

Original Research Article

Effect of *Carica papaya* leaf extract (CPLE) on thrombocytopenia among dengue patients of tertiary care hospital, Chitradurga, India

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ABSTRACT

Background: Dengue is a global public health problem and thrombocytopenia associated with it is a serious complication for which there is no specific treatment available. This study was done to assess the effect of *Carica papaya* Leaf Extract (CPLE) on thrombocytopenia associated with Dengue and to study other clinical parameters of dengue.

Methods: A longitudinal study conducted in Department of General Medicine, BMCH, Chitradurga, from September 2017 to March 2018. All the participants were randomized into two groups by simple randomization by lot method. Study group was given *Carica papaya* Leaf Extract (CPLE) and routine supportive treatment for other group. The patients were followed from the day of admission till their discharge from hospital. The platelet counts and other baseline hematological investigations, duration of hospital stay in both the groups were compared statistically by unpaired t-test.

Results: There were total 127 males and 73 females. Age groups were comparable in both the groups. Most common presenting complaints were fever (100%) followed by headache (85%), myalgia (81.4%), fatigue (75%), arthralgia (65%). On admission baseline investigations were done and mean levels of both groups were compared. It was found that there was only significant difference of mean RBC levels ($p=0.045$). When followed up with daily platelet counts of both the groups, it was seen that there was increase in platelet counts in study group compared to placebo group and on third day there was significant difference between both ($p=0.002$). It was also found that discharge rate is earlier in study group than placebo group.

Conclusions: *Carica papaya* leaf extract accelerates the increase in platelet count and reduces the hospital stay. So, it can be used as supplementary drug to reduce complications.

Keywords: *Carica papaya*, Dengue fever, Complications, Thrombocytopenia

INTRODUCTION

Dengue is one of the most common arboviral infection in humans which is transmitted by *Aedes* mosquitoes, mainly *Aedes* (*Stegomyia*) *aegypti* and also *Ae. albopictus*. The infection causes flulike illness, and occasionally develops into a potentially lethal complication or severe dengue, such as dengue

haemorrhagic fever and dengue shock syndrome. As per the World Health Organization, dengue has shown a 30-fold increase globally over the past five decades. Some 50 to 100 million new infections are estimated to occur annually in more than 100 endemic countries. Every year, hundreds of thousands of severe cases arise resulting in 20,000 deaths. Dengue is found in tropical and sub-

tropical climates worldwide, mostly in urban and semiurban areas.¹

Based on the data of National Vector Borne Disease Control Programme, in India during 2016, 129166 cases of dengue were reported with 245 deaths. Where as in Karnataka in 2016, 6083 cases of dengue with 8 deaths were reported.²

Four main characteristic manifestations of dengue illness are; continuous high fever lasting 2-7 days; haemorrhagic tendency as shown by a positive tourniquet test, petechiae or epistaxis; thrombocytopenia (platelet count < 100 x 10⁹/L); and evidence of plasma leakage manifested by haemoconcentration (an increase in haematocrit 20% above average for age, sex and population), pleural effusion and ascites.³

Any patient of fever with thrombocytopenia causes panic amongst the patient and their relatives about possibility of dengue. Thrombocytopenia is an important pointer to the diagnosis of dengue for the lay-person and the general physician. Also, thrombocytopenia is a contributor to bleeding, which appears to be the root cause to the patient and relatives, and therefore correction of the same may be a priority for the patient, although correction of thrombocytopenia does not figure as one of the mainline principles of dengue management.⁴

The management of dengue virus infection is essentially supportive and symptomatic. No specific treatment is available.³ There remains a lot of hue and cry about lack of agents, which can raise platelet counts, and shortage of platelet transfusions in the dengue season. People resort to a number of untested and unverified preparations and local remedies in order to increase their platelet counts with or without success.⁴ Therefore, there is an urgent need of development of alternative therapy for dengue.³

Several studies have been conducted to determine the usefulness of herbal medicine in curing dengue. Researchers have indicated that the juice of the leaves of the Carica papaya plant from the family Caricaceae helps to increase the platelet levels and have demonstrated definitive beneficial effects in these patients.⁵

So, authors conducted this study to know the effect of Carica Papaya Leaf Extract (CPLE) on thrombocytopenia associated with Dengue and to study other clinical parameters of dengue.

METHODS

This study was conducted in Department of General Medicine, BMCH, Chitradurga, from September 2017 to March 2018.

Inclusion criteria

- Age more than 18 years

- Diagnosed as dengue fever by NS1 or IgM antibody or Platelet count less than 1.5 lakh/mm³.

Exclusion criteria

- Patients with thrombocytopenia due to other causes
- Leukemia
- Idiopathic thrombocytopenic purpura
- Other fevers with thrombocytopenia like malaria, brucellosis, enteric fever

All the participants were randomized into two groups by simple randomization by lot method. Study group was given Carica Papaya Leaf Extract (CPLE) and routine supportive treatment for other group. Complete blood counts, platelet counts, haematocrit level, liver function test and renal function test for both groups were screened daily. The patients were followed from the day of admission till their discharge from hospital.

Statistical analysis

Data of both groups were entered in Microsoft Excel 2007 and analysed using SPSS software, version 20. Data tabulated as frequency tables and bar diagrams with comparison of both groups. The platelet counts and other baseline hematological investigations, duration of hospital stay in both the groups compared statistically by unpaired t-test.

RESULTS

Among 200 study participants, 100 were given regular supportive treatment and 100 were given caripill along with supportive treatment. There were total 127 males and 73 females. Age groups were comparable in both the groups i.e. majority belonged to the age group of 21-40 yrs (56% in study group and 57% in placebo group).

Table 1: Socio-demographic data of study participants.

Socio-demographic variables		Caripill	Placebo
Gender	Male	65	62
	Female	35	38
Age	<20 years	20	17
	21-40 years	56	57
	41-60 years	20	21
	>60 years	04	05
Religion	Hindu	85	94
	Muslim	15	06
Education	Graduate	05	14
	PUC	27	29
	High school	42	37
	Primary	24	12
	Illiterate	02	08
Marital status	Married	56	66
	Unmarried	44	34

Table 2: Baseline hematological investigations of study participants.

Baseline hematology investigations	Caripill	Placebo group	P value
Mean Platelet count	95247	98470	0.971
Mean Hb%	13.46	14.65	0.491
Mean RBC levels	4.89	4.76	0.045*
Mean WBC	4042.9	4523.06	0.456

Table 3: Comparison of mean platelet counts of both groups on hospitalized days.

Days	Caripill		Placebo		P value
	N	Mean PC	N	Mean PC	
Baseline	100	95247	100	98470	0.971
Day 2	100	94950	99	81141	0.211
Day 3	95	97270	95	71663	0.002*
Day 4	63	101936	94	81372	0.218
Day 5	54	111936	61	78098	0.04*
Day 6	44	82291	50	81860	0.768
Day 7	40	77770	43	36920	<0.01*

Most of them i.e. 85% and 94% in study group and placebo group respectively were Hindus. 42% and 37% of study group and placebo group respectively were educated upto high school (Table 1). Most common presenting complaints were fever (100%) followed by headache (85%), myalgia (81.4%), fatigue (75%), arthralgia (65%). Least common presenting features were melena (2.5%) and excess menstrual bleed (1.2%).

On admission baseline investigations were done and mean levels of both groups were compared. It was found that there was only significant difference of mean RBC levels (p=0.045) (Table 2).

On admission mean platelet count of study group was 95247 where as in placebo group it was 98470. (p=0.971). On 2nd day mean platelet counts of both the groups decreased to 94950 and 81141 respectively (p=0.211). But on third day among study group mean platelet count rose to 97270, where as in placebo group it was still 71663.

The mean difference among these two groups was found significant. (p=0.002). On 5th day, mean platelet count of study group and placebo group were 111936 and 78098 respectively (p= 0.04). But 6th day onwards platelet counts reduced in both groups. This may be due to increased rate of discharge among study group than the placebo group and also due to change in baseline levels of platelet counts. Overall this indicates that caripill (Carica Papaya Leaf Extract) tends to fasten the natural course of rate of platelet rise in dengue fever (Table 3).

When compared about the discharge rate among two groups, it was seen that discharge rate is earlier in study

group than placebo group. This shows that caripill is effective in treatment of dengue (Figure 1).

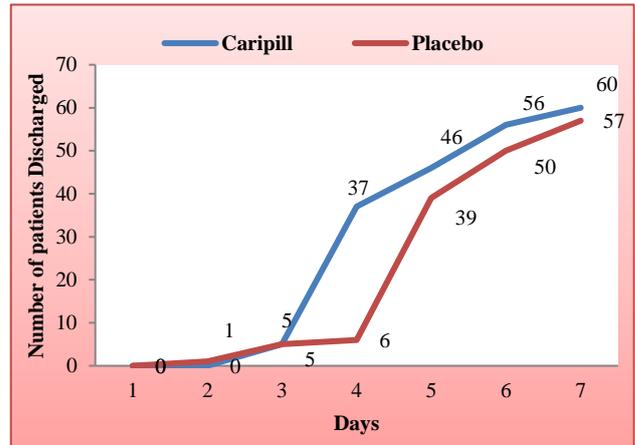


Figure 1: Number of patients getting discharged on respective days.

DISCUSSION

Thrombocytopenia is one of the associated conditions in dengue cases and can lead to DHF further aggravating the shock leading to a fatal state.

With respect to clinical features in present study, similar results were observed in a study conducted by Adarsh et al in Gulbarga, most common presenting features were fever (100%) followed by myalgia (82.5%), headache (75%), fatigue (55%), arthralgia (55%).⁶ Similar studies by Agarwal et al where fever, myalgias, headaches were predominant symptoms.⁷

In present study it is demonstrable that the subjects in the study group that received CPLE (Caripill) can reach faster and higher increase in platelet count as compared to the placebo group. In a similar study conducted in Malaysia by Subenthiran et al comparison of mean platelet count between intervention and control group showed that mean platelet count in intervention group was significantly higher than control group. (P < 0.01).⁸ Th results were also similar to a pilot study conducted by Gowda et al, and also by Kasture et al in Bangalore where it showed that after the treatment at the end of day 5, the median platelet count showed a significant increase in the intervention group and an insignificant rise in the control group as compared to baseline values.^{5,9} Another study by Juneja et al in Indore showed significantly increased the platelet count (p<0.05).¹⁰

A similar study conducted in Rajasthan by Gadhwal et al showed that 90% of control group patients were discharged as compared to 99% discharged in study group.³ This is similar to present study where discharge rate is earlier in study group than placebo group but in slower rate.

CONCLUSION

With rapid urbanization and global travel leading to drastic demographic changes, dengue is a threat to almost 40% of the world's population. There is still no specific treatment for dengue. *Carica papaya* leaf extract can be used as supplementary drug in acute febrile illness patients with thrombocytopenia. It accelerates the increase in platelet count and reduces the hospital stay thereby reducing the cost of hospitalization.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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