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ORIGINAL ARTICLE **OPEN ACCESS**

Study of Effectiveness of *Carica papaya* Leaf Extract (Caripill) Iin Management of Thrombocytopenia In Dengue

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ABSTRACT

Introduction: Dengue is a rapidly expanding global health problem. It is the most rapidly spreading mosquito borne viral disease with major failure complications. Dengue Virus is an arthropod- borne flavivirus associated with both hemorrhagic fever and shock. Aims and objective: To monitor the effect of caripill in increasing the platelet count in dengue so that the people can be treated with minimal side effects as offered by corticosteroids, by utilization of a natural product. Method: 40 subjects (n=40) diagnosed dengue cases were enrolled. Of these, 20 were randomized to a study group where they received a Caripill tablet in addition to the standard management of dengue. The remaining 20 in the control group received the routine standard management of dengue only. Results: Most subjects infected were between 18-35 years and the distribution in both the groups did not show any significant difference. The result showed a significant difference in the platelet rise in Test and the Control group. The rise in platelets in the test group was almost 64% as compared to the control group which was almost only 17%. The monitoring of platelet count clearly indicated that change in the platelet count is faster in the test group as compared to the control group. Conclusion: Drastic fall in platelet count is a matter of major concern in dengue. Caripill offers simple convenient cost effective safe and efficacious treatment for thrombocytopenia in dengue fever.

Key words: Dengue, Shock, Caripill, thrombocytopenia.

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INTRODUCTION

Dengue is a rapidly expanding global health problem. It is the most rapidly spreading mosquito borne viral disease with major failure complications. Dengue Virus is an arthropod- borne flavivirus associated with both hemorrhagic fever and shock.[1] The classical clinical presentation of Dengue Virus infection is characterized by abrupt onset of headache, myalgia and high fever, in addition to arthralgia, retro-orbital pain and hemorrhagic manifestations.

Dengue belongs to Flaviviridae with four serotypes of the virus. The epidemiology of the dengue fever in the Indian subcontinent has been very complex and has largely changed over almost six decades in terms of prevalent strains, affected geographical locations and severity of disease. [2] WHO currently estimates there may be 50-100 million dengue infections with half a million Dengue Hemorrhagic Fever worldwide every year, with an average fatality rate of around 5%. [3] The average total economic burden was estimated to be US$27.4 million (US$25.7-29.1). [4]

The mechanism behind the platelet reduction is not clear till date due to lack of suitable animal model studies. [5] Different mechanisms have been suggested to explain dengue associated thrombocytopenia, including bone marrow suppression and peripheral destruction of platelets. [6] In support of theory of bone marrow suppression studies have suggested reduced megakaryopoiesis at the onset of infection, which is normal at the time of clinical recovery. [7] The other main mechanism proposed is the increased autoimmune platelet destruction by DENV.

Currently there is no specific treatment for dengue; intensive supportive care is the most important aspect of management. Till now there is no vaccine or drug against dengue virus, therefore there is an urgent need of development of alternative solutions for dengue. The standard protocol for management includes symptomatic treatment with fluid management. The thrombocytopenia is not addressed till it gets lowered down to levels less than 20000per micro liters, where platelet transfusion is advocated. Corticosteroid is advised by some which is supposed to halt platelet destruction; however it is not preferred by all. [8, 9]The evolution of Caripill in the management of thrombocytopenia associated with dengue is significant as it would be better and viable options in fever associated with thrombocytopenia.

It is palatable, fewer side effects, decreases cost of hospitalization, cost effective, affordable and accessible.
The primary objective of this research is to monitor the effect of caripill in increasing the platelet count in dengue in a tertiary care hospital so that the people can be treated with minimal side effects as offered by corticosteroids by utilization of a natural product.

MATERIAL AND METHODS

Type of study: Open, labeled, randomized comparative study in a tertiary care hospital.
Place of study: Department of Medicine
Duration of Study: 2 months
A total of 40 subjects (n=40) diagnosed as dengue cases by NS1 antigen test admitted in a hospital were enrolled and randomized in this study. Exclusion and Inclusion criteria was set up and those meeting all the inclusion criteria's were allowed to participate. Of the total subjects, 20 will be randomized to study group where they received Caripill tablet 3 times a day for 5 days, in addition to the standard management of dengue. The remaining 20 in control group received the routine standard management of dengue, only. All the subjects were followed up every day for 5 days and their platelet counts were monitored daily.
Inclusion criteria:

- Subjects between 18-60 years of age
- Patient should be confirmed with the diagnosis of DF or DHF Grade 1, Grade 2.
- Platelet count of the Patient is below 100,000 and above 30,000per micro liter
- The patient's ALT/SGPT level is less than 165U/L
- The subject should give a willingly informed consent

Exclusion criteria:

- Patients diagnosed with Dengue Hemorrhagic Fever Grade 3 or 4
- Patient's platelet levels are less than 30,000 per micro liters
- Patient is either pregnant or lactating
- The patient has received blood products or blood transfusion during the current hospital stay or during last one month
- Serum creatinine of the patient is more than 1.4mg/dl (if female) or 1.5 mg/dl (if male)
- Patient has participated in another clinical trial within past one month.
- The investigator can exclude patient at his/her discretion depending on the condition of the patient.

RESULTS

All the 40 subjects enrolled were diagnosed as dengue cases by NS1 Antigen test. After administering Caripill and standard management (Corticosteroid) to the test group (n=20) and only Standard management to control group (n=20); everyday platelets of both groups were monitored.
Demographic Characteristics:

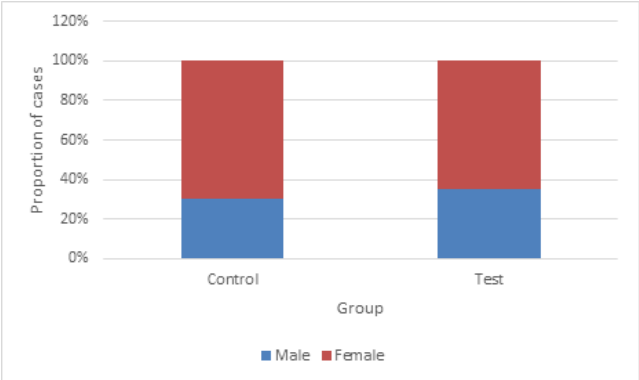
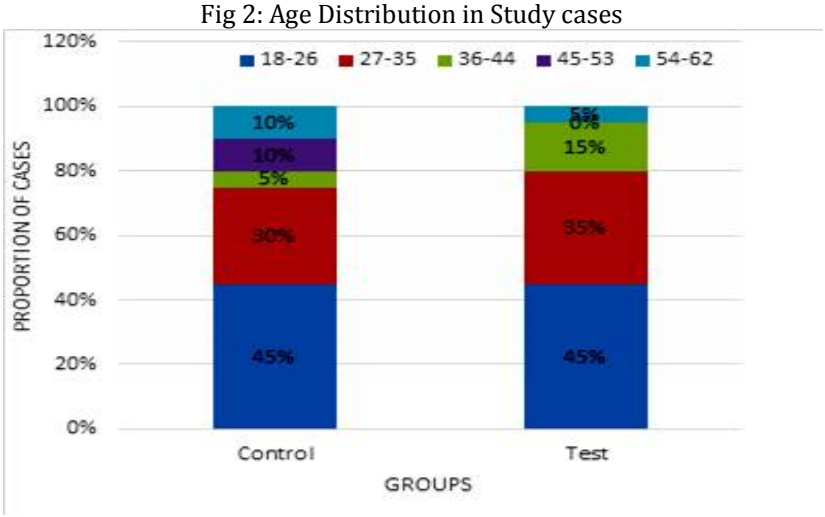


Fig 1: Sex Distribution in Study Cases

The above distribution reveals that 70% cases in the control group were females, which is comparable to the test group in which 65% were females and the difference was not significant [Fig 1].

Fig 2: Age Distribution in Study cases



Above data states that, 80.0% of cases among test were between 18-35 years (major age group affected) which was comparable to 75.0 % of cases of control group and the difference was not significant [Fig 2]. Majority of patients were febrile (97%) in both the groups and had associated headache and muscular pain as predominating symptoms (67.3% and 91.1%). The other symptoms observed in study subjects were rash (43.3%), joint pain (50%), retro orbital pain (45.1%) and vomiting (10.4%). The monitoring of platelet count clearly indicated that change in the platelet count is faster in the test group as compared to the control group. (Fig-3)

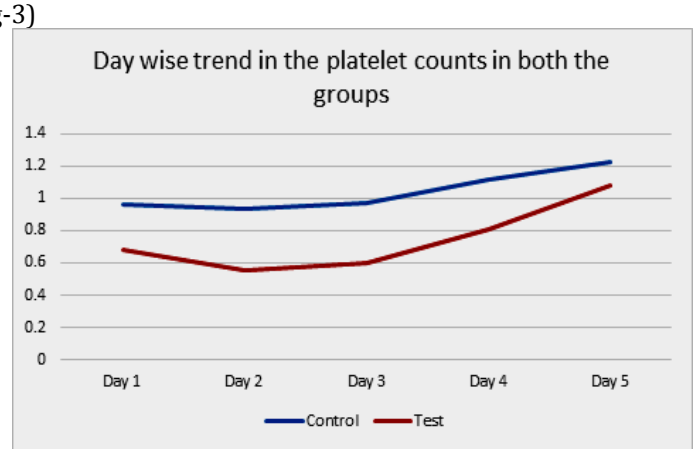


Fig 3: Showing mean platelet count for Control and Test Group

As seen from the above line graph the percentage change in platelet count in test group is significantly higher than that in the control group

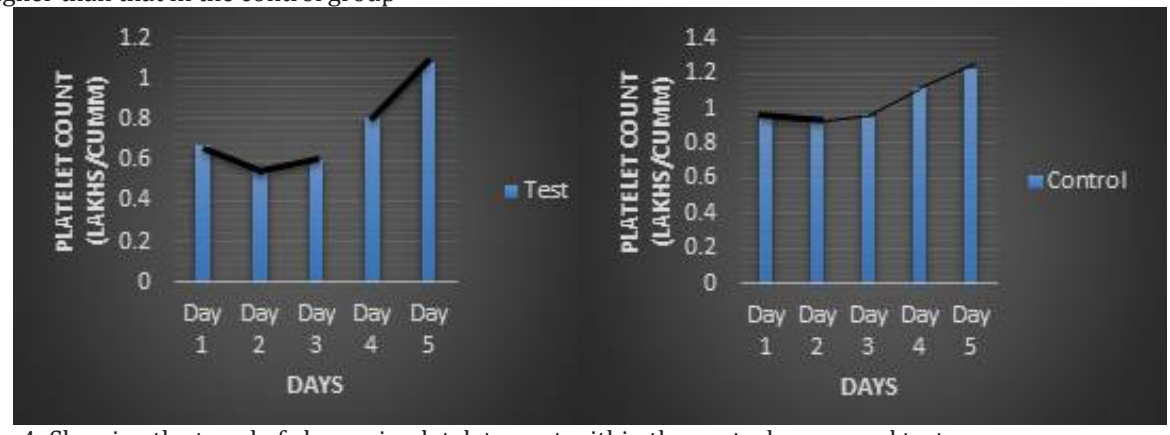


Fig 4: Showing the trend of change in platelet count within the control group and test group:

Fig 4 above clearly indicated a rising trend (steep) in the platelets of the test group, whereas in the control group there was a gradual rise (shallow) on 4th and 5th day. In the test group there was a significant increase in the platelet count after 2nd day onwards which was very much evident at the end of 5th day. The trend line is 'J' shaped where on the 2nd day onwards a steep rise was observed in the test

group. When compared to the control group rise which showed a shallow rise increasing gradually only on the 4th and 5th day.

Table 1(below) shows that the baseline of the data is significantly different for the test groups as given by p value for day 1 by Student t test as 0.004 which is statistically significant. After the treatment at the end of day 5 we see that the p value has gone up to 0.93 which is not statistically significant which means that the platelet of two groups are somewhat similar even though both groups started with a huge baseline difference and the test group was able to overcome the difference.

Table 1: Comparison of changes in the mean platelet counts between the two groups

	Mean Platelet Count (X+- SD)		
	Test Group (N=20)	Control Group (N=20)	Comparison (p value)
Day 1	0.68+-0.30	0.96+-0.26	*0.004
.Day 2	0.55+-0.24	0.92+-0.26	
Day 3	0.65+-0.25	0.95+-0.24	
Day 4	0.84+-0.31	1.03+-0.24	
Day 5	1.11+-0.34	1.12+-0.24	
Difference (Day 1- Day 5) (P value)	*0.43+-0.35(p value -0.93)	0.16+-0.26	

DISCUSSION

In scientific literature, it is proved that the *C. papaya* leaf extract does have a beneficial effect on dengue mainly in increasing the platelet count.

Thrombocytopenia is one of the major associated problem with the dengue leading to Dengue Hemorrhagic Fever and Dengue Shock Syndrome.

In this research it is shown that the subjects in the test group that received caripill showed faster increase in platelet count.

Caripill consumption during the course of dengue infection has the potential to induce rapid production of platelets [8-10]. It was demonstrated by the significant increase in the mean platelet count in the test group.

There were a few side effects reported related to GI disturbances like nausea, vomiting which were common in both the groups and not related to the drugs displaying the tolerability and safety of Caripill.

The above findings, thus reaffirm the platelet increasing capacity of Caripill as concluded by other pilot studies conducted in the past.

CONCLUSION

Drastic fall in platelet count is a matter of major concern in dengue. Caripill offers simple convenient cost effective safe and efficacy treatment for thrombocytopenia in dengue fever. Various clinical and preclinical studies have been conducted to demonstrate the positive effect of Caripill in dengue. This study was done in a way that the test groups were given corticosteroid therapy along with the Caripill. So studies should be done in which the test people are given only Caripill, so as to establish its role completely and to avoid the unnecessary side effects offered by corticosteroids.

LIMITATIONS

Since in this study effectiveness of Caripill on platelets was studied, other parameters were not monitored. The sample size was not representative and thus large scale studies should be conducted to establish the role of Caripill. Severe cases of DHF Grade 3 and 4 were excluded from the study, therefore the efficaciousness of the drug could not be established in these individuals.

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