased children from the same socio-economic and age group.

In spite of the putative role of oxidative stress in conditions like viral infections, inflammatory bowel diseases, immune response, atherosclerosis and neurodegenerative disorders [3–5] and childhood diseases, [6] vitamin E and C did not beneficially influence the course of illness in children with measles and pneumonia. While the TBARS values, an indicator of oxidative stress, were high antioxidant vitamins did not improve them. Oxidative stress may even play a beneficial role in diverse processes in nature that includes cell-proliferation, gene activation and expression, and activation of spermatozoa [7]. We need a better understanding of oxidative processes in growing children that would allow us to better define the role of nutritional antioxidants.

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