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RESEARCH ARTICLE

Study of Effect of Vitamin C on Thrombocytopenia in Patients of Simple Dengue Fever

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ABSTRACT:
Introduction: Dengue is the most common arboviral disease worldwide. Patients with dengue can experience a variety of serious complications including thrombocytopenia, bleeding and shock. These problems are thought to be a result of oxidative damage. Vitamin C, a potent anti-oxidant, is recommended in many viral diseases empirically. Hence this study was conducted to assess the efficacy of vitamin C in simple dengue fever.
Methods: Patients (Age:18-60 y) of simple dengue fever, diagnosed by NS-1 test were included in the study, after obtaining informed written consent. Vitamin C was administered as Tab. CELIN or Tab. Bio-C orally (p.o.). They were divided into three treatment groups viz. Control, CELIN and Bio-C. They were assessed clinically and biochemically, on day 1,3,5 and 7. Laboratory parameters included hemogram, BSL, platelet count, SALT and serum creatinine. Results were analyzed by ANOVA.
Results: Between August 2010 and September 2012, 110 patients of simple dengue fever, attending the OPD of Dhanashree Hospital, New Sangavi, Pune 411027 were enrolled in the study. They were given one of the three treatments viz. CELIN-50,Bio-C-38 and Control-22.Ten patients were lost in follow up. Data of 100 patients, who attended all 5 visits were subjected to statistical analysis. Baseline characteristics were similar across the groups. All patients recovered fully and there were no serious adverse events. Vitamin C treatment, either CELIN or Bio-C, was associated with better clinical response ($P<0.05$) and significantly ($P<0.05$) lesser decline in platelet count as compared to control. Patients in BIO-C (n=35) group recovered faster.
Conclusions: Use of vitamin C was associated with rapid clinical & biochemical recovery in patients of simple dengue fever. Considering the low cost and lack of toxicity, vitamin C may be recommended in all patients of dengue fever.
Key words: BIO-C, Dengue fever, Thrombocytopenia, Vitamin C.

INTRODUCTION

Dengue is a flavi-virus infection, which has become a worldwide public health concern. In India, epidemics are becoming more frequent and are exhausting the limited public health resources.[1]The major threat of dengue fever is from thrombocytopenia, bleeding manifestations and shock. There is as yet no satisfactory treatment for thrombocytopenia, which might be caused by oxidative damage.[2]Vitamin C, a well known potent anti-oxidant, has been used in common cold and idiopathic thrombocytopenic purpura.[3,4]It has been recommended empirically in the treatment of viral infections. However, there are no controlled studies evaluating its efficacy. Hence, the present study was designed to assess the efficacy of vitamin C in patients of simple dengue fever.

Patients & Methods:

This was an observational study. Patients attending the OPD of Dhanashree Hospital, New Sangavi, Pune 411027, likely to be suffering from dengue fever were screened by platelet count and were included in the study if tested positive for NS-1 antigen.

Patients were excluded if they fulfilled one or more of the following criteria :

1.Patients with platelet count<10,000/cmm or requiring transfusion of platelets,2.patients with overt bleeding manifestations or with family history of bleeding disorders,3.patients with severe dengue and 4.those on drugs affecting platelet function.

Informed written consent was obtained and then they were divided into three groups viz. **Control, CELIN and Bio-C.** CELIN group was given Tab. CELIN **(Glaxo)** containing ascorbic acid 500mg two tablets twice daily, Bio-C **(Amway)** group received one tablet twice daily, while patients in the control were treated symptomatically with paracetamol, domperidone or pantoprazole. This treatment was common to all the groups. Each tablet of Bio-C contains 1000 mg ascorbic acid and citrus multi-flavonoid complex containing phytonutrients. These drugs were given for seven days. Patients were assessed clinically and biochemically on days 1,3,5 and 7. Findings of clinical examination like fever, bodyache, retro-orbital pain, rash etc. were scored on a scale of 0 to 4,as absent, mild, moderate and severe respectively. Laboratory investigations included hemogram, including platelet count which was done on days 1,3,5 and day 7; while BSL,NS-1,Serum alanine aminotransferase (SALT) and serum creatinine were estimated on day 1 and day 7. Compliance to the drugs was assessed by return tablet counting. The patients were closely observed for any bleeding manifestations. Side effects to treatment if any were recorded with the help of a questionnaire. Patients requiring platelet transfusion after enrolment in the study were given platelets and thereafter the study was terminated in them.

STATISTICAL ANALYSIS:

Results obtained were analyzed by ANOVA and post-hoc test and P value < 0.05 was considered as statistically significant.

RESULTS:

Total 135 patients were screened. Out of these, 11 cases were NS-1 negative, 14 patients did not attend all the visits and 10 patients developed complications and required platelet transfusions (**Control**=5, **CELIN**=3 & **Bio-C**=2). Hence total patients in the study were 100. Out of these, 45 were treated with CELIN, 35 received Bio-C while 20 were in the control group. There was no significant difference in the baseline clinical and biochemical features between the groups (Table 1).

Table 1: Baseline Characteristics of patients in different treatment groups:

Parameters	**Control (n=20)**	**Celin (n=45)**	**Bio-C (n=35)**
Age (y)	35±11	34±12	38±13
Sex (M/F)	14/6	30/15	24/11
Hb (g/dl)	12.5 ±1.4	12.8±1.5	13.1±1.7
WBC (cells/cmm)	3200±140	3500±160	3400±150
BSL (mg/dl)	103±18	110±12	108±17
SALT (IU/l)	32±5	30±6	28±7
S. creatinine (mg/dl)	0.8 ±0.1	1.2±0.1	0.9±0.1
Platelets (10^3/L)	144±31	135±35	142±34

Figures are expressed as Mean ± SD. No significant difference between the groups.

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It was found that in patients treated with Vitamin C, either **CELIN** or **Bio-C**, the severity of illness decreased significantly on day 3 and day 5. However patients in all the groups improved clinically by the end of 7 days. **(Table 2 & Figure 1)**.

Table 2: Effects of different treatments on clinical severity of illness

Group/ Day of assessment	**Control (n=20)**	**CELIN (n=45)**	**Bio-C (n=35)**
Day 1	12.4+/-2.5	12.0+/-3.2	12.2+/-2.8
Day 3	10.8+/-2.3	**9.1+/-2.2***	**8.0+/-2.1***
Day 5	7.0+/-1.8	**4.8+/-1.1#**	**3.8+/-0.9#**
Day 7	2.0+/-0.8	1.6+/-0.7	1.0+/-0.5

Figures are expressed in Mean+/-SD,*,#:P<0.05 as compared to control.

Platelet counts reduced in all groups on day 3 and began to increase later. However, the increase was more rapid in Vitamin C treated groups, especially in Bio-C group. Counts greater than 1,00,000/cmm were achieved in significantly (P<0.05) more number of patients treated with Vitamin C (**C**: 5/20, **CELIN**: 25/45, **Bio-C**:28/35) **(Table 3 and Fig.2).**Similarly higher number of patients became NS-1 antigen negative in CELIN and Bio-C groups as compared to control. The changes in SALT,BSL and serum creatinine levels were not statistically significant.

Table 3: Effect of different treatments on laboratory parameters in patients of simple dengue fever

Parameters	CONTROL				CELIN				Bio-C			
	D1	D3	D5	D7	D1	D3	D5	D7	D1	D3	D5	D7
Hematocrit (%)	50 ± 3.5	47 ± 3.2	45 ± 3.1	45± 3.0*	52 ± 3.7	47 ± 3.3	44 ± 3.2	40.7 ± 2.8*#	51± 3.6	46± 3.1	44± 2.9	41± 2.8*#
SALT (iu/l)	38.50± 11.5			35.80± 10.7	40.40 ± 12.5			36.4 ± 11.3	38.8± 12.3			32.6 ± 11.6
Plat.Count ($\times 10^3$)	95± 21	35 ± 4.5*	52 ± 14*	70± 17.5*	97 ± 22.5	52 ± 14*	65 ± 16*#	100 ± 20.5#	93± 19.3	61± 15.2*	77± 18.5*#	110± 22.4#
NS-1 (positive/negative)	20/0			12/8	45/0			24/21*	35/0			11/24*

Figures are expressed in mean ± SD

* denotes comparison with D1 value, # denotes comparison with control,
* # P< 0.05

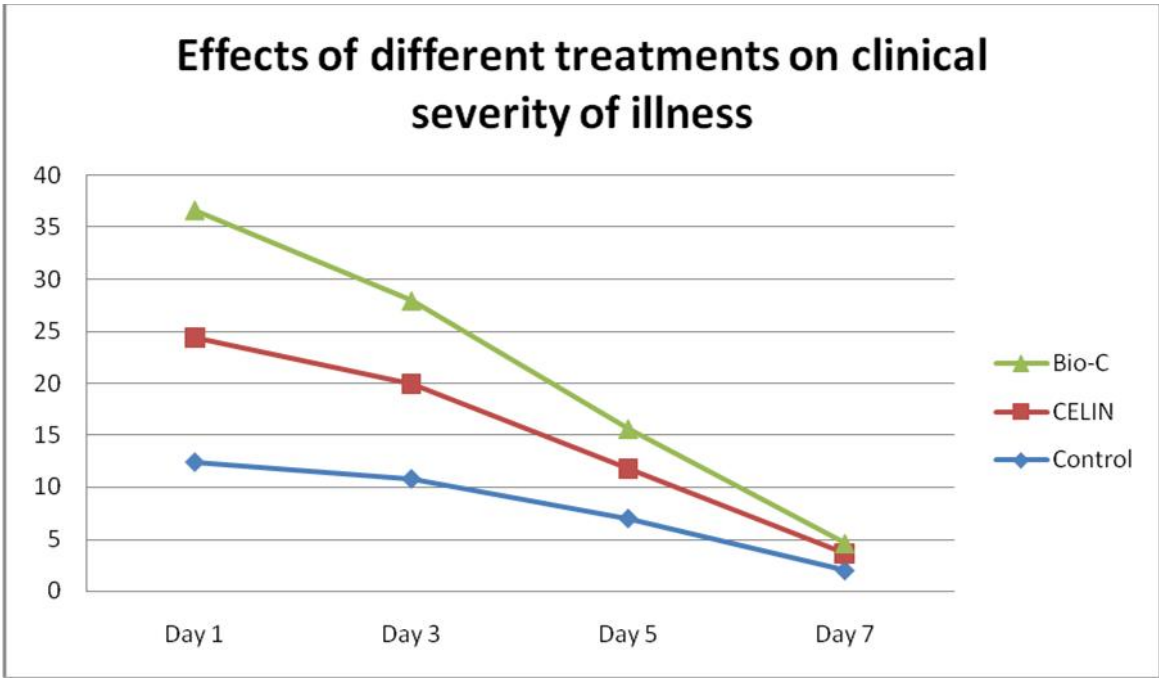

Figure 1: Effects of different treatments on clinical severity of illness

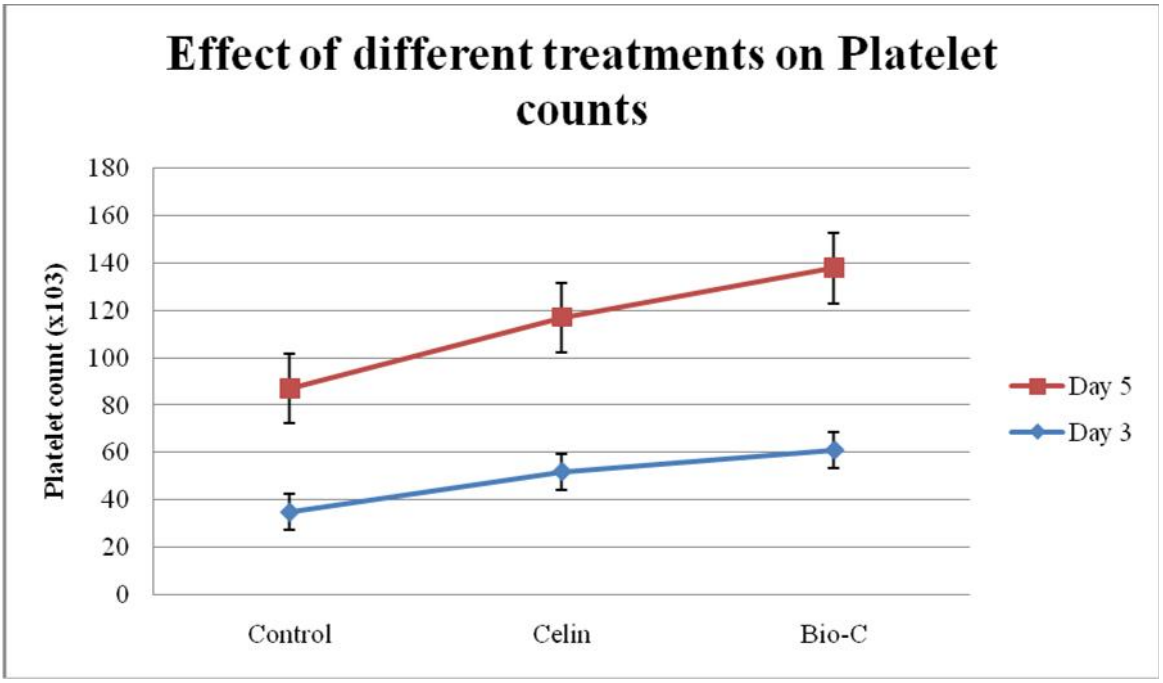

Figure 2: Effects of different treatments on platelet counts

DISCUSSION:

Results of this study show that administration of vitamin C to patients of simple dengue fever led to rapid improvement in clinical features and early restoration of thrombocytopenia. Although with passage of time, the platelet counts increased in all the groups, the increase was faster and greater in the groups receiving vitamin C, with significant differences being apparent on day 5 and day 7.The proportion of cases achieving platelet counts > 1,00,000/cmm was also significantly greater in groups receiving vitamin C on day 5 as compared to the control group.

The greatest danger of dengue fever is from the ensuing thrombocytopenia with its attendant consequences. There is as yet no satisfactory treatment for the dengue virus induced thrombocytopenia, except platelet transfusion.[5] Use of vitamin C may decrease the need for platelet transfusion and prevent its overuse in such cases.

The pathogenesis of thrombocytopenia in dengue fever is also not well known. [6] There is some evidence that increased oxidative stress might play some role.[5] Vitamin E, a fat soluble vitamin, is a powerful anti-oxidant.[7]Previously, Vaish et al [8] have obtained similar results with vitamin E. They enrolled 66 cases of dengue fever with similar degree of thrombocytopenia,27,000 to 28,000/cmm. Thirty three patients were treated with vitamin E 400mg/d for seven days. The platelet count improved faster by day 4 and greater in these patients as compared to control group. Only two patients from vitamin E group required platelet transfusion as compared to 5 out of 33 in the control group.

Our results are similar to this study. However our patients did not have severe degree of thrombocytopenia, as we included only early cases of dengue fever with mild thrombocytopenia. Ascorbic acid, a water soluble vitamin, is also reported to exert anti-oxidant action[9],which might explain the benefits observed in the present study. The results were better in patients receiving BIO-C than those treated with CELIN; which might be due to phytonutrients present in BIO-C. However, this difference did not achieve statistical level of significance. Better clinical improvement in patients treated with vitamin C cannot be explained at present.

Our study has many limitations like, small sample size, single centre, mild cases etc. However, we are not aware of any similar study done with vitamin C in such cases so far. The combination of vitamin C and E may be more beneficial due to probability of exerting actions, both intra & extracellularly and additive anti-oxidant effects**.** However, further multicentric,double blind randomized studies with large sample size are necessary.

CONCLUSIONS:

This study provides some rationale for the use of vitamin C in dengue fever. It appears from our study that Vitamin C may accelerate the replenishment of the circulation with platelets in dengue fever, thereby reducing the risk of bleeding and the need for platelet transfusion. As vitamin C is cheap,and relatively free of serious adverse effects, it may be recommended in all patients of simple dengue fever.

REFERENCES:

1. Yeolekar ME. Dengue. In: Shah SN, editor. API textbook of medicine, 8th edition. The Association of Physicians of India; 2008:Vol 1:p. 113-116.
2. World Health Organization. Dengue: Guidelines for diagnosis, treatment, prevention and control, NewEdition, 2009. Available from:http://www.who.int/rpc/guidelines/9789241547871/en/.[accessed on 2011 Jun 4].
3. Cohen HAet al. Treatment of chronic idiopathic thrombocytopenic purpura with ascorbate.ClinPediatr (Phila)1993;32:300-302.
4. Hemila H, et al. Vitamin C for preventing and treating the common cold. Available in the Cochrane Database of Systemic Reviews; Issue 4,Chichester:John Wiley;2004.
5. Gil L, Martínez G, Tápanes R, Castro O, González D, Bernardo L, *et al.* Oxidative stress in adult dengue patients. Am J Trop Med Hyg 2004; 71: 652-7.

6. Chairulfatah A, Setiabudi D, Agoes R, Colebunders R. Thrombocytopenia and Platelet Transfusions in Dengue Haemorrhagic Fever and Dengue Shock Syndrome. Dengue Bull 2003;27:138-43.
7. Sies H, Stahl W. Vitamins E and C, beta-carotene, and other carotenoids as antioxidants.Am J ClinNutr 1995; 62: 1315-21.
8. Vaish A, Verma S, AgarwalA, GuptaL, Gutch M. Effect of vitamin E on thrombocytopenia in dengue fever. 2012; 5 (4): 282-285.
9. Lei HY, Huang KJ, Lin YS, Yeh TM, Liu HS, Liu CC. Immunopathogenesis of Dengue Hemorrhagic Fever. Am J Infect Dis 2008;4:1-9.

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